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Experimental Investigation of Porous Concrete for Concrete Pavement

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***Abstract*:- Porous Concrete may be an extraordinary strong structure utilized in the progression field, another name of it is dry concrete other than broken concrete, no fines concrete and porous concrete. Water is a noteworthy constituent. Penetrable concrete is an uncommon kind of strong, which includes concrete, coarse aggregates, water and at whatever point required, admixtures and distinctive cementations materials. As there are no fine aggregates used in the strong cross section, the void substance is more which allows the water to travel through its body. Permeable concrete fuses solid, water and if vital, course masses, admixtures and unmistakable cementations constituents. There is bundle of exploration work is going in the field of porous concrete. The quality traits and structure of porous concrete is less when appeared differently in relation to the standard concrete on account of its porosity and voids. Thus, the utilization of porous concrete is compelled in spite of the way that it has some portion of good conditions. If the compressive quality and flexural nature of porous concrete is extended, by then it might be used for logically number of uses. For the present, the utilization of penetrable concrete is generally limited to light traffic lanes so to speak. If the properties are improved, by then it can similarly be used for medium and significant traffic inflexible pavements besides. Close by that, the penetrable concrete takes out surface overflow of storm water, empowers the ground water restore and makes the fruitful use of open land. This guideline purpose of our endeavor deals with the connection of flexural quality, compressive quality and porosity of concrete between porous concrete with no fine masses with replacement of cement and structure of penetrable concrete. However, it will in general be seen that with increase in quality, the permeability of penetrable strong will be diminished.**

Keywords: Porous Concrete, Compressive Strength, Flexural Strength, Porosity of Cement Concrete Pavement.

I. INTRODUCTION

Permeable solid which is otherwise called the no-fines, Porous, hole reviewed, and penetrable cement and Enhance porosity concrete are a dependable tempest water the executive's device. By definition, permeable cement is a blend of rock or rock stone, concrete, water, practically zero sand (fine total). At the point when permeable cement is utilized for clearing, the open cell structures permit storm water to channel through the asphalt and into the fundamental soils. As it were, permeable solid aides in securing the outside of the asphalt and its condition. As expressed above, permeable cement has indistinguishable essential constituents from ordinary solid, 15 - 30% of its volume comprises of interconnected void system, which permits water to go through the solid. Permeable cement can permit the section of 11.35-18.97 liters of water every moment through its open cells for each square foot (0.0929m2) of surface region which is far more noteworthy than most downpour events. Aside from being utilized to kill or lessen the requirement for costly maintenance lakes, engineers and other privately owned businesses are likewise utilizing it to let loose important land for advancement, while as yet giving a cleared park. Permeable cement is likewise an interesting and viable intends to address significant ecological issues and supportable development. At the point when it downpours, permeable cement consequently goes about as a waste framework, in this manner returning water where it has a place. Permeable cement is harsh finished, and has a honeycombed surface, with a moderate measure of surface raveling which happens on intensely voyaged streets. The painstakingly controlled measure of water and cementations' materials are utilized to make a glue. The glue at that point frames a thick covering around total particles, to forestall the streaming off of the glue during blending and putting. Utilizing enough glue to cover the particles keep up an arrangement of interconnected voids which permit water and air to go through. The absence of sand in permeable solid outcomes in a brutal blend that adversely influences blending, conveyance, and situation. Additionally, because of the high void substance, permeable cement is light in weight (around 1600 to 2000 kg/m3). Permeable cement can be utilized in a wide scope of utilizations, in spite of the fact that its essential use is in asphalts which are in private streets, rear entryways, and carports, low volume asphalts, low water intersections, walkways and pathways, stopping regions, tennis courts, incline adjustment, sub-base for regular solid asphalts, and so on.

1.2 ADVANTAGES

- Easy Installation
- Durable
- Sustainable
- Low Cost
- Can Be Temporary
- Can Be Used for Lawn Parking
- Can Create Temporary Roads
- Eliminates Costly Drainage Systems
- Can be Used for Erosion Control
- Natural drainage reduces puddles
- Natural filtration
- Flood prevention
- Reduces the heat island affect
- Natural and sustainable materials

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1.3 Applications for Porous Concrete

- Low-volume pavements
- Residential roads, alleys, and driveways
- Sidewalks and pathways
- Parking areas
- Low water crossings
- Tennis courts
- Sub-base for conventional concrete pavements
- Patios
- Artificial reefs
- Slope stabilization
- Well linings
- Tree grates in sidewalks
- Foundations/floors for greenhouses, fish hatcheries, aquatic amusement centers, and zoos
- Hydraulic structures
- Swimming pool decks
- Pavement edge drains
- Groins and seawalls
- Noise barriers
- Walls (including load-bearing)

II. LITERATURE REVIEW

Penetrable Concrete (PC) can decrease street upheaval, improve sprinkle and sprinkle, and improve granulating as a surface wearing course. A penetrable strong mix plan for a surface wearing course should meet the models of adequate quality and toughness under site-unequivocal stacking and regular conditions. As of recently, two key issues that have deterred the usage of Porous Concretein the United States are that characteristics of Porous Concretehave been lower than would regularly be suitable for required applications and the freeze-defrost strength of Porous Concretehas been suspect.

V.M. Malhotra (1976). Inspected Porous concrete as it relates to applications and properties. He gave nuances on such properties as consistency, degrees of materials, unit weight, similitude, and reestablishing attempting to intensify vulnerability in the Porous concrete. Malhotra furthermore coordinated various preliminaries on various test chambers attempting to find a connection between compressive quality and any of the material's properties. He induced that the compressive nature of Porous concrete was dependent upon the water solid extent and the all out solid extent.

Richard Meininger (1988). Released results on research focus investigations he had driven on Porous concrete. Examination was finished on various models with changing material properties. These properties included water solid extent, all out solid extent, compaction, and reestablishing time.

Nader Ghafoori (1995) wide exploration was driven by on various pieces of Porous concrete. In one assessment, he investigated various areas all through the United States that have utilized Porous strong clearing systems. His assessment incited a connection of compressive quality achieved at all of these districts. He furthermore investigated disillusionments in the various pavements if any had occurred close by the water concrete and absolute solid extents.

Ghafoori (1995), researched usages of Porous concrete outside the United States and eventually took a gander at the compressive characteristics. He is similarly looks at, in detail, black-top thickness plan for Porous concrete. He finds that compressive quality depends upon the water solid extent, the complete solid extent, compaction, and calming. He similarly gives a blueprint which shows the effects of fluctuating the all out solid extent and compaction imperativeness have on the compressive quality and permeability.

Paul Klieger (2003) performed tests thinking about the effects of entrained air on the quality and robustness of customary concrete. But never utilizing the proportion of voids seen in Porous concrete (15%-35%), his investigation evidently shows the impact the closeness of air has on the introduction of concrete. He construed that the abatement in compressive quality with the proximity of air reduces as the size of complete decays and as the solid substance decreases. These are both in light of the abatement in water.

Yang and Jing (2003). It ensured the reduction of all out size provoked higher Porous strong quality, coming about on account of the development of the interface quality between the aggregate and solid paste. Using the ordinary material and method, the nature of the Porous concrete is low. However, using smaller aggregate, silica smoke and super plasticizer in the past strong quality can be extended altogether. Furthermore by growing the solid paste latch district and updating the nature of solid folio Porous strong quality can in like manner be extended. The Porous black-top materials that made out of a surface layer and a base layer were made.

Tennis Paul et. Al I (2004). Examined the copied simples of Porous concrete surrounded from two stone hotspots for coarse aggregates and particular size parts to choose hydrologic associations. Straight associations were found among thickness and porosity, thickness and permeability, porosity and vulnerability, porosity and unequivocal yield. The results suggest that properties, for instance, permeability, porosity and unequivocal yield are not in a general sense impacted by different absolute sorts.

III.EXPERIMENTAL MATERIALS:

Permeable Concrete is a blend of Cement, Coarse Aggregate practically no sand and Water. Fine Aggregates are not utilized for making Porous properties in concrete. Now and again admixtures are utilized for accomplishing additional quality and unique properties of Porous cement.

3.1 CEMENT:

Concrete is a key to system industry and is used for various purposes and moreover made in various structures. Improvement of amazingly high compressive quality in starting periods helps in early covering. Intense Concrete Feasible for commonsense strong mix structures.

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Figure3.1: Ordinary Portland cement

Table 1: - Properties of Cement

Property	Values of Cement (PPC)	AS per IS: 12269-1987
Specific Gravity	2.93	3.10-3.15
Consistency (%)	31.5%	30 -35(%)
Initial setting time (Min)	34 minutes	30 minutes
Final setting time (Min)	240 minutes	600 minutes
Compressive strength at 7 days (N/mm^2)	39.50 N/mm^2	43 N/mm^2
Compressive strength at 28 days (N/mm2)	51 N/mm^2	53 N/mm^2

3.2 AGGREGATES

Coarse Aggregates is the section of the strong which is included the greater stones embedded in the mix. Concrete contains three fixings; Water, cement, and aggregate. particle shape and size, surface, and digestion. The standard kind total for use in pervious cement is commonly squashed stone or waterway rock. Run of the mill sizes are from 10mm t 25mm.

Figure 3.2: Coarse Aggregates

Table 2: - Properties of Coarse Aggregates

S.No	Particulars	Values
1	Density (Kg/m^3)	1830
2	Fineness Modulus	7.53
3	Specific Gravity	2.78
4	Water absorptions (%)	1.60
5	Surface moisture	Nil

3.3 WATER

While any consumable water can be used for mixing, the proportion of water is fundamental for the improvement of the voids in pervious concrete. Water-to-cement extents can run from 0.27 to 0.30 with extents as high as 0.40. Wary control of water is fundamental.

Fig 3.3 (a) little water

Fig 3.3 (b). Correct amount of water

Figure 3.3. (c) Much water.

3.4 METAKAOLIN

Metakaolin is an admixture utilized as an incomplete substitution of concrete. A solid is expressed to be over the top power concrete if its compressive quality is more than 40Mpa. Metakaolin is prepared by method for calcination of kaolin (clay mineral) at a temperature of 650-800ºC .It has pozzolanic homes. It responds with Ca (OH) 2 one of the through-results of hydration reaction of concrete and impacts in extra C-S-H gel which prompts expanded quality.

3.5.1 MIX DESIGN

- Grade designation:M40
- Maximum nominal aggregate size : 20mm
- Minimum cement content : 320 kg/m3
- Maximum water cement ratio : 0.38
- Workability : 100mm (Slump)
- Exposure condition : Severe
- Degree of supervision : Good
- Type of aggregate : Crushed angular aggregate
- Maximum cement content (OPC) : 400 kg/m3
- Chemical admixture type : Super plasticizer confirming to IS-9103

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3.5.2 MATERIALS REQUIRED FOR M40 GRADE OF CONCRETE

Cement	466.66 kg
Coarse aggregate	1140 kg
Admixture	7 kg
Water	140 litres

3.5.3 MIX PROPORTIONS

MIXES	CEMENT	METAKOLIN	C.A
Mix-1	1.00	0	2.44
Mix-2	0.95	0.05	2.44
Mix-3	0.90	0.10	2.44
Mix-4	0.85	0.15	2.44
Mix-5	0.80	0.20	2.44

IV. RESULTS AND DISCUSSION

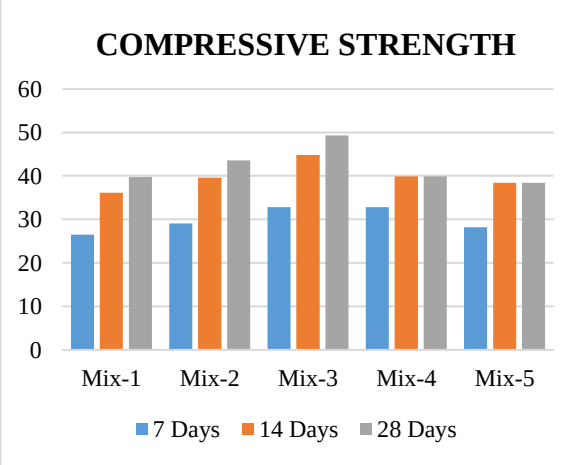
4.1 COMPRESSIVE TEST

Compressive strength is dependent on size of coarse aggregate, void ratio, bond between mortar and coarse aggregate.

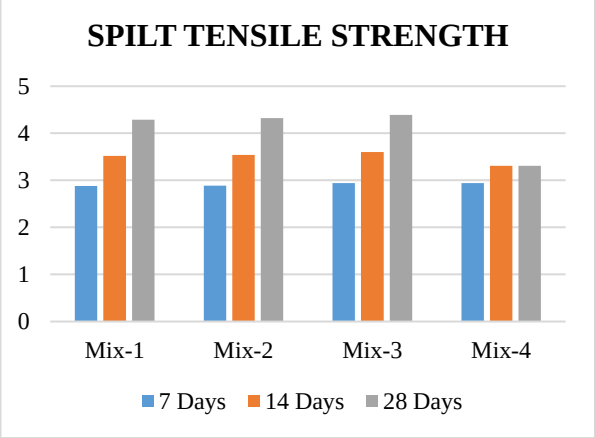
4.2. SPLIT TENSILE STRENGTH

In this project we conducted the split tensile test for cylinder. In pervious concrete tensile strength vary from 1 to 3.5 Mpa.

4.4 TEST RESULTS



4.4.2 SPILT TENSILE STRENGTH



CONCLUSION

In view of test examination, following perceptions are made on the new and solidified properties of Pervious cement.

- Pervious concrete have less compressive quality contrasted with traditional cement.
- Permeability is high because of high void substance.
- The utilization of pervious cement ought to be constrained to zones not exposed to high volumes of traffic.
- Even however the compressive quality of the pervious cement is extensively not as much as that of customary cement. The entirety of the blends tried, be that as it may, didn't accomplish compressive quality sufficiently able to continue such high vehicle loadings.
- Suggestions are that pervious concrete be compelled to regions that are presented to little vehicle loads with intermittent use by greater vehicles. Pervious concrete, in spite of the fact that not as solid as customary cement, gives a worthy elective when utilized in low volume and low effect regions.
- Strength is relinquished for penetrability however not to any degree which would deliver the pervious cement non-practical.

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PERFORMANCE OF GEOSYNTHETIC IN LANDFILL SYSTEM

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Abstract: *Geosynthetics have multi facet applications like separation, reinforcement, filtration, drainage and hydraulic/gas barrier in waste containment facilities, which include barriers and covers. In the liners, Geosynthetics are subjected to water and contaminant interaction where as in covers, it mostly interacts with water. Therefore, in covers the hydraulic performance of Geosynthetics is important for its use as barrier, filter or drainage layer. The various experimental methodologies for characterizing the type of Geosynthetics and evaluation of hydraulic characteristics of soil- Geosynthetics composites is discussed in detail.*

The main objective of this study is to evaluate the hydraulic performance of individual geosynthetics and also to find out the compatibility of different combinations of soil-geotextile in the landfill cover system. Comparative studies of change in permeability of soil-geosynthetic composites due to external factors like change in the type of soil change in the gradation of the soil, types of geosynthetics and increase in number of geosynthetic layers is carried out. Accordingly, the best geosynthetic type for a particular soil composition meeting the filtration requirements in the landfill cover system is determined. Improvement factors of permeability due to introduction of geosynthetics in top cover soils is ascertained taking into account the ratio of the permeability of soil- geosynthetic composition to the permeability of the soil alone. Gradient ratio tests and long term filtration tests is conducted to investigate the compatibility and clogging potential of the soil- geosynthetic system.

Keywords: *Geosynthetics, landfill system, covers, permeability, soil, gradient ratio, long term filtration test, clogging potential.*

1. Introduction.

Geosynthetics have multi facet applications in waste containment facilities, which include barriers and covers. The main advantage of geosynthetics is its cost effectiveness, versatility, easy installation and their mechanical and hydraulic properties best suited for barriers and covers (Querio and Lundell 1992). Geosynthetics are applied in the landfill liners and covers for the purpose of separation, reinforcement, filtration, drainage and hydraulic/gas barrier. Different forms of geosynthetics available are (1) Geotextiles, (2) Geogrids, (3) Geonets, (4) Geomembranes, (5) Geosynthetic clay liners, (6) Geopipe (buried plastic pipe) (7) Geofoam and (8) Geocomposites.

Geotextiles can be utilized in the landfills for any one of the following purpose:

separation, filtration, drainage, reinforcement or protection of geomembranes from puncture (Christopher 1991). Geogrids are used to reinforce slopes beneath the waste so as to resist the differential settlement caused by the overlying waste as well as to reinforce cover soils above geomembrane (Carroll and Curtis 1991; Palmeira and Vienna 2003). Geonets are used for in- plane drainage (Austin 1991). Geomembranes are thin impervious polymeric sheet primarily used for containment of liquids or vapors in the landfill system (Mackey 1996). Geosynthetic clay linersare thin layers of bentonite clay sandwiched between two geotextiles or bonded to a geomembrane connected through needle punching, stitching or adhesives and are used as infiltration/ hydraulic barriers in landfill system (US EPA 2001). Geopipe are used for draining out leachate and water from sand and gravel layers in landfills to sump or removal system. Geofoam are used as separators. Geocomposites are combinations of two or more geosynthetics that can be used for drainage, filtration or separation. These geosynthetics are used in combination with soils in liners and covers. In the liners, geosynthetics are subjected to water and contaminant interaction where as in covers, it mostly interacts with water. In real field situations, the geosynthetics are placed beneath the top soil layer as filters and as such there is no standard documentation of the type of soil that can be used as topsoil in the literature. Hence, locally available red soil and mixture of 50% red soil and 50% fly ash in combination with different geosynthetics such as geotextiles and geocomposites can be explored to check its effectiveness as filters for landfill cover system.

Many researchers have used the in-plane and cross plane permeability of different combinations of soil- geosynthetics in the landfill cover system by using laboratory and field tests (Raisinghani and Viswanadham 2010; Shan et al. 2001; Fannin et al. 1996; Fannin et al. 1994; Bhatia et al. 1990; Williams and Abouzakhm 1989). The laboratory tests that were conducted as per the literature, to evaluate the cross plane flow characteristics of the soil- geotextile systems in covers are hydraulic conductivity ratio test, flexible wall permeameter test, permittivity test, gradient ratio test, long term clogging flow test. Transmissivity tests were also conducted to determine the in-plane flow characteristics in the laboratory. Gradient ratio test were preferred over the hydraulic conductivity ratio test as it is simpler to operate and provides clogging resistance values along with permeability values unlike the hydraulic conductivity ratio test which gives only the permeability values (Shan et al. 2001).

The opening size and permeability of geotextile alone cannot determine the filtration efficiency of soil-geocomposite in the long run. So, in order to evaluate the actual field condition, test has to be carried out for hydraulic behavior of soil-geotextile composite also. Initially, the base soil lying above geotextile plays a major role in the permeability characteristics but with the passage of time, geotextile also starts contributing in

permeability. Since stable or equilibrium permeability is achieved after a long run, hence long term permeability test of soil-geotextile composite is done. One of the major concerns in the compatibility of the soil-geosynthetic composition is the clogging of soil particles in the voids of the geosynthetics. This will decrease the efficiency of the geotextile as filters and drainage layers in the cover system. Studies have been conducted to evaluate the clogging behavior of non woven geotextiles with silty and gap graded sands using long term filtration tests at constant head (Bhatia et al.1990). Several tests using gradient ratio apparatus have also been performed to determine the clogging potential. US Army Corps of Engineers have recommended the clogging limit of soil-geosynthetic composite as gradient ratio greater than 3. The main objective of this study is to evaluate the hydraulic performance of individual geosynthetics and to find out the hydraulic compatibility of different combinations of soil- geotextile composites in the landfill cover system by gradient ratio and tests and long term filtration tests. Gradient ratio tests and long term filtration tests will be conducted to investigate the clogging potential of the soil- geosynthetic system.

Comparative studies of change in permeability of soil-geosynthetic composites due to factors like change in the type of soil, gradation of soil, type of geosynthetics and increase in number of geosynthetic layers will be carried out. Accordingly, the best geosynthetic type for a particular soil composition meeting the filtration requirements for a particular boundary condition will be determined. Improvement factors of permeability will be ascertained taking into account the ratio of the permeability of soil- geosynthetic composition to the permeability of the soil alone.

A need to understand the hydraulic characteristics and clogging potential of soil - geosynthetic systems used in waste containment cover system has motivated this study.

2. Testing Methodology

Permeability, both cross plane and in-plane, are very important criteria for filtration and drainage characteristics in the design of landfill cover system. This chapter deals with the details of various instruments and their working principle which are used in the present study for measurement of permeability. Instruments and procedures adopted for physical and mechanical characterization of geosynthetics are also discussed.

2.1 Physical Characterization

2.1.1 Mass per unit area of geosynthetics:- ASTM D 5261-10 states that mass per unit area of geosynthetics are measured by weighing geosynthetic specimens of known area, cut from different locations of the laboratory samples. Measured average value gives

mean mass per unit area of that geosynthetics. This test is only for quality conformance. Usually non woven geotextiles lies in the range of 100 to 1000 g/m^2 and 100-300 g/m^2 grade is the most commonly used. Woven geotextiles are comparatively heavier and weigh about 100 to 2000 g/m^2, 100- 200 g/m^2 grade is the common type available. Lighter types of geotextiles are used as separators; heavier woven fabrics are used for reinforcement and the heavier non woven geotextiles for filters or protection.

2.2 Mechanical Properties

2.2.1 Cone Drop Test:- IS 13162 (Part 4) specifies that cone drop test is conducted to determine the puncture resistance offered by the geotextiles under impact load. Geotextile specimens of 250 mm diameter were cut and clamped into the lower clamping ring. Cone was placed in the trigger mechanism ensuring that the distance between the tip of cone and the geotextile specimen is 500 mm. The trigger is pulled to release the cone to fall into the geotextile specimen and make a hole. The fallen cone is removed and the diameter of the hole is measured with penetration measuring cone. Penetration strength is denoted by the size of the hole. Smaller the diameter of cone, higher will be the puncture resistance of the geotextile.

2.3 Hydraulic Characterization

2.3.1 Apparent Opening size (AOS) of geosynthetics by dry sieving method:- Dry sieving is conducted to determine the apparent opening size (AOS) of a geotextile which is an indication of largest opening size of a geotextile. ASTM D4751-12 recommends that 50 grams of uniform glass bead size is made to pass through a geotextile inserted in a sieve frame. The apparatus is placed in a sieve shaker to induce vibration to the sieve for 10 minutes. The weight of the beads passing through the geotextile is measured. The same procedure is repeated for other sizes of glass beads until 5% of the total weight of glass beads is passed. The diameter corresponding to this is called O_{95} which is expressed in mm. The apparent opening size is denoted by standard sieve number.

2.3.2 In plane permeability test/ transmissivity test:- This test method is used to determine the volumetric flow rate per unit width of geosynthetics parallel to its plane under varying normal compressive load and constant head. The test apparatus can be designed for parallel or for radial flow. The apparatus used in the laboratory are mostly radial flow type.

2.3.3 Radial in-plane flow: - This method is adopted for the geotextiles whose transmissivity value is lesser than or equal to $2x10^{-4}$ m^2/sec. The water enters through the central circular hole and it flows to the periphery of the circular specimen.

2.3.4 Cross permeability test /permittivity test:- Cross permeability test is conducted to determine the volumetric flow rate per unit crossectional area per unit hydraulic head across the plane of geotextile. It is meant for the geotextiles that exhibit filtration properties. In the field, permeability of the geotextile must be greater than the

permeability of the soil so that water can easily pass through the geotextile and prevent the buildup of hydrostatic pressure.

2.3.5 Gradient ratio test:- ASTM D5101 -01(2006) describe the procedure for measuring the soil- geotextile system clogging potential by the gradient ratio (GR) test. GR test is used to determine permeability and soil-geotextile system clogging potential. Gradient ratio of 1 or preferably less than 1 is desirable for soil-geotextile system compatibility. Gradient ratio excessively less or more than 1 may lead to piping or clogging respectively. As depicted in Fig. 3.4.3.1 (b), the permeameter apparatus consist of three sections- top, center and bottom section lying over base. It is furnished with support stand, soil geotextile, support screen, piping barriers, clamping brackets and plastic tubing. Six manometer ports namely 1, 2,3,4,5 and 6 attached in the permeameter body are connected to the manometer board to study the head readings. Inlet and outlet valves are connected to adjustable inflow constant head device (CHD) and stationary outflow constant head device (CHD) respectively with hose pipes. The hydraulic gradient is maintained by adjusting the height of inflow CHD with respect to outflow CHD.

3. Experimental Investigations and Discussions.

For the present study, five types of geotextiles which include woven multifilament geotextile, woven slit film geotextile, non-woven geotextile and two geocomposites (woven and non-woven combinations) were selected. The soil chosen for the study were locally available red soil of two different gradations – red soil finer than 4.75 mm sieve size and red soil finer than 425 micron; and 50% red soil-50% farraka fly ash mix . Basic geosynthetic characterization has been done using different methodologies. Gradient ratio test and long term permeability test have been carried out to check the soil-geosynthetic compatibility in terms of permeability and clogging potential.

3.1 Physical Characterization

3.1.1 Specific Gravity:- Specific gravity of the material (G) has been conducted by using density bottle method as per ASTM D 854-92. The values are listed in the table below:

Table 3.1.1.1: Specific gravity of the materials used

Type of Materials	Specific Gravity (G)
Red soil	2.69
Farraka fly ash	2.07

3.1.2 Gradational Characteristics:- The gradational characteristics of material were determined according to the guidelines specified in ASTM D 422-63. The results are shown in Fig 4.1.2.1 and percentage size fractions are listed in the table 4.2

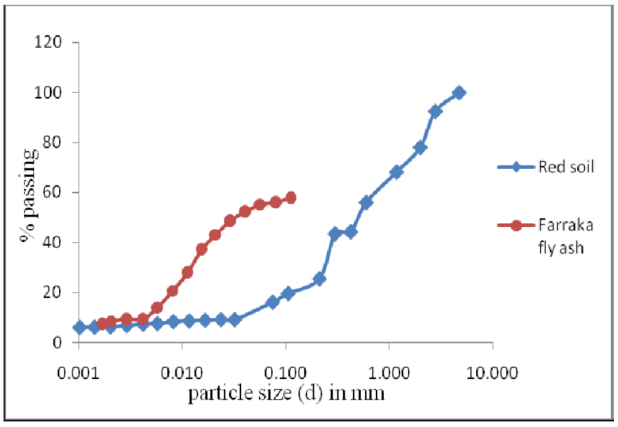

Fig 3.1.2.1 Gradational Characteristics of the material used

3.1.3 Atterberg limits:- The liquid limit, plastic limit and shrinkage limit of the material were determined as per ASTM D 4318-93. The values are listed in the table below:

Table 3.1.3.1 Physical characteristics of material used in study

Property	Material Used	
	Red soil	Farraka Fly ash
Particle size distribution in %		
Coarse sand (4.75-2mm)	22	0
Medium sand (2-0.425mm)	34	2
Fine sand (0.425-0.075mm)	28	24.0
Silt size (0.075-0.002mm)	10	74.0
Clay size (<0.002mm)	6	0
Atterberg's limit		
Liquid limit	41	NA
Plastic limit	25	NA
Shrinkage limit	23	NA

3.2 Geotechnical characterization

3.2.1 Proctor compaction characteristics:- The compaction characteristics of the material have been determined by following the procedure adopted in ASTM D 698. The relationship between dry density γ_d and moisture content w is plotted in Fig. 4.1.4.1 . Maximum dry density (MDD) and optimum moisture content (OMC) values are presented in table below.

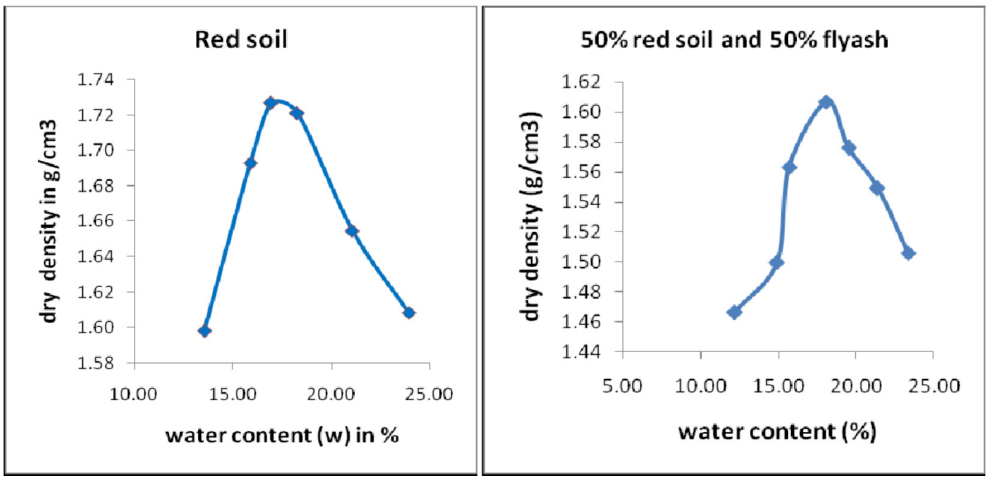

Fig 3.2.1.1: Compaction characteristics of different soils used

Table 3.2.1.1 Compaction characteristics of materials used

Property	Materials Used	
	Red soil	Mixture of 50% red and 50% flyash
MDD (g/cc)	1.73	1.61
OMC (%)	16.92	18.12

3.2.2 Mass per unit area of geosynthetics:- The test has been executed in accordance with ASTM D5261-10 and listed in table below.

Table 3.2.2.1 Details of mass per unit area of geosynthetics.

S. No	Type of Geosynthetics	Mass per unit area in (gm/sqm)
1	Woven Slit film Geotextile	167.13
2	Woven multifilament geotextile	1031.34
3	Non Woven Geotextile	958.76
4	Geocomposite- 1	785.34
5	Geocomposite-2	658.34

Mass per unit are of geotextiles is an important property as it decides the cost of fabric. Usually the non-woven geotextiles lies in the range of 100 to 1000 g/m2 , the 100-300 g/m2 grade is the most commonly used. Woven geotextiles are comparatively heavier and weigh about 100 to 2000 g/m2 , the 100-200 g/m2 grade is the most common type available. Lighter types of geotextiles are generally used as separators; heavier woven fabrics are used for reinforcement and the heavier non-woven for filters or protection.

3.3 Mechanical properties

3.3.1 Cone drop test:- This test is performed to check the strength of the geotextiles against puncture. Resistance is denoted by the average size of the hole. The procedure of the test has been followed as per IS 13162 (Part 4) standard.

Table 3.3.1.1 Details of cone drop test of geosynthetics

Sl No	Type of Geosynthetic	Size of the hole in mm
1	Woven Slit film Geotextile	15
2	Woven multifilament geotextile	4.5
3	Non Woven Geotextile	16
4	Geocomposite- 1	16
5	Geocomposite-2	9

Out of all the available materials, woven multifilament geotextile has the highest resistance to puncture followed by geocomposite-2. Woven slit film geotextile, non-woven geotextile and geocomposite-1 exhibit nearly similar amount of resistance to puncture. Smaller the hole, larger will be the resistance of geotextile against damage. Some materials like geonets that tear apart when cone is dropped on it, should not be placed directly beneath the aggregate layers in the landfill cover system. Non-woven geotextiles are generally placed above geonets in the field to impart protection from aggregate layers placed above it.

3.4 Hydraulic characterization of Geosynthetics

3.4.1 Apparent opening size (AOS) test:- This test has been carried out in accordance with ASTM D 4751-12 by passing glass beads of known diameter through a geotextile held by sieve frame. The AOS or O95 gives an approximate idea of the largest opening size of the geotextile fabric. Geosynthetics having larger O95 value result in larger hydraulic conductivity. The summary of AOS value has been tabulated below:

Table 3.4.1.1: Summary of AOS (095)values of geosynthetics

S. No	Types of Geosynthetics	O_{95} in mm	Remarks
1	Woven slit film geotextile	lesser than 75 micron	No passing of 0.075 mm beads
2	Woven multifilament-geotextile		thickness of the textile is higher than the limitations of apparatus (2.3mm) and hence O95 value could not be determined
3	Non-woven geotextile	lesser than 75 micron	No passing of 0.075 mm beads
4	Geocomposite -I	lesser than 75 micron	No passing of 0.075 mm beads
5	Geocomposite-II	lesser than 75 micron	No passing of 0.075 mm beads

The graphs could not be plotted for geotextiles as their opening sizes are smaller than smallest bead size (75 micron) available with us. So, their sizes have been approximated as <75 μ.

3.4.2 In-plane permeability test of geosynthetics:- In-plane permeability is a very important characteristic of geosynthetics which assess its drainage potential. The procedure of radial flow test adopted for this study has been taken from ASTM D6574-00.

Table 3.4.1.1 Details of in plane permeability values obtained:

Sl No	Geosynthetic Type	transmissivity in m2/sec	in plane permeability coefficient in m/sec
1	Woven slit film geotextile	5.27E-05	5.27E-02
2	Woven multifilament geotextile	2.197E-06	1.10E-02
3	Non woven geotextile	1.758E-06	4.40E-02
4	Geocomposite -I	1.494E-06	4.98E-03
5	Geocomposite-2	1.846E-06	9.23E-02

Woven multifilament geotextiles contribute highest cross plane flow. Woven slit film geotextiles comparatively exhibited lowest filtration performance but the overall performance of other geotextiles is comparable. Good filters need to maintain retention criteria and permeability criteria. It is very difficult to specify the good filtration ability of geotextiles based only on its cross plane permeability parameter alone. Tests have to be conducted with soil- geosynthetic system to draw any conclusion about its filtration capability and its compatibility in terms of clogging.

4. Conclusions

Cross plane permeability of woven multifilament geotextile is highest compared to other geotextiles considered for the study. However, it was observed that woven multifilament geotextile-red soil composite does not give highest permeability in case of red soil finer than 4.75 mm. This confirms that the hydraulic characteristic of geotextile alone does not determine its efficiency as effective filter. In order to evaluate the actual field condition, test has to be carried out for hydraulic behavior of soil- geotextile composite. Locally available red soil finer than 4.75 mm and 50% red soil- 50% fly ash mix can be used as top soil in landfill covers under the tested boundary conditions as they were found compatible with, geotextiles taken for study, by gradient ratio test. It was verified that variation of permeability values and gradient ratio values of soil- geotextile composite with time are inversely proportional. Long term permeability test results also confirmed the compatibility of different combinations of soil-geotextile composite in the stabilised condition marked by zero slope of the permeability vs time response curve. Improvement factor helped in comparing suitability of various geotextiles as filter in landfill covers. Woven slit film geotextiles, non-woven geotextiles and geocomposite-I showed comparatively better performance as filter media in red soil finer than 4.75 mm for a

hydraulic gradient i= 20 and compacted at maximum dry density Woven multifilament geotextiles delivers better performance as filter for red soils finer than 425 micron and 50% red soil – 50% fly ash mix for a hydraulic gradient i= 20 and compacted at maximum dry density.

The study of increase in filtration ability by increasing the number of geotextile layers in landfill soil cover system has to be investigated further in detail as no concrete conclusion could be drawn. Red soil finer than 425 micron compared to other two soils compacted at dry density and hydraulic gradient of i= 20 is more suitable to be used as top soil since it is compatible with the geotextiles fulfilling the clogging and permeability criteria. The long term permeability results of geotextile-soil composite initially increase, then there is a series of decreasing and increasing response of the curve till system permeability stabilizes with time.

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STUDY OF CURRENT SCENARIO & IMPROVEMENT SUGGESTION FOR THE MUNICIPAL SOLID WASTE MANAGEMENT PRACTICES IN PURNEA CITY

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Abstract - Rapid growth in urban population coupled with economic growth and rise in community living standards has resulted in the generation of huge quantities of municipal solid waste posing a serious problem to municipal corporations. Approximately 59.3 tons/day of waste is generated in Purnea city, out of which only 30% of waste is collected by Purnea Municipal Corporation directly, and the 70% of municipal solid waste is collected and transported through NGO Shivam. The current scenario and status of the Municipal Solid Waste (MSW) for Purnea city is studied. The results indicated that organic waste was highest among other components of the wastes. A considerable proportion of organic carbon was found which causes health problems to the dwellers of the city. To avoid this situation small community bins are placed in the nook and corner of the city, besides, the litter bins are provided as per requirement. Disposal vehicles, small auto-rickshaws, hand carts, and tricycles are provided to maximize the collection of waste. The current municipal waste treatment methods in Purnea are unsustainable and will burden future generations. The main goal of this paper is an ardent need for proper suggestions to improve municipal solid waste in Purnea City, especially technical solutions based on the conditions of Purnea municipal solid waste management. The municipal solid waste is changing its composition over the time; moreover due to several issues, there is no properly operating sanitary landfill. Some of the landfills are either closed or badly managed. So, much of municipal solid waste gets dumped in the open dumps, posing health risks to residents in their vicinity. This may cause a high risk of contamination of groundwater/surface water, soil, and air. Further to improve the MSWM in Purnea City, we analyzed the gaps, strengths and weaknesses; several recommendations were proposed in need to improve the existing system complying with the MSW (H & M) rules, 2016. The site should be planned as an integrated facility for compost plant and sanitary landfill. The solution must be carried out as soon as possible by Purnea Municipal Corporation to close the open dumping situation. Purnea Municipal Corporations should arrange an adequate area that is required for sanitary land-filling to reduce the MSW at the disposal site. Apart from this, it is suggested that the Purnea Municipal Corporation should create awareness on storage, segregation, antilittering with the help of NGOs and also organize the workshop for the awareness and involvement of citizens and NGOs.

***Key Words*: Contamination, Landfill, MSW (H & M) Rules 2016, Municipal Solid Waste, Municipal Solid Waste, Open Dump, Purnea Municipal Corporation**

1. INTRODUCTION

The municipal solid waste management is one of the essential duties of municipal bodies to arrange for daily street sweeping, cleaning, collection, transportation processing, and disposal of waste in a scientific way at the appropriate site. Improper handling and disposal practices of solid wastes continue to be a serious problem [1]. Municipal Solid Waste Management is (MSWM) is one of the environmental problems in Purnea city. Improper management of Municipal Solid Waste (MSW) IS causing hazards to the inhabitants. In studies, it was revealed that about 85%-90% of MSW is disposed of unscientifically in open land and landfills in Purnea, creating problems to public health and overall environment [2].

Urbanization and Industrialization have increased the quantity and diverse nature of wastes, which need proper handling and treatment. Purnea City has a mixed demographic profile with about 3, 61, 371 of the total population living in the municipal area [3]. Most of the municipal areas are highly unsatisfactory managed due to inadequate services, limited finances, and municipal authorities as well as people's apathetic behaviour towards MSWM [4].

2. STUDY AREA PURNEA CITY

The Municipal Solid Waste (MSW) consists of organic and inorganic waste materials generated by various societal activities. The improper disposal of MSW pollutes all the vital components of the living environment, i.e. air, land, and water. Purnea is located in the east of Bihar state. It is situated at 25^0 46' 15" N and 87^0 28' 55" E covers an area of 92 Km^2 at an average elevation of 36 meters [2]. Purnea city has earned the name "Mini Darjeeling", as it experiences favorable weather throughout

the year [5]. In summers, the maximum temperature rises to 44°C. In winter months the temperature varies between 9°C [6] and the annual rainfall is about 1427 mm [7].

2.1 Dimension of Solid Waste Problem

Currently, Purnea city generates around 59.3 T/day of MSW at an average of 0.55 kg/day/per capita with a population of about 3, 61, 371 [2]. Purnea city is facing serious problems due to existing disposal practices of generated waste incurring high cost due to lack of proper infrastructural facilities, also the open dumping in the expanding zone of the city poses serious problems to the structures constructed on these old dumps in addition to the groundwater quality due to improper leachate management [3]. However, with an increasing population, the local authorities are struggling to provide the proper municipal solid waste management system to a satisfactory level. Recently, the authorities have taken initiatives and measures to organize the municipal solid waste management (MSWM) sector. Purnea city has several narrow streets and gulleys, high population density, and has pockets of the rural area which have been amalgamated with developed areas, posing serious problems for the collection and transport of municipal waste. The phenomenal growth of vehicles on roads makes the task even more difficult.

Table -1: Future population and Future Solid Waste Generation – Projection

Year	Projected Population	Waste Generated (Tons/day)
2011	2,82,248	46.8
2015	3,27,070	51.9
2020	3,61,371	59.3
2025	4,10,433	67.3
2030	4,64,918	76.6

In the year 2030, Purnea will generate 76.6 Tons/day of solid waste as per data provided by Purnea Municipal Corporation. Table 1 presents the projected solid waste to be generated in the projected years [2].

2.2 Characteristics of Municipal Solid Waste

The biodegradable matter in the waste collected from Purnea city is about 56% and can be converted into manure. Recyclable materials such as paper, cardboard, glass, metal, plastic, electronics are 15% and at present only 10% of the waste has been going recycling properly. 29% of inert materials have been used for landfilling purposes. The average composition of waste on a wet weight basis is shown in Figure 1. The testing was done in PHED Laboratory, Purnea. A total of seven samples were tested. Organic matter based on test results was found to be 56% while inorganic matter was 29%, and rest constitutes other matter [2].

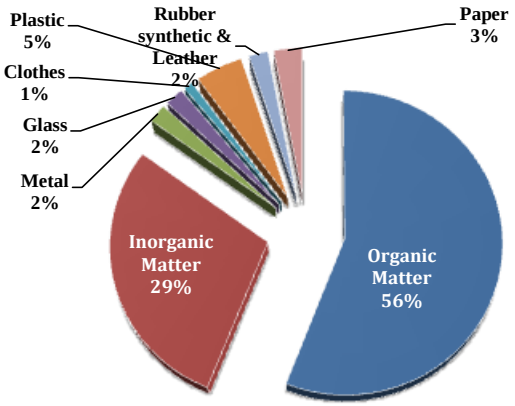

Fig -1: Average physical characteristics

These percentages differ from city to city depending upon food habits. Also, it has been noted that the characteristics of the waste are changing with time.

Table -2: Chemical characteristics of waste

Parameter	Average
pH	7.70
Moisture	39.1
Organic carbon	11.37
Total Kjeldhal Nitrogen	0.57
C/N Ratio	30.94
Total Phosphorus	17.20
Total Potassium	19.4
Density	550 kg/cum
Calorific value	1000 kcal/kg

The data provided by Purnea Municipal Corporation for the chemical characteristics of waste generated from various sources are tabulated above. Table 2 showed that the Organic carbon of the waste is 11.37, the C/N ratio of the waste is 30.94 and the average density based on test results was found to be 550 kg/m^3. The gross calorific value was been observed as 1000 kcal/kg [2].

3. PRESENT PRACTICE OF SOLID WASTE MANAGEMENT

Presently, the Shivam NGO and Purnea municipal corporation, the agency vested with the responsibility of collection and disposal of solid waste, is engaged in a series of approaches such as involvement of citizen, investment in infrastructure and technology, as well as monitoring the various systems that are involved in managing the present mix of actions and techniques. The Municipal Corporation has divided into 46 wards. As per the present practice, collection carriage and disposal of solid waste is done by engaging 282 sweepers, under the supervision of 02 sanitary inspectors. The tractor, trolleys, Handcarts, and tricycles are engaged on alternate day for the carriage of municipal solid waste from community bins to disposal site. The household waste is collected in the community bins daily through handcart vehicles and is disposed of off to the site twice a week. The tricycles and trolleys are being used in collecting household waste from the roadside to the community bins. The dumped garbage is allowed to decompose and shrink at the spot, spreading and levelling are often done by dozer/excavators as and when required [3].

3.1 Collection

Source segregation is still a concern in Purnea City. Purnea Municipal Corporation manages about 30% of MSW and the Rest 70% of MSW manages through NGOs from primary collection to disposal sites [2]. The collection of municipal solid waste is carried out in two phases. The first stage is a primary collection, in which the municipal solid waste is collected on auto tipper & pushcarts. An Auto tipper has been provided for every 1000 households and a pushcart for every 200 households. About 282 Sweepers are being utilized (both Purnea Municipal Corporation and contractors) in the door-to-door collection, street sweeping, and transportation of MSW [3]. The waste collected from the households is brought and transferred to landfill sites through tipper trucks & trolley tractor.

The Purnea Municipal Corporation has assigned the primary collection and transportation activity to Self Help Groups (SHG's) which are basically below poverty women's groups and landfill sites are operated by the private sector based on public-private partnership (PPP). Annually about 1 crore is spent on municipal solid waste management salaries for both 100 Sweepers by Purnea Municipal Corporation directly and for 182 Sweepers, through a contractor who performs the door-to-door collection, Tipping fees, etc. [3]. The system and practice continued to be outdated and inefficient. There are no clear plans to enhance their efficiency or improve working conditions through the provision of modern equipment and protective gear. There is a lack of knowledge of the characteristics of MSW aid in the preparation of a long-term plan for an MSWM system. Hence, it was deemed necessary by the Purnea Municipal Corporation to assess the existing status of the MSWM system in Purnea city.

3.2 Transportation

Transportation of solid waste from collection centers to the final disposal site/landfill is another important step in municipal solid waste management. Currently, transportation of municipal solid waste is using small auto-rickshaws, hand carts, tricycles, and auto, etc. Which brings the municipal solid waste to primary collection centers. From there trolley tractor collects the municipal solid waste and transport it to waste disposal sites/landfills [3].

Major issues in transporting waste are:

1. Due to open beds in tractors and trucks, the waste spills from the truck, during transport, thereby causing a nuisance.
2. Loading of waste by manual without the use of protective gear is dangerous to the health of workers.
3. The secondary storage system is not synchronized with the transport system. Problems arise when a transport fleet is modernized because waste at the secondary storage system is still dumped on the ground.
4. Due to an inadequate number of vehicles, the area cannot be serviced properly.
5. Due to inadequate workshop facilities and maintenance procedures, the vehicles are poorly maintained. This problem leads to a breakdown of trucks and becomes out of service for a long time.

Table -3: Waste collection

Category	Quantity of waste (tons/day)
Waste collected by Vehicles	36
Uncollected waste	13.3
Waste collected by rag pickers	10 (including paper)
Total Waste Generated	59.3

As per data provided by Purnea Municipal Corporation (see table 3), The total quantity of waste generated in the Purnea city is found to be 59.3 ton/day, Out of which the vehicles collect only 36 ton/day, 13.3 ton/day is not collected and 10 ton/day picked by the rag pickers.

Table -4: Waste collected by the vehicles[3]

Type of vehicle	No of vehicle	Waste Capacity (tons)	Trips/ day	Carrying capacity	Vehicle running	Waste carried	Actual waste collected
Tata Dumper	1	7	4	28	4	4	9
JCB	2	9	3	54	0	5	0
Tractor trolley	11	3	3	99	10	2	15
Tempo	30	5	3	450	3	3	12
						Total	**36**

3.3 Current Disposal Practices in Purnea City

Presently, Purnea does not have any scientific treatment method facilities for municipal solid waste generated by municipal and industries around Purnea. This has led to the development of several illegal and unauthorized dumpsites in Purnea [2]. The waste produced by the bulk generators such as hotels, restaurants, markets, etc., is being directly collected and transported to the treatment/disposal sites.

3.3.1 Sanitary Landfill Site

At present, Purnea is handling the municipal solid waste of about 59.3 tons/day only [2]. There is no waste treatment facility existing at Purnea. The government has not sanctioned new facilities.

3.3.2 Illegal Dump Sites

There are more than 10 dump sites and it consists of both municipal and industrial waste existing in and around Purnea city area [2]. While the Purnea Municipal Corporation and the Bihar State Pollution Control Board (BSPCB) close these sites, the new ones emerge elsewhere posing health risks to residents in their vicinity. The Purnea Municipal Corporation is merely collecting waste instead of disposal after collection.

3.4 Strength and Weakness Analysis of MSW Management

Table -5: Strengths and Weaknesses of MSW management of Purnea City[8]

Strengths	Weaknesses
• Private sectors have a strong capacity to manage MSW, including collection, transport, treatment, and dispose of while applying environmentally sound technologies. • Availability of strong human resources (including manual labor) to meet the demand for MSW management. • Informal sectors play an important role in the recycling of MSW.	• Weak legal and institutional framework for solid waste management (SWM), especially implementation, monitoring, and evaluation (M&E). • Policy and standards do not meet the ability of stakeholders (e.g. private sectors). • Lack of experts and staff who have technical knowledge and skills in SWM. • Lack of financial support from the government. • Lack of technologies for SWM. • Poor infrastructure (e.g. landfill design and operation is not efficient. • Weak environmental protection in landfills • It does not take advantage of the private sector role in SWM. • Lack of waste separation at source due to lack of environmental awareness of local people

Table 5 illustrated the SW (Strength and Weakness) analysis for MSW management in Purnea City. The SW (Strengths and Weaknesses) analysis is a tool to identify the positive and negative points of the performance of any process, organization, project, and company. SW analysis was done on the MSW management of Purnea City to rectify the current issues on the MSW practices; while enhancing the positive points and minimizing the negative ones for future city strategies.

4. DISCUSSION AND SUGGESTIONS

In this work, a detailed study of the collection, storage, transport, and disposal practices were conducted for Purnea city. An improvement to the existing system has been proposed to meet the MSW (H & M) rules 2016. It was found that the disposal site has been planned as an integrated facility for compost plant and sanitary landfill. Private sectors, NGOs, and rag pickers are to be brought in to the institutional framework for effective management of MSW.

The following key points are suggested to practice for minimization of waste:

- ❖ Prohibit the littering: The notification should be issued which is not done yet. Also, it is required to increase the number of litter bins. Litterbins should be provided at strategic locations for the citizens to dispose the waste. This will reduce the waste coming on the street as well as the requirement for sweeping and thus reduces the cost of MSW management. Legal notification to this effect to the citizens will enable the corporation to enforce antilittering.

- Segregation of Waste: At present, there is no segregation of waste at source. Segregation of waste at the point of generation i.e. homes, offices, shops must be done into two categories:
  - Wet waste comprising of biodegradable waste such as food waste etc.
  - Dry waste comprising of plastics, tins, etc. The Purnea Municipal Corporation must enforce this by notifying the citizens to do so.
- Generation of waste: The waste generation in the city is 300 to 550 gm/Capita/Day. Since the weight of the waste is only an estimate, Therefore It is suggested that the Purnea Municipal Corporation will collect information on the exact quantity of waste generation. It is also suggested that the physical examination of the waste to be carried out into four categories:
  - Biodegradable Waste
  - Recyclable Waste
  - Non-Biodegradable Waste
  - Green waste

  This will enable the Purnea Municipal Corporation to plan the recycling and processing of the waste.
- Employ sufficient no. of staff: In Purnea Municipal Corporation 46 wards are covering an area of 92 km^2. The Corporation has employed only 100 sweepers for street cleansing which are insufficient for the work. Hence it is suggested that the Purnea Municipal Corporation should employ a sufficient number of sweepers so that the daily cleaning should be done.
- Waste Collection: Purnea Municipal Corporation has not implemented the appropriate method of collection and it is suggested that the Purnea Municipal Corporation should provide house to house collection.
- Transportation of Waste: The Purnea Municipal Corporation has only 11 Tractors with trolleys which are inadequate. Though the generation of waste is 59.3 T/Day, only 36 T/Day is collected by Vehicles. Hence it is suggested that the Purnea Municipal Corporation should increase the number of vehicles and laborers to fulfill the requirement.
- Waste Processing: Currently the Purnea municipal corporation has no arrangement for processing hence it is suggested that the Purnea municipal corporation should make an adequate number of incinerators to reduce the MSW at the disposal site.
- Waste Disposal: Presently, Purnea Municipal Corporation does not have any scientific treatment method facilities for municipal solid waste generated by municipal and industries around Purnea. Hence it is suggested that the Purnea Municipal Corporation should make an adequate area is required for sanitary land-filling to reduce the MSW at the disposal site.
- Awareness and Involvement Programs: There is no awareness and involvement of citizens and NGOs. Hence it is suggested that the Purnea Municipal Corporation should create awareness on storage, segregation, and antilittering with the help of NGOs. Also, it is suggested to organize the workshop for the awareness and involvement of citizens and NGOs.
- Feasibility of Disposal Site: The porosity and permeability of the soil at the disposal site is very high. Hence, the possibility of groundwater pollution. Therefore the present site is not suitable for disposal of solid waste.
- Composting Plant: The C/N ratio of the waste generated at Purnea city is found to be 30.94, (Shown in Table 2) which is ideal for composting. Hence it is advisable to make a composting plant.

5. CONCLUSION

In this work, a detailed study of the collection, storage, transport, and disposal practices were conducted for Purnea city. The total quantity of MSW generated in Purnea City 59.3 T/Day and the rate of generation of MSW is 300 to 550 gm/Capita/Day. Current practices of municipal solid waste management in Purnea City are open dumping. About 90% of municipal solid waste is open dumping at trenching grounds in Ward 37 and the rest 10% is recycled. Paper, plastic, and metals are among the major

recyclable waste. The Gaps analysis revealed that there are several gaps in the regulation and economic policies, institutions framework and arrangements, technologies and infrastructure, capacity building, participation of stakeholders, and financing mechanism. One of the most important gaps is that there is a lack of clear responsibility and accountability of several institutions for the MSW management in Purnea City due to the involvement of multi agencies. The Gap and SW (Strength and Weakness) analysis pointed out that the private sector could play a pivotal role, as strength of the city, in MSW management, if the regulatory and policy-related weaknesses are resolved. Based on gaps and SW (Strengths and Weaknesses) analysis, several recommendations were proposed, such as, in an existing system is need to follow the MSW (H & M) rules 2016. The disposal site need to the planned as an integrated facility for compost plant and sanitary landfill. Organizing public awareness programs, which could start from the schools; increasing efforts for recycling, resource recovery, building transport stations for efficient transport of waste, renewing transport vehicles; capacity building programs for staff including abroad training and courses on waste management; and encouraging public-private partnerships in SWM are the practices recommended in present study.

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Study of lime Stabilized Expansive Soil

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Abstract: **Expansive soils are the soils which expand as they get wet and shrink as they dry out. In other words, soils which show large volumetric changes due to changes in their moisture content are expansive soil. They are one of the prevalent causes for damage of infra**structures because of the large **swelling pressure exerted by the soil during the process of swelling and shrinkage. Mechanical stabilization, chemical stabilization, stabilization with additives, thermal stabilization and electrical stabilization are common methods for improvement or stabilization of expansive soil. At present, chemical stabilization is the most effective and cheap method where the soil properties are altered and made less plastic, less expansive, more workable and of more strength. Chemical treatment mainly includes treatment by lime, cement, gypsum, magnesium oxide etc. Among these lime treatment is the most effective method till date. The study on beneficial use of lime in treatment of expansive soil has been done by many researchers (Bell, 1988; Al- Rawas et al., 2005; Sharma et al., 2008; Sivapullaiah et al., 1998). Other additives like coal fly ash, rice husk fly ash, sand etc also used successfully in treatment of expansive soil (Kumar et al., 2007; Ameta et al.,2007) Performance improvement of expansive soil by the application of geo-reinforcement like geogrid, geomesh, fibers etc. is a new approach (AI-Omari, 1990; Rao, 2011). Also combined treatment on expansive soil with lime and such reinforcement has been used with great success in recent past (Cai et al., 2006; Ramesh et al., 2010 etc). Such techniques may contribute to a relaxation in the specifications of fill materials and also to the degree of chemical treatment that would have been used otherwise. In this investigation an attempt has been made to carry out a systematic study on strength behaviour of lime treated soil with different percentages of lime (i.e. 2, 4, 8, 12 and16%) and also with combined application of lime with geonet/ geomesh and glass fiber. In the initial stage of the investigation, some basic properties of the swelling soil (liquid limit, plastic limit, specific gravity etc) have been determined to categorize the soil. Compaction test for each lime-soil mixes (soil with 0, 2, 4, 8, 12 and 16% lime) has been done using mini compaction test (Prashanth, 1998; Sridharan and Sivapullaiah, 2005). Result from these tests shows that upon addition of lime upto 2% the dry density of the mix reduces** with a **corresponding increase of OMC. This is because of the card house structure that forms due to flocculation which resists the compactive effort and also holds more water. But upon increasing lime content beyond 2%, dry density continuously increases while OMC decreases. This is because of the relatively dispersed structure formed due to higher addition of lime, which is less resistive to the compactive effort applied. However at 12% and 16% lime content, dry density and OMC both increases, though mechanism for this change (increase in OMC) is not understood clearly. Also lime addition makes the compaction curves flatter; it implies that the targeted density can be achieved in a wide range of moisture content.**

To study the strength characteristics of lime treated soil unconfined compressive strength test has been done on soil samples prepared by mixing soil with different percentage of lime (i.e. 0, 2, 4, 8, 12 and 16%) by dry weight of soil, compacting at their respective Proctor MDD and OMC conditions and keeping for different curing periods (i.e. 3, 7, 14 and 28 days). To compare the strength improvement upon various treatments of lime and reinforcement, a term "improvement factor" has been used in this study which can be defined as the unconfined compressive stress of treated soil to the unconfined compressive stress of the untreated soil at the corresponding point of strain or at the point of failure. From the tests, it has been observed that 2 % lime addition almost increases the strength to two times (improvement factor 2.49) than to untreated soil. With further increasing in lime content the pozzolanic reaction accelerates forming more of cementitious compound leading to increased strength. 12% lime to expansive soil has shown maximum strength of 2051 kPa at 28 days of curing periods which is 8.69 fold (improvement factor 8.69) to that of expansive soil which had initial strength 235.93 kPa. Further addition of lime brought decrease in unconfined compressive strength of the soil.

Geomesh reinforced soil-lime mix also shows superior strength characteristics than only soil- lime mixes. At 8, 12 and 16% lime content, the unconfined compressive strength of soil-lime- geomesh mix obtained are 2035.31 kPa, 2245.11 kPa and 2667.63 kPa with improvement factor of 8.63, 9.52 and 11.31 respectively.

To further improve the strength of geomesh reinforced lime treated soil and also to improve its ductility characteristics, glass fiber (of the property mentioned in chapter 3), has been used in fixed amount of 1% and of fixed length of 10 mm. Expansive soil treated with 8%, 12% and 16% of lime, reinforced with 3 layers of geomesh in equal spacing and fibers, are tested for their unconfined compressive strength at different curing periods (3, 7, 14 and 28 days). The results showed that at 28 days curing period the improvement factor of the mentioned mixes significantly increases and are 9.57, 11.81 and

16.99 respectively. Therefore fiber and geomesh reinforced soil with higher lime content shows better strength characteristics than both only geomesh reinforced lime treated soil and only lime treated soil, particularly at higher curing periods.

Keywords: Expansive soil, lime, reinforcement, stabilization, compressive strength

1.0 INTRODUCTION

Expansive soils are those problematic soils which swell as they get wet and shrink as they dry out. And so during monsoon season, these soils increase in volume by absorbing water, and in dry season they reduce in volume by evaporation of water. Consequently, expansive soil causes distress and damage to structures founded on them. These soils are also called as swelling, montmorillinitic or black cotton soil. These soils are characterized by following properties;

a) Small particle size,
b) A large specific surface area(SSA)
c) A high Cation Exchange Capacity(CEC).
d) High liquid limit and plasticity index.

The mineral that expansive soils mostly contain is montmorillonite, which is capable of absorbing large quantities of water. Volume of swelling soil may expand 100 percent or more as it get wet. The powerful force of expansion is capable of exerting excessive pressure particularly on the lightly loaded structures such as pavements, canal beds and linings and residential buildings and can cause damage to them. This in turn can be an immense loss to a nation's economy. In United States, it has been recorded from last few decades that damages from expansive soil has exceeded the average annual damage caused by floods, hurricanes earthquakes and tornados (Buhler and Cerato, 2007). In India, expansive soil covers almost 30% of its land area. They mostly found in Maharashtra, Gujarat, Southern part of Utter Pradesh, Eastern part of Rajasthan, Southern and western part of Madhya Pradesh and few parts of Andhra Pradesh and Chennai (Kumar et al., 2007). Therefore being such a big part of the area, it is becoming a potential source of problem for this country.

Expansive soils are one of the most prevalent causes of damage to buildings and infrastructures because of its swelling-shrinking and very poor strength characteristics. Therefore it is extremely important to stabilize and improve the quality of swelling soil prior to any construction upon them. The damages due to construction on untreated swelling soil are mainly- severe structural damage, cracked driveways, sidewalks and basement floors, heaving of roads and highway structures and disruption of pipelines, irrigation systems and sewer lines etc. Fig.1.1 shows the damage in a building founded in such soil, while fig. 1.2 and fig. 1.3 shows the damages (heaving and cracking) it does to road pavement. Fig. 1.4 shows the heaving of a floor built on expansive soil.

Fig. 1.1 Damage to superstructure of a building

Fig. 1.2 Heaving and cracking of roads

Fig. 1.3 Heaving of roads

Fig. 1.4 Cracks in floors

2.0 MATERIALS AND METHODS

2.1 Introduction

In this section the properties and other details of the testing materials i.e. expansive soil, lime and reinforcements (i.e. geomesh and fiber) are presented. Also planning of the tests conducted, procedures for different test, standards followed etc. will be the topic of the discussion.

2.2 Materials

2.2.1 Expansive soil: Expansive soil used in this study is a commercially available bentonite, which is highly expansive in nature with very poor strength. It is mainly consist of the montmorillonite mineral. The bentonite or the expansive soil (ES) being finer than 425 µm is directly used in the experiments. It is also assumed to be consisting of 100 % clay size particles because of its difficulty of particle size determination. The basic properties of the soil are presented in table 3.1.

Table 2.2.1 Properties of expansive soil

Property	Quantity
Specific gravity	2.64
Liquid limit (%)	450.4
Plastic limit (%)	48.2
Plasticity index	402.2

Based on the above properties the soil can be classified as inorganic clay with high plasticity or flat clay (CH) as per guidelines provided by ASTM D 2487 standard.

2.2.2 Lime: The limeused in the present investigation is a commercially available Laboratory reagent grade quick lime (CaO) obtained from S.D. Fine-Chem. Ltd. Mumbai, India. Quicklime is manufactured by chemically transforming calcium carbonate (limestone $CaCO_3$) into calcium oxide. Its properties are presented in Table 2.2.2

Table 2.2.2 Properties of Lime

Property	Quantity
Physical appearance	Dry powder
Colour	White
Chemical formula	CaO
Molecular weight	56.08
Specific gravity	3.1
Minimum assay (%)	95

2.2.3 Geomesh: The geomesh used in this study is the commercially available mosquito net. Its properties are presented in Table3.3

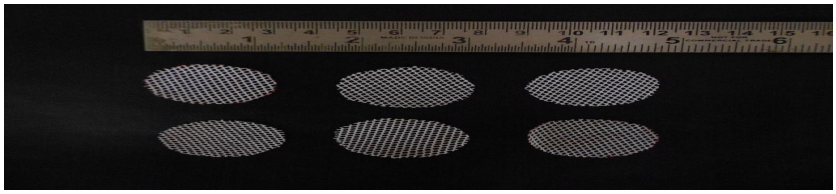

Fig. 2.2.3 Geomesh used in the investigation

Table 2.2.3.1 Properties of geomesh

Property	Quantity	Remarks
Thickness (mm)	0.4	Measured following ASTM D 5199-11
gm/cm^2	9.76×10^{-3}	Measured following ASTM D 5261-10
Tensile strength (kN/m)	5.7	Measured following ASTM D 4595-11
Secant modulus at 5% strain (kN/m)	5.5	Measured following ASTM D 4595-11

2.2.4 Fiber: The fiber used in this study is commercially available glass fiber. Its properties are presented in Table3.4

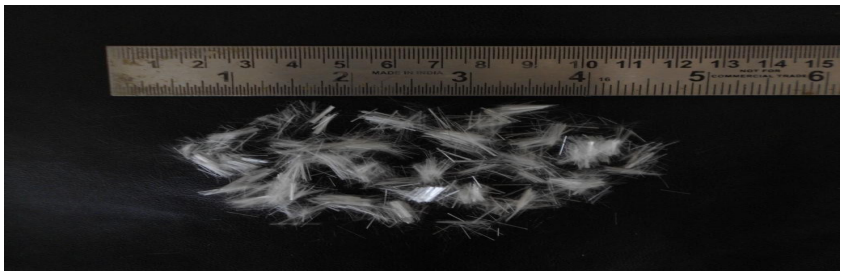

Fig. 3.2 Glass fiber used in the investigation

Table 2.2.4 Properties of fiber

Property	Quantity	Remarks
Diameter (mm)	0.16	-
Specific gravity	2.55	Measured following ASTM D 792-08 Measured following ASTM D2256-10
Tensile strength (GN/m^2)	151.9	Measured following ASTM D2256-10
Modulus of elasticity (GN/m^2)		

2.2.5 Unconsolidated undrained triaxial test

A series of unconsolidated undrained triaxial test has been conducted to further study the stress strain responses of soil-lime mix and reinforced soil-lime mix. The results from this test will also assist in finalizing an optimum combination of reinforced soil- lime mix which can be used beneficially for such soil. The tests were conducted in accordance with ASTM D 2850-03a. The sample preparation and curing process etc were all similar to those adopted in case of unconfined compressive strength test. At the end of desired curing periods, the samples were tested in the triaxial testing machine, maintaining a strain rate of 0.14mm/min for all the samples. The strain rate was so selected that all the samples attain their respective ultimate stress within 5-15 minutes as suggested by the mentioned standard. The triaxial compression testing machine used for this purpose was an electronic type. The main advantage of the electronic system is that it provides an effective alternative to mercury and water constant pressure system,especially where the

laboratory head room is insufficient. The photographic view of the system and the set up made for this test is shown in fig. 2.2.5.

Fig. 2.2.5 Photographic view of the triaxial test set up

3.0 RESULTS AND DISCUSSION

3.1 Strength behavior from unconfined compressive strength test

3.1.1 Strength behavior of Expansive soil- lime mixes

The stress-strain responses of expansive soil-lime mixes obtained from unconfined compressive strength test are presented here In fig.4.1 the response shown is of 3 days curing period. The stress- strain response of untreated soil (i.e. 0% lime) is also shown for comparison purpose of the strength gain due to subsequent lime addition. It has been observed that the curves attain higher peak on increasing in lime content upto12 %, while at 16 % lime content the peak stress decreases.

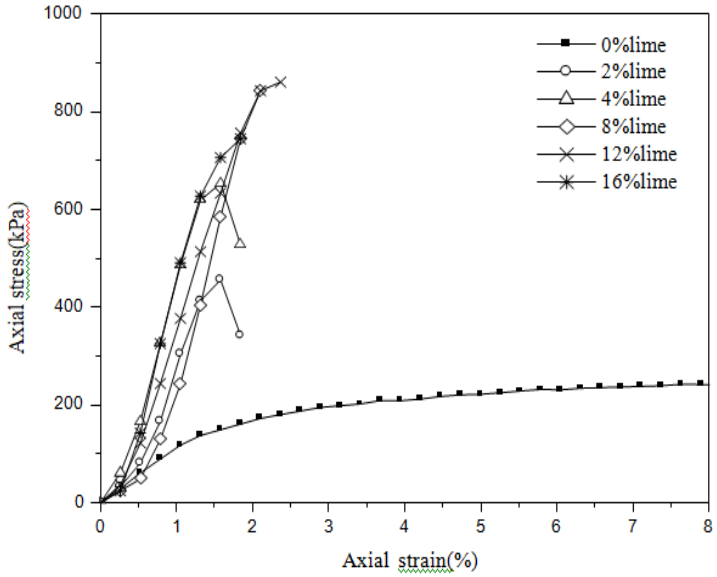

Fig. 3.1.1.1 Stress – strain responses of lime treated expansive soil at 3 days curing period

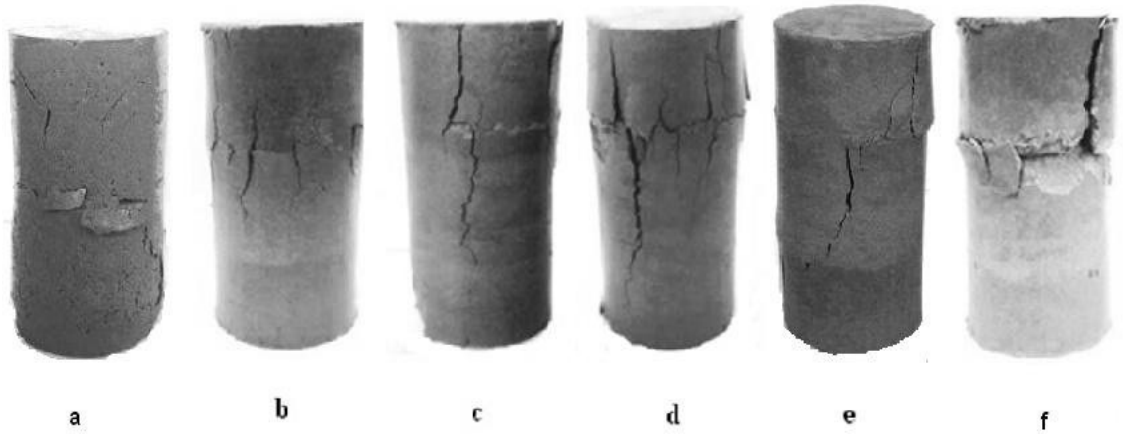

Fig. 3.1.1.2 Failure patterns of lime treated expansive soil at 3 days curing period (a) 0 % lime (b)2% lime (c) 4% lime (d) 8% lime (e) 12 % lime (f) 16 %lime

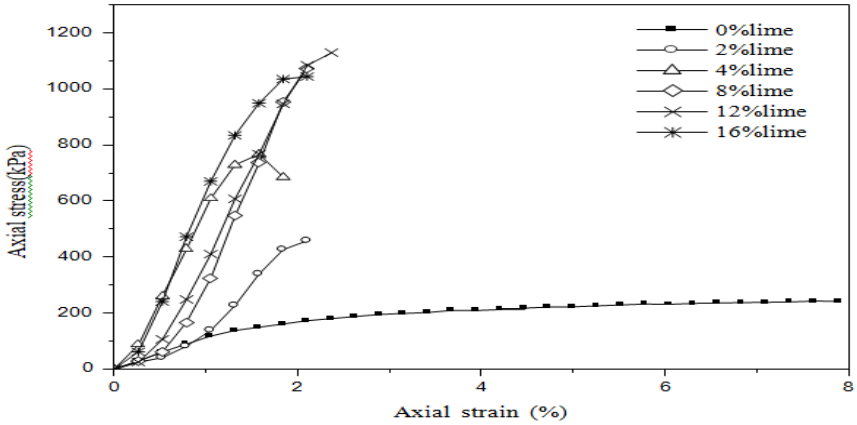

Fig. 3.1.1.3 Stress – strain responses of lime treated expansive soil at 7 days curing period

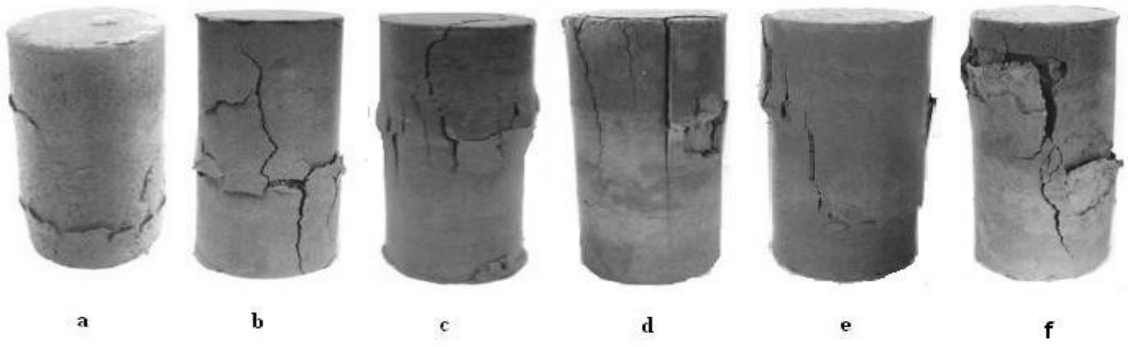

Fig. 3.1.1.4 Failure patterns of lime treated expansive soil at 7 days curing period (a) 0 % lime (b) 2 % lime (c) 4% lime (d) 8% lime (e) 12% lime (f) 16% lime

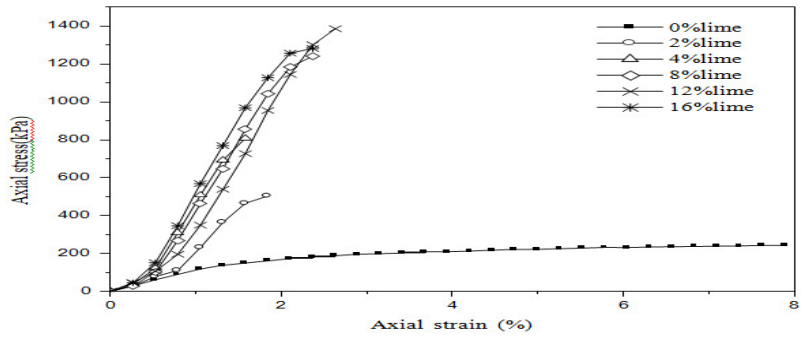

Fig. 3.1.1.5 Stress-strain responses of lime treated expansive soil at 14 days curing period.

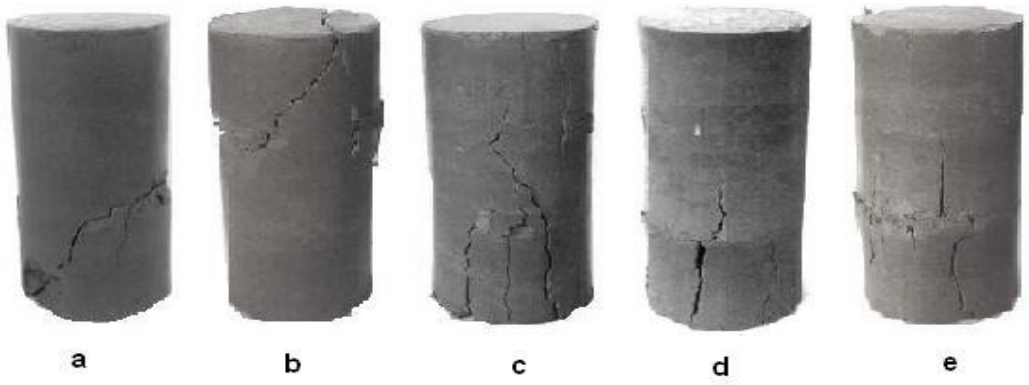

Fig. 3.1.1.6 Failure patterns of lime treated expansive soil at 14 days curing period (a) 2% lime (b) 4% lime (c) 8% lime (d) 12% lime (e) 16 % lime

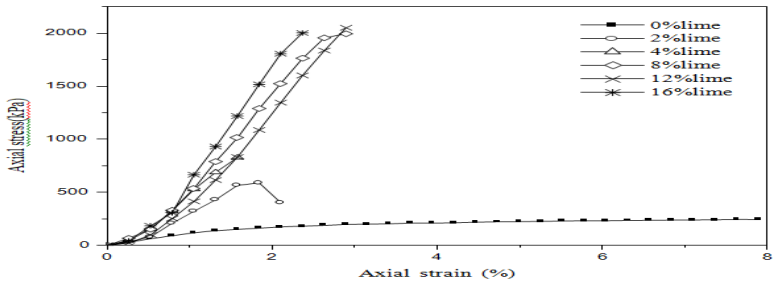

Fig. 3.1.1.7 Stress-strain responses of lime treated expansive soil at 28 days curing period

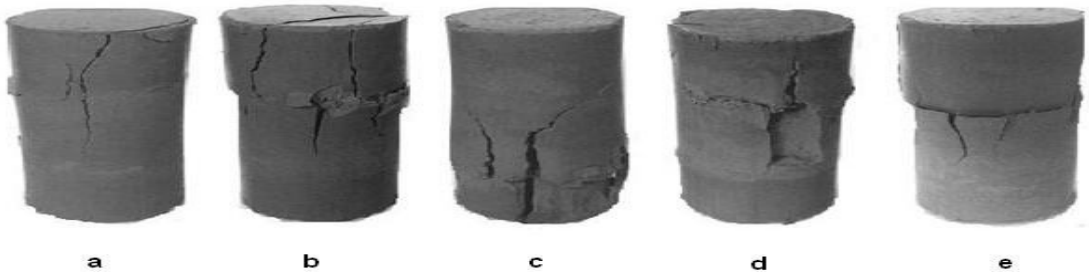

Fig. 3.1.1.8 Failure patterns of lime treated expansive soil at 28 days curing period (a) 2% lime (b)4% lime (c) 8% lime (d) 12% lime (e) 16 %lime

The variation of unconfined compressive strength of the expansive soil and expansive soil treated with lime, with respect to lime content at varied curing period has been shown. It should be mentioned here that the peak compressive stress (average of the three sample's peak stress) at which failure takes place is reported as the unconfined compressive strength of the soil sample. It has been seen that at 2 % lime addition, strength of the swelling soil increases from 235.93 kPa to 456.34, 457.92, 503.454 and 588.035 kPa at 3, 7, 14 and 28 days of curing periods. So at the end of 28 days, increase of strength is almost 2.5 times. With further increase in lime content, the pozzolanic reaction accelerates forming more of cementitious compound leading to increased strength. At 4, 8, 12 and 16% lime content, strength achieved at the end of 28 days are 827.879, 1996.202, 2051.00 and 2003.019 kPa respectively, which are 3.51, 8.46, 8.69 and 8.49 times of the unconfined compressive strength of expansive soil alone. The graph shows clearly the significant effect of curing on strength of soil-lime mixes. Therefore it is clear from the results that 12% lime content shows highest strength gain, though 8% lime content also shows almost same strength gain at all the curing periods with 12% lime content. Further addition of lime content beyond 12% (i.e. at 16% lime content), some reduction in strength has been observed. It may be because of the fact that lime has neither appreciable friction nor cohesion, and a high lime content serve as a lubricant within the soil particles leading to lesser strength.

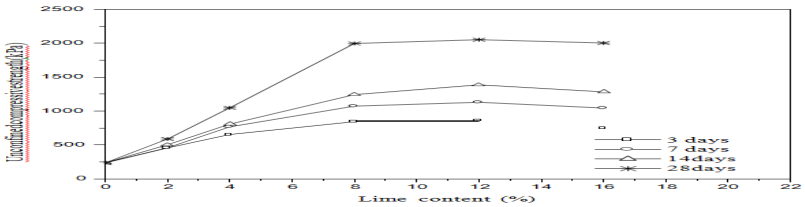

Fig. 3.1.1.9 Unconfined compressive strength v/s lime content for expansive soil-lime mix

3.1.2 Improvement factor for lime treated expansive soil (IF_l): This term has been used to clearly define the improvement of expansive soil upon treatment of lime. It can be defined as the ratio of unconfined compressive strength of lime treated soil to the unconfined compressive strength of untreated expansive soil. This is denoted as IF_l

Table 3.1.2 Improvement factor of lime treated soil IF_l

Lime content	Curing period	Improvement factor IF_l	
		1.36 % strain	Failure stress
0%	-		-
2%	3 days	4.08	1.93
	7 days	2.24	1.94
	14 days	3.60	2.13
	28 days	4.24	2.49
4%	3 days	6.12	2.77
	7 days	7.20	3.25
	14 days	6.84	3.42
	28 days	6.80	3.51
	3 days	4.00	3.58

8%	7 days	5.40	4.55
	14 days	6.40	5.26
	28 days	7.80	8.46
12%	3 days	5.08	3.65
	7 days	6.00	4.79
	14 days	5.32	5.88
	28 days	6.08	8.69
16%	3 days	6.20	3.16
	7 days	8.24	4.43
	14 days	7.60	5.43
	28 days	9.20	8.49

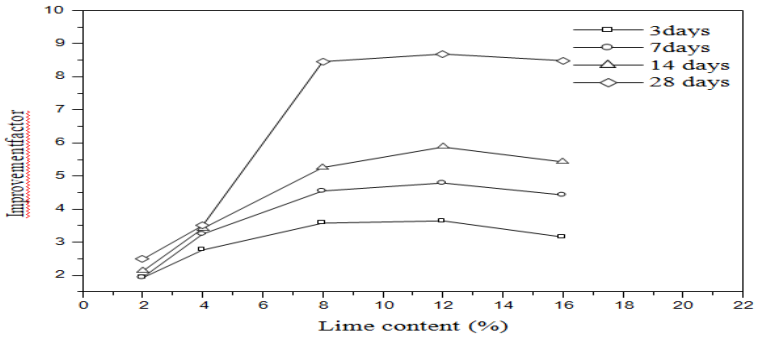

Fig. 3.1.3 Improvement factor vs. lime content at failure stress for expansive soil-lime mixes.

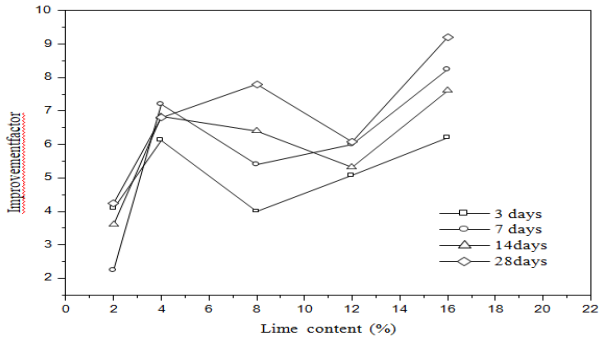

Fig. 3.1.4 Improvement factor vs. lime content at 1.36% strain for expansive soil-lime mixes.

3.1.3 Strength behavior of Geomesh reinforced Expansive soil- lime mixes

In this section stress strain responses of reinforced soil- lime mixes and the improvement in strength will be discussed. The geomesh that has been used as reinforcement material is a commercially available mosquito net. It has been cut in circular sections of 34 mm diameter and introduced in number of layers within the soil samples. In earlier stage, soil with 2 and 3 layers of the geomesh with 0, 2, 8 and 12% of lime were tested for its unconfined compressive strength to obtain the optimum numbers of layers which would give maximum strength. In fig. 4.12, 4.13, 4.14 and 4.15, the stress- strain responses of expansive soil, expansive soil-2% lime- geomesh, expansive soil-8% lime- geomesh and expansive soil-12% lime- geomesh at 7 days curing periods are shown. From all the three graphs it has been observed that with 3 layers of geomesh both expansive soil and

expansive soil treated with lime shows superior results (higher unconfined compressive strength) than with 2 layers of reinforcement. Therefore it is decided to use 3 layers of geomesh in one soil sample in all the cases in rest of theinvestigation.

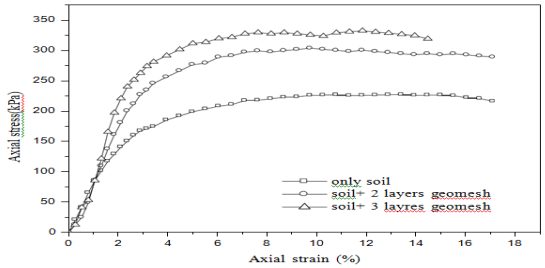

Fig. 3.1.3.1 Stress-strain response of expansive soil-0% lime with different no. of reinforcement layers.

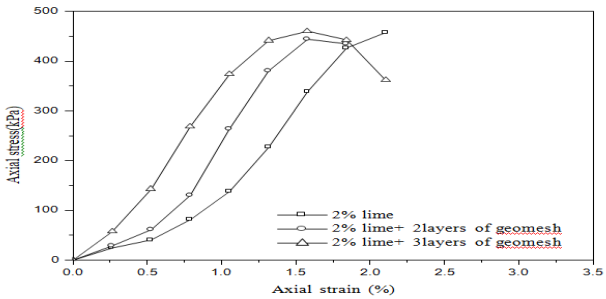

Fig. 3.1.3.2 Stress-strain response of expansive soil-2% lime with different no. of reinforcement layers at 7days curing period.

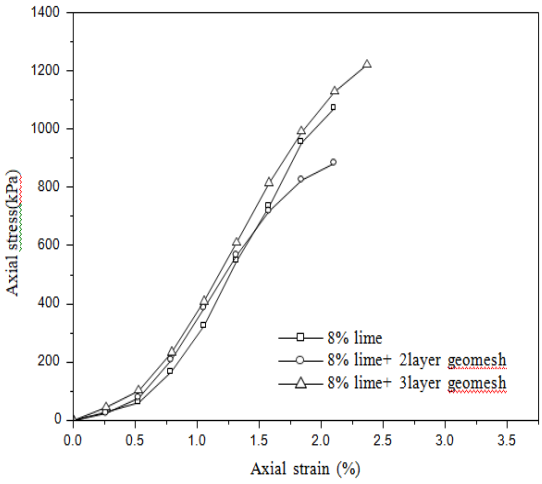

Fig. 3.1.3.3 Stress-strain response of expansive soil-8% lime with different no. of reinforcement layers at 7days curing period.

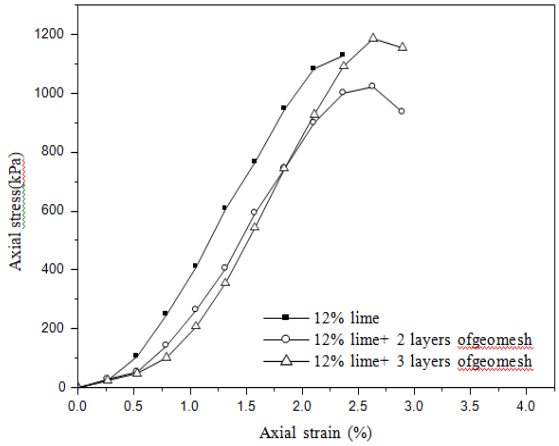

Fig. 3.1.3.4 Stress-strain response of expansive soil-12% lime with different no. of reinforcement layers at 7days curing period

Now, a comparative study of geomesh reinforced lime treated expansive soil with only lime treated soil to evaluate percentage strength improvement in reinforced soil with respect to unreinforced soil will be done. Fig. 4.16, 4.17, 4.18 and 4.19 shows relative stress-strain responses of 2% lime treated expansive soil and 2% lime treated geomesh reinforced expansive soil at 3, 7, 14 and 28 days respectively. From these responses it is observed that with geomesh reinforcement, lime treated soil shows higher unconfined compressive strength than that of only lime treated soil. At 3 days curing period soil-lime mix gives UCS of 456.34 kPa, and soil-lime-geomesh mix gives 463.18 kPa i.e. an improvement of 1.4%. Similarly at 7, 14 and 28 days the percentage improvement in geomesh reinforced soil lime mixes are 5.7%, 7.7% and 6.8% respectively in compared to lime treated soil at the corresponding curing periods.

3.1.4 Improvement factor for Lime treated & geomesh reinforced soil (IF_{lg}): It can be defined as the ratio of unconfined compressive strength of geomesh reinforced lime treated soil to the unconfined compressive strength of untreated expansive soil. It is denoted as IF_{lg}

Table 3.1.4 Improvement factor for lime treated & geomesh reinforced expansive soil IF_{lg}

Lime content	Curing period	Improvement factor IF_{lg}	
		1.36 % strain	Failure stress
0%	-	1.20	1.41
2%	3 days	3.88	1.96
	7 days	4.36	2.05
	14 days	5.36	2.30
	28 days	5.20	2.66
4%	3 days	5.36	3.07
	7 days	5.16	3.52
	14 days	4.40	3.76

	28 days	7.12	3.83
8%	3 days	4.20	4.16
	7 days	6.04	5.09
	14 days	5.88	6.25
	28 days	4.00	8.63
12%	3 days	4.36	4.03
	7 days	3.52	5.03
	14 days	3.80	6.76
	28 days	7.40	9.52
16%	3 days	5.64	3.42
	7 days	7.00	4.44
	14 days	5.20	7.08
	28 days	4.40	11.31

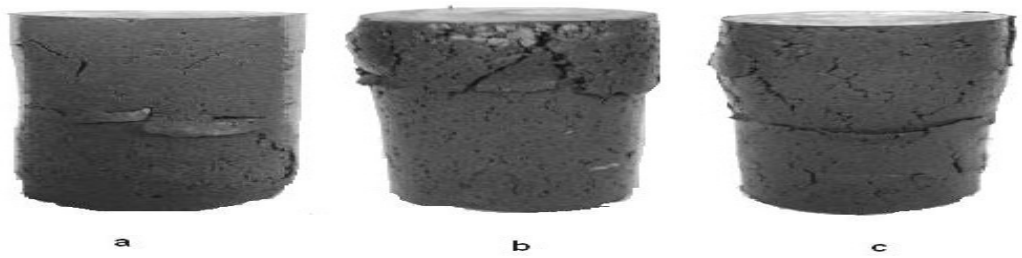

Fig. 3.1.4.1 Failure patterns of expansive soil+0% lime with (a) 0 layer geomesh (b) 2 layer geomesh (c) 3 layer geomesh

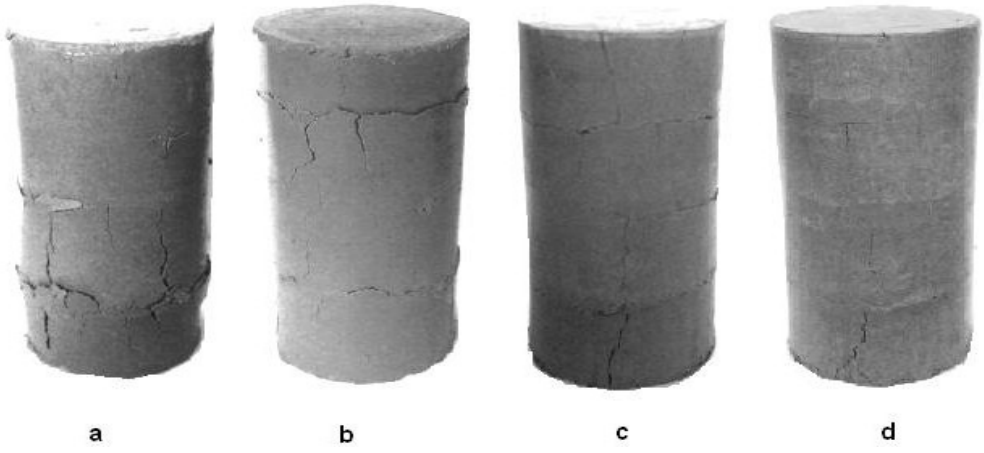

Fig. 3.1.4.2 Failure patterns of expansive soil-2% lime-geomesh mixes at (a) 3 days (b) 7 days (c)14 days (d) 28days

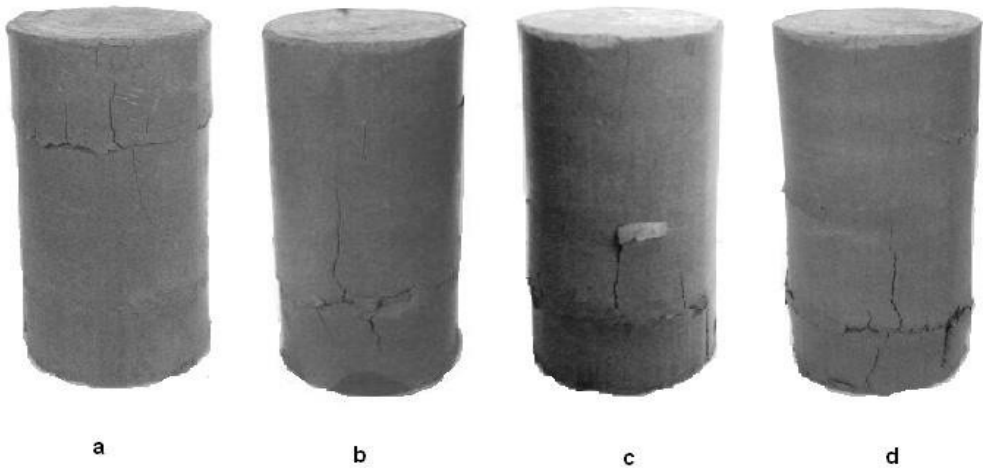

Fig. 3.1.4.3 Failure patterns of expansive soil-4% lime-geomesh mixes at (a) 3 days (b) 7 days (c) 14 days (d) 28 days

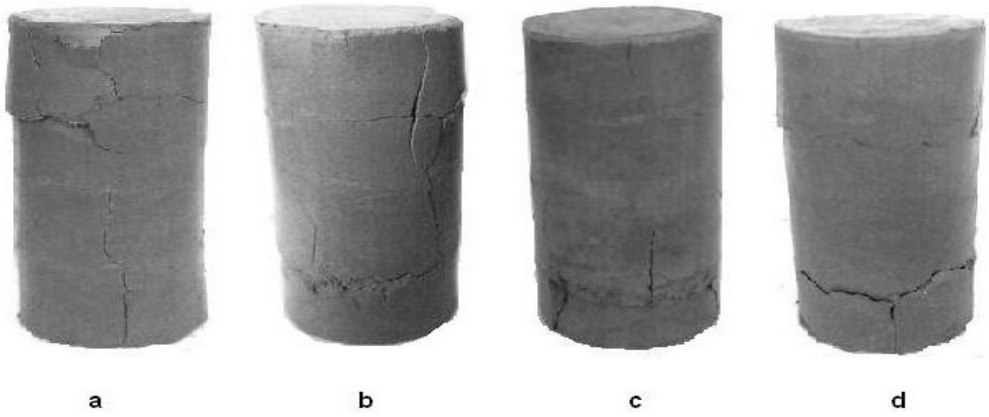

Fig. 3.1.4.4 Failure patterns of expansive soil-8% lime-geomesh mixes at (a) 3 days (b) 7 days (c) 14 days (d) 28 days

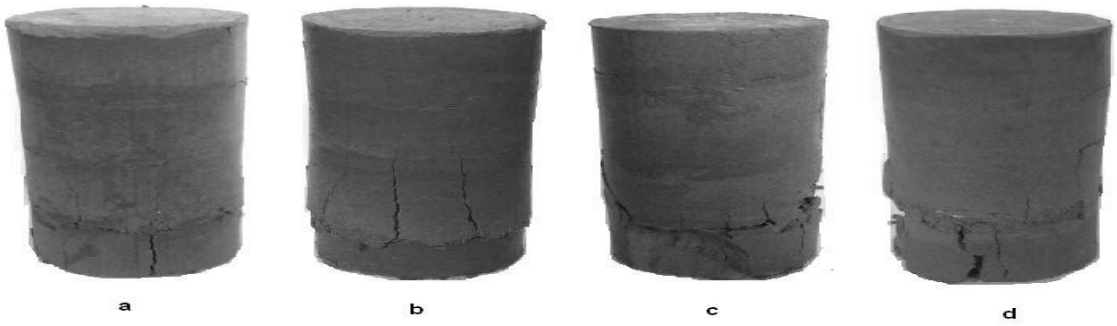

Fig. 3.1.4.5 Failure patterns of expansive soil-12% lime-geomesh mixes at (a) 3 days (b) 7 days (c) 14 days (d) 28 days

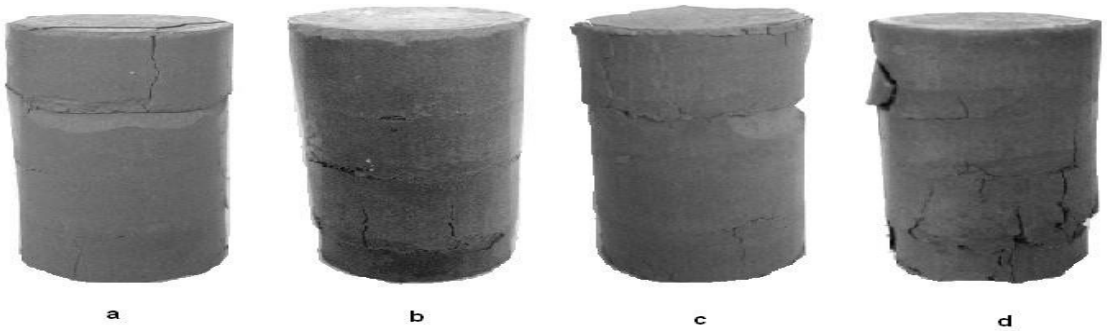

Fig. 3.1.4.6 Failure patterns of expansive soil-16% lime-geomesh mixes at (a) 3 days (b) 7 days (c) 14 days (d) 28 days

3.1.5 Strength behavior of geomesh and fiber reinforced ES- limemixes

From the studies of the results obtained from unconfined compressive strength test and unconsolidated undrained triaxial test, it has been now well understood that geomesh reinforcement in soil lime mix shows superior strength than only lime treatment. Especially soil with higher lime content (i.e. with 8%, 12%. 16%) shows highest strength improvement.

Looking for further improvement of geomesh reinforced lime treated soil; glass fiber has been used in this study. In this section the effects of fiber on strength characteristics of geomesh reinforced lime stabilized soil with lime content of 8%, 12% and 16% will be studied. The fiber used is commercially available glass fiber. The length of the fiber used is fixed to 10mm. Also it has been used in a constant percentage of 1% to the dry weight of soil in all cases. Geomesh were used in three layers at equal spacing in a soil sample alike in the previous cases.

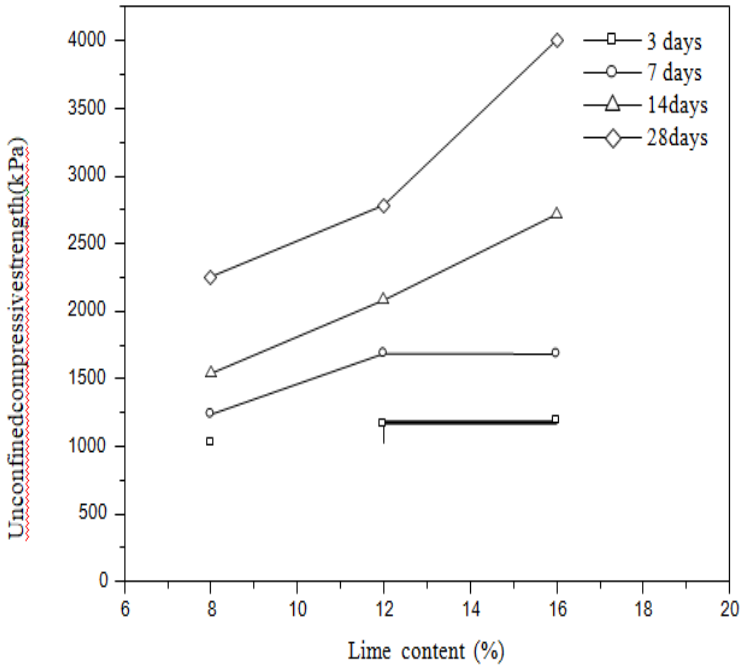

Fig. 3.1.5.1 Unconfined compressive strength vs. lime content for expansive soil-lime-geomesh- fiber mixes.

Table 3.1.5.1 Improvement factor for lime treated & fiber and geomesh reinforced soil IF_{lgf}

Lime content	Curing days	Improvement factor IF_{lgf}	
		1.36% strain	Failure stress
8%	3 days	4.56	4.37
	7 days	5.6	5.25
	14 days	5.56	6.54
	28 days	9.6	9.57
12%	3 days	6.6	4.95
	7 days	9	7.16
	14 days	9.2	8.83
	28 days	6.2	11.81
16%	3 days	6.6	5.05
	7 days	7.64	7.14
	14 days	7	11.52
	28 days	10.04	16.99

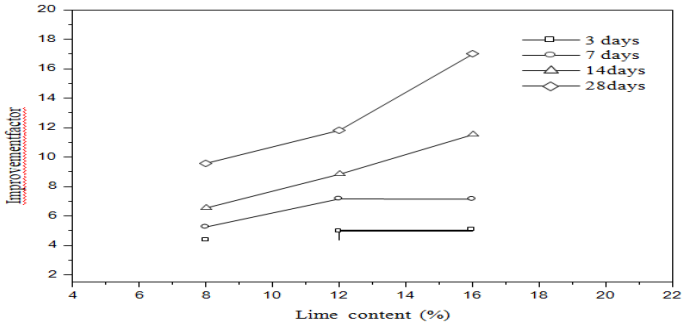

Fig. 3.1.5.2 Improvement factor vs. lime content at failure stress for expansive soil-lime-geomesh-fiber mixes

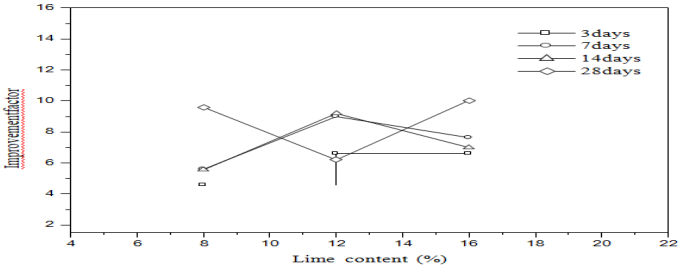

Fig. 3.1.5.3 Improvement factor vs. lime content at 1.36% strain for expansive soil-lime-geomesh-fiber mixes.

4.0 CONCLUSION

Expansive soils exist in several countries across the world and constitute more than 20 % of India's land area. It is a major cause for damage and rapture of structures. Economic loss due to expansive soil in many countries is more than any other natural disaster like earthquake, tsunami or flood etc. Through the time, various treatment methods have been discovered to improve the performance of expansive soil and mainly are mechanical stabilization, chemical stabilization, stabilization with additives, thermal stabilization and electrical stabilization etc. Among these various methods, chemical treatment (treatment using lime, cement etc) has been proved to be the most performance as well as cost efficient method. Lime treatment is the most popular method within this category for expansive soil treatment. From the literature review it has been observed that with an optimum lime addition to expansive soil its swelling potential can be reduced significantly, and with further addition its strength can be increased to many folds than to its initial strength.

Other chemical and non chemical additives those have been tested successfully for performance improvement of swelling soil are cement, sand, fly ash, gypsum, magnesium oxide, calcium chloride etc. Improvement of swelling soil by geogrid, geomesh, and other fibers etc. along with lime or other treatment is a modern approach. In this investigation lime treatment with and without application of such geo-materials (geomesh and fiber) have been studied. The findings from this kind of research may contribute to a relaxation in the specifications of fill materials and also to the degree of chemical treatment that would have been otherwise applied to the same.

In this investigation, the main purpose was to observe strength characteristics of expansive soil upon combined treatment of reinforcement and lime. For this, unconfined compressive strength test and unconsolidated undrained triaxial have been conducted on different mixes of expansive soil with different percentages of lime (0, 2, 4, 8, 12 and 16% by dry weight of soil) and reinforcement (3 layer of geomesh and 1% of fiber). Samples were prepared compacting at their respective Proctor MDD and OMC conditions. They were kept for different curing periods (i.e. 3, 7, 14 and 28 days). Geomesh and fiber reinforced soil also tested under similar conditions of lime content and curing periods. The details of the methods

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TO ENHANCE MECHANICAL PROPERTIES OF CONCRETE BY USING LATHE STEEL SCRAP AS REINFORCED MATERIAL

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Abstract— Every day about 8 to 10 kg of lathe waste are generated by each lathe industry in the Rajasthan region and through away in the barren soil, thereby contaminating the soil and ground water, which produces an environmental issue. Hence, by adopting actual management by recycling the lathe scrap with concrete is observed to be one of the best compounds. The test was conducted as per the Indian standard procedure for its mechanical properties such as flexural strength, split tensile strength, compressive strength, and compared normal PCC. The 7 days strength of the Lathe scrap reinforced concrete communicates an increase in its compressive strength when compared with PCC, and has practically become equal to the strength when tested on 28 days under normal curing. The addition of steel scrap in concrete has enhanced the performance of beam in flexural by 40% when compared with plain cement concrete. There is only a sizable increase in the split tensile strength of concrete with steel scrap when compared with plain cement concrete. The workability of fresh concrete that accommodate different ratios of lathe scrap was carried out by using slump test. The result showed that addition of lathe scrap into plain cement concrete mixture increased its compressive strength while it decreased the workability of the fresh concrete containing the steel scrap.

Comparatively the population of the world is increasing there is an emerging necessity of mass constructions or multi storied constructions which can accommodate a larger number of people. In this situation high strength concrete is required, which is eco-friendly, i.e. it must be moreover sustainable and effort worthy. To speed up the properties of concrete we can add some fibrous material to the concrete, which are uniformly distributed and randomly oriented and helps to enhance the compressive strength, shear resistance, crack résistance, modulus of elasticity, toughness and reduction of shrinkage of concrete. And also, by keeping sustainability in mind, we have used Lathe steel scrap as a fibrous material in the concrete, which is non-bio-degradable solid waste generate by Lathe machinery in fabricate industries, land stuffing by these waste materials causes land pollution and also influence the quality of ground water at such places. In consideration of environmental pollution and the huge availability of these scrap material we have used Lathe steel scrap as partial adding to concrete at 0%, 0.5%, 1%, 1.5%, and 2% by volume proportions for M30 grade concrete and the properties like compressive strength, split tensile strength, flexural beam strength, modules of elasticity are tested for 7 and 28 days and compared with normal M30 concrete.

Keywords— Lathe Steel Scrap, Compressive Strength, Split Tensile Strength, Flexural Strength, Workability, Waste Material, Sustainable Material.

1.0 INTRODUCTION

In the current scenario, the world is facing the construction of very challenging and difficult engineering structures. Concrete is the most important and widely used material for construction of engineering structure, pavements etc. it is called upon to possess very high compressive strength and sufficient workability properties and efforts are made in the field of concrete technology to develop the properties of concrete by using fibers and other admixtures in concrete up to certain proportions. In the view of the global sustainable development, it is imperative that Fiber Reinforced Concrete (FRC) provide improvements in tensile strength, toughness, ductility, post cracking resistance, fatigue characteristics, durability, shrinkage characteristics, impact, cavitations, erosion resistance and

serviceability of concrete. Due to these benefits, the use of FRC has increased during last two decades.

In the present experimental work, an attempt will be made to analyze the compressive strength of the waste lathe steel scrap material which is available from the lathe machine, is used as a steel fiber in concrete for various construction works and to optimize fiber content. Lathe Scarp is easily available in mechanical workshops, car pantry shops etc. with minimum cost. By adding lathe scrap as a reinforced fibre, we can reduce the construction cost as well as material. As we know concrete has more compressive strength, but less in tensile, so by using some waste as a additional material so we can increase the tensile strength as well as compressive strength.

1.1 Lathe Steel Scrap

Waste usages are an attractive substitute to disposal in that disposal cost and likely pollution problems are decreased or even eliminated along with the achievement of measurable conservation. However, the utilization strategy must be coupled with environmental and energy reflection to use available materials most efficiently. Steel slag, the by-product of steel and iron manufacture processes, started to be used in civil engineering projects during the past 12 years. The secondary waste from steel is the iron filing, which is produced locally in large amounts from steel workshops and factories. This product has a refuse impact on the environment when disposed from this reason the research project started. Most of the previous researches were discussed with steel slag where a rare of it was concerned with iron filing.

Scrap from lathe machine is built from different manufacturing processes which are carried out by lathe machine. Scrap which is a waste can be used as a reinforcing material in concrete to strengthen the various properties of concrete. Scrap from the machine can react in a same way as steel fiber. Steel scrap which is a lathe waste generated by each lathe industry and dumping of such wastes in barren soil causes contamination of soil and ground water, which generate harmful environment. In adding to get sustainable development and environmental profit, lathe scrap can be used as a reuse fiber with concrete. With expanded in population and industrial activities, the amount of waste fibers generated will increase in coming years.

Figure 1.1: Steel Scrap from Lathe Machine

These industrial waste fibers can be effectively used for manufacturing high-strength, low cost Fibre Reinforced Concrete after exploring their suitability. Plain reinforced concrete is brittle material due to adding of steel fibers in concrete, considerably expand the tensile strength, static flexural strength, durability, impact strength and shock resistance.

Concrete is a substance which is weak in tension and fails in a brittle manner when subjected to tension and flexure. When steel scrap is put into concrete, the performance of composite material is superior to plane concrete. A good waste, solid management is to occur a way to make use of it. In this experimental study was carried out to study the practicability of using steel scrap obtained from lathe machine in concrete by inspecting the compressive strength, splitting tensile strength and flexural strength of M30 concrete and thus boost the fiber proportions. Lathe steel scrap reinforced concrete (LSSRC) is a costly essential replacement for fiber reinforced concrete (FRC).

Steel scraps gets from lathe machines has similar physical properties as that of steel fibers. The essential utilization of localized available lathe waste material is certainly a great have to in the recent years. The lathe waste was ready manually to get an aspect ratio from 50-110. It is known that too long fibers cause balling effect.

1.2 BENEFITS OF USING LATHE STEEL SCRAP IN CONCRETE

- To reach high strength concrete economically.
- To explore the proper replacement percentage for lathe steel scraps and lathe scraps based on the strength and workability parameters.
- To study the degree of workability of concrete on all present replacement percentages.
- To study and compare the showing of usual concrete and high strength concrete using Lathe scraps and Steel fibers

- To understand the effectiveness of Lathe and Steel fibers in betterment of concrete strength
- To study the carry out of varying percentage of replacement of fine aggregate by lathe steel scraps and steel fibre on concrete.
- To study the advantage of Lathe steel scraps and Steel fibers as an supplement in concrete

2.0 MATERIAL AND METHODOLOGY

2.1 MATERIALS USED

Concrete Material mainly consists of cement, fine aggregate, coarse aggregate, lathe scrap waste, anti corrosive agent and water.

2.2 Cement

The Aditya Birla brand of Ordinary Portland cement (OPC) of grade-43 used in this study was purchased from the local market of Chittorgarh. Cement is an artificial material, generally available in powder form, which can be made into paste form by the mixing of water and it will set into solid mass when it is moulded or poured. Various organic compounds used for fastening and adhering materials, are called cements, but cement classified as adhesives, and cement alone means a construction material.

2.3 Fine Aggregate

Fine aggregate is a naturally occurring granular material. Sand is collected of finely divided rock and mineral particles. The main ingredient of sand is, in non-tropical coastal settings and inland continental settings, is silica (SiO_2), usually it is in the form of quartz. It is the most usual mineral resistant to weathering. It is used as fine aggregate in concrete and mortar.

Sand is a collection of grains of mineral matter derived from the disintegration of rocks. Sand is specifying from gravel only by the size of the particles or grains, but is differ from clays which contain organic materials. Sands that has been and separated from the organic material by winds or by the action of currents of water across arid lands are generally quite uniform in size of the grains. Commonly, commercial sand is obtained from sand dunes formed by the action of winds and from riverbeds.

2.4 Coarse Aggregate

Crushed stone aggregate with particle size less than 20mm size was used for the present investigation. The specific gravity of the coarse aggregate was tested as per IS 2386:1963 (PART 3) and it was found to be 2.89.

Aggregates are immobile granular materials such as sand, gravel, or crushed stone that, along with water and Portland cement, are a basic ingredient in concrete.

For an actual concrete mix, aggregate needs to be cleaned, hard, strong particles unconfined of absorbed chemicals and other fine materials that could end the deterioration of concrete. Aggregates, which account for 60 to 75 percent of the total volume of concrete, are split into two distinct categories--fine and coarse. Gravels constitute the majority of coarse aggregate used in concrete with crushed stone making up most of the residue.

S.NO.	Properties	Values
1	Cross –section	Straight and deformed
2	Diameter(mm)	0.3-0.75
3	Length (mm)	25-40
4	Density kg/m3	7850
5	Young modulus(N/mm²)	2 x 105
6	Tensile strength (N/mm²)	500-3000
7	Specific gravity	7.85
8	Aspect ratio	45-100
9	Elongation (%)	5-35

2.5 lathe Steel Scrap

To make concrete more economical and clean with a remarkable quality, application of Computer Numeric Controlled (CNC) Lathe machine waste can have massive importance. By using this large amount of (according to ICI 1200 million tons annually) CNC waste can help to generate large quantities of eco-friendly concrete and decrease large amount of land pollution.

At this present time when the unbelievable demand of steel is at its maximum, this nature of blindly following the broadening strategy not only leads toward development, but it heads to a throwaway ground of Industrial Waste as well. To utilize this large quantity of steel the CNC Lathe Machines are used and due to their usage a large amount of waste is generated.

From the previous many researchers during their research work have come across many profits and obstacles. Lathe waste is a material through lathe machines and that can be used as a steel fiber. Now manually processed lathe waste with an aspect ratio range from 45 to 100 was used. The thickness varies from 0.3 to 0.75 mm and length from 25 mm to 40 mm was included in Lathe Steel Scrap Fiber Reinforced Concrete (LSSFRC).

Figure 2.5: Lathe Steel Scrap of various length

Table 2.5.1: Properties of Scrap Steel Fibre

2.6 Water

Potable water available from the laboratory which satisfies the drinking standard was used for mixing and curing.

2.7 Anti Corrosive Agent

These when added to concrete reduces the corrosion of steel fibers in it. These are water soluble and easy to mix with water. Here, "CORROMIN W" containing alkyl phosphonate salt mixture has been used.

3.0 Methodology

3.1 Working Procedure

The working procedure applied in this research is shown in the flow diagram below:

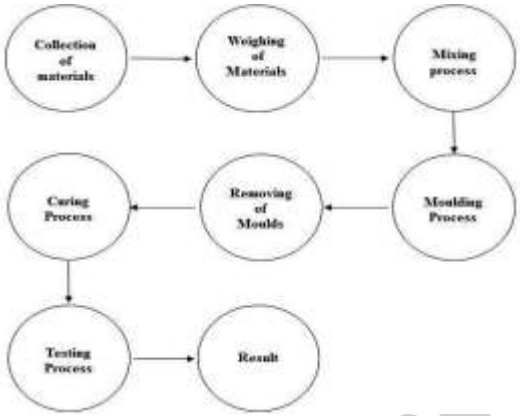

Figure 3.1: Schematic flow diagram of methodological approach

3.2 Concrete Mix Proportion

In this study M30 grade concrete mix design as per IS: 10262-2009 is carried out. The concrete mix proportion was 1:1.73:3.3 and water content was 197 l/m3

In this present study, all the properties are tested for M30 concrete as per IS 456-2000. The design mix is prepared as per the specifications of the materials mentioned above. And the quantities of the materials are shown in the table 3.2.1

Table 3.2.1: Mix Proportion per m3 of Concrete for Lathe steel Scrap

Material	Mix 1	Mix 2	Mix 3	Mix 4	Mix 5
% Addition of steel scrap	0	0.5	1	1.5	2
Cement (kg)	370	370	370	370	370
Coarse aggregate (kg)	1242.58	1242.58	1242.58	1242.58	1242.58
Fine aggregate (kg)	639.88	639.88	639.88	639.88	639.88
Steel scrap weight (kg)	0	11.26	22.52	33.78	45.04
Chemical admixture (litre)	0	0.34	0.68	1.04	1.14
Water (litre)	169	169	169	169	169

4.0 RESULT AND DISCUSSION

4.1 Workability: The workability of fresh Lathe Steel Scrap Fibre Reinforced Concrete (LSSFRC) is a measured of its ability to be mixed, handled,

transported and importantly place and consolidated. Slump test is a common, convenient and inexpensive test, but refer only for small fiber contents, for high volume contents inverted cone or Vee Bee test is referred (IS 1199-1959).

Figure 4.1.1: Workability Measured by Slump Test Apparatus

Table 4.1.1: Slump Value of lathe Steel Scrap Reinforced Concrete (LSSRC)

S. No	Addition of Lathe Steel Scrap (%)	Slump Value(mm)
1	0	85
2	0.5	80
3	1.0	75
4	1.5	70
5	2.0	70

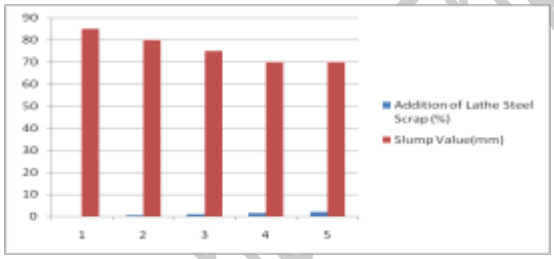

Figure 4.1.2: Graphical arrangement of Slump Value

4.2 Compressive Strength: (IS 516-1959): Fibers usually minor effects on compressive strength, slightly increasing or decreasing the result. Cubes moulds are used to prepare 30 cubes testing under the Compressive testing machine.

Figure 4.2.1: Concrete Cube under CTM

Table 4.2.1: Compressive Strength of LSSRC at 7 days (MPa)

S. No	Addition of Lathe Steel Scrap (%)	Compressive strength at 7 days (MPa)
1	0	31.2
2	0.5	36.43
3	1.0	37.2
4	1.5	44.2
5	2.0	33.3

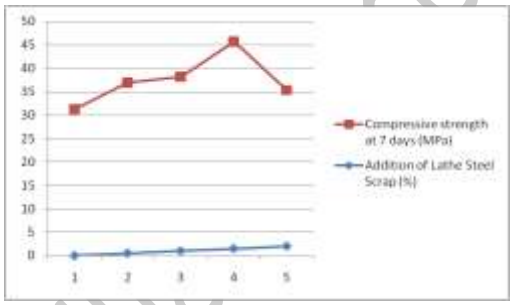

Figure 4.2.2: Graphical Arrangement of Compressive Strength of LSSRC at 7 days

Table 4.2.2: Compressive strength of LSSRC at 28 days (MPa)

S. No	Addition of Lathe Steel Scrap (%)	Compressive strength at 28 days (MPa)
1	0	41.2
2	0.5	42.52
3	1.0	42.83
4	1.5	49.32
5	2.0	44.42

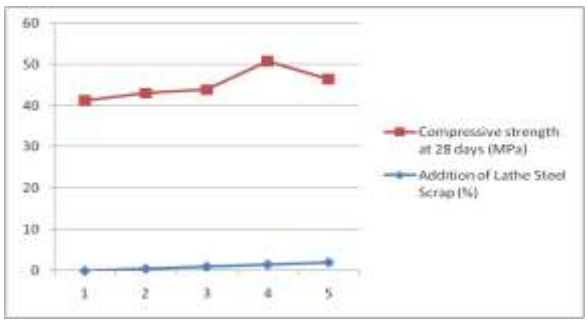

Figure 4.2.3: Graphical Arrangement of Compressive Strength of LSSRC at 28 days

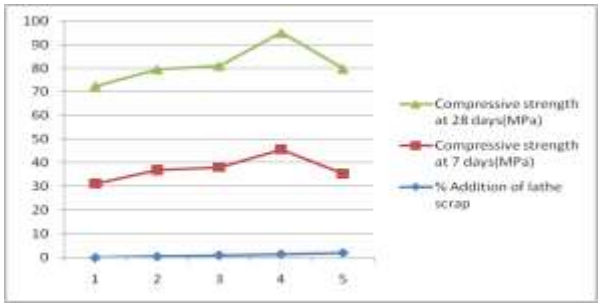

Figure 4.2.4: Graphical Comparison of Compressive Strength of LSSRC at 7 & 28 day

4.3 Flexural strength (I.S. 516 - 1959): The flexural strength of the beams tested for different proportion shows a gradual increase in flexural strength up to 1.2% of fiber added concrete and then a gradual decrease in the strength up to 2%.

Table 4.3.1: Flexural Strength of LSSRC at 28 days (MPa)

S. No	Addition of Lathe Steel Scrap (%)	Flexural Strength at 28 days(MPa)
1	0	4.13
2	0.5	4.56
3	1.0	5.86
4	1.5	6.34
5	2.0	4.83

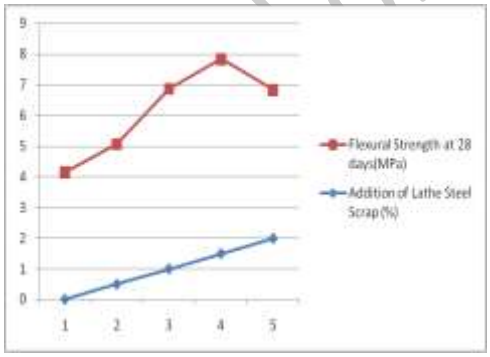

Figure 4.3.1: Graphical Arrangement of Flexural Strength of LSSRC at 28 days

4.4 Split Tensile strength (I.S. 5816 - 1999): The split tensile strength of the concrete varies with the proportion of fiber added in concrete. The maximum strength is observed in 1.2% of fiber added to concrete.

Table 4.4.1: Split Tensile Strength of LSSRC at 28 days (MPa)

S. No	Addition of Lathe Steel Scrap (%)	Tensile Strength at 28 days (MPa)
1	0	2.83
2	0.5	2.98
3	1.0	3.33
4	1.5	4.23
5	2.0	3.45

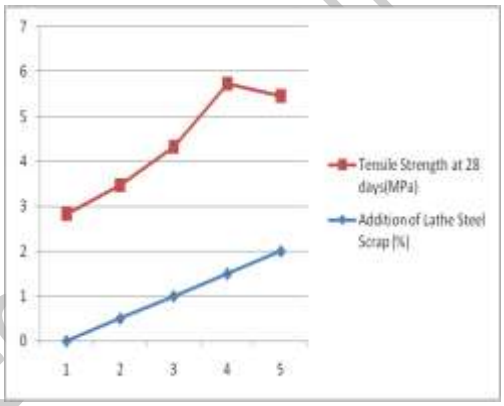

Figure 4.4.1: Graphical Arrangement of Tensile Strength of LSSRC at 28 days

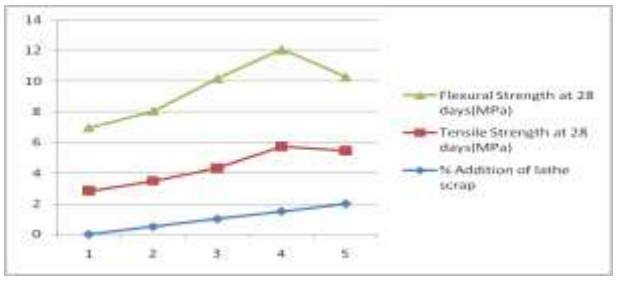

Figure 4.4.2: Graphical Comparison of Flexural and Tensile Strength

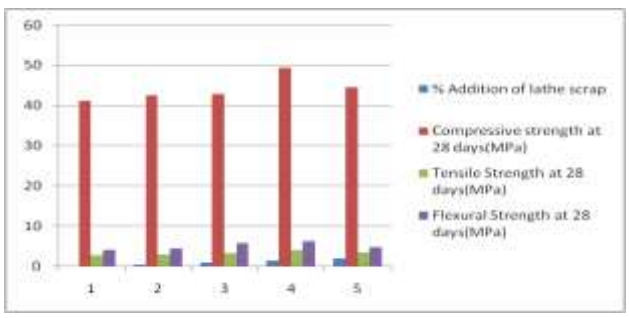

Figure 4.4.3: Graphical Comparison of Compressive Strength, Flexural Strength and Tensile Strength at 28 days

5.0 Conclusion

This study shows that restore of lathe waste enhance mechanical properties of concrete. Different tests were done at 7 and 28 days after casting the specimens. The following conclusions were made from the test results and discussions of this investigation:

The mechanical properties of the concrete are increased by increasing the proportion of the lathe steel scrap from 0.5% up to 1.5%. From 1.5% to 2.0% it shows slight decrease in the mechanical strength. At 2.0% of lathe scrap proportion there is a considerable reduction in the mechanical strength of LSSRC .The compressive strength of LSSRC increased by 10% for 7 days strength when compared to Plain Cement Concrete for all the tested proportions of lathe scrap and steel fiber. For the 28 days strength the Lathe Steel Scrap Reinforced Concrete (LSSRC) poses almost the same compressive strength as plain cement concrete for all the tested proportion. The addition of lathe steel scrap has significantly increased the performance of beam in flexural nearly 40% when compared with plain cement concrete .There is a considerable increase in split tensile strength of about 10% when compared to plain cement concrete. The result published that addition of lathe scrap in to plain cement concrete mixture enhanced its compressive strength while it decreased the workability of the fresh concrete containing the lathe scrap. In general from the above study it was incurred that, the performance of lathe scrap reinforced concrete proves to be better than the normal concrete and very much comparable with SFRC regarding its mechanical properties.

Natural maneuver are not immense and also, there is a global need to preserve to our environment and preserve our scarce natural resources for next generation. Use of lathe waste in concrete is beneficial as compared to conventional concrete decrease the environmental pollution as well as providing economical value for the waste material.

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Utilization of Construction & Demolition Waste as Coarse Aggregate in Rigid Pavement Construction

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Abstract: ***The main objective of this research is to investigate the possibility of utilizing construction & demolition waste aggregate in rigid pavement construction. In the present study compressive strength of concrete at 7, 14, and 28 days was checked, and this concrete is prepared by mixing cement, sand, aggregate, and water. In a further study, coarse aggregate is replaced by aggregates obtained from C&D (Construction & Demolition) waste, and then M35 mix design concrete is prepared. From the result obtained in the present experimental investigation, it was found that the desired strength concrete can be obtained from replacing the conventional coarse aggregate with recycled aggregate obtained from C&D waste with a substitution rate of 20 %. Thus the use of C&D waste in concrete manufacturing will not only solve the problem of availability of material but also reduces the cost of the construction and problems caused due to dumping of C&D waste. The utilization of C&D waste in the construction industry also ensures sustainable development in an environmentally friendly manner by the conservation of natural resources.***

Keywords: Compressive Strength; Construction & Demolition Waste; Recycled Aggregate; Road Construction; Rigid Pavement

I. INTRODUCTION

A pavement is a structure consisting of superimposed layers of processed materials above the natural soil surface, whose primary function is to distribute the vehicular loads to the stable strata below the normal ground level lies at a considerable depth. The pavement structure should be able to provide a surface of acceptable riding quality, adequate skid resistance, favourable light reflecting characteristics, and low noise pollution. Two types of pavements are generally recognized as serving this purpose, namely flexible pavements and rigid pavements (Mathew, 2009).

Flexible pavements are those, which on the whole have low or negligible flexural strength and are rather flexible in their structural action under the loads. The flexible pavements layers reflect the deformation of the lower layers on to the surface of the layer (Anusha & Avinash, 2017). Rigid pavements have sufficient flexural strength to transmit the wheel load stresses to a wider area below. In rigid pavement, the load is distributed by the slab action, and the pavement behaves like an elastic plate resting on a viscous medium; assuming the concrete slab as a medium thick plate which is plane before loading and to remain plane after loading. Compare to the flexible pavement, rigid pavement is placed either directly on the prepared sub-grade or a single layer of granular or stabilized material. Construction of rigid pavement is now-a-days most widely used in the road construction industry. Rigid pavement has a life span of 40 years compared to the bituminous which has 10 years life span. Also, rigid pavement distributes load much more widely than the flexible pavement (Chandra, 2017). Rigid pavement requires little maintenance; whereas bituminous roads need frequent repairs due to damage occurred by traffic and weather. The main disadvantage of rigid pavement requires high initial cost for rectification compare to bitumen roads as the entire concrete slab needs to be replaced when it damages(Jain et al., 2013).

Because of the continuous use of construction material has led to a fast decrease in natural available resources. Today we are faced with an important consumption and a growing need for aggregates because of the growth in industrial production, the situation has led to a fast decrease of available resources. (Hebhoub et al., 2011a) With the advancement of technology and on-going research in development, the use of various materials other than conventional material has been increased. Now-a-days in the road construction works, waste is being used as a substitute for the conventional materials; gives the same strength and bearing capacity to concrete. This type of wastes comes from mining sites and thermal power plants (Miller & Collins, 1976).

In India, Road Construction works have witnessed a significant change over the last few decades due to the adoption of advanced technology, new as well as improved construction methods, the involvement of private firms with huge finances, changes in policies, and willing to provide better infrastructure facilities by the government. Utilization of waste/recycled material in construction works has several merits: cost reduction, reduction in disposal/waste/dumpling load, promoting recycling of waste material, natural resource conservation, pollution reduction, and many other environmental benefits.

This will not only ensure that the construction industry follows the path of sustainability but also addressing the problem of resource scarcity (Bakash et al., 2013). Nearly 12 million tons of CD (construction & demolition) waste is being produced annually in developing nations like India. In major parts of the world, the population explosion in urban areas has lead to the exploitation of natural resources due to fast-growing construction works. The utilization of CD waste as a construction material will not only reduce the burden on landfill sites but also help in the conservation of natural resources (Jagadeesh & Rao, 2018).

Natural aggregate consists of rock fragments that are used in their natural state or are used after mechanical processing such as crushing, washing, and sizing (Kulkarni et al., 2015). Quarried or excavated stone that has been crushed and screened to the desired standard particle size and make them suitable to use in construction works are crushed stone aggregates (Joanna, Hydzik-Wiśniewska Anna, Łukasz, & Sebastian, 2018). Artificial aggregates are sometimes produced for special purposes (Priyadharshini et al., 2012). Recycled aggregate is derived from crushing inert construction and demolition waste. It may be classified as recycled concrete aggregate (RCA) when consisting primarily of crushed concrete or more general recycled aggregate (RA) when it contains substantial quantities of material other than crushed concrete. The characteristic of recycled aggregates could be different from its parent concrete because the parent concrete was designed for its purposes such as permeable, durable, and high strength concrete. Recycling of concrete is a relatively simple process. It involves breaking, removing, and crushing existing concrete into a material with a specified size and quality. Reinforcing steel and other embedded items, if any, must be removed, and care must be taken to prevent contamination by other materials that can be troublesome, such as asphalt, soil and clay balls, chlorides, glass, gypsum board, sealants, paper, plaster, wood, and roofing materials (PCA, 2019). In general, recycled aggregates without any processing are being used in many types of general bulk fill, Bank protection, Base or fill for drainage structures, Road construction, Noise barriers, embankments etc., while after processing of recycled aggregates, can be used in pavements, shoulders, median barriers, sidewalks, curbs, and gutters, Bridge foundations, Concrete bases, Bituminous concrete (Steven et al., 2002).

In this paper, an attempt has been made to access the utilization of waste materials collected from construction and demolition waste as coarse aggregate in concrete production. Utilization of waste generated from construction and demolition activities not only solves the problem of material availability and economical feasibility but also helps in maintaining environmental sustainability by waste reduction.

II. METHODOLOGY

The Methodology adopted for the present study is depicted in the figure given below:

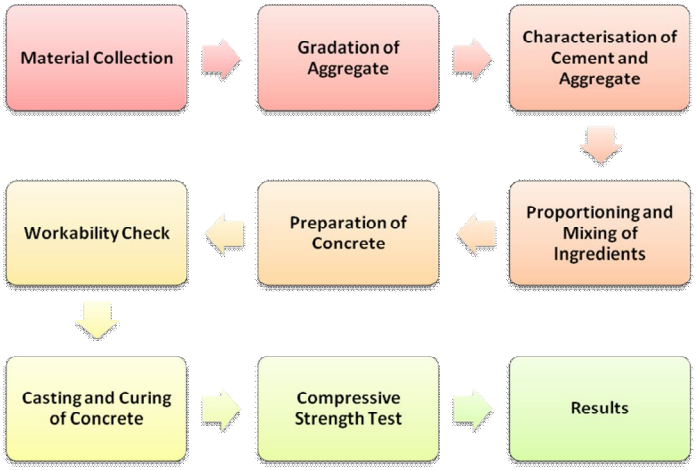

Figure 1: Methodology Adopted

III.EXPERIMENTAL STUDY AND LABORATORY TESTS

In this study, natural coarse aggregate is replaced by aggregates collected out of construction and demolition waste and then designed mix concrete is prepared by mixing cement, aggregate, water, and sand. For the present study, compressive strength as a prime variable for quality assessment of concrete was checked at 7, 14, and 28 days. For preparing the concrete of desired strength, the material like cement of OPC grade 43 conforming to IS: 8112-2013, the conventional coarse aggregate of size 10 – 20 mm, the recycled aggregate of size 10 – 20 mm, sand Particle of size below 4.75 mm and potable tap water free from any kind of impurity was used in this study (BIS, 2013).

For experimental work the waste material (construction and demolition waste) was collected from the construction and demolition site of the classroom turned into a pharmacological laboratory, located inside the Mewar University Campus. As per the requirement and specification recommended by IS: 383-1970, segregation of material was done to extract the usable material as coarse aggregates (BIS, 1970).

In this experiment program test specimens of M35 concrete mix were prepared to have a constant water-cement ratio of 0.35. The physical properties of cement are presented in Table 1. The concrete was prepared by replacing the natural coarse aggregate by recycled aggregate. Replacement was done in different proportions such as 0%, 20%, 40%, 60%, 80% and 100% by weight. The physical properties of natural coarse aggregate and recycled coarse aggregate are presented in Table 2. All the material was mixed manually in the desired proportion as per the requirement and concrete mixes were prepared. The mix proportions are presented in Table 3. Concrete cubes of size 150 mm × 150 mm × 150 mm were cast by filling the molds with concrete in three layers and each layer was compacted with the help of a vibrating Table as per procedure defined in Indian standard IS: 516-1959 (BIS, 1959). All specimens were de-molded after 24± 1h of casting and cured in water at room temperature until their testing was done.

IV. RESULTS & DISCUSSION

The characterization of cement, natural aggregate, and recycled aggregate were done before the preparation of the concrete mix by performing various tests in the laboratory. the workability check of the fresh concrete was done before casting of concrete cubes by using a slump cone and compaction factor test. for determination of compressive strength, 150 mm × 150 mm × 150 mm cube specimens were tested under compression testing machine or CTM.

Table 1: Observed Properties of Cement

Sr. No.	Test	Result
1.	Specific Gravity	3.15
2.	Initial Setting Time	40 - 45 min
3.	Standard Consistency	33P

1) *Aggregate Impact Value Test:* The aggregate impact value indicates resistance offered by aggregates to sudden impact or shock, which may be different for the gradually applied compressive load. The impact value presented in Table 2 shows that natural coarse aggregate and recycled aggregate is strong enough to be used in rigid pavement.
2) *Los Angeles Abrasion Test:* Los Angeles abrasion test shows the aggregate toughness and abrasion resistance such as Crushing, degradation, and disintegration. From the results, it is clear that natural coarse aggregate is stronger but recycled also have sufficient strength to be used as aggregate in the rigid pavement.
3) *Specific Gravity and Water Absorption:* The observed value of Specific gravity and water absorption for natural coarse aggregate and recycled are presented in table 2 Aggregates having low specific gravity are generally weaker than those with higher specific gravity values and water absorption shall not be more than 0.6 per unit by weight. From the result, it is clear that recycled aggregates are weaker than natural aggregates. Since the recycled aggregates were obtained from construction and demolition waste consisting of crushed, broken, and fragmented material with old mortar adhering it owing to lower specific gravity and high water absorption characteristics.

Table 2: Observed Properties of Natural Coarse Aggregate and Recycled Coarse Aggregate

Sr. No.	Property	Natural Aggregate	Recycled Aggregate
1.	Specific gravity	3.08	2.72
2.	Water absorption	0.63%	1.95%
3.	Impact value	6.17%	18.76%
4.	Abrasion Resistance	12.79%	28.32%

Table 3: Mix Proportion Details

Mix Designation	Mix of RA (%)	Water content (in liter)	Cement (in kg)	Sand (in kg)	Natural Coarse Aggregate (in kg)	Recycled Coarse Aggregate (in kg)
NC (Control Concrete)	0%	3.15	9.00	4.5	9.00	0.00
RC20	20%	3.15	9.00	4.5	7.20	1.80
RC40	40%	3.15	9.00	4.5	5.40	3.60
RC60	60%	3.15	9.00	4.5	3.60	5.40
RC80	80%	3.15	9.00	4.5	1.80	7.20
RC100	100%	3.15	9.00	4.5	0.00	9.00

4) *Workability:* The workability of fresh concrete being a measure of consistency is an important characteristic of quality control in concrete production. For workability checks, an empirical test such as the slump cone test was performed. Table 4 suggests that the workability of the concrete got reduced with the increment in replacement of natural coarse aggregate by recycled aggregates. The decrease in the workability of the concrete mix was due to the high water absorption rate of recycled aggregate. The low workability of the concrete is suitable for pavement construction.

Table 4: Workability of Design Mix Concrete

Mix Designation	NC (Control Concrete)	RC20	RC40	RC60	RC80	RC100
Mix of RA (%)	0%	20%	40%	60%	80%	100%
Slump Value	7	7	5	4	3	2

5) *Compressive Strength:* Compressive strength of concrete is the most prominent characteristic as it can provide comprehensive information about the quality of concrete because of the direct relationship with the other properties. The concrete cube specimens were cast and tested at 7, 14, 28 days and the results are presented in Figure 1. The compressive strength of the concrete mix containing 20% recycled aggregates was approximately equal to that of control concrete. The decrease in compressive strength in the concrete mix has 40%, 60%, 80% and 100% replacement of natural coarse aggregate with recycled aggregate are since recycled aggregate losses it strength because of very small fractures developed while breaking down the C&D waste material into small pieces and unevenness of the composition of the material. Improper bond action also gets developed due to different types of material that adhere to the surface of the recycled aggregate leads to a loss in strength characteristic of concrete.

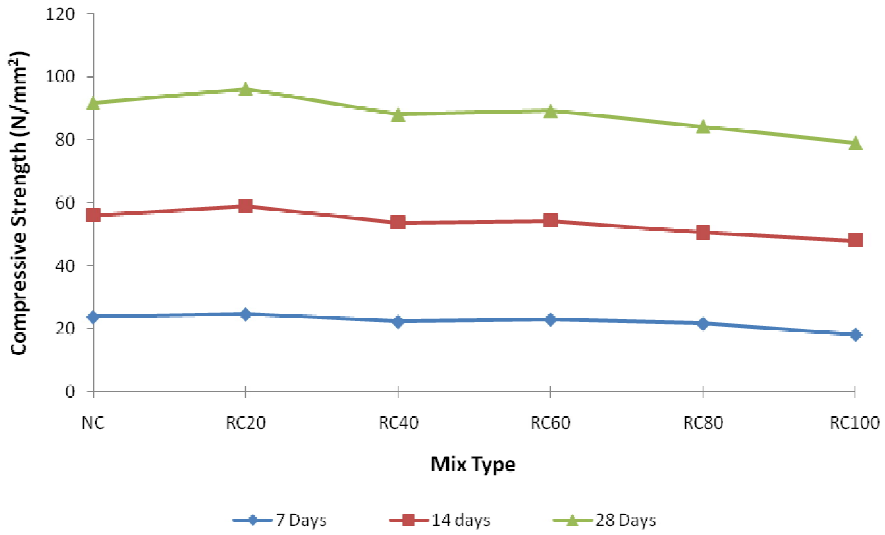

Fig. 1: Compressive Strength Test of Concrete at 7, 14 and 28days

V. CONCLUSIONS

The use of construction & demolition waste in road works not only results in a reduction in construction cost but also a very important environmental management tool for achieving sustainable development. On the other hand, recycling waste without properly scientific research and development can result in environmental problems greater than the waste itself. Therefore, many countries have still been working on how to re-use the waste material. Now-a-days the cost of material is increasing so if we use the waste material in the production of the concrete so we decrease the price. Exposing the waste material to the environment directly can cause problems to the environment as well as the flora and fauna present on the planet.

In the present study, replacement of natural coarse aggregate by recycled aggregates obtained from C&D waste in the M35 design mix concrete in the order of 0%, 20%, 40%, 60%, 80%, and 100% was done. The experimental result shows that the compressive strength of concrete prepared with recycled aggregate was found to be very much close to the concrete produced with conventional/natural aggregate up to 20% substitution rate after 28 days of concrete casting and after 20% compressive strength started decreasing. However, a replacement ratio of 100% can be used for minor works of lower importance. The impact value and Los Angeles abrasion test value are within limits as per BIS: 2386 (part IV), 1963 (BIS, 1963). From the result, it is also clear that recycled aggregates are weaker than natural aggregates but can provide considerable strength when used in concrete production. The use of waste and by-products as aggregates has potential because 75% of the concrete is composed of aggregates. The results of this study show that recycled aggregate can be used as a replacement of natural coarse aggregate in pavement construction.

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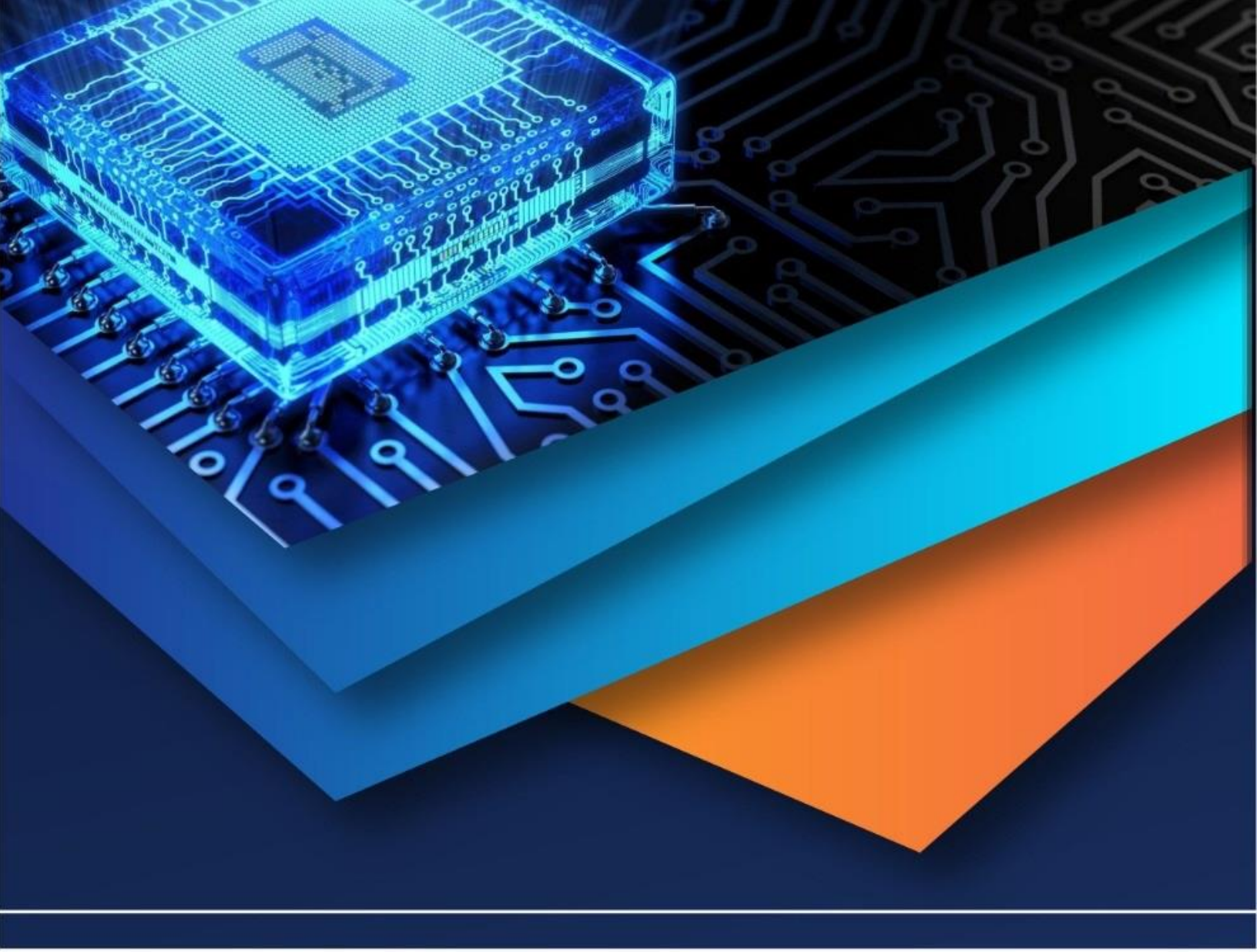

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IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

UTILIZATION OF WASTE POLYETHYLENE IN HOT BITUMINOUS MIXES (DRY PROCESS) IN WEARING COURSE

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***Abstract*— This paper examines the utilization of waste plastic in bituminous mixes thereby enhancing the bituminous properties to ensure the long-term performance of HMA mixtures. Worldwide, Bitumen is used as binder in flexible pavements for highway and road construction and the type of binder differs with their chemical properties. Addition of additives to bitumen enhances its properties to suit climatic requirement. Waste plastic is one such additive. Safe disposal of used plastic is a major concern for environment as it does not decay over time and occupies lot of earths space. Unsafe disposal of plastic with its toxic waste into sea affects the aquatic animals by large. Burning of plastic waste produces toxic gases and smoke which is unsafe for humans and produces increase in earth's temperature. Also, the unsafe disposal into idle fields cause grazing animals to getting infected causing illness by the chemicals in the plastic. It is indeed a matter of great concern that even in this advanced world, methods of safe disposal of nonbiodegradable material like plastic are inadequate and more attention is required for the research community. Additives are added to bitumen binders to improve their properties. In this research paper, plastic is added to bitumen by partially replacing the bitumen content in bituminous mixes thereby enhances its properties and also its strength. Graded and shredded waste plastic is mixed with hot bitumen and aggregates and the modified mix is made and used for pavement construction. The plastic added mix strengthens the pavement and also increases the stability and durability. In this paper, we have discussed about the mix design of Bituminous mixes by addition of waste plastic. A small amount (6-10% by weight of bitumen) of plastic is added to bitumen and bituminous mixes made in laboratory (asphalt), and the results found showed better durability pavement stability, and strength. This results in saving of bitumen, utilization of waste plastic in the form of recycling thereby reducing the product cost.**

***Keywords*— Eradication of pot holes, flexible pavement, plastic waste, stability, strength, durability.**

I. INTRODUCTION

The cumulative production of plastics as of 2015 can wrap the entire earth in a 52 layer of cling film, and project production of plastics by 2050, that is about 40 billion tons, can 53 wrap the Earth by six layers. In the present context, recycling of waste plastic appears to be the best method for the safe disposal of plastic and different types of by-products can be made. Throughout the world, huge quantity of bitumen is required for constructing roads and requires huge amount of investments by the state and central governments. In developing countries, huge investment is made in the highway projects. Therefore, replacing small fraction % of bitumen with waste plastic is a relatively new idea and can have a vast positive effect of the environment. Reduction of costs is observed when roads are constructed with plastic mixed bitumen. The method also contributes to longer road service life. The use of waste plastic thus is in the interest of pollution free environment. Important ingredients of plastic in the form of Polyethylene is used which can be derived mainly from PET bottles, packets of polyethylene, plastic carry-bags, disposable cups which are collected from garbage.

II. OBJECTIVES

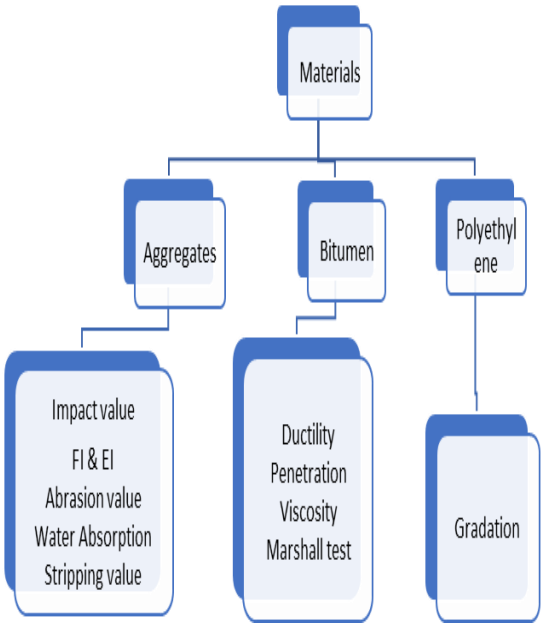
- To reduce the bitumen consumption by partially adding waste plastic in the form of polyethylene.
- To increase the durability, stability of the bituminous mix, tested by Marshall stability tests
- To economise the construction cost.
- To utilize the waste plastic hazardous to the environment.

III. MATERIALS USED

- **Bitumen:** Bitumen is an important ingredient when flexible pavements are constructed. Types generally available are viscosity grade VG 30 and VG 40. Binder content acts an important role to achieve maximum density, desires stability and flow and air voids. An easy way to comply with IJRASET paper formatting requirements is to use this document as a template and simply type your text into it.
- **Aggregates:** Bituminous mix generally constitutes aggregates by 92 to 96% of its volume. This are required to be graded to sizes as per the grading requirement. This have to satisfy the requirements of laboratory before using.
- **Filler:** Fillers is used to fill up the voids in the HMA mix. Generally, stone dust, limestone is used. Lime filler @ 2% is added in the present study.
- **Polyethylene:** IRC states that LDPE, HDPE, PET and Polyurethane shall only be used in pavement construction. In this study polyethylene used for plastic bottles packaging which is locally available is used. National Highway Authority of India has approved vendors for the supply of Polyethylene as per the IRC requirement. The shredded size requirement is passing the 2.36 mm sieve and retained on 600-micron sieve.

IV. METHODOLOGY

The materials constituting the bituminous mix are subjected to tests as under:



A. Tests conducted

As first stage, physical properties of aggregates and bitumen are tested in the laboratory. The results obtained are as below:

i. Physical properties of aggregates as per IS codes

TABLE 1

Property	Test Method	Test Result	Required
Aggregate Impact Value (%)	IS: 2386 (P IV)	10.74	Not more than 25
Aggregate crushing Value (%)	IS: 2386 (P IV)	14.50	Not more than 30
Los Angels Abrasion Value (%)	IS: 2386 (P IV)	18 %	Max 30 %
Flakiness Index (%)	IS: 2386 (P I)	6.75%	Max 15 %
Elongation Index (%)	IS: 2386 (P I)	10.55%	Max 20 %
Water Absorption (%)	IS: 2386 (P III)	0.1 %	Max 2 %
Soundness by Sodium sulphate	IS: 2386 (P III)	1.95 %	Max 12 %

ii. Physical properties of binder VG 40 bitumen as per IS codes.

TABLE 2

iii.

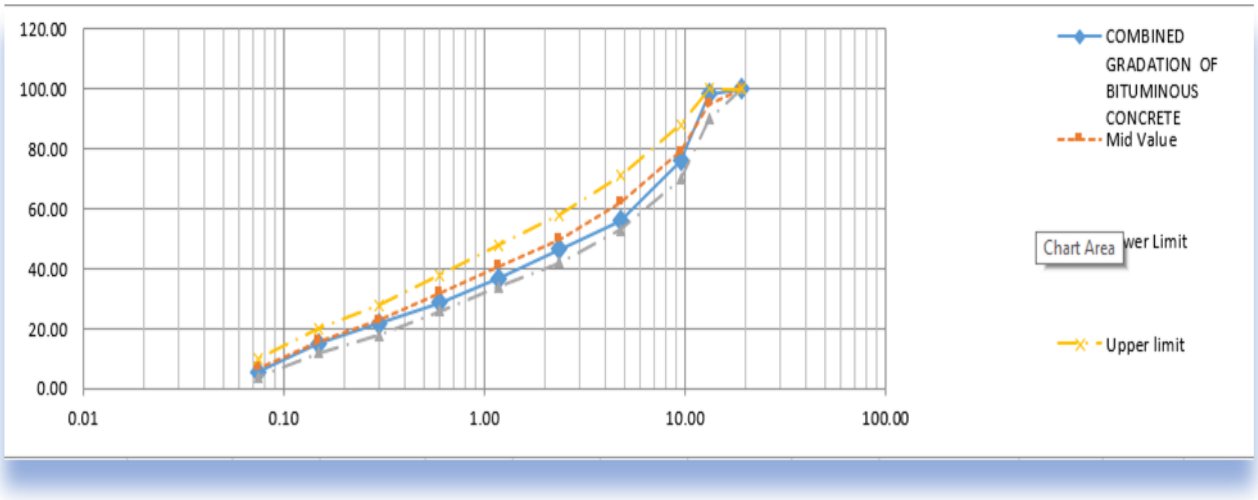
Property	Test Method	Value	Required
Penetration at 135℃ (mm)	IS : 73-2013	45.67	Min. 35
Softening Point (℃)	IS : 73-2013	53.35	Min. 50
Ductility @ 25℃	IS : 73-2013	41.12	Min. 25
Kinematic Viscosity @ 135℃	IS : 73-2013	441.50	Min. 400
Absolute Viscosity @ 60℃	IS : 73-2013	3701	3200-4800
Specific gravity @ 27 ℃	IS : 73-2013	1.01	Min. 0.99
Flash Point ℃	IS : 73-2013	295	220 ℃ Min.

iii. Blending of aggregates. After selection, sampling and testing of the ingredients, sieve analysis of the aggregate material is carried out. The combined gradation of the aggregate blending is as under:

TABLE 3

IS Sieve (mm)	Total % Passing	Specific Limits as per MoRT&H Table 500-17		
		Mid Value	Lower Limit	Upper limit
19.00	100.00	100.00	100	100
13.20	98.29	95.00	90	100
9.50	76.15	79.00	70	88
4.75	55.91	62.00	53	71
2.36	46.56	50.00	42	58
1.18	36.93	41.00	34	48
0.60	28.86	32.00	26	38
0.30	21.84	23.00	18	28
0.150	15.17	16.00	12	20
0.075	5.52	7.00	4	10

TABLE 4



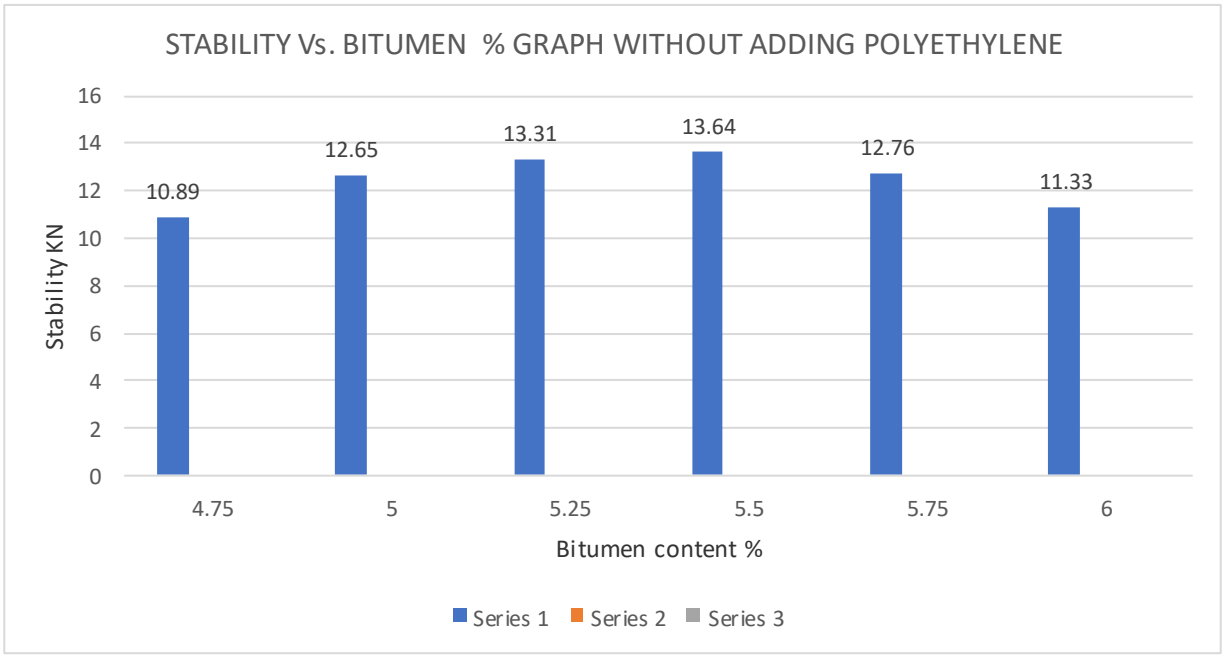
iv. The materials are mixed and cores are formed as per the details mentioned din the Marshalls stability test Review of the sieve analysis clearly indicate that blending required to fulfil the gradation requirement of aggregates for bituminous concrete grade 1 as per table 500-17 of MORT&H Rev. 5

To evaluate optimum binder content, Marshall mould were casted at various binder contents as per MS2.By testing of the Marshall mould, the following properties are found.

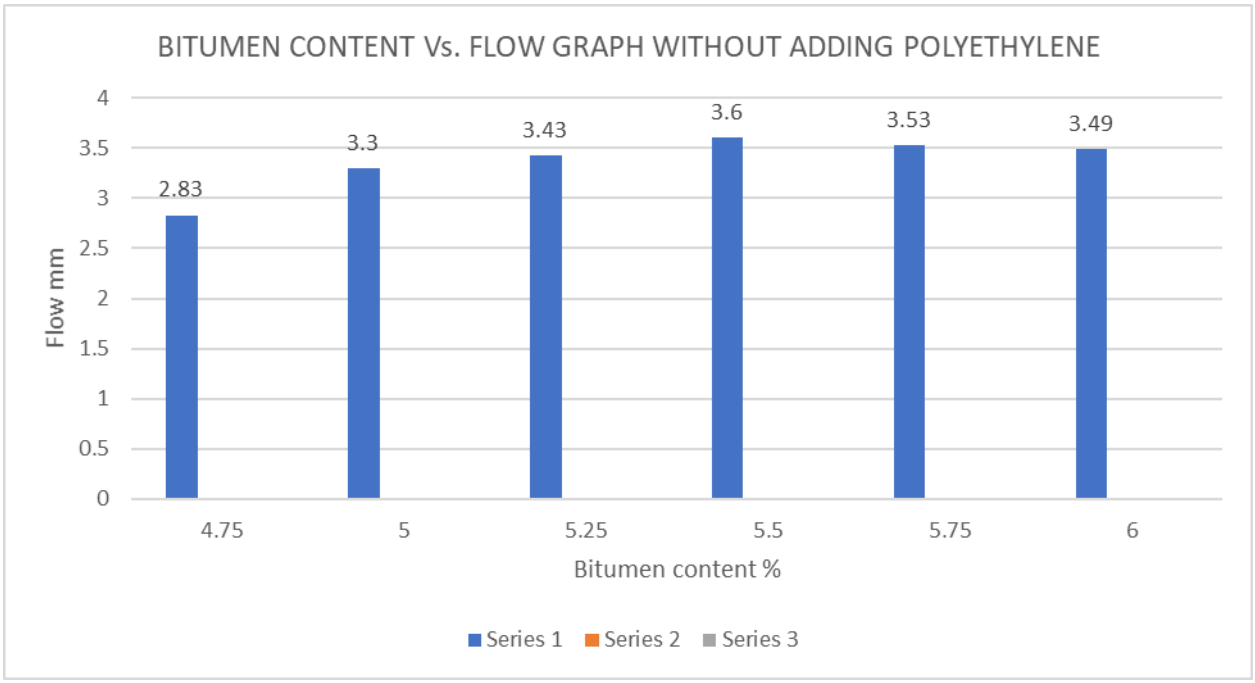
TABLE 5

a) Marshall test data for optimum binder

Bitumen (%)	**Stability (KN)**	**Flow(mm)**
4.75	1089	2.83
5.0	1265	3.30
5.25	1331	3.43
5.50	1364	3.60
5.75	1276	3.53
6.0	1133	3.57



GRAPH 1

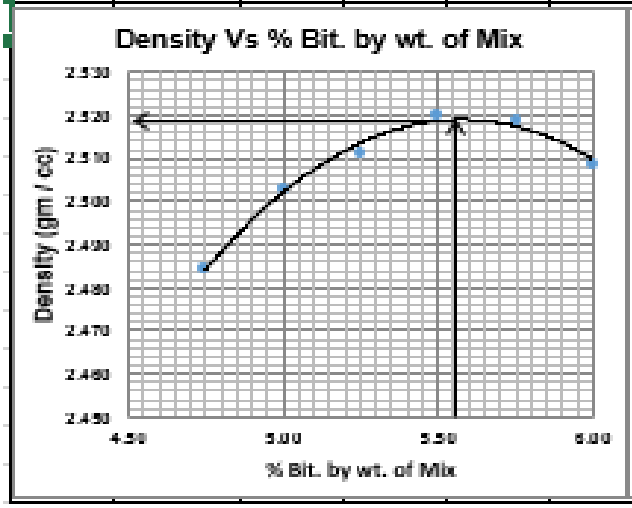


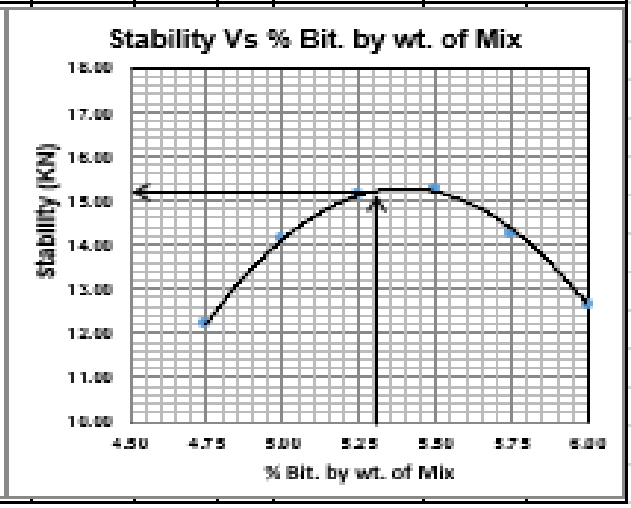
GRAPH 2

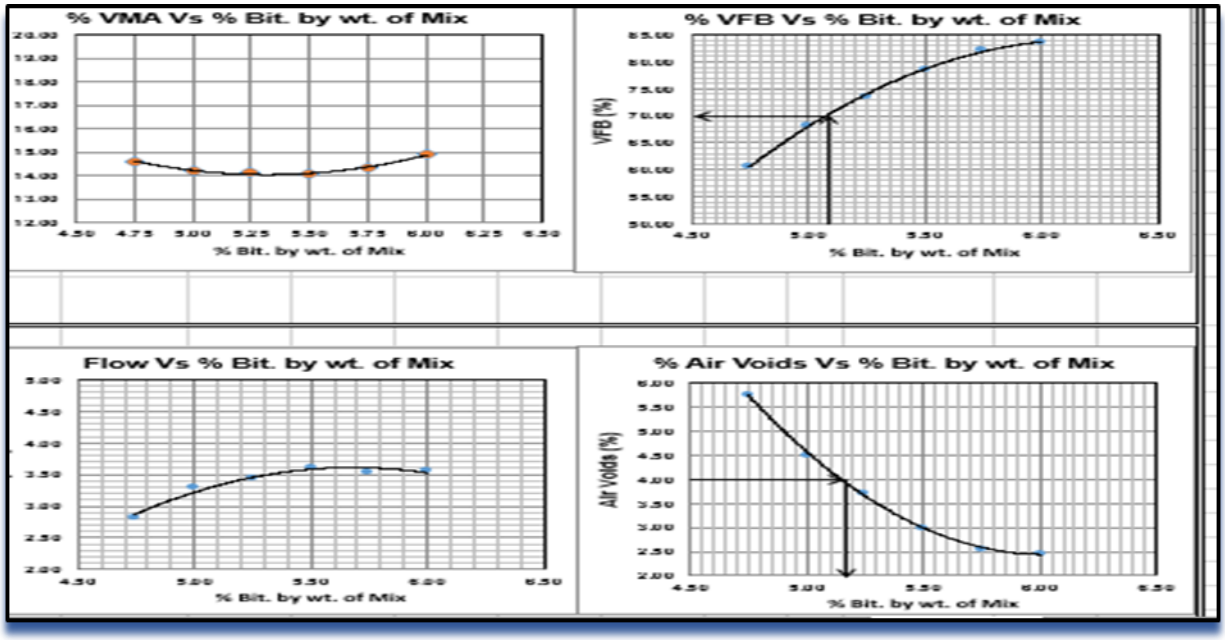
TABLE 6

b) Other mix properties

% Bit. By Weight of Mix	Bulk Sp. Gr. (Gmb)	Stability (KN)	Voids in Mineral Agg.	Voids Filled with Bitumen	Flow (mm)	Air Voids VA (%)				
4.75	2.484	12.18	14.61	60.51	2.83	5.77			**Properties**	**OBC**
5.00	2.503	14.15	14.18	68.27	3.30	4.50			Bulk Density	5.55
5.25	2.511	15.10	14.13	73.67	3.43	3.72			Stability	5.30
5.50	2.520	15.25	14.05	78.65	3.60	3.00			VFB	5.07
5.75	2.519	14.27	14.32	82.19	3.53	2.55			AV	5.15
6.00	2.509	12.67	14.89	83.55	3.57	2.45			**Avg. OBC**	**5.27**







GRAPH 3

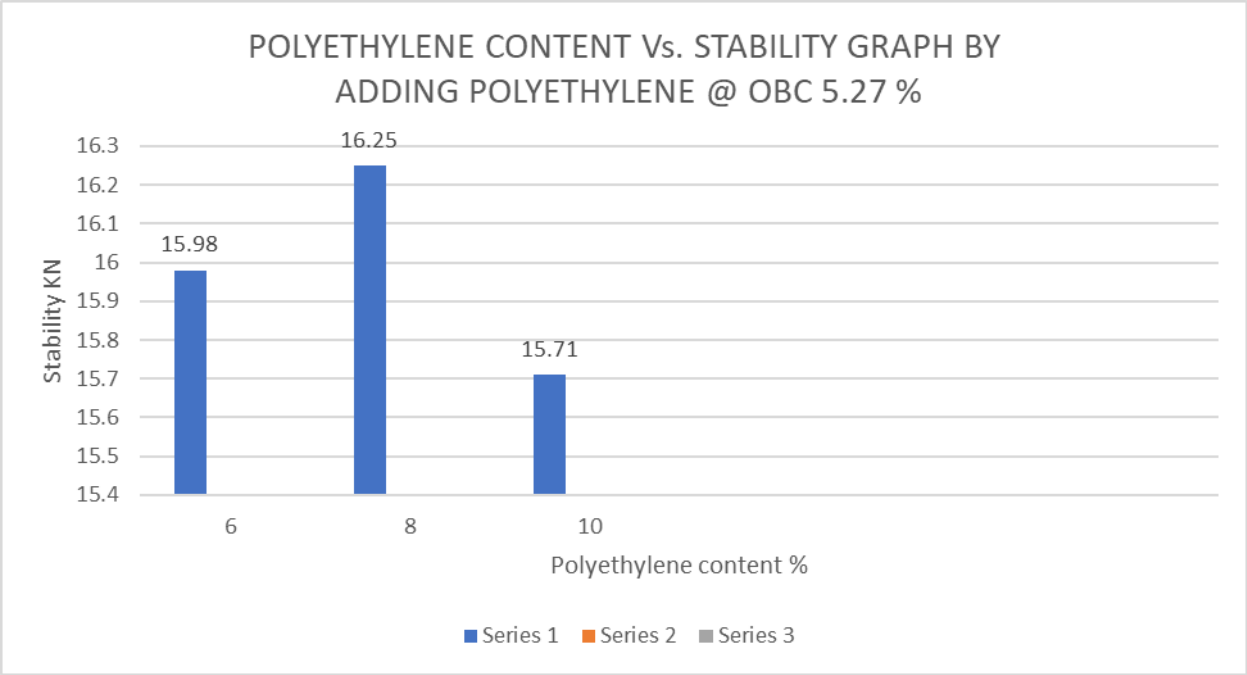
Optimum Binder Content achieved as per the above graph is 5.27 % with stability of 1331 KN and flow of 3.61 mm.

v) Effect of Replacing Polyethylene at different percentages on the properties of Bituminous mix @ OBC.

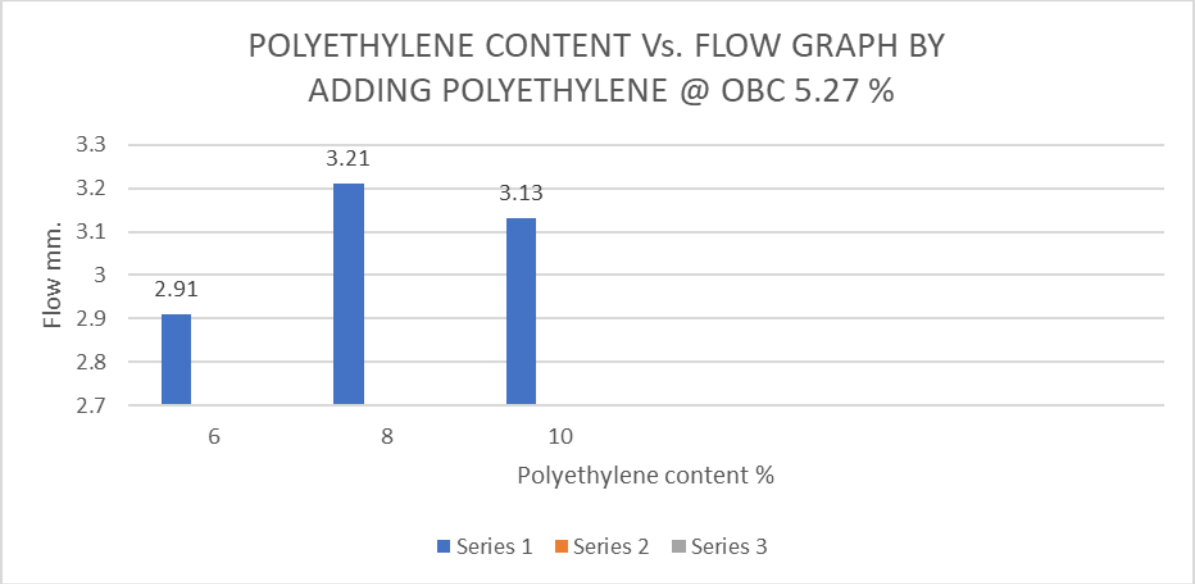
Now at the optimum bitumen content, different % of polyethylene is added to check the mix properties as per the table below.

TABLE 7

Optimum Bitumen Content (%)	Polyethylene added (%)	Stability observed (KN)	Flow observed (mm)
5.27	6%	1598	2.91
5.27	**8%**	**1625**	**3.21**
5.27	10%	1571	3.13



GRAPH 4



GRAPH 5

VI COST COMPARISON CHART

TABLE 8

Material required	Plain Bitumen Process	Addition Polyethylene
VG 40 Bitumen	131.75 MT	121.21tonnes
Saving	-	10.54 tonnes
Cost	Rs. 52,70,000.00	Rs. 48,48,400.00
Saving in Rs.		Rs. 4,21,600.00
% Saving		8 %

As can be seen from above, for 1450 meter for 4 lane highway with 8.75 m. wide carriageway, and 40 mm. thickness, 10.54 MT of plastic waste is utilized.

VII CONCLUSION

In this research paper study, BC mixes are prepared with VG 40 grade bitumen used as a binder. The effect of addition of waste polyethylene in form of locally available plastic bottles in the bituminous mixes has been studied by addition of polyethylene at 6 to 10 % by wt. of bitumen.

In this study, the optimum bitumen content (OBC) and optimum polyethylene content (OPC) have been determined for different types of mixes by using the Marshall Method of mix design. It has been observed that addition of 8 % polyethylene of bitumen for BC mixes results in optimum Marshall Properties and flow value. The Optimum binder content in BC mix is found 5.27 %.

- The result illustrates that there is cost saving of 8 % when compared to ordinary mix.
- The addition of 8% polyethylene increases the stability, durability which results in long lasting wearing course of flexible pavements.
- The flow value also reduces which is better for resistance to water penetration, stripping and rutting.
- There is a cost saving of 8% compared to normal bituminous mix.
- The waste nonbiodegradable plastic hazardous to the environment is utilized in pavement layers in significant quantity, the disposal of which is a cause of concern

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A Comparative Study on T Girder Bridge Deck using Grillage Analogy and Finite Element Method

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Abstract **- Concrete slabs and t- girder bridges have been the dominant bridges in India. Especially in recent years, many road constructions are underway, some are under construction, and some road projects are planned to be carried out in the future. As the project becomes larger, it is necessary to improve the design method and make it more effective every day. It summarizes the requirements of the new bridge and the important features of the planned site and makes it the basis for each design. Initially, the dimensions of the structural members were chosen according to the designer's experience, and at a later stage, the engineering software was used to compare the alternative software and optimize the part size. Finally, a complete analysis and analysis of all important construction phases and detailed shop drawings will be carried out.**

Key Words: Skewed bridges, bending stress, shear stress

1. INTRODUCTION

The bridge is a structure that can access the barrier without closing the barrier. The necessary accesses are roads, railways, pedestrians, pipes or canals. The obstacle to overcome may be a river, a road, a railroad or a valley. From the engineering point of view, the bridge can be described as plain (or right) or sloping. A typical bridge is a bridge with a vertical axis perpendicular to the platform pillar. Further, in a conventional bridge, the deck and the support beam are disposed symmetrically with respect to the center of the bridge, and the center line is the same as the longitudinal axis thereof. This arrangement is ideal and ideal. Because bridge analysis and construction are simplified, leading to an economical structure. To analyze this, it is necessary to divide the superstructure of the bridge into smaller, more manageable components consisting of rays, deck panels, barrier systems, sections and membranes.

It summarizes the requirements of the new bridge and the important features of the planned site and makes it the basis for each design. Initially, the dimensions of the structural members were chosen according to the designer's experience, and at a later stage, the engineering software was used to compare the alternative software and optimize the part size. Finally, a complete analysis and analysis of all important construction phases and detailed shop drawings will be carried out.

1.1 Main Components of a Bridge

A typical bridge consists of the following components:
a) Deck slab.
b) Cantilever slab portion.
c) Footpaths, if provided, kerb and handrails or crash barriers.
d) Longitudinal girders, considered in design to be of T-section.
e) Cross beams or diaphragms, intermediate and end ones.
f) Wearing coat.
g) Abutments and piers.
h) Foundation (pile cap and piles).

1.2 Type of Bridge Decks

(a) **Slab Bridges**

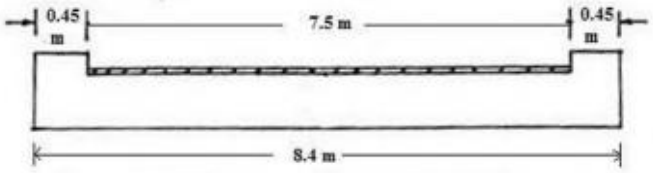

Figure 1.1: Typical Cross-section of solid slab deck

(b) **Box Girder bridges**

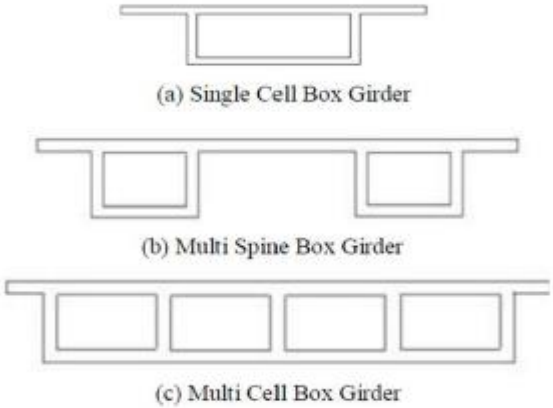

Figure 1.2: Typical Cross-Section of box Girder Bridge

(c) T-Beam Bridges

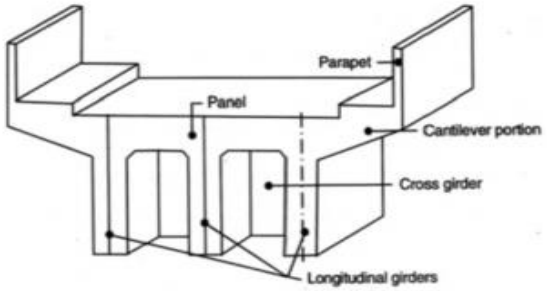

Figure 1.3: Typical Cross-section of T-girder for two lane traffic

1.4 Objective of the Study

A relative investigation of T-Beam arrangement of deck piece with various IRC loadings considered for the examination. FEM investigation is finished utilizing STAAD Pro. V8i In this investigation, the destinations are accomplished by basic grouping:

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- To set up and exhibit a helpful, solid, and precise philosophy for dissecting solid structures with specific accentuation on T-Girder solid extension decks
- Approving FEM Analysis and looking at grillage similarity Method of examination for shifting lengths.
- To propose which model can give more efficient plan.
- Performing FEM and GA Analysis on T-pillar arrangement by considering greatest Shear compel, most extreme twisting minute and most extreme torsional snapshots of parameters of correlation

2. LITERATURE REVIEW

The essential target of this examination was to set up and exhibit an advantageous, solid, and exact technique for breaking down fortified solid structures with specific accentuation on strengthened solid extension decks. An optional target was to build up a capacity for foreseeing anxiety dispersion through the thickness of fortified solid scaffold decks. Such data isn't effortlessly gotten through experimentation. The extension has broken down for single traverse with length changing from 12m,15m and 18m and twofold path width subjected to various IRC stacking design class An and 70R . The aggregate length of the extension Deck framework is made of cast in situ T molded cement longitudinal braces and cross supports. The extension is straight and has no skew. The standard extension models are created. The outcomes are acquired regarding examination of various parameters.

Menessa (2007) this examination work led FEA for just upheld, one-traverse, multi-path fortified solid piece spans. Four traverse lengths were considered in this parametric examination as 7.2, 10.8, 13.8, and 16.2 m with comparing chunk thickness of 450, 525, 600 and 675 mm separately. The outcomes were contrasted and straight scaffolds. SAP2000 was utilized to produce three-dimensional (3D) limited component models.

Qaqish et al (2008) In this exploration a straightforward traverse T-beam connect pivoted toward one side and opposite end sliding the longitudinal way was broke down by utilizing AASHTO particulars and stacking as a one dimensional structure, at that point a three-dimensional structure was completed by utilizing limited component plate for the deck section and shaft components for the principle pillar. The two models were subjected to AASHTO Loadings and at specific areas to create greatest bowing minute and most extreme shear. The outcomes were broke down and it was discovered that the outcomes got from the limited component demonstrate are littler than the outcomes acquired from one dimensional examination, which implies that the outcomes got from AASHTO loadings are moderate.

Shreedhar, et al (2012) a straightforward traverse T-beam connect was examined by utilizing I.R.C. particulars and stacking (dead load and live load) as a one dimensional structure. A similar T-bar Bridge was dissected as a three-dimensional structure utilizing limited component plate for the deck section and shaft components for the fundamental bar utilizing programming STAAD ProV8i. By contributing certain qualities for traverse, clear roadway width, cross brace interims and plate thickness. The two models were subjected to I.R.C. Stacking (Class AA and Class A) to deliver greatest twisting minute. The outcomes were broke down and it was discovered that the outcomes got from the limited component demonstrate were lesser than the outcomes acquired from one dimensional examination, which implies that the outcomes got from I.R.C. loadings are traditionalist and FEM gives sparing outline.

Khatri, et al (2012) their study led on grillage similarity technique for investigation of extensions. A sum of nine distinctive matrix sizes (4 to 12 divisions) are made utilizing grillage relationship with various skew edges 30°, 45° and 60° to decide the best lattice estimate. It is watched that FEM and Grillage strategy comes about are not comparative for each framework estimate contingent upon different parameters. Variety in response esteem is same in FEM and Grillage strategy however variety of B.M and torsion in FEM is lower than grillage comes about.

Samuel (2016) in his thesis endeavored to examine the consequences of T Girder superstructure utilizing both the estimated strategy which depends on the conveyance factor idea and grillage similarity technique. Both these strategies were utilized to break down RCC T and box brace superstructure and comparing to change in rush hour gridlock paths, traverse length and stomach (for e.g,: 10.3 m width and 20 m traverse) and valuable data was acquired with respect to the variety of bowing minute and shear constrain. It was presumed that outcomes got from grillage similarity strategy were littler than rough technique aside from shear power of inside brace of T-Girder connect.

Arun L (2018) Grillage analogy is probably one of the most popular computer-aided analysis for analyzing bridge decks. The method consists of representing the actual decking system of the bridge by an equivalent grillage of beams. The dispersed bending and torsional stiffness of the decking system are assumed, for the purpose of analysis, to be concentrated in these beams. The actual deck loading is replaced by an equivalent nodal loading. The requirement of analysis is the evaluation of internal member forces, stresses and deformations of structures. After the analysis, distribution of member forces will be ascertained.

3. METHODOLOGY AND MODELLING OF T-GIRDER BRIDGE DECK

Numerous exploratory and scientific works has been finished by numerous analysts in the zone of limited component displaying and nonlinear FE analysis of RC bridges. Moreover, much research has been directed concerning the general utilization of PCs to strengthened cement. STAAD. Pro is a generally utilized basic examination program fit for breaking down several auxiliary individuals under various stacking conditions. It includes a cutting edge UI, representation instruments, intense investigation and outline motors with cutting edge limited component and dynamic examination abilities. From display age, investigation and configuration to perception and result confirmation, STAAD.Pro V8i is the expert's decision for steel, solid, timber, aluminum and cool framed steel outline of low and tall structures, courses, petrochemical plants, burrows, extensions, heaps and considerably more.

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3.1 Refined Methods of Analysis

Refined strategies for examination for dissecting roadway connect superstructures and deciding brace minutes and burdens can be characterized into following classifications:

1. **The orthotropic plate approach** romanticizes the real extension structure as a proportionate orthotropic plate, which is then treated by established hypothesis. This approach was first created by Guyon for grillages with insignificant torsional solidness and later for isotropic chunks. Massonnet expanded this approach by including the impacts of torsion. The joined work of Guyon and Massonnet, alluded to as the Guyon-Massonnet stack conveyance hypothesis, has been stretched out by others.
2. **The harmonic analysis procedure,** created in the 1950's by Hendry and Jaeger, considers an indistinguishable flexural and torsional rigidities from the orthotropic plate examination, yet dismisses the torsional unbending nature the transverse way. Burdens are disseminated to the individual braces just as the section were a constant shaft over non avoiding bolsters. The stacking is communicated as a consonant arrangement or Fourier sine arrangement. Articulations for shear, minute, incline, and redirection are found by progressive mix of this heap arrangement. Support twisting minutes are controlled by thinking about the above arrangement in conjunction with transverse power balance and incline diversion articulations the transverse way.
3. **The grillage analogy method** idealizes the bridge structure using an equivalent grid system, which is then analyzed by:
   Slope-deflection and compatibility equations;
   Moment or torque distribution;
   Shear distribution;
   Reaction distribution

   This method usually involves the solution of a large number of simultaneous equations or numerous arithmetic calculations.

3.2 Load Distribution Mechanism

It is realized that the bridge loads are transmitted from the deck to the superstructure and afterward to the supporting substructure components. It is fairly hard to envision how these heaps get exchanged. On the off chance that a vehicle is proceeding onward the highest point of a specific shaft, it is sensible to state that, this specific bar is opposing the vehicle or truckload. In any case, this pillar isn't the only one; it is associated with adjoining individuals through the section and cross braces. This availability enables distinctive individuals to cooperate in opposing burdens. The supporting braces share the live load in shifting extents relying upon the flexural solidness of the deck and the situation of the live load on the deck.

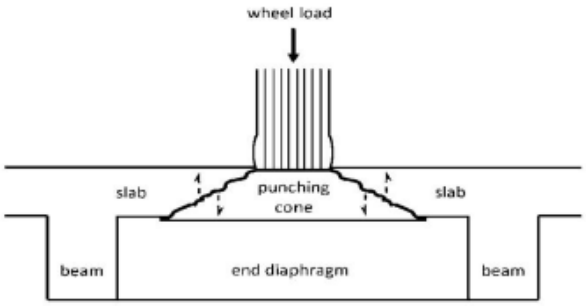

Figure 3.1: wheel load distribution in beam-slab girder

3.3 Bridge Deck Data

T-girder bridges: It has been broke down for a chunk thickness of 200 mm in the present examination. The width of carriage way has been taken as 7.5m and 8.7m in the wake of including width of kerbs and railings on the two sides.
The bridges has been broke down for 12m, 15m and 18m clear traverse with individual compelling ranges of 12.6m, 15.6m and 18.6m with skew edge of 0

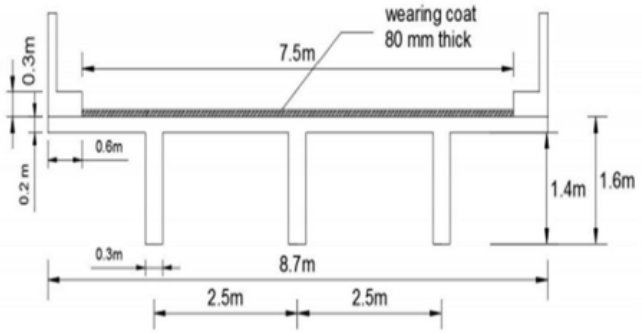

Figure 3.2: Cross-Section of T-girder deck

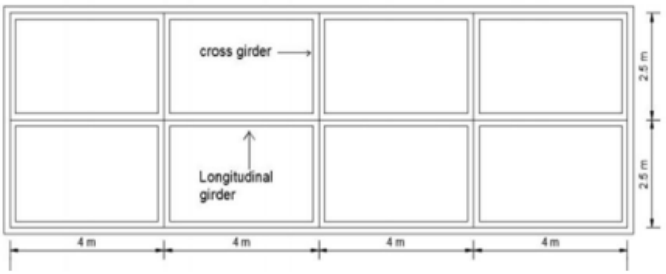

Figure 3.3: Plan view of T-girder deck

3.4 Methodology

3.4.1 Grillage Analogy Method

As of late, the Grillage Analogy Method, which is a PC arranged procedure, is progressively being utilized as a part of the examination and outline of extensions. The technique is additionally appropriate in situations where connect displays convoluting highlights, for example, overwhelming skew, edge solidifying and disengaged underpins .The utilization of PC encourages the examination of a few load cases in briefest conceivable time. The technique is adaptable in nature and the commitment of kerb bars and the impact of differential sinking of support closes over yielding course, (for example, neoprene bearing) can likewise be considered and extensive assortment of scaffold decks can be broke down with adequate functional exactness. Moreover, the grillage portrayal is helpful for give the originator a 'vibe' for the auxiliary conduct of the extension

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and the way in which the scaffold loadings are disseminated and in the long run taken to the backings.

3.4.1.1 Idealization of Physical Deck into Equivalent Grillage

The strategy for grillage investigation includes the glorification of the extension deck as a plane grillage of discrete between associated shafts. This is the primary vital advance to be taken by the creator and requirements most extreme care and under-remaining of the basic conduct of the scaffold decks. It is hard to make exact general standards for picking a grillage work and much relies on the idea of the deck to be dissected, its help conditions, exactness required, quantum of processing office accessible and so on and just an arrangement of rules can be proposed for setting matrix lines. It might be noticed that such admiration of the deck isn't without traps and the framework lines embraced in one case may not be effective in another comparable case and the experience and judgment of the planner will dependably assume a noteworthy part.

3.4.1.2 General Guidelines for Grillage Layout

In view of the gigantic assortment of deck shapes and bolster conditions, it is hard to embrace immovable tenets for picking a grillage spread out of the genuine structure. In any case, some fundamental rules with respect to the area, heading, number, separating and so on of the longitudinal and transverse framework lines shaping the glorified grillage work, are depicted here. Be that as it may, each kind of deck has its own exceptional highlights and may require some specific game plans for setting admired framework lines and along these lines grillage glorification of section needs most extreme care.

3.4.1.3 General Guidelines for Grillage Layout

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3.4.2 Grillage Mesh for T-Girder Bridge

The sensible decision of longitudinal lattice lines for T-beam bridge decks is to make them incidental with the middle lines of physical girders and these longitudinal girders are given the properties of the supports in addition to the related slab of the piece, which they speak to. Extra lattice lines between physical girders may likewise be set so as to enhance the exactness of the outcome. Edge gridlines might be given at the edges of the deck or at appropriate separation from the edge.

At the point when middle of the road cross supports exist in the genuine deck, the transverse framework lines speak to the properties of the cross braces and related deck sections. The grid lines are set in along the inside lines of cross supports. Grid lines are likewise set in the middle of these transverse physical cross girders, if in the wake of considering the successful rib width of these supports, bits of the slab are forgotten. A commonplace T-beam bridge with grillage layout is appeared in Figure 3.4.

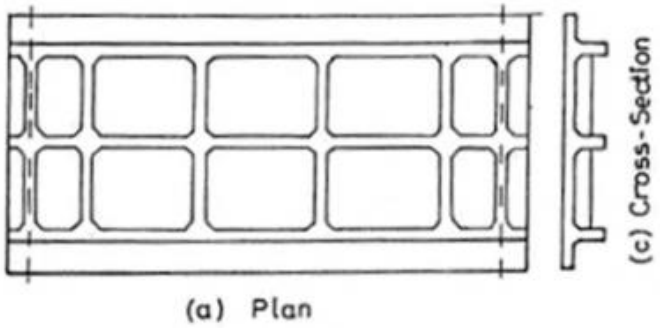

Figure 3.4(a): (a) Plan and (c) cross-section of T-Girder Bridge

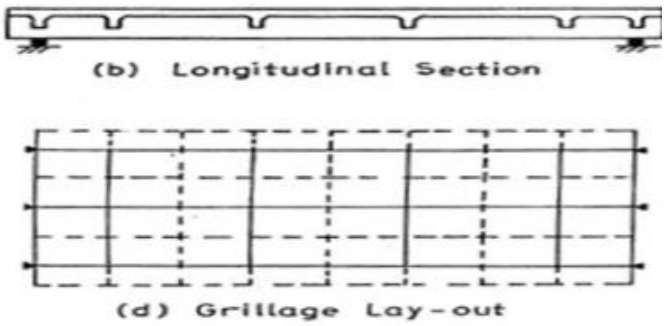

Figure 3.4(b): (b) longitudinal section and (d) grillage layout

3.4.3 Evaluation of Equivalent Elastic Properties

After the real extension structure is reenacted into equal grillage, comprising of longitudinal and transverse matrix lines meeting at discrete hubs, the second imperative advance in grillage relationship technique is to allocate suitable versatile properties i.e. flexural and torsional firmness' to every individual from the grillage so admired. This needs the calculation of proportionate flexural snapshot of inactivity I and torsional idleness J for the\ individuals from the grillage work. This is refined by considering secluded segments of the deck as though they are singular shafts and the idleness's are ascertained for each area and designated to the comparing grillage bars speaking to that segment.

3.4.3.1 Flexural and Torsional Inertias of Grillage Members for T-Girder bridges:

Slab-on-girders bridge decks comprise of various beams spreading over longitudinally between projections with a thin piece traversing transversely over the best. T- beam bridges are the normal cases under this classification. The beams might be thrown solidly with the section or the precast beams with in-situ slab might be utilized. The decks might be with or without middle of the road or potentially end stomachs. With the end goal of estimation of flexural and torsional dormancies, the powerful width of piece, to work as the pressure spine of T-beam or L-beam, is required. A thorough investigation for its assurance is greatly unpredictable and without more exact methodology for its assessment, IRC proposals are taken after.

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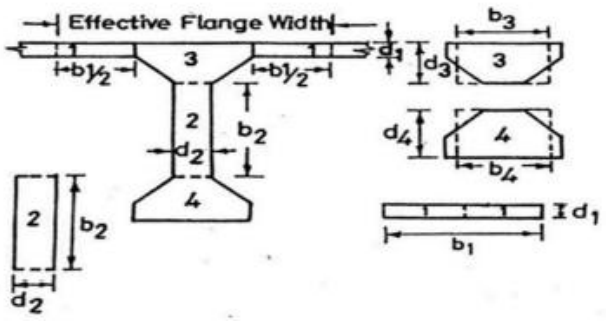

Figure 3.5: Sub-division of T-section

3.4.4 Application and Transfer of Loads to Various Nodes of Grillage

The bridge deck has been changed into an equal grillage comprising of longitudinal and transverse framework individuals with the end goal that the romanticized grillage is near the physical deck. Every individual from the grillage is apportioned flexural and torsional latencies which are proportional to the relating physical properties of the bridge deck. The longitudinal and transverse matrix lines shape a work having number of hubs. The scaffold is basically subjected to vertical burdens containing dead, live and affect loads. Grillage examination requires that these connected burdens be changed into equal burdens at hubs.

3.4.5 Design Constants

The various constants used in the analysis of bridge decks are given below:
Grade of Concrete = M30
Modulus of Elasticity, Ec =3.05×107kN/m2 for all members
Density of RCC = 24 kN/m3
Poisson's Ratio = 0.15
Modular Ratio = 10

3.4.6 Finite Element Method

3.4.6.1 Basic theory

The limited component strategy has been a conspicuous decision for the displaying and investigation of strengthened solid frameworks for a long time. Limited components have the one of a kind capacity to fit in with essentially any geometry that could be physically executed. Along these lines, the limited component strategy has picked up acknowledgment as a proper instrument for the examination of level plates, particularly those with exceptionally sporadic or bizarre geometries where the immediate outline and equal edge methods are not substantial. In sporadic chunks, the limited component strategy can be appeared to precisely explain for the dissemination of stress where various approximations and suspicions would be summoned if the yield line or strip plan procedure were connected. The arrangement approach is construct either with respect to taking out the differential condition totally (relentless state issues), or rendering the PDE into an approximating arrangement of common differential conditions, which are then numerically incorporated utilizing standard systems. In illuminating halfway differential conditions, the essential test is to make a condition that approximates the condition to be considered, however is numerically steady, implying that blunders in the info information and middle of the road counts don't gather and cause the subsequent yield to be pointless. The Finite Element Method is a decent decision for unraveling halfway differential conditions over complex areas.

3.4.6.2 The matrix displacement method used in FEM

The matrix relocation technique for investigation is utilized. The continuum structure is isolated into various sub- regions, called limited components, which are thought to be interconnected at the nodal focuses as it were. Inexact dislodging capacities are expected over each limited component. Dislodging similarity conditions are fulfilled and the overseeing harmony conditions that are created are tackled to yield the obscure nodal relocations. Once the removals are known, the strains may then be assessed from the strain-dislodging relations, lastly the anxieties are resolved from the pressure strain relations.

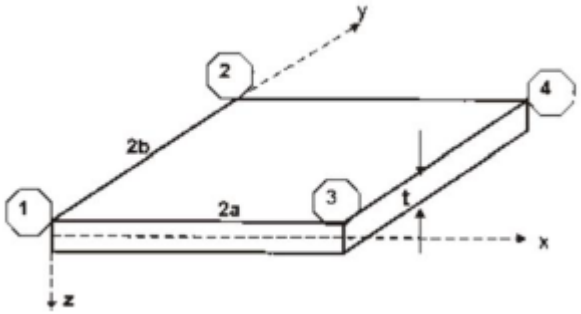

Figure 3.6: Co-ordinate system of plate element

The slab of the T-beam bridge deck is spoken to by non-adjusting yet entire rectangular plate bowing components with three degrees of flexibility for each hub (w, θx, θy) and a cubic dislodging model, (Fig 3.6). Concentrates by Gallagher demonstrated that this component is productive and yields arrangements of satisfactory precision.

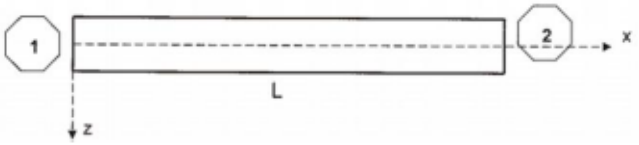

Figure 3.7: Co-ordinate system of beam element

3.5 Grillage Modelling of T-Girder Bridge Deck

The grillage displaying and investigation performed in this examination were finished utilizing a broadly useful basic examination and configuration program, STAAD. Master V8i is a business basic examination and configuration program created by Bentley Solutions Center. The program is accessible for PC. The examinations in this proposal were performed utilizing STAAD. Genius Version 2008. In this area illustrative examination is introduced thinking about 8.7m scaffold width and 12m, 15m and 18m extension traverse (length) like the regular segment appeared.

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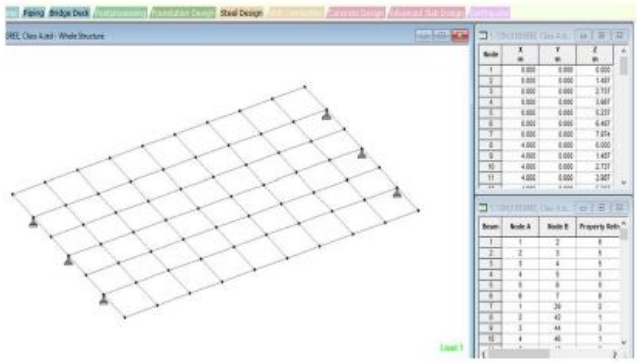


Figure 3.8(a): grillage geometry of T-girder deck in STAAD Pro V8i

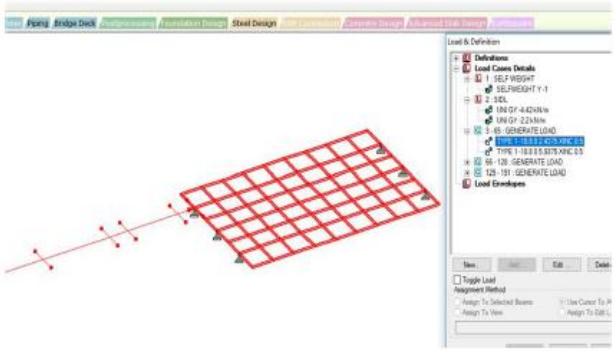


Figure 3.9 (a): IRC Class A initial vehicle position case 1 (Moving Load) in STAAD.Pro V8i software.

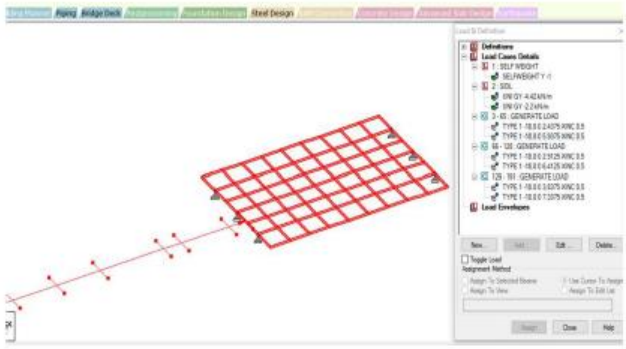


Figure 3.9 (b): IRC Class A Moving load configuration case 2 in STAAD.Pro V8i Software

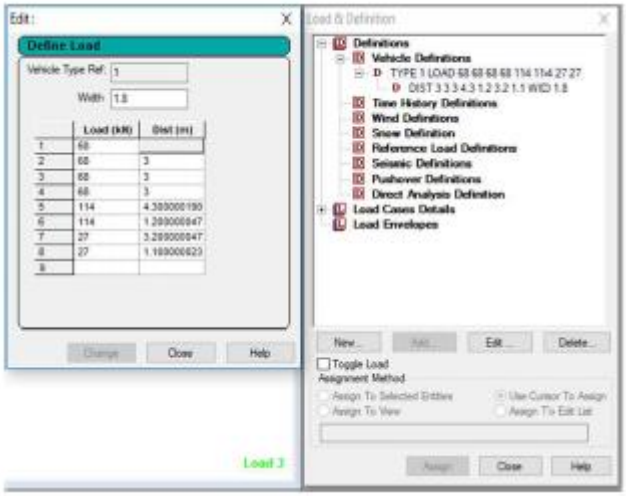


Figure 3.9 (c): Definition IRC Class a Moving load configuration in STAAD.Pro V8i Software.

The last advance is translation of the outcome, the yield acquired from the examination of grillage comprises of vertical redirection and X and Z revolution of every hub, shear drive and torsional snapshot of each shaft component, twisting minute at the two finishes of each bar component

3.6 Finite Element Modelling of T-Girder Bridge Deck

3.6.1 Modelling of Structure

The piece is demonstrated utilizing a plate component and it is discretized into limited component work which comprises of quadrilateral shell components. The shell components speaking to the section are 0.5m X 0.5m quadrilateral shell components with four hubs and six degrees of flexibility for each hub. The chunk has steady length of 12m and consistent width of 8.7m. This brought about a chunk show with 620 hubs, 732 plates and 3,720 degrees of opportunity. A draw of the limited component work is appeared in Fig 3.12. These plates have every one of the qualities as same as the solid piece all in all. These plates can deal with stresses independently. The flat components utilized are the standard shaft components.

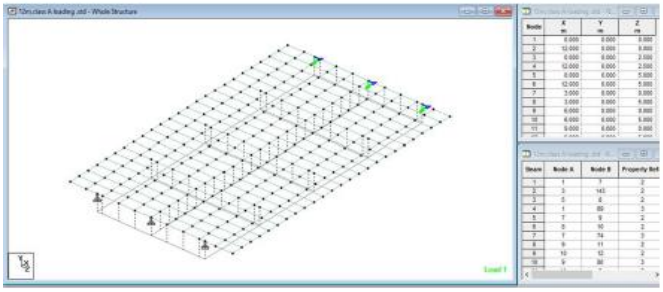
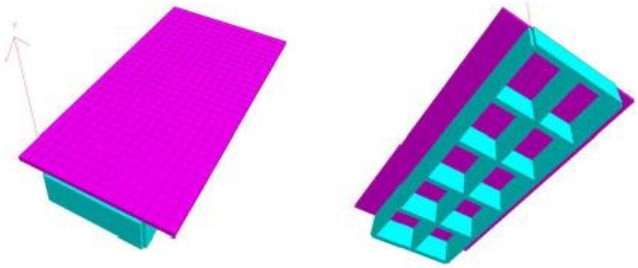


Figure 3.10: Geometry of the structure showing finite beam and plate element in STAAD.Pro V8i software.



(a) Showing deck slab with quadrilateral (b) longitudinal and cross beam girders plate element

Figure 3.11: Rendered view of the structure in STAAD.Pro V8i software.

3.7 Loading Data

The following IRC 6:2014 loadings have been considered in the analysis of the bridge decks:

Dead Load: The dead load took care of by a scaffold part comprises of its fair share and bits of the heaviness of the superstructure and any settled burdens upheld by the individuals regarding super-forced dead load (SIDL).

IRC Class 70R Wheeled loading:

IRC Class70R wheeled loadings is of two types:

i) 70R Bogie loading weighing 400kN through two axles each weighing 200kN.

ii) 70R train loading weighing 1000kN through seven ales, one axle of 80kN, two axles of 120kN each and four axles of 170kN each. The wheeled vehicle is 15.22m long. The dimensions of the Class 70R wheeled loading vehicle.

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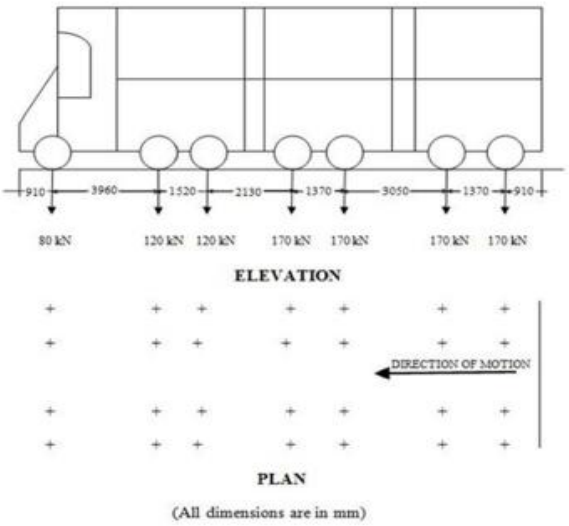

Figure 3.12: IRC 70R wheeled loading

3.8 Output Data

The two different types of bridge decks as mentioned in the objectives have been
Analyzed for the following forces:

- Maximum Longitudinal Bending MomentsMaximum
- Torsional Moments
- Maximum Shear Forces

4. Results and Discussion

In the present investigation the subtle elements have been examined and broke down for the two models of T-support kind of scaffold deck utilizing grillage similarity and limited component examination keeping in see the multifaceted nature required in the outline of extension decks for various traverses utilizing STAAD PRO V8i programming. Along these lines show work encourages in to set up and exhibit a helpful, solid, and precise procedure for breaking down strengthened solid structures with specific accentuation on fortified solid extension decks. The outcomes are thought about as far as longitudinal bowing minutes, shear powers, torsional minutes, and bolster responses for the two sorts of extension decks in the both graphical and forbidden frame.

4.1 Discussion of Results

4.1.1 Longitudinal Bending Moments (kN-m)

1. **Self-Weight:** The varieties of longitudinal bowing minute for various traverses running from 12m to 18m because of self-weight of the structure are exhibited in Table 4.1 and Figure 4.1. Variety of longitudinal BM of traverse 12m in grillage relationship and FEM is appeared in Figure 4.2(a) and 4.2(b) individually

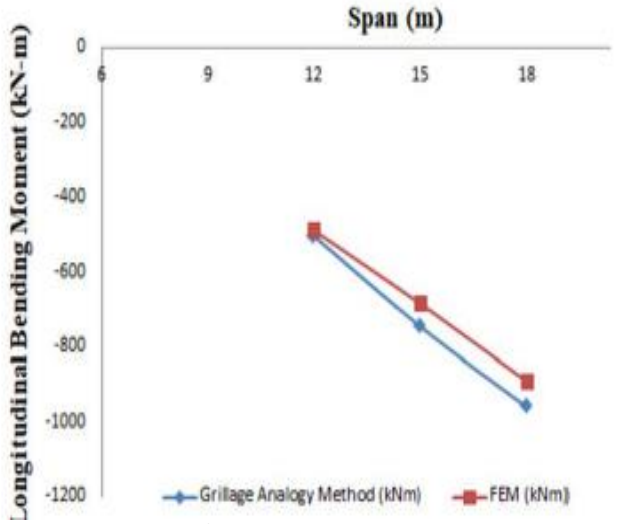

Figure 4.1: Variations of maximum longitudinal B.M. with varying span

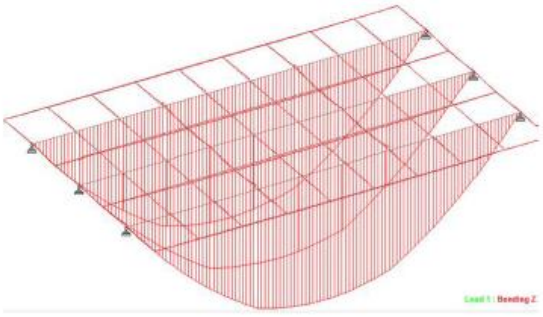

Figure 4.2(a): Variations of maximum longitudinal B.M. of span12m Under self-weight using grillage analogy

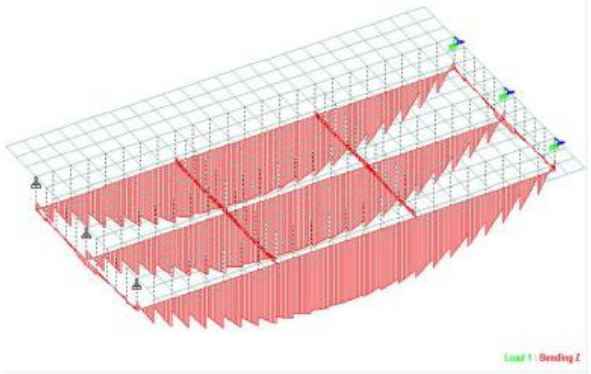

Figure 4.2(b): Variations of maximum longitudinal B.M. of span12m Under self-weight using FEM

Limited component gives the littlest positive and negative in light of the distinction in work (more discretization), while every one of the shafts are symmetrical in properties (thickness, width, materials, stacking) and the benefit of stacking is same for each model. Limited component demonstrate gives less reaction than grillage display.

2. **SIDL:** Variety of longitudinal BM of traverse 12m in grillage similarity and FEM is appeared in Figure 4.4(a) and 4.4(b) individually

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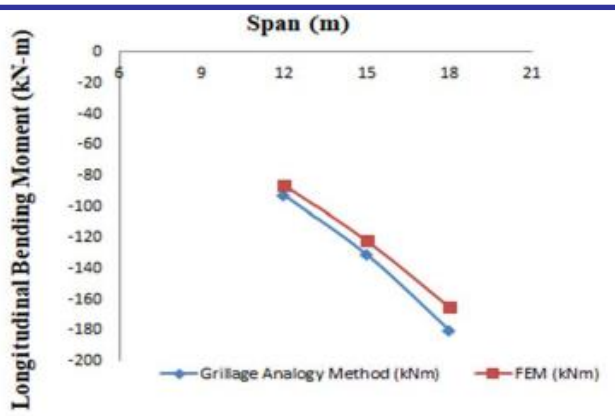

Figure 4.3: Variations of maximum longitudinal B.M. (in case of SIDL)

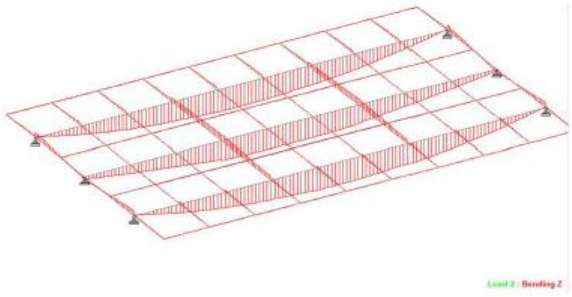

Figure 4.4(a): Variations of maximum longitudinal B.M. of span 12m under SIDL using grillage analogy

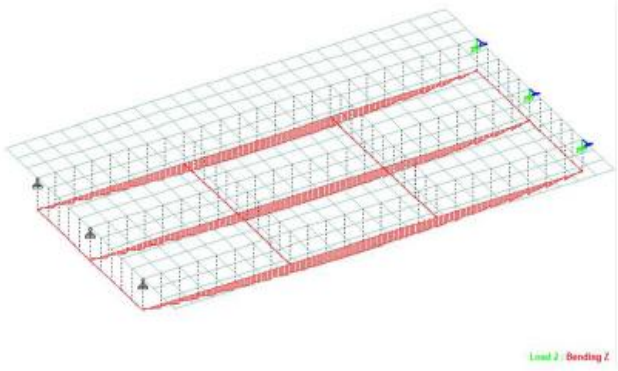

Figure 4.4(b): Variations of maximum longitudinal B.M. of span 12m under SIDL using FEM

3 Live Load Conditions: The extension deck has been examined according to IRC 6:2014 rules for two instances of IRC live loadings i.e. IRC Class 70R wheeled stacking and IRC Class A stacking.

IRC Class 70R(W) loading: The variety of twisting minute initiated in connect for IRC Class 70R wheeled stacking vehicle for various ranges has been exhibited in Table 4.3 and the graphical portrayal of the same has been introduced in Figure 4.5, Figure 4.6(a) and Figure 4.6(b). It has been watched that longitudinal twisting minutes demonstrate an expanding pattern for the live stacking condition 70R in both FEM and grillage similarity with increment in traverse.

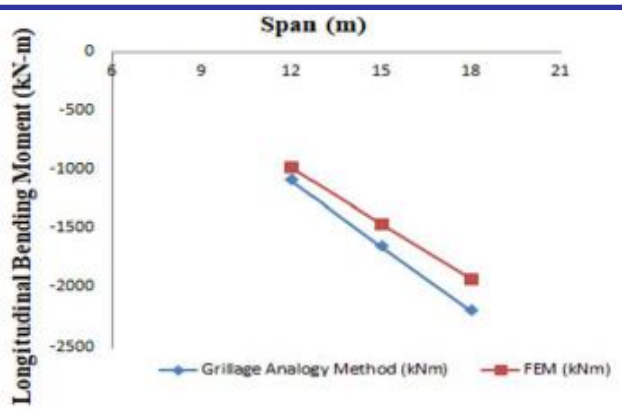

Figure 4.5: Variations of maximum longitudinal B.M. with varying span (in case of IRC 70R loading)

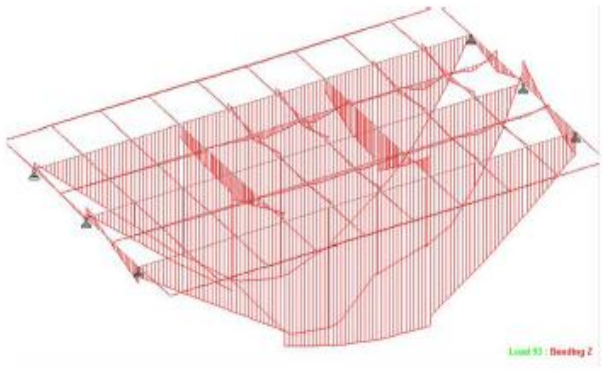

Figure 4.6(a): Variations of maximum longitudinal B.M. of span 12m IRC Class 70R (W) Using grillage analogy

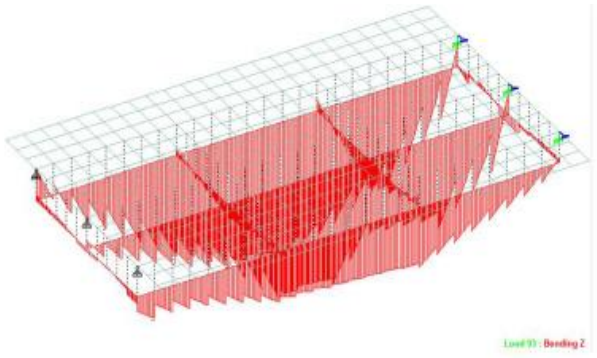

Figure 4.6(b): Variations of maximum longitudinal B.M. of span 12m IRC Class 70R (W) Using grillage analogy

4. IRC Class A loading: The varieties of plan longitudinal bowing minute in the extension deck for expanding ranges under IRC Class A live stacking have been exhibited in Table 4.4 and Figure 4.7. Variety of longitudinal BM of traverse 12m in grillage relationship and FEM is appeared in Figure 4.8(a) and 4.8(b) individually.

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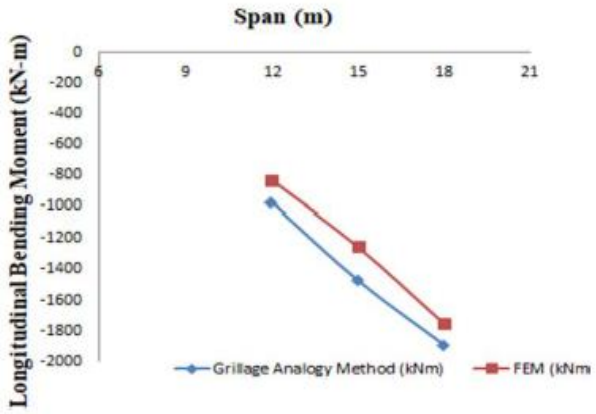

Figure 4.7: Variations of maximum longitudinal B.M. with varying span (in case of IRC Class A loading)

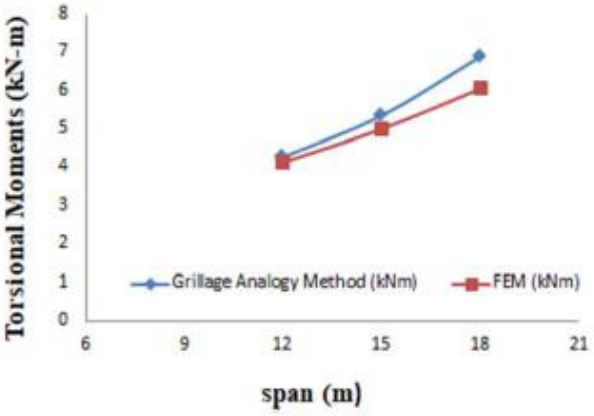

Figure 4.9: Variations of maximum Torsional moment with varying span (in case Self-weight)

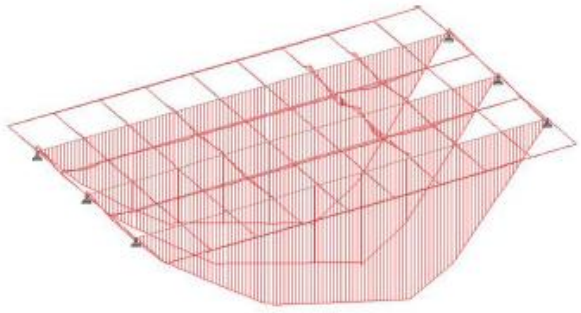

Figure 4.8(a): Variations of maximum longitudinal B.M. of span 12m under IRC Class A loading using grillage analogy

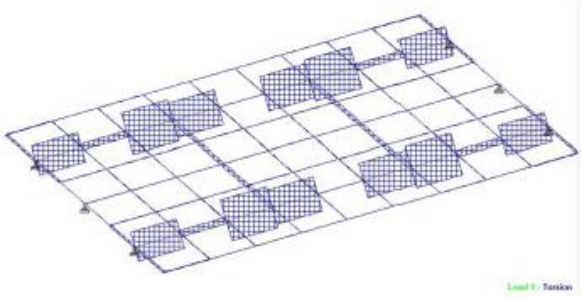

Figure 4.10(a): Variations of maximum Torsional moment of span 12m under Self weight using Grillage Analogy

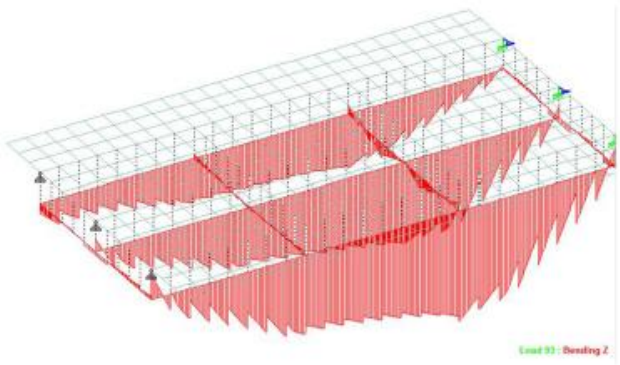

Figure 4.8(b): Variations of maximum longitudinal B.M. of span 12m under IRC Class A loading using FEM

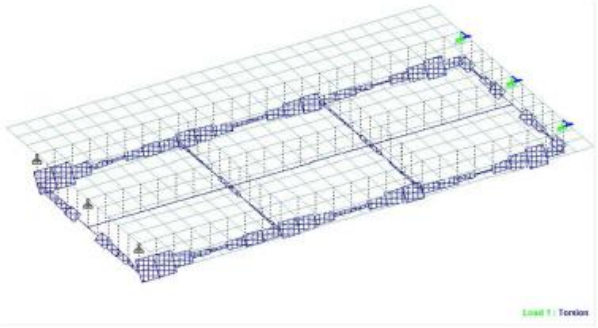

Figure 4.10(b): Variations of maximum Torsional moment of span 12m under Self weight using FEM

4.1.2 Torsional Moments (kN-m)

1. **Self-weight:** The variety of torsional minutes for traverses going from 12m to 15m because of self-weight of the structure is displayed in Table 4.5 and spoke to graphically in Figure 4.9. The investigation comes about demonstrates those most extreme torsional minutes were observed to be accumulated more at closures of the scaffold deck when contrasted with the focal point of the deck as appeared in Figure 4.10(a) and Figure 4.10(b).

2. **SIDL :** The torsional minutes incited in the scaffold deck were found to increment with the expansion in traverse as saw from the Table 4.6 and similar varieties are spoken to graphically in Figure 4.11. It is likewise watched that variety in the torsional minute in 12m traverse between grillage relationship and FEM is 3% where as it indicates expanding nature when traverse length increases\ independently in both the techniques as appeared.

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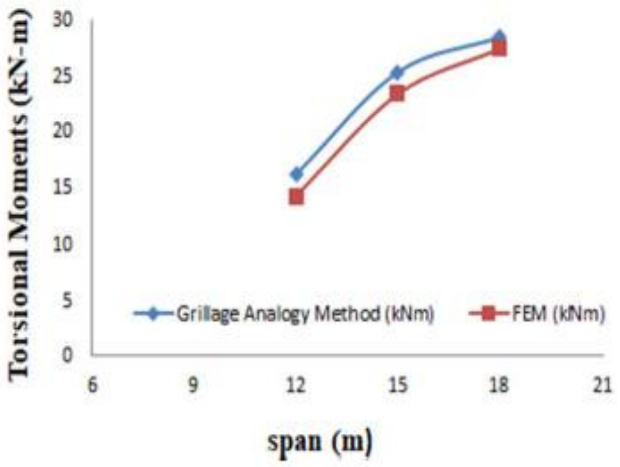

Figure 4.11: Variations of maximum torsional moment with varying span (in case of SIDL)

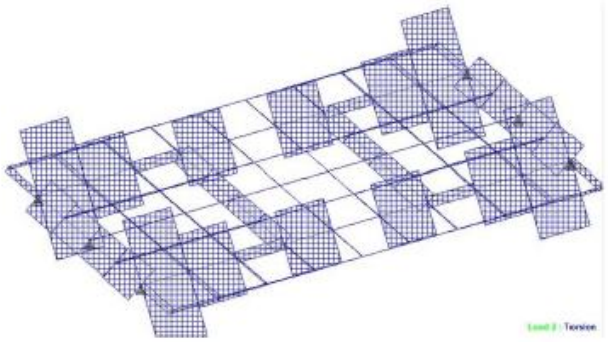

Figure 4.12(a): Variations of maximum torsional moment of span 12m under SIDL Using Grillage Analogy

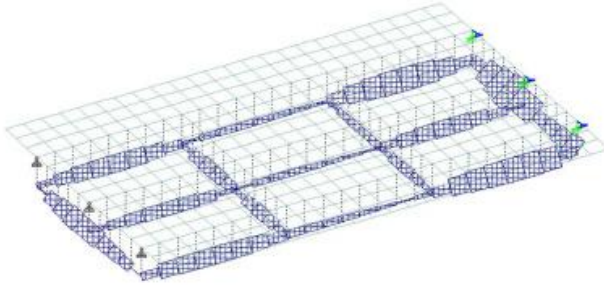

Figure 4.12(b): Variations of maximum torsional moment of span 12m under SIDL Using FEM

3. Live load conditions: The extension deck has been investigated according to IRC 6:2014 rules for two classes of IRC live loadings-IRC Class 70R haggled Class A stacking. The investigation comes about are examined underneath:

a) IRC Class 70R(W) loading: The variety of torsional minutes because of IRC Class 70R stacking case for traverses extending from 12m to 18m has been exhibited and Figure 4.13. Varieties of most extreme torsional snapshot of traverse 12m under IRC Class 70R (w) utilizing Grillage Analogy and FEM is appeared in Figure 4.14(a) and Figure 4.14(b)

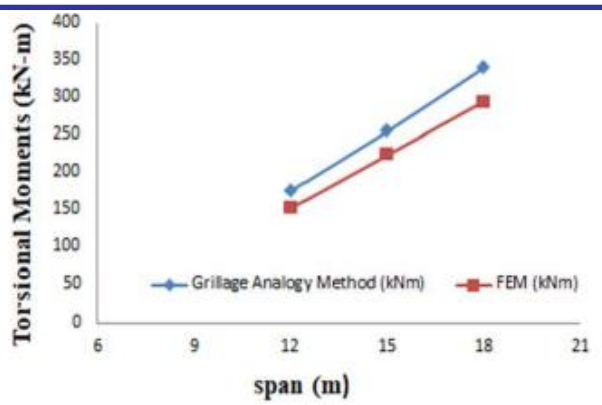

Figure 4.13: Variations of maximum Torsional Moment with varying span (in case of IRC 70R loading)

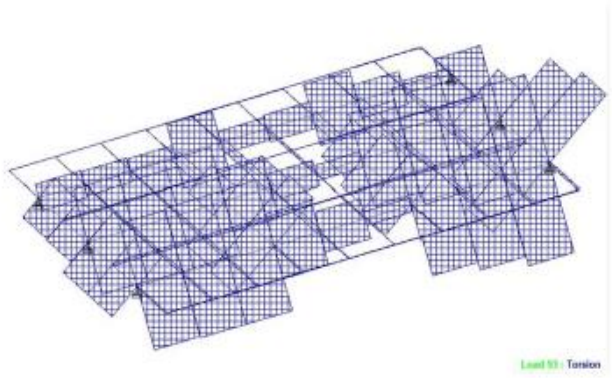

Figure 4.14(a): Variations of maximum Torsional Moment of 12m span under IRC 70R loading using Grillage Analogy

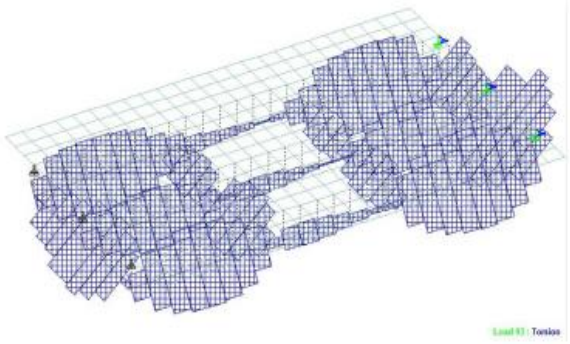

Figure 4.14(b): Variations of maximum Torsional Moment of 12m span under IRC70R loading using FEM

b) IRC Class A loading: IRC Class A loading: The torsional minutes have been found to have more prominent incentive in grillage similarity technique then FEM with the expansion in traverse under IRC Class A stacking and the same is spoken to graphically in Figure 4.15. Varieties of most extreme torsional snapshot of traverse 12m under IRC Class An utilizing Grillage Analogy and FEM is appeared in Figure 4.16(a) and Figure 4.16(b)

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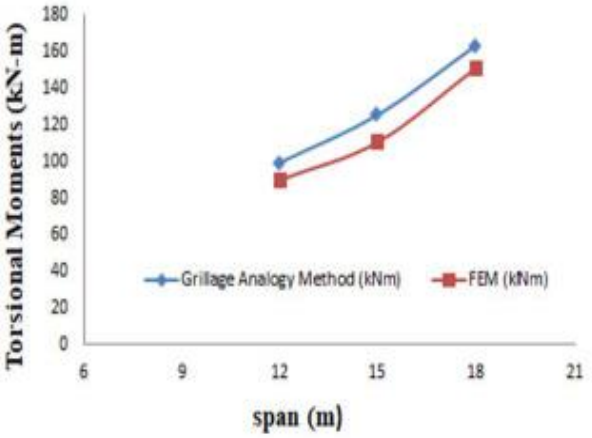

Figure 4.15: Variations of maximum Torsional Moment with varying span (in case of IRC Class A loading)

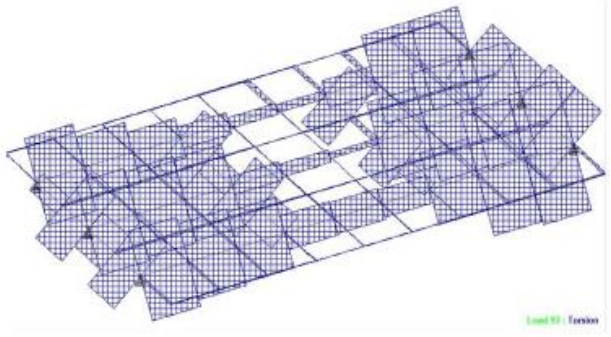

Figure 4.16(a): Variations of maximum Torsional Moment of 12m span under IRC Class A loading using Grillage Analogy

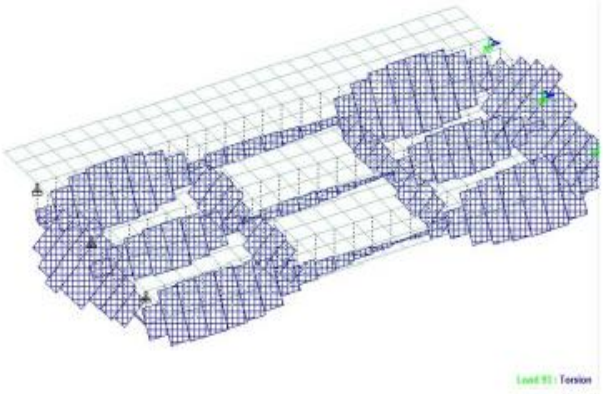

Figure 4.16(b): Variations of maximum Torsional Moment of 12m span under IRC Class A loading using FEM

4.1.3 Shear force (kN)

1. **Self-Weight**: The variation of maximum shear force for right spans ranging from 12 m to 18m due to self-weight of the structure has been presented in Figure 4.17.

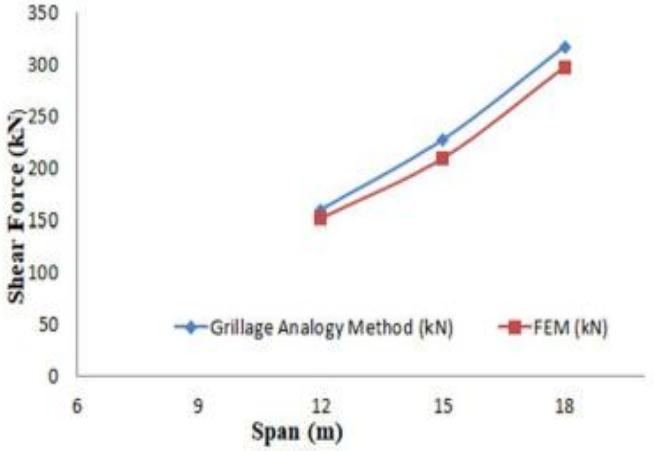

Figure 4.17: Variations of shear force with varying span (in case of self-weight)

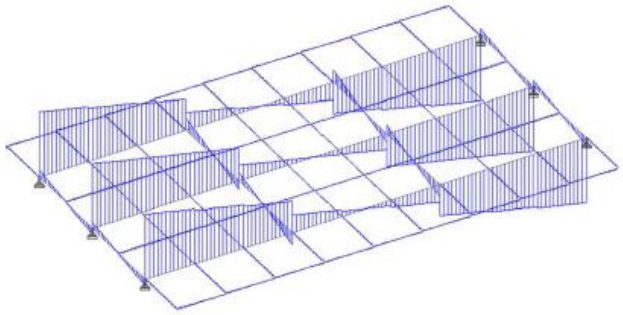

Figure 4.18(a): Variations of shear force of 12m span under self-weight using Grillage Analogy

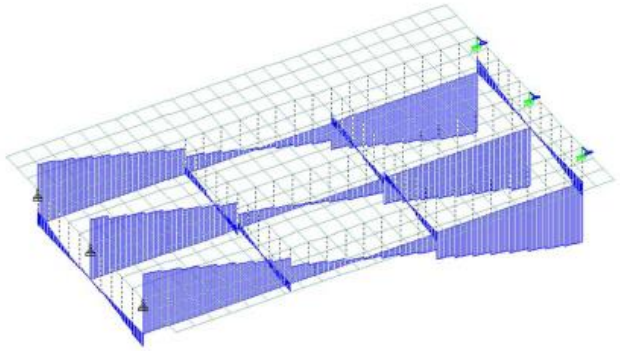

Figure 4.18(b): Variations of shear force of 12m span under self-weight using FEM

2. SIDL: The relatively same pattern for the outline shear powers has been gotten for SIDL case as got on account of self-weight stacking case, the variety in the consequences of FEM and Grillage Analogy all the more yet relatively same for various traverse length, as exhibited in Table 4.10 and graphically looked at as appeared. Varieties of shear power of 12m traverse under self-weight utilizing Grillage and FEM is appeared in Figure 4.20(a) and Figure 4.20(b)

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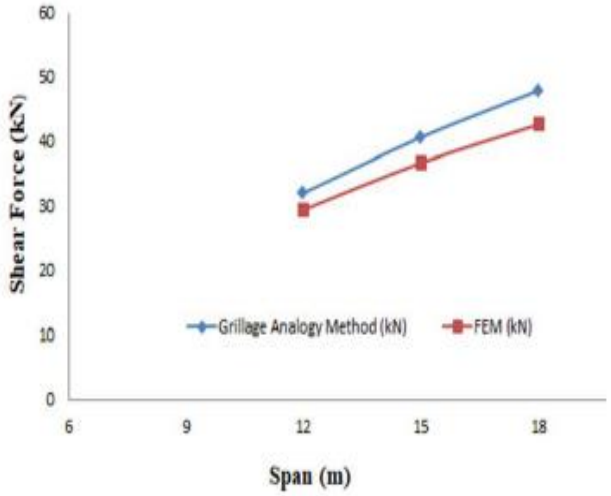

Figure 4.19: Variations of maximum shear force with varying span (in case of SIDL)

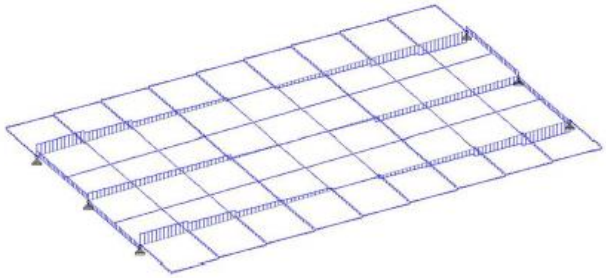

Figure 4.20(a): Variations of maximum shear force of 12m span under SIDL using Grillage Analogy

3. Live Load Conditions: The extension deck has been dissected according to IRC 6:2014 rules for two classes of IRC live loadings-Class 70R wheeled stacking and Class A stacking. The examination comes about for the two kinds are talked about underneath:

IRC Class 70R(W) stacking: The most extreme shear powers have been found to increment with increment in traverse in both the models under IRC Class 70R wheeled stacking as saw and the varieties are spoken to graphically in Figure 4.21. Varieties of shear power of 12m traverse under self-weight utilizing Grillage and FEM is appeared in Figure 4.22(a) and Figure 4.22(b)

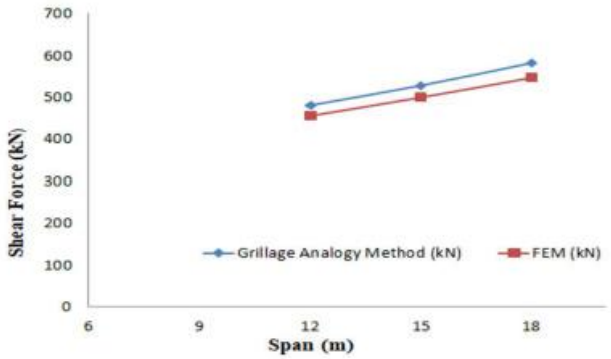

Figure 4.21: Variations of maximum shear force with varying span (in case of class 70R (W) live loading)

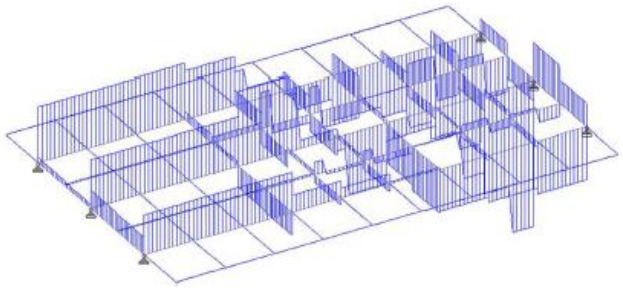

Figure 4.22(a): Variations of maximum shear force of 12m span under class 70R (W)

Live loading using Grillage Analogy

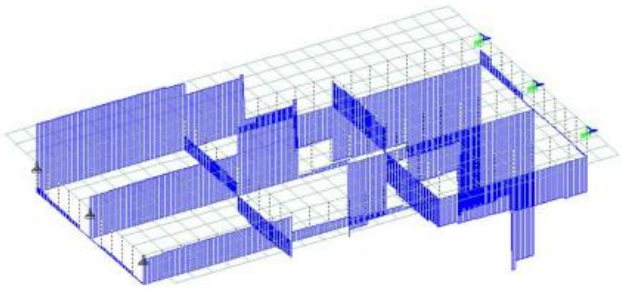

Figure 4.22(b): Variations of maximum shear force of 12m span under class 70R (W) live loading using FEM

a) IRC Class A loading: The greatest shear powers have been found to increment with increment in traverse in both the models under IRC Class A stacking and the varieties are spoken to graphically in Figure 4.23. A similar rising pattern for this situation likewise has been seen as on account of the power reactions got from the use of IRC Class 70R live stacking. . Varieties of shear power of 12m traverse under self-weight utilizing Grillage and FEM is appeared in Figure 4.24(a) and Figure 4.24(b)

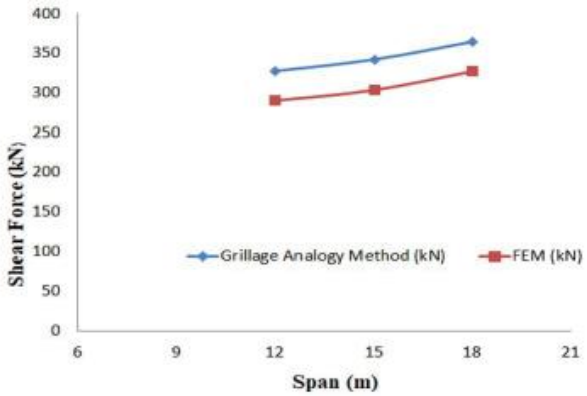

Figure 4.23: Variations of maximum shear force with varying span (in case of IRC

Class A loading)

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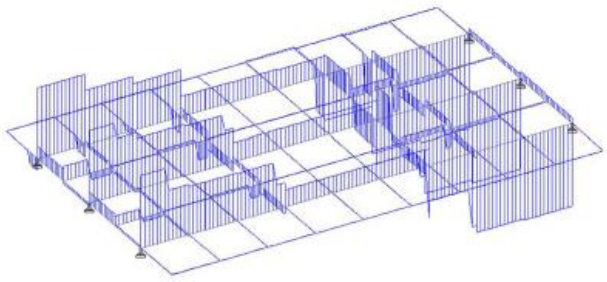

Figure 4.24(a): Variations of maximum shear force of 12m span under IRC Class A

loading using Grillage Analogy

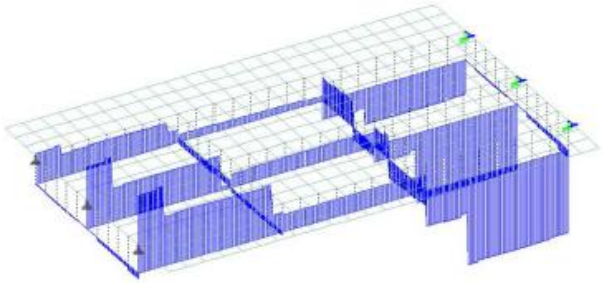

Figure 4.24(b): Variations of maximum shear force of 12m span under IRC Class A loading using FEM

Thus for all the considered load cases, the shear force tends to increase with the increase in span ranges also with methodology. The variations in shear forces in percentage difference along the span for all the loading cases are as follows:

Self-weight- in the range of 5% to 8%

SIDL- in the range of 8% to 10%

Live IRC Class 70R wheeled loading- in the range of 5 % to 6.5 %

Live IRC Class A loading- in the range of 10% to 12%

5. CONCLUSIONS

Bridges are a standout amongst the most difficult activity of all considerate designing works. The number and sizes of scaffolds have persistently expanded in the previous couple of years. This has\ required to grow new plan systems. To adapt up to this request, gigantic endeavors everywhere throughout the world as dynamic research in the investigation, plan and development of Bridges are proceeding. The focal point of this demonstrating is to discover the reason of the outcomes' disparities of the two models, while the goal of this proposal is to recreate the conduct of scaffold structure as far as (shear drive, twisting minute, and torsion) by fluctuating the traverse. All done by STAAD.Pro V8i programming. In the present work, it has been watched that more drawn out traverse spans are one of real worry due to conjusted urban regions and in addition expanded activity development rate. The parametric investigation on T-Girder solid extension for differing traverse length has been led, the parameters like bowing minutes, torsional minutes and shear powers have been dissected for IRC Class An and 70R stacking on T-support spans. The near investigation was directed in light of the expository demonstrating of just upheld RC T-bar Bridge by grillage similarity technique and Finite component strategy utilizing Staad Pro V8i. Based on the examinations, it has been presumed that:

- Based on this examination grillage relationship technique gives the moderate outcome with deference BM esteems in the longitudinal brace when contrasted with limited component strategy.
- In the instance of T-Girder bridges, it has been watched that the longitudinal bowing minutes demonstrates a rising pattern with increment in ranges. In any case, the mid traverse longitudinal twisting snapshots of the external girders, were observed to be relatively higher than then the longitudinal bowing minutes in the center support. The varieties in rate contrast for right edge straight bridges between grillage similarity and limited component technique are found in the scope of 2% to 8 % for dead load cases and 10% to 14.5% for live load cases, which are stopped worthy qualities.

  In the instance of T-Girder bridges, it has been watched that the torsional minutes increments with increment in traverse and furthermore external brace demonstrates more torsional minute at that point center support. The varieties in rate contrast between two strategies are found in the scope of 3% to 12% for dead load cases and 12% to14% for live load cases.
- In the instance of T-Girder bridges, it has been watched that the shear compel additionally increments with increment in ranges. Likewise, it has been discovered that most extreme shear powers tend to increment close to the edge backings of the external supports for every one of the traverses considered in the investigation. The varieties in rate distinction between the grillage similarity technique and limited component strategy are found in the scope of 5% to 10% for dead load cases and 5% to 12% for live load cases.
- When the explanatory outcomes are looked at for IRC Class 70 R (W) and IRC Class A stacking, it has been discovered that the plan esteems with IRC Class 70 R (W) give relatively high reactions and in this way are represented to be utilized as a part of the outline of the extensions.
- In conclusion, Finite Element show has more discretization (more exact), so the plan base of this reaction with the littler component gives less measure of materials et cetera (that is the conservative factor), therefore limited component demonstrate is more temperate outline than grillage display.
- Maximum BM happens for class 70R wheeled vehicle. Thus class 70R vehicle case is the most basic case for greatest BM in longitudinal brace.
- Maximum SF happens for class 70R wheeled vehicle. Thus class 70R wheeled vehicle case is the most basic case for greatest Shear compel in longitudinal brace.

6. FUTURE SCOPE

However during the course of this study, it has been found that there are still some grey areas. In order to find the more details, further studies can be recommended in the following ways:

- In request to discover the points of interest, the investigation can be led on more extraordinary kind of RCC spans and diverse span cases.
- The study can be additionally stretched out to multi-lane bridges.

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- The study has been led on basically upheld deck chunk. An examination might be led on consistent deck slabs.
- The study can be additionally stretched out for breaking down the impact of skew edges by considering stress and strain parameters.

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Experimental Study on Partial Replacement of Cement with Sugarcane Bagasse Ash in High Strength Concrete

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Abstract: *There are lots of environmental impacts of cement on our ecology. Cement industry creating environmental problem by emission of CO2 during manufacturing of cement. Today researchers are more focusing towards the environment issue globally. Portland cement is the conventional building material that actually is responsible for about 5%-8% of global CO2 emissions. On the other side Sugar cane Bagasse ash generated in sugar mill creating environment issue as most of the part is used as a land fill. In this research work the suitability of sugarcane bagasse ash (SCBA) in concrete used as partial replacement with cement and sand. The cement and sand was partially replaced by SCBA at 10%, 20%, 30% and 40%, by weight in normal strength concrete. Sugarcane bagasse ash which is taken from one of the sugar mill of Amroha district of Uttar Pradesh used in M25 grade of concrete by replacing cement and sand in percentage by weight and compare with conventional concrete to check the feasibility of sugarcane bagasse ash in concrete. Fresh concrete tests like compaction factor test and slump cone test must examined as well as hardened concrete tests like compressive strength at the age of 7, 14 and 28 days , and flexural strength at the age of 7 and 28 days is to be obtained.*

Keywords: Sugarcane Bagasse Ash (SCBA), Concrete, Compressive Strength, Flexural Strength, Waste Material, Durability

1. INTRODUCTION

Concrete is a complex composite comprises of aggregate and sand which is clenched unitedly with hydrous cement which after desiccation forms a compound stuff. When the aggregate and sand is assorted in-concert with cement and water, the concoction frames fluent slurry that is easily poured and molded into precise shape. Oftentimes habituation (such as fibrous) is included in the mixture to amend the physical properties of wet mix. Since aggregates occupy about 60-70% of the volume of a concrete mix, they play a significant role on the properties of concrete, including rheological properties of fresh concrete mix, reflex behavior and durability of hardened concrete which directly depends on the presence of C-S-H gel in concrete mass.

1.1 SUGARCANE BAGASSE ASH (SCBA)

Sugarcane bagasse is a fibrous waste-product of the sugar refining industry, along with ethanol vapor. This waste product (Sugar-cane Bagasse ash) is already causing serious environmental pollution, which calls for urgent ways of handling the waste. Bagasse ash mainly contains aluminum ion and silica. Utilization of agricultural, industrial and agroindustrial by-products in the form of processed ash attracting researchers to explore their potential as cement replacement material or mineral admixture to the properties of concrete at multiple levels. Utilization of established materials such as silica fume, fly ash and ground granulated blast furnace slag has proved as the high performance concrete ingredients. Today researches all over the world are focusing on ways of utilizing either industrial or agricultural wastes as a source of raw materials for the construction industry. These wastes utilization would not only be economical, but may also help to create a sustainable and pollution free environment. Sugar-cane bagasse is one such fibrous waste-product of the sugar refining industry, along with ethanol vapor. Bagasse ash mainly contains aluminum ion and silica. Sugarcane is one of the major crops grown in over 110 countries and its total production is over 1500 million tons. In India only, sugarcane production is over 300 million tons/year that cause about 10 million tons of sugarcane bagasse ash as an un-utilized and waste material. After the extraction of all economical sugar from sugarcane, about 40-45% fibrous residue is obtained, which is reused in the

same industry as fuel in boilers for heat generation leaving behind 8 -10 % ash as waste, known as sugarcane bagasse ash (SCBA). The SCBA contains high amounts of un-burnt matter, silicon, aluminum and calcium oxides. But the ashes obtained directly from the mill are not reactive because of these are burnt under uncontrolled conditions and at very high temperatures. The ash, therefore, becomes an industrial waste and poses disposal problems. With increasing demand and consumption of cement, researchers and scientist are in search of developing alternate binders that are ecofriendly and contribute towards waste management. The utilization of industrial and agricultural waste produced by industrial processes has been the focus on waste reduction. One of the agro waste sugar cane bagasse ash (SCBA) which is a fibrous waste product obtained from sugar mills as byproduct. Juice is extracted from sugar cane then ash produced by burning bagasse in uncontrolled condition and at very high temperature.

1.2 OBJECTIVE OF THE STUDY

This study can be done in many ways and with many parameters, but according to further clear objective are as follows:

- To compare the effect of concrete using Sugarcane Bagasse Ash (SCBA) as a partial replacement of cement and sand.
- To analyze the behavior of concrete using untreated Sugarcane Bagasse Ash by partially replacement in the proportion of 10%, 20%, 30% and 40% by weight of cement in concrete.
- Fresh concrete tests like slump cone test and compaction factor test were undertaken along with hardened concrete tests like compressive strength at 7, 14 and 28 days and flexural strength test at the age of 7 and 28 days.
- To find the best mix for the concrete in terms of strength, waste disposal and cost reduction from obtained results.

2. MATERIALS AND EXPERIMENTAL DETAILS

2.1 Experiment Background

For the analysis of determining strength and behavior of sustainable sugarcane bagasse ash(SCBA) concrete, the concretes formed as plain and SCBA concrete of various parameters are molded as cube of side 150 mm and beam of size (700 x 150 x 150) mm. The load is applied on the cube block under universal testing machine for compressive strength and 3-point loading (ASTM) on beam for flexural strength, which causes crack or fracture developed on the surface of cube and beam. For this, a proper maintained proportion of SCBA is used to achieve various resultant data. The determination of the behavior of freshly green concrete is also analyzed using this sustained proportion of SCBA.

2.2 Materials Used

2.2.1. Cement - Ordinary Portland Cement of 43 grade having properties as mentioned in Table No.3.1 was used.

Table No. 3.2.1 - Properties of cement

Physical Properties		IS Specification
Soundness	Le Chat Expansion (mm)	2.0
	Auto Clave Expansion (%)	0.10
Fineness (cm^2/gm.)		2850
Standard Consistency (%)		30
Initial setting time (minutes)		120
Final setting time (minutes)		200
Specific gravity		3.15

2.2.2 Aggregate

Aggregates constitute a skeleton of concrete. Approximately three-quarters of the volume of conventional concrete are occupied by aggregate. It is predictable that a constituent conquering such a huge percentage of the mass should contribute significant properties to both the fresh and hardened product.

Coarse aggregate: Aggregates predominately retained on a No.4 (4.75-mm) sieve are classified as coarse aggregate. Generally, the size of coarse aggregate ranges from 5 to 150 mm. For normal concrete used for structural members such as beams and columns, the maximum size of coarse aggregate is about 25 mm. For mass concrete used for dams or deep foundations, the maximum size can be as large as 150 mm.

Fine aggregate: Aggregates passing through a No.4 (4.75 mm) sieve and predominately retained on a No.200 (75 μm) sieve are classified as fine aggregate. River sand is the most commonly used fine aggregate. In addition, crushed rock fines can be used as fine aggregate. However, the finish of concrete with crushed rock fines is not as good as that with river sand. For this study we have used we have used natural sand excavated from local river site.

2.2.3 Sugarcane Bagasse Ash (SCBA)

Portland cement is recognized as a major construction material throughout the world. Researchers all over the world today are focusing on ways of utilizing either industrial or agricultural waste, as a source of supplement raw materials for in construction industry. This waste, utilization would not only be economical, but may also result in foreign exchange earning and environmental pollution control. Industrial wastes, such as blast furnace slag, fly ash and silica fume are being used as supplementary cement replacement materials. Along with industrial wastes; agricultural wastes like rice husk, wheat hay, sugarcane bagasse are also being tried to be supplement material.

Currently, there has been an attempt to utilize the large amount of bagasse ash, the residue from an in-line sugar industry and the bagasse-biomass fuel in electric generation industry. When this waste is burned under controlled conditions, it produces ash having amorphous silica, which has pozzolanic properties.

The potential production capacity of burnt sugarcane bagasse residue is around 7-8% of total bagasse consumed. A few studies have been carried out on the ashes obtained directly from the industries to study pozzolanic activity and their suitability as binders, partially replacing cement. Therefore it is possible to use sugarcane bagasse ash (SCBA) as cement replacement material to improve quality and reduce the cost of construction materials such as mortar, concrete pavers, concrete roof tiles and soil cement interlocking block.

Figure No. 2.2.3-Sugarcane Bagasse As

Table No. 2.2.3 - Composition of Sugarcane Bagasse Ash

S. No	Chemical compound	Abbreviation	Percentage (%)
1	Silica	SiO_2	68.42
2	Aluminum Oxide	Al_2O_3	5.812
3	Ferric Oxide	Fe_2O_3	0.216
4	Calcium Oxide	CaO	2.554
5	Phosphorous Oxide	P_2O_5	1.258
6	Magnesium Oxide	MgO	0.572
7	Sulphide Oxide	SO_3	4.327
8	Loss on Ignition	LOI	15.86

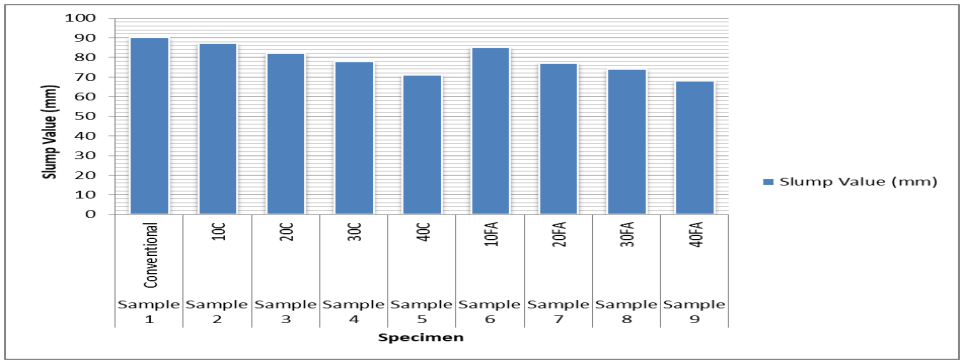
Table No. 2.3 Batch Description

Batch Description		Cement	Fine Aggregate	Coarse Aggregate	SCBA
For conventional concrete					
S1	Proportion	1	1.68	2.86	0
	Wt. (kg/m^3)	394.32	658.26	1123.62	0
For 10% replacement of Cement by SCBA					
S2	Proportion	0.90	1.68	2.86	0.10
	Wt. (kg/m^3)	354.89	658.26	1123.62	39.43
For 20% replacement of Cement by SCBA					
S3	Proportion	0.80	1.68	2.86	0.20
	Wt. (kg/m^3)	315.43	658.26	1123.62	78.86
For 30% replacement of Cement by SCBA					
S4	Proportion	0.70	1.68	2.86	0.30
	Wt. (kg/m^3)	276.02	658.26	1123.62	118.30
For 40% replacement of Cement by SCBA					
S5	Proportion	0.60	1.68	2.86	0.40
	Wt. (kg/m^3)	236.59	658.26	1123.62	157.73
For 10% replacement of Fine Aggregate by SCBA					
S6	Proportion	1	1.58	2.86	0.10
	Wt. (kg/m^3)	394.32	592.44	1123.62	65.82
For 20% replacement of Fine Aggregate by SCBA					
S7	Proportion	1	1.38	2.86	0.20
	Wt. (kg/m^3)	394.32	526.61	1123.62	131.65
For 30% replacement of Fine Aggregate by SCBA					
S8	Proportion	1	1.08	2.86	0.30
	Wt. (kg/m^3)	394.32	460.78	1123.62	197.48
For 40% replacement of Fine Aggregate by SCBA					
S9	Proportion	1	0.68	2.86	0.40
	Wt. (kg/m^3)	394.32	394.96	1123.62	263.30

3.0 RESULT ANALYSIS AND DISCUSSIONS

3.1 Results of Slump cone test and Compaction factor test

The results of slump test and compaction factor tests are represented in graphically form.

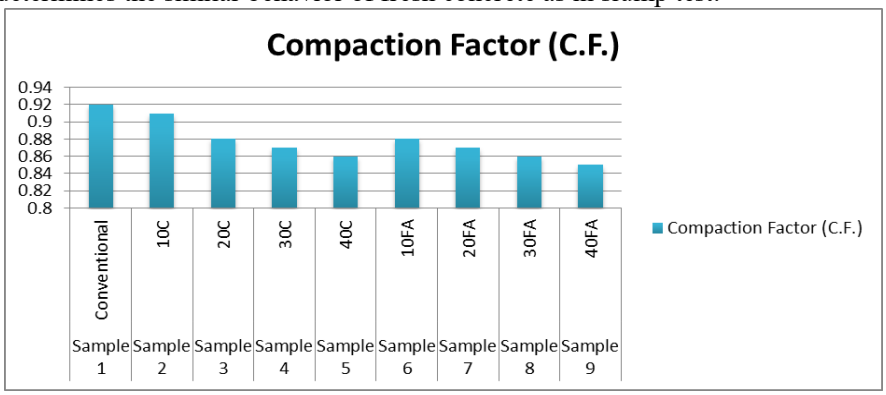


Graph No. 3.1.1 Slump test results

It can examined from the Graph No. 3.1.1, when replacement of cement by sugarcane bagasse ash (SCBA) is increased by percentage (10%-40%), with increase in sugarcane bagasse (SCBA) in the concrete mix there is decrease in slump value. There is an indication of less water cement ratio and hence value of slump decreases with increase in sugarcane bagasse ash (SCBA).This can be explained as, more the sugarcane bagasse ash (SCBA) in concrete mix; less will be the water in the concrete mix. This can clarified with the fact that sugarcane bagasse ash (SCBA) is more porous than cement, which requires more amount of water for lubrication process.

Similar trends of result obtained when replacement of sand by sugarcane bagasse ash (SCBA) is used in concrete mix. As sugarcane bagasse ash (SCBA) is more permeable than sand, so the slump value obtained are quite higher than case of cement replacement for the same proportioning.

Similarly, Graph No. 3.1.2 shows the results of compaction factor test for all different sample or parameters used in the experimental study. The result of compaction factor tests also determines the similar behavior of fresh concrete as in slump test.



Graph No. 3.1.2 Compaction factor test results

3.2 Results of Compressive strength test of concrete cubes

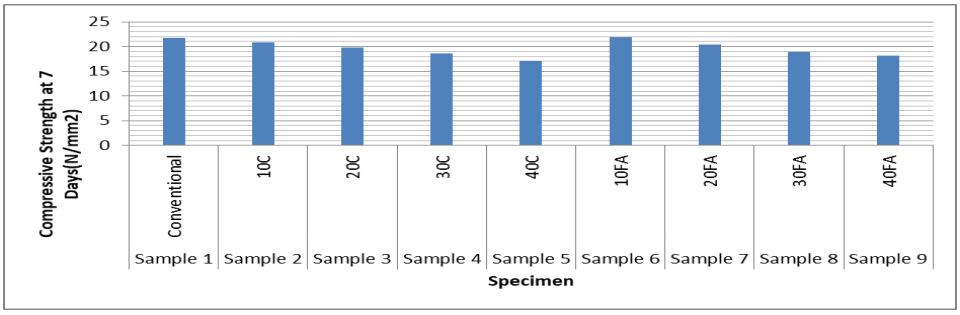
The characteristic compressive strength of concrete at 7 days, 14 days and 28 days was found in N/mm^2. The results are shown below in tabular form in Table No. 3.2.1 and are represented graphically in Graph No. 3.2.1, Graph No. 3.2.2, & Graph No. 3.2.3 respectively for all the specimens. Average results of 3 samples for each parameter

(specimen/days of test) are evaluated by using universal testing machine.

Table No. 3.2.1 Compressive strength of cube specimen

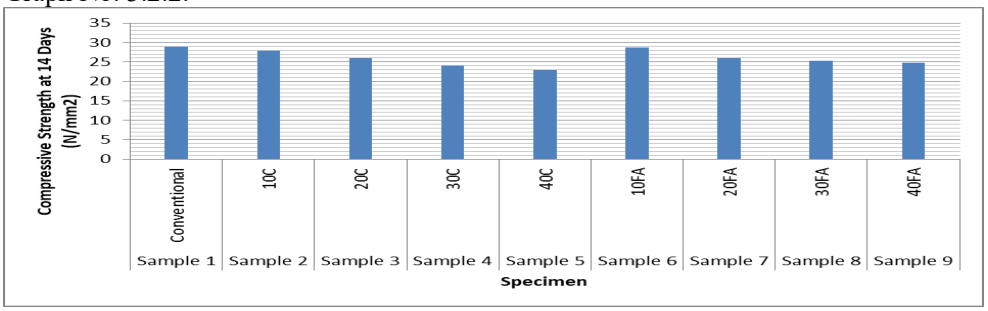
Specimen	Abbreviation	Average Compressive Strength of Cubes (N/mm^2)		
		7 days	14 days	28 days
Sample 1	Conventional	21.73	28.90	31.95
Sample 2	10C	20.83	27.92	29.83
Sample 3	20C	19.73	25.95	27.92
Sample 4	30C	18.61	24.02	26.63
Sample 5	40C	17.07	22.92	26.08
Sample 6	10FA	21.96	28.75	31.45
Sample 7	20FA	20.35	26.05	29.32
Sample 8	30FA	18.95	25.21	28.16
Sample 9	40FA	18.19	24.73	27.39

Result showed a continuous decrease in the strength with addition of SCBA in the concrete. Decrease in compressive strength with the increase SCBA can be justified by the fact that SCBA does not have such binding property as compared to cement. At the same time, SCBA imparts more strengthen properties comparing to sand because it is finer than sand thus results in less voids in the concrete specimen.
The results of compressive strength at 7 days are represented graphically below in Graph No. 3.2.1.



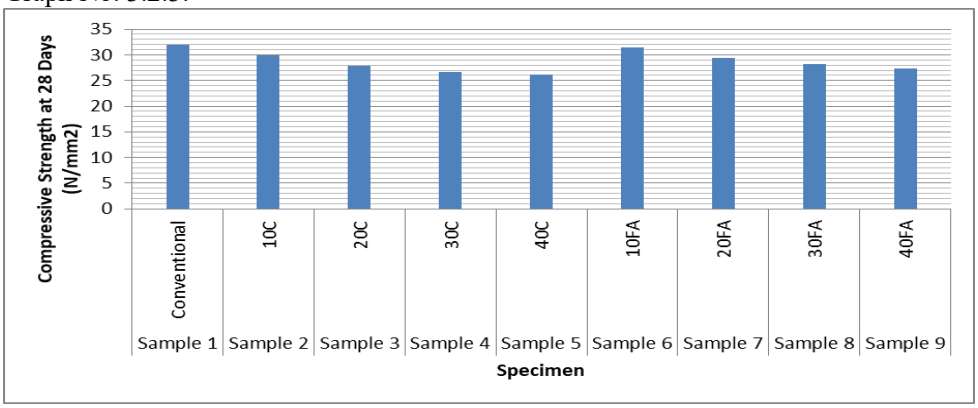
Graph No.3.2.1- Results of compressive strength test of cube at 7 day's

The results of compressive strength at 14 days are represented graphically below in Graph No. 3.2.2.



Graph No.3.2.2- Results of compressive strength test of cube at 14 day's

The results of compressive strength at 28 days are represented graphically below in Graph No. 3.2.3.



Graph No.3.2.3 Results of compressive strength test of cube at 28 day's

3.3 Results of Flexural tensile strength test of concrete beam

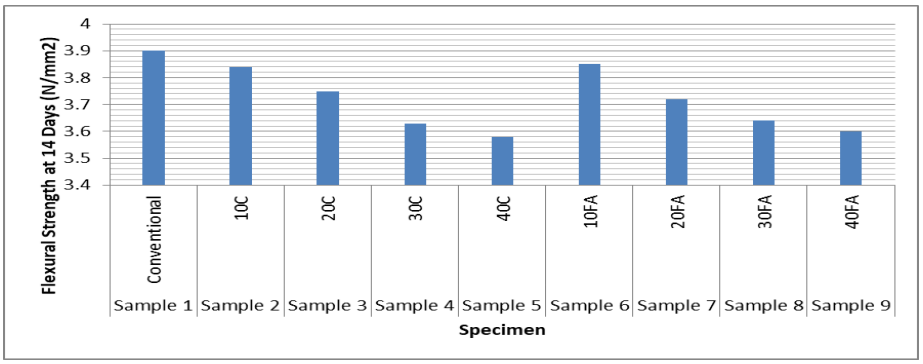
The flexural strength of concrete beam at 14 days and 28 days was found in N/mm^2. The results are shown below in tabular form in Table No. 3.3.1 and are represented graphically in Graph No. 3.3.1 & Graph No. 3.3.2 respectively for all the specimens. Average results of 3 samples for each parameter (specimen/days of test) are evaluated by using BIS: 456-2000 specification.

Table No. 3.3.1- Flexural strength of concrete beam specimen

Specimen	Abbreviation	Flexural Strength of Beam (N/mm^2)	
		14 Days	28 Days
Sample 1	Conventional	3.90	4.38
Sample 2	10C	3.84	4.29
Sample 3	20C	3.75	4.19
Sample 4	30C	3.63	3.99
Sample 5	40C	3.58	3.95
Sample 6	10FA	3.85	4.35
Sample 7	20FA	3.72	4.20
Sample 8	30FA	3.64	4.13
Sample 9	40FA	3.60	3.98

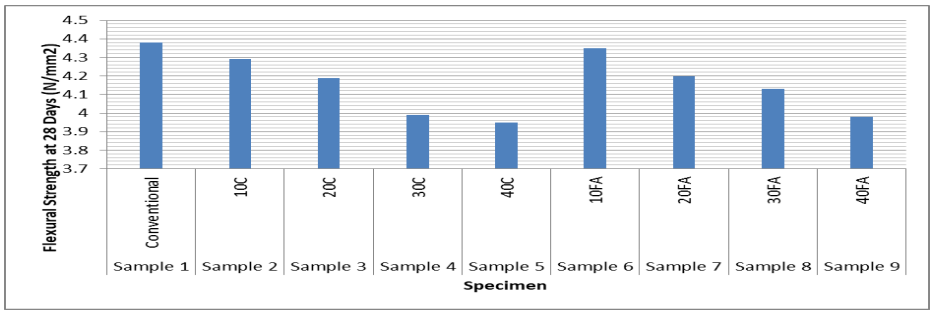
Result showed a continuous decrease in the flexural strength with addition of SCBA in the concrete beam. Decrease in flexural strength with the increase SCBA can be justified by the fact that doesn't have tensile properties. SCBA provides minimum voids in the concrete due to finer than sand thus helpful in decreasing cracks on concrete beam.

The test results of 14 days are represented below in Graph No. 3.3.1.



Graph No.3.3.1- Results of flexural strength test of beam at 14 day (N/mm^2)

The test results of 28 days are represented below in Graph No. 3.3.2.



Graph No.3.3.2- Results of flexural strength test of beam at 28 day (N/mm^2)

4.0 CONCLUSION

1. Decrease in slump value by 25% and compaction factor by 9% is examined when the replacement of sand by SCBA in the concrete mix from 0% to 40%.
2. Compressive strength of concrete decreases initially with the inclusion of SCBA.
3. Compressive strength of concrete cube at 7 days, 14 days and 28 days are decreased by 20%, 19% and 18% respectively when 40% SCBA was used to replace cement.
4. Flexural strength of concrete at 14 days and 28 days are decreased by 6% and 5% respectively when 40% SCBA was used to replace cement.
5. There will be a reduction in cost of material for the same strength of concrete if SCBA this is because SCBA is a waste and was obtained free of cost from the factory.

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TOWARD THE RESILIENT SMARTMANUFACTURING

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ABSTRACT

The focus of this paper is to highlight general overview reliability and resilience of smart manufacturing inthe nearest future, the current system of smart manufacturing is at infancy stage even with the emergence and integration of smart sensors, internet of things, artificial intelligence, Cloud computing and powerful software into it. its benefits are to all parties involved in the supply chain, which was hindered by different factors such as lack of policymakers' intervention, funding, skilled workforce and widen the gap between industries and academia. Therefore, there is an urgent need to allocate a very huge amount to thesector, equipped with enough skilled manpower, as well as special package to support both small and medium scaled industries. Through the implementation of proposed recommendations made, the future of smart manufacturing especially in developed countries can safely be guaranteed.

Keyword: Resilience, Smart Supply Chain, Intervention, System

I. INTRODUCTION

Over the past few years, smart manufacturing is one of the most top topics of discussion between professionals and experts in the industrial sector especially the technology industries. which can be the most competitive scenario in the future industrial revolution. The world competition in smart manufacturing transformation is taking new shape among technological industries in Europe, U.S.A and Asia. This competitive moves between these industries in recent time hasbrought about a rapid change toward their activities and help manufacturers to smartly transform and change their entire system of production into digitized one. an industrial revolution for implementing smart production and artificial intelligence would bring about progress in economic development, meeting costumers demand, time reduction, improved quality as well as the flexibility to suit the demanding market through an integrated human-machine interaction. The recent innovation would drastically minimize the manpower requirement, increased product quality. Cyclic, undisrupted and connected supply chain of production in manufacturing process. This has brought about transparency in the industrial hierarchy thereby increasing the effectivenessof productivity. However, up to now very few manufacturingindustries have been able to rapidly adopt these technologies. Many attempts have been made by professionals to give anexcellent definition of smart manufacturing but the mostrobust definition is given by the [1] of the United State o America as it's

"fully-integrated, collaborative manufacturing systems thatrespond in real-time to meet changing demands and conditions in the factory, in the supply network, and in customer needs."

But the above definition is not considering the possible effect caused to the environment by the activities of smart manufacturing, therefore the smart manufacturing can be redefined as the process of applying advanced automation, control, simulation, and modelling in production which will result in safer, quicker, efficient, effective, cheaper productsor service that meet the demand of the consumer withoutcausing due effects to the habitat and environment. in the simplest way it's the future system of which machinery, components will automatically be communicating between themselves through wireless interconnectivity for the output of relatively high quality in lesser time, less emission of pollutant and without causing the degradation to the environment. It also involves the integration of automation, computation, networking, cloud computing and adoption of advanced information technology for the production ofreliable and updated goods and services.

The main objective of resilience in smart manufacturing is to have a sustainable innovation by using state-of-the-art Advanced automation and control, simulations and modelling system that will be incorporated with the utilization of energy, manpower, cost, other resources an intended aim of satisfying customer needs without compromising the manufacturing processes and causing disturbance to the environment also thisinnovation will remain capable of considering political, economic and social demand of the society and also capable of resisting future possible disruption from unforeseen circumstances such as natural pandemic, which can be achieved by ongoing competitive and initiation of innovative

ideas of world-leading technologies companies in developed and developing countries such as china USA, India etc.

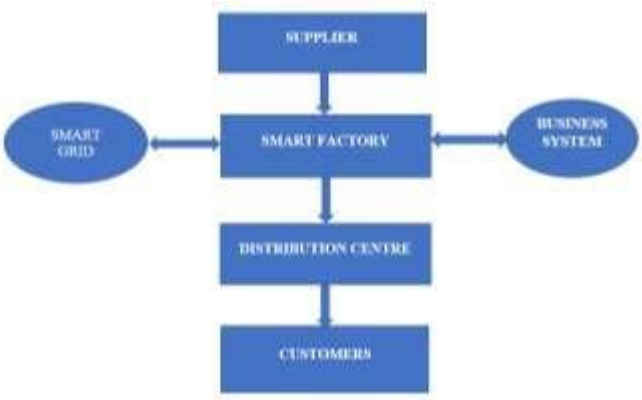

Fig 1: System of Resilient Smart Manufacturing [2]

II. IDEA BEHIND THE RESILIENT SMART MANUFACTURING

Production exists long ago in the human history starting from the stone age down to the current digital world, for example, the British industrial revolution of 18th century was empowered, secured and successful due to its capacity in manufacturing in utilizing steam engine and iron, while USA and China as the two main competitors in the world economy and leaders of fourth industrial transformation are still in the race of dominating the emerging fifth era of smart manufacturing which include the integration of wireless communication especially the 5G, cloud computing, internetof things, artificial intelligence and even forecasting the digitized way of the real-time interface between visible and virtual world. all these superpower countries rely heavily on

manufacturing industries, therefore there is a need for continuous improvement to sustain the system. Also, another factor that necessitates the smart manufacturing is thelimitation of the small and medium manufacturers to access the costlier business model. Also, besides most traditionalindustrial processes are now been replaced with the current technology of industry 4.0 and may in the nearest future going to be replace with the system which was equipped with smart sensors to have flexible, simpler, transformed, the real-time products that would satisfy the consumer's need. [3]

III. KEY DRIVERS TO THE RESILIENT SMART MANUFACTURING

The Keys technologies enabling the smart manufacturing are sensors, wireless connection, data analysis, generative design, computer-aided design, and advanced robotics. But Technological industries are faced with two challenges: these are, visible one which includes detectable machine fault, decrease in output, which can be detected and be appropriately solved depending on the problem encountered using normal manufacturing approach and non-visible one which includes wear and tear of a component part, the main problem of these industries they just focused on implementing program and methodology to foster the costumers demand in preference to the solving problems. i.e. they only consider their profit output.Therefore, implementing artificial intelligence as part of smart manufacturing processing will yield a very fruitful result as it can be used to detects both the visible and non-visible defect, as mentioned by [4] using artificial intelligence in smart manufacturing can lead to a reduction of work, waste, championing other competitors, providing costumers demand and improve the quality of the manufactured goods.

Also, the emergence of Artificial Intelligence (AI) gives the breakthrough to the development of the smart manufacturing due to its multipurpose characteristics of capable storing, computing, sharing huge data which gives the technological manufacturers ability to improve the level of production and increase their competitiveness. Internet of Things (IoT) which sometimes correlated with the cloud computing which serves as the main storage of Internet of Things (IoT) data and provide medium to which the users can interact and retrieve data, the innovation of Internet of Things (IoT) and cloud computing provides an opportunity to manufacturers to save a lot by avoiding them to unnecessarily to create individual sites and communication platforms for their product which can be they can be accessed by other independent service providers companies. [5]

IV. REQUIREMENTS FOR RESILIENT SMARTMANUFACTURING

For successful smart manufacturing, the following driving points need to be considered which was described by [6] Providing Universal interactive platform to share the idea for industries in the new research obtained in the field of smart manufacturing,

i. Cheaper, Reliable, Accessible and Robust System for collection processing retrieving and management of data in smart manufacturing.
ii. Sustained, optimized and valued supply chain system.
iii. Establishment of an organized and well-integrated educational system to which the smart manufacturing industrials will rely on [7].

BENEFITS OF RESILIENT SMART MANUFACTURING TO THE SUPPLY CHAIN PROCESSES

All the parties involved in the supply chain benefit from the smart manufacturing

i. **To the Supplier:** as the supply chain include the continuous and cyclic processes from manufacturer, supplier to the final consumer. The supplier might use the opportunity of using smart manufacturing to optimize the end-user requirement especially in an environment where there is limited medium to which he can interact with the end-user directly.

ii To the Manufacturer: the most important factorthat enhances supply chain is better and effectiveinteracting medium. Therefore, implementing the resilient smart manufacturing in production will lead to a sustained and valuable product that can be traced, tracked and apply simulation processes to detect possible variation in the supply chain.

iii To the End User: The basic consumer needs are to have an assurance of quality and timely delivery of the product. he can also be able to access different alternatives of his demand. And also send feedback and suggestion to the other parties in the supply chain using smart manufacturing technology.

V. CHALLENGE TO THE RESILIENT SMARTMANUFACTURING IMPLEMENTATION

Besides this rapid development in resilient smart manufacturing still, most of the companies have little knowledge about these innovations. Therefore, there is a need to explore those benefits of resilient smart manufacturing and let those companies strictly adhere to them promptly [8]. Other challenges faced by the smart manufacturing industries as identified by [6]. include, 1. No evidence or any reliable ordependable fact that for them to embrace the innovations in manufacturing, 2. Complex and wider range variability in datato be processed by the machines. 3. No system that can beused to detect the machine failure which may lead to output with high possible errors. 4. Some Complex industrial processes may be impossible for machine to handle without human intervention. Other challenges as describe by [9] include Data Management and Lifecycle Challenges, data Processing Architectures Challenges, Data Analytics Challenges, Data Protection and Security Challenges, and lastly Data Visualization Challenges.

VI. CONCLUSION

The existence of the digital world in the production and manufacturing industries has been the key factor in the revolutionary movement of resilient smart manufacturing which may lead to the fifth edition of the industrial revolution. Also, considering the current challenges and disruption in supply chain and value chain activities, implementing the smart manufacturing in the production industries will help in alleviating them. Also, the successful trends in smart manufacturing is likely to be the conditional advancement to the change in the current perspective in global manufacturing competition. However, most of the industries embarked on this trend are still at the infancy stage crippled with the funding scarcity, poor and unavailability of well-trained and skilled manpower and lack proper support from their government. And lastly, to have a robust, resilient, reliable, less costly, environmentally friendly smart manufacturing it is necessary for both private and public sectors especially in the production sector to work hand in hand with the provisional guidelines prescribes by the policy makers.

VII. RECOMMENDATIONS

To have long-lasting, sustained and resilient smart manufacturing especially in the production sector there is a need to implement the following recommendations.

1. A very huge amount needs to be allocated by the manufacturers in the countries interesting and competing to lead the advancement in smart manufacturing, the allocation should uniformly be distributed to the whole digital system which includes modern tools, installing state of the art plants and equipment, sophisticated sensors and strong cloud for proper communication in the sector.
2. Enough manpower in cooperated with updated required essential skills is needed by industries to speed up the smart manufacturing revolution in the world. This can be achieved by improving the consistency and quality of manufacturing education.
3. To bust the economy and speed up the process of smart manufacturing its prerequisite to all the nations interested to invest and gain in resilient smart manufacturing for the inclusion of research activities in the universities. which should be encouraged by supportive effort through special grant allocation to these kinds of research and also strengthens the bond between industries and academia.
4. Several conferences and seminars have to be organized on a timely basis by professionals and experts in such fields for sharing ideas and otherupdated and innovative information.
5. another factor which needs to be considered to have successful, resilient smart manufacturing is the integrational intervention to support both small and medium scale industries in those countries which may lead to economic improvement for them.

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Plastic Pollution: A Major Environmental Threat

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***Abstract*- Plastic pollution is the increase of plastic bottles and much more in the Earth's environment that adversely affects wildlife, wildlife habitat, and humans. Plastics that act as pollutants are categorized into micro-, meso-, or macro debris, based on size. Plastics are inexpensive and durable, and as a result levels of plastic production by humans are high. However, the chemical structure of most plastics renders them resistant to many natural processes of degradation and as a result they are slow to degrade. Together, these two factors have led to a high prominence of plastic pollution in the environment. Plastic is a polymeric material—that is, a material whose molecules are very large, often resembling long chains made up of a seemingly endless series of interconnected links. Natural polymers such as rubber and silk exist in abundance, but nature's plastics have not been implicated in environmental pollution, because they do not persist in the environment. Today, however, the average consumer comes into daily contact with all kinds of plastic materials that have been developed specifically to defeat natural decay processes—materials derived mainly from petroleum that can be molded, cast, spun, or applied as a coating.**

***Index terms*- degradation, prominence, durable**

I.INTRODUCTION

Plastic pollution is the increase of plastic bottles and much more in the Earth's environment that adversely affects wildlife habitat, and humans. Plastics that act as pollutants are categorized into micro-, meso-, or macro debris, based on size. Plastics are inexpensive and durable, and as a result levels of plastic production by humans are high. However, the chemical structure of most plastics renders them resistant to many natural processes of degradation and as a result they are slow to degrade. Together, these two factors have led to a high prominence of plastic pollution in the environment. This pollution can afflict land, waterways and oceans. It is estimated that 1.4 to 8.8 million metric tons (MT) of plastic waste enters the ocean from coastal communities each year. Living organisms, particularly marine animals, can be harmed either by mechanical effects, such as entanglement in plastic objects, problems related to ingestion of plastic waste, or through exposure to chemicals within plastics that interfere with their physiology. Effects on humans include disruption of various hormonal mechanisms. As of 2019, about 400 million tons of plastic is produced worldwide each year. From the 1950s up to 2019, an estimated 7.3 billion tons of plastic has been produced worldwide, of which an estimated 12% has been recycled and another 15% has been incinerated. This large amount of plastic waste enters the environment, with studies suggesting that the bodies of 90% of seabirds contain plastic debris. In some areas there have been significant efforts to reduce the prominence of free range plastic pollution, through reducing plastic consumption, litter cleanup, and promoting plastic recycling

II.TYPES OF PLASTIC DEBRIS

There are three major forms of plastic that contribute to plastic pollution: micro plastics as well as mega and macro-plastics. Mega and micro plastics have accumulated in highest densities in the Northern Hemisphere, concentrated around urban centers and water fronts. Plastic can be found off the coast of some islands because of currents carrying the debris. Both mega- and macro-plastics are found in packaging, footwear, and other domestic items that have been washed off of ships or discarded in landfills. Fishing-related items are more likely to be found around remote islands. These may also be referred to as micro-, meso-, and macro debris. Plastic debris is categorized as either primary or secondary. Primary plastics are in their original form when collected. Examples of these would be bottle

caps, cigarette butts, and micro beads. Secondary plastics, on the other hand, account for smaller plastics that have resulted from the degradation of primary plastics.

III.CAUSES OF PLASTIC POLLUTION

In 2019 a new report "Plastic and Climate" was published. According to the report, in 2019, plastic will contribute greenhouse gases in the equivalent of 850 million tons of carbon dioxide (CO2) to the atmosphere. In current trend, annual emissions will grow to 1.34 billion tons by 2030. By 2050 plastic could emit 56 billion tons of Greenhouse gas emissions, as much as 14 percent of the earth's remaining carbon budget.[24] By 2100 it will emit 260 billion tons, more than half of the carbon budget. Those are emission from production, transportation, incineration, but there are also effects on Phytoplankton.

IV.PROBLEM OF PLASTIC POLLUTION

Plastic is a polymeric material—that is, a material whose molecules are very large, often resembling long chains made up of a seemingly endless series of interconnected links. Natural polymers such as rubber and silk exist in abundance, but nature's "plastics" have not been implicated in environmental pollution, because they do not persist in the environment. Today, however, the average consumer comes into daily contact with all kinds of plastic materials that have been developed specifically to defeat natural decay processes—materials derived mainly from petroleum that can be molded, cast, spun, or applied as a coating. Since synthetic plastics are largely non biodegradable, they tend to persist in natural environments. Moreover, many lightweight single-use plastic products and packaging materials, which account for approximately 50 percent of all plastics produced, are not deposited in containers for subsequent removal to landfills, recycling centres, or incinerators. Instead, they are improperly disposed of at or near the location where they end their usefulness to the consumer. Dropped on the ground, thrown out of a car window, heaped onto an already full rubbish bin, or inadvertently carried off by a gust of wind, they immediately begin to pollute the environment. Indeed, landscapes littered by plastic packaging have become common in many parts of the world. Studies from around the world have not shown any particular country or demographic group to be most responsible, though population centres generate the most litter. The causes and effects of plastic pollution are truly worldwide.

V.EFFECTS OF PLASTIC ON THE ENVIRONMENT

The distribution of plastic debris is highly variable as a result of certain factors such as wind and ocean currents, coastline geography, urban areas, and trade routes. Human population in certain areas also plays a large role in this. Plastics are more likely to be found in enclosed regions such as the Caribbean. It serves as a means of distribution of organisms to remote coasts that are not their native environments. This could potentially increase the variability and dispersal of organisms in specific areas that are less biologically diverse. Plastics can also be used as vectors for chemical contaminants such as persistent organic pollutants and heavy metals.

VI. EFFECTS OF PLASTIC ON HUMANS

Due to the use of chemical additives during plastic production, plastics have potentially harmful effects that could prove to be carcinogenic or promote endocrine disruption. Some of the additives are used as phthalate plasticizers and brominated flame retardants. Through bio monitoring, chemicals in plastics, such as BPA and phthalates, have been identified in the human population. Humans can be exposed to these chemicals through the nose, mouth, or skin. Although the level of exposure varies depending on age and geography, most humans experience simultaneous exposure to many of these chemicals. Average levels of daily exposure are below the levels deemed to be unsafe, but more research needs to be done on the effects of low dose exposure on humans. A lot is unknown on how severely humans are physically affected by these chemicals. Some of the chemicals used in plastic production can cause dermatitis upon contact with human skin. In many plastics, these toxic chemicals are only used in trace amounts, but significant testing is often required to ensure that the toxic elements are contained within the plastic by inert material or

polymer. It can also affect humans because it may create an eyesore that interferes with enjoyment of the natural environment.

VII. EFFECTS OF PLASTIC ON OCEANS

In 2012, it was estimated that there was approximately 165 million tons of plastic pollution in the world's oceans. The Ocean Conservancy reported that China, Indonesia, Philippines, Thailand, and Vietnam dump more plastic in the sea than all other countries combined. One study estimated that there are more than 5 trillion plastic pieces (defined into the four classes of small microplastics, large microplastics, meso- and macroplastics) afloat at sea. The litter that is being delivered into the oceans is toxic to marine life, and humans. The toxins that are components of plastic include diethylhexyl phthalate, which is a toxic carcinogen, as well as lead, cadmium, and mercury. Plankton, fish, and ultimately the human race, through the food chain, ingest these highly toxic carcinogens and chemicals. Consuming the fish that contain these toxins can cause an increase in cancer, immune disorders, and birth defects. The majority of the litter near and in the ocean is made up of plastics and is a persistent pervasive source of marine pollution. According to Dr. Marcus Eriksen of The 5 Gyres Institute, there are 5.25 trillion particles of plastic pollution that weigh as much as 270,000 tons (2016). This plastic is taken by the ocean currents and accumulates in large vortexes known as ocean gyres. The majority of the gyres become pollution dumps filled with plastic.

VIII. EFFECTS OF PLASTIC ON ANIMALS

Plastic pollution has the potential to poison animals, which can then adversely affect human food supplies. Plastic pollution has been described as being highly detrimental to large marine mammals, described in the book Introduction to Marine Biology as posing the "single greatest threat" to them. Some marine species, such as sea turtles, have been found to contain large proportions of plastics in their stomach. When this occurs, the animal typically starves, because the plastic blocks the animal's digestive tract. Sometimes Marine mammals are entangled in plastic products such as nets, which can harm or kill them

IX. EFFORTS TO REDUCE PLASTIC

Efforts to reduce the use of plastics and to promote plastic recycling have occurred. Some supermarkets charge their customers for plastic bags, and in some places more efficient reusable or biodegradable materials are being used in place of plastics. Some communities and businesses have put a ban on some commonly used plastic items, such as bottled water and plastic bags. In January 2019 a "Global Alliance to End Plastic Waste" was created. The alliance aims to clean the environment from existing waste and increase recycling, but it does not mention reduction in plastic production as one of its targets. The Ministry of Drinking Water and Sanitation, Government of India, has requested various governmental departments to avoid the use of plastic bottles to provide drinking water during governmental meetings, etc., and to instead make arrangements for providing drinking water that do not generate plastic waste. The state of Sikkim has restricted the usage of plastic water bottles (in government functions and meetings) and styrofoam products. The state of Bihar has banned the usage of plastic water bottles in governmental meetings. The 2015 National Games of India, organised in Thiruvananthapuram, was associated with green protocols. This was initiated by Suchitwa Mission that aimed for "zero-waste" venues. To make the event "disposable-free", there was ban on the usage of disposable water bottles. The event witnessed the usage of reusable tableware and stainless steel tumblers. Athletes were provided with refillable steel flasks. It is estimated that these green practices stopped the generation of 120 metric tonnes of disposable waste.

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STUDY OF TRAFFIC VOLUME OF NH- 79 SIX LANE (BHL TO COR AND COR TO BHL) AND ITS SAFETY MEASURES ON NATIONAL HIGHWAYS

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Abstract: National Highway 79 passes through the districts of Bhilwara and Chittorgarh and connects Udaipur via NH 76 in Rajasthan. The corridor traverses through major settlement stretches such as Nasirabad, Gulabpura, Bhilwara (Textile city of India), Chittorgarh (Asia's largest fort), Mangalwara and finally Udaipur (Lake city of Rajasthan). Chittorgarh- Nimbahera area is also famous for its cement factories. There are many cement plants like (JK Cement, Wonder Cement, Lafarge Cement, Birla Cement etc). Chittorgarh is also famous for Marbles and Granites. Chittorgarh Fort, is the largest fort in India and Asia[1].Hindustan Zinc Limited is also located in Chittorgarh District; Chanderiya Lead-Zinc Smelter is the one of the largest zinc-lead smelting complexes in the world. Its current metal production capacity is 610,000 tonnes per annum (525,000 tonnes per annum of zinc and 85,000 tons per annum of lead)[2]. In the year ended March 2013, Chanderiya produced 443,000 MT of zinc and 60,000 MT of lead. The main products are special high grade (SHG) zinc, continuous galvanizing grade (CGG) zinc, prime western (PW) zinc and pure lead. It also produces a number of valuable by-products including silver and cadmium[3].
Bhilwara is known as '*Textile City of India*', is a famous industrial town in Rajasthan. Located in the western part of Rajasthan, Bhilwara is well connected with all major cities in India. Bhilwara emerged as India's largest manufacturer of suiting's, fabrics and yarn[4].

The safe and efficient movement of the people and goods is dependent on traffic flow, which is directly connected to the traffic characteristics .The three main parameters of a traffic flow are volume, speed and density[5]. There are four main methods of Traffic Volume namely Manual Count Method, Automatic Method, Combination of Manual and Automatic Method and Photographic Methods. For better understanding of the current state of traffic flow on the highway, traffic surveys are organized. With the help of data collection, an attempt was made to understand traffic patterns during different time periods[5]. Traffic control on that highway is also dependent on traffic flow characteristics. Therefore, the results of the current study help in controlling traffic on tampering and some measures also suggest measures to improve traffic safety in national highway.

Index Terms - Volume, Demand, Road Capacity, Traffic Volume, PCU, Traffic Control

1. INTRODUCTION

Transportation engineering is the application of technology and scientific principles to the planning, functional design, operation and management of facilities for any mode of transportation in order to provide for the safe, efficient, rapid, comfortable, convenient, economical, and environmentally compatible movement of people and goods. The planning aspects of transportation engineering relate to elements of urban planning, and involve technical forecasting decisions and political factors. Passenger trips are the focus of transportation engineering because they often represent the peak of demand on any transportation system.
Operations and management involve traffic engineering, so that vehicles move smoothly on the road or track. Other techniques include signs, signals, markings, and tolling. Newer technologies involve intelligent transportation systems, including advanced traveler information systems (such as informatory sign, warning sign and regulatory sign), advanced traffic control systems, and vehicle infrastructure integration. Human factors are an aspect of transportation engineering, particularly concerning driver-vehicle interface and user interface of road signs, signals, and markings[6].
While designing any structure it is necessary to calculate the loads coming on it to determine the reinforcement to be provided for safe functioning of the structure. In transportation volume serves the identical purpose[7]. For planning, designing, scheduling, safe operation and development of transportation system the prime requisite is traffic volume.

1.1 Traffic Volume

The number of vehicles moving in a specified direction on a road way that pass a given point during a specified unit of time is called traffic volume[7]. Traffic volume researches are performed to determine the count, movement and classification of roadway vehicles at a given location so as to become aware of critical time flow periods, the influence of heavy vehicles or pedestrians on vehicular traffic flow or traffic volume trends.

1.2 Traffic Density

The number of vehicles occupying a unit length of a roadway at a given instant is called traffic density[8].

1.3 Theoretical Capacity

The maximum number of passenger's cars that can pass a given point on roadway during one hour under the most ideal road and traffic condition is called basic capacity it is sometimes called theoretical capacity[8].

1.4 Practical Capacity

The maximum number of vehicles that can pass a given point on a roadway during one hour without imposing any restrictions to the driver's freedom for driving the vehicles underprivileged road and traffic condition is called practical capacity[8].

2.0 METHODOLOGY

Firstly, traffic volume at study of national highway will be determined. After that, traffic safety measures along national highways will be discussed[9]. We have adapted Manual Count Method for counting traffic volume of NH 79. In this method, One observer group will record the count of the number of vehicles passing through NH 79 (BHILWARA TO CHITTORGARH) in each fifteen-minute interval of time and the other observer group will count the number of vehicles passing through NH79 (CHITTORGARH TO BHILWARA) in each fifteen-minute interval of time. Data is collected and recorded on data sheets, data can be recorded with tick mark on a pre prepared field form. A stopwatch is used to measures desired count interval.

Manual counting method

i) Direct Method.

ii) Indirect Method.

Direct Method: - By this method data can be collected immediately and we can obtain the traffic volume as well as vehicle classification. We will be using this method during off peak hours[7].

Indirect Method: - In this method the traffic volume data is collected by the video camera. Video is captured & after that detail collected by rewinding. At morning and evening time, we will be using this method because of high traffic flow[7].

After calculating the traffic volume data of the selected national highway stretch the data will be used for implementing various safety measures by suggesting the means to reduce the congestion on the highway. Moreover, various means to enable the smooth movement of vehicles and pedestrians on the road could be suggested to avoid the delay in travel time. Thus, limits the possible conflicts within the traffic.

3.0 OBJECTIVES

The main objective of the traffic study is as follows:

1. To find out various traffic volumes on selected sections of National Highway 79.
2. To find out the traffic flow pattern on weekdays and weekends for 15 minute interval variation.
3. To minimize the traffic congestion through different ideas and provide more on-road security features of national highway 79.
4. To decide about the measures for the safety of moving Traffic.

Location: We have chosen the location National Highway-79 from Bhilwara to Chittorgarh and Chittorgarh to Bhilwara in front of Mewar University.

- By standing the side of the road different vehicles were counted by group members.
- We have selected one member who was in charge of time, he commanded us when we have to Stop and Start our time watch.

Date: Data for volume study was collected on 29 March 2019.It was Friday and it was a week day.
Time: Time of data collection for volume study was divided in four times and the time interval is 15 minutes.
Weather Condition: It was Sunny day.
Observation: Classified vehicle counts
Duration: 15 minutes (short count)
Equipment: Mobile Camera (Video recorder), Stopwatch, rough copy

Traffic Characteristics: The different type of vehicles presents at NH 79 in front of Mewar University:

- Motorized two wheelers which include bikes and scooters.
- Motorized three wheelers which include auto rickshaws and tempos.
- Four wheelers which includes cars and jeeps.
- Light commercial vehicles (L.C.V) which includes small vans and four wheelers.
- Six Wheeler
- Heavy Vehicle
- Extra Heavy Vehicle

Data Collection and Analysis

The data is collected after carefully studying the location area. The study was conducted on a sunny day when the pavement was dry and no repairing was going at that time.

Method used for volume study

We have adapted Manual Count Method for counting traffic volume of NH 79. In this method, One observer group will record the count of the number of vehicles passing through NH 79 (BHILWARA TO CHITTORGARH) in each fifteen-minute interval of time and the other observer group will count the number of vehicles passing through NH79 (CHITTORGARH TO BHILWARA) in each fifteen-minute interval of time[9]. Data is collected and recorded on data sheets, data can be recorded with tick mark on a pre prepared field form. A stopwatch is used to measures desired count interval. From the applied manual method these are the following data were observed:

Table 1: PCU factors used for traffic signal design according to IRC

Vehicle	PCU Factors
Car	1
3-wheeler	1
2-wheeler	0.5
Bus/Truck	3
Rickshaw	1.5
Cycle	0.5
Tractor	4.5
LCV	1.5

Table 2: No. of vehicle passing through NH-79 (Bhilwara to Chittorgarh)

BHILWARA TO CHITTORGARH 26/03/2019 Friday Timing (10:00 AM to 11:45 AM)					
Time		10:00 to 11:15 AM	10:30 to 10:45 AM	11:00 to 11:15 AM	11:30 to 11:45 AM
No of vehicles	Two Wheelers	56	54	60	29
	Three Wheelers	9	13	3	11
	Four Wheeler	33	22	33	47
	Six Wheeler	18	15	12	3
	Heavy Vehicle	14	21	11	51
	Extra Heavy Vehicle	25	14	21	21

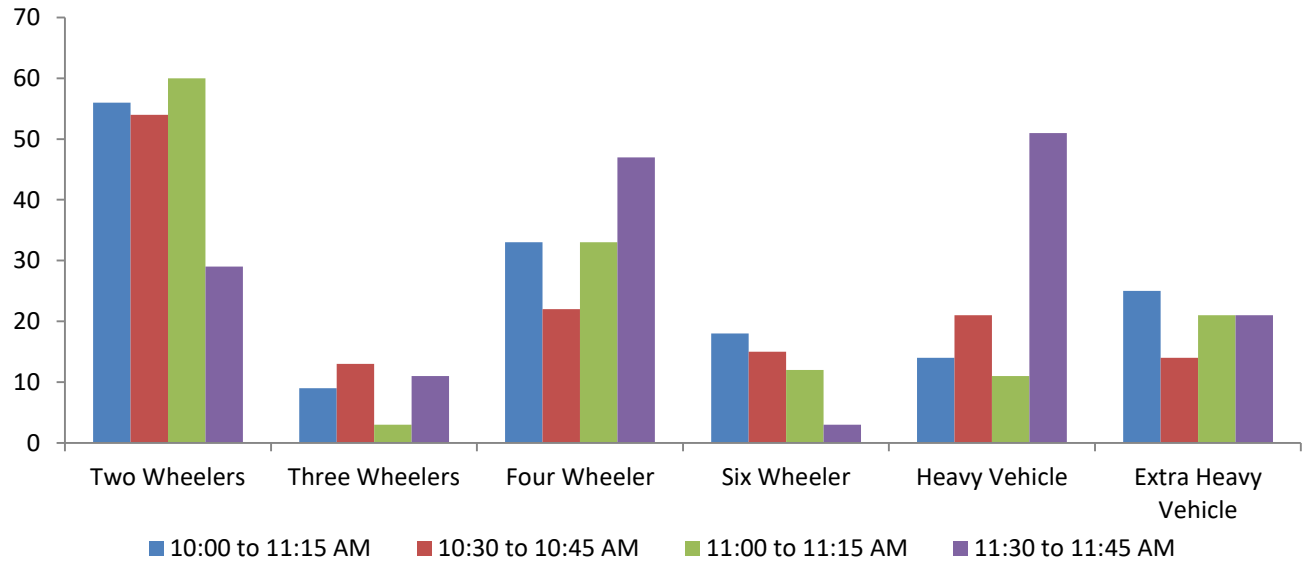

Fig- Graph between No of Vehicles Vs Time (BHL TO COR)

Table 3: No. of vehicle passing through NH-79 (Bhilwara to Chittorgarh)

CHITTORGARH TO BHILWARA 26/03/2019 Friday Timing (10:00 AM to 11:45 AM)					
Time		10:00 to 11:15 AM	10:30 to 10:45 AM	11:00 to 11:15 AM	11:30 to 11:45 AM
No of vehicles	Two Wheelers	47	43	33	41
	Three Wheelers	7	5	6	7
	Four Wheeler	29	27	35	31
	Six Wheeler	11	16	10	12
	Heavy Vehicle	13	22	14	16
	Extra Heavy Vehicle	27	23	13	17

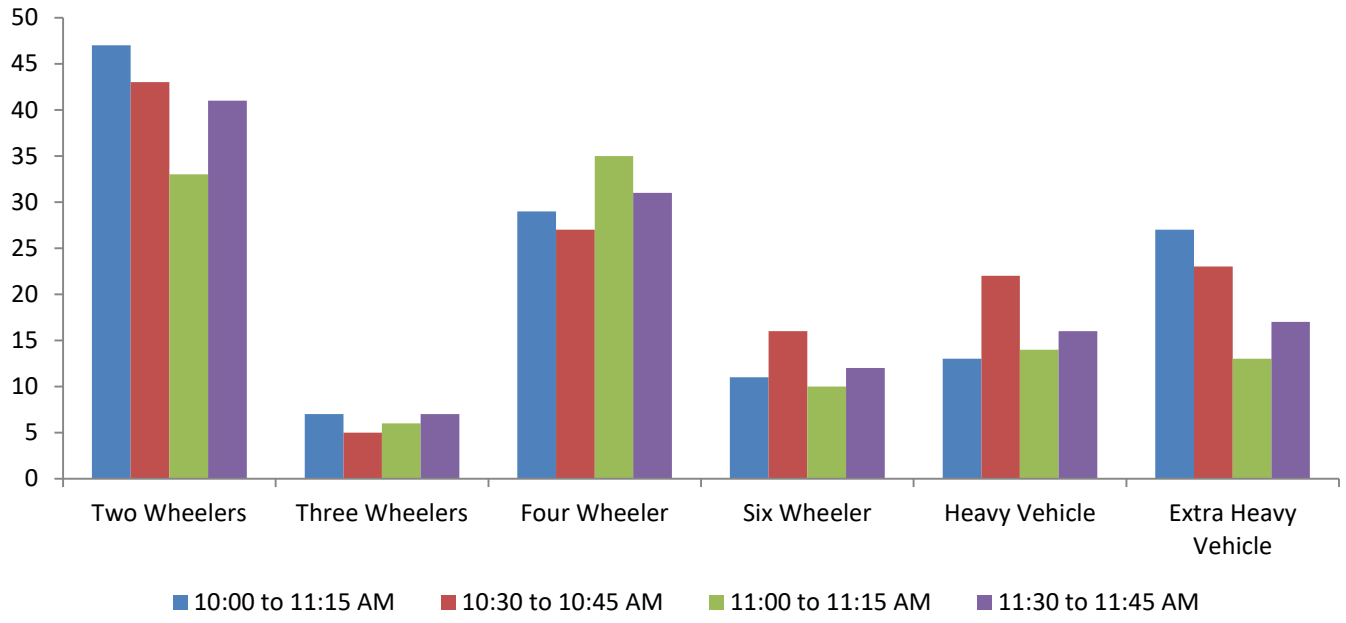

Fig- Graph between No of Vehicles Vs Time (COR TO BHL)

Table 4: No. of vehicle passing through NH-79 (Bhilwara to Chittorgarh)

Bhilwara to Chittorgarh 26/03/2019 Friday Timing (06:00 PM to 07:45 PM)					
Time		6:00 to 6:15 pm	6:30 to 6:45 pm	7:00 to 7:15 pm	7:30 to 7:45 pm
No of vehicles	Two Wheelers	46	38	27	17
	Three Wheelers	9	15	12	17
	Four Wheeler	47	49	41	35
	Six Wheeler	4	2	6	3
	Heavy Vehicle	35	42	51	56
	Extra Heavy Vehicle	28	29	35	39

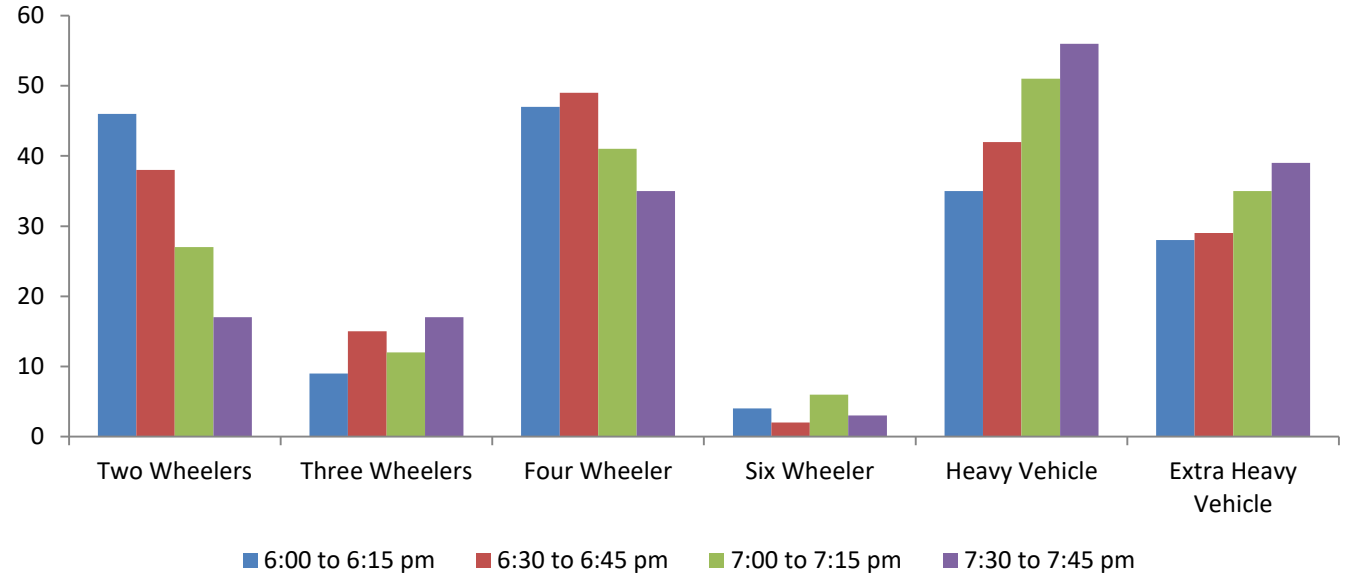

Fig- Graph between No of Vehicles VS Time (BHL TO COR)

Table 5: No. of vehicle passing through NH-79 (Chittorgarh to Bhilwara)

Chittorgarh to Bhilwara 26/03/2019 Friday Timing (06:00 PM to 07:45 PM)					
Time		6:00 to 6:15 pm	6:30 to 6:45 pm	7:00 to 7:15 pm	7:30 to 7:45 pm
No of vehicles	Two Wheelers	34	37	31	29
	Three Wheelers	6	9	10	11
	Four Wheeler	32	36	41	47
	Six Wheeler	2	4	5	3
	Heavy Vehicle	33	35	43	51
	Extra Heavy Vehicle	22	28	34	21

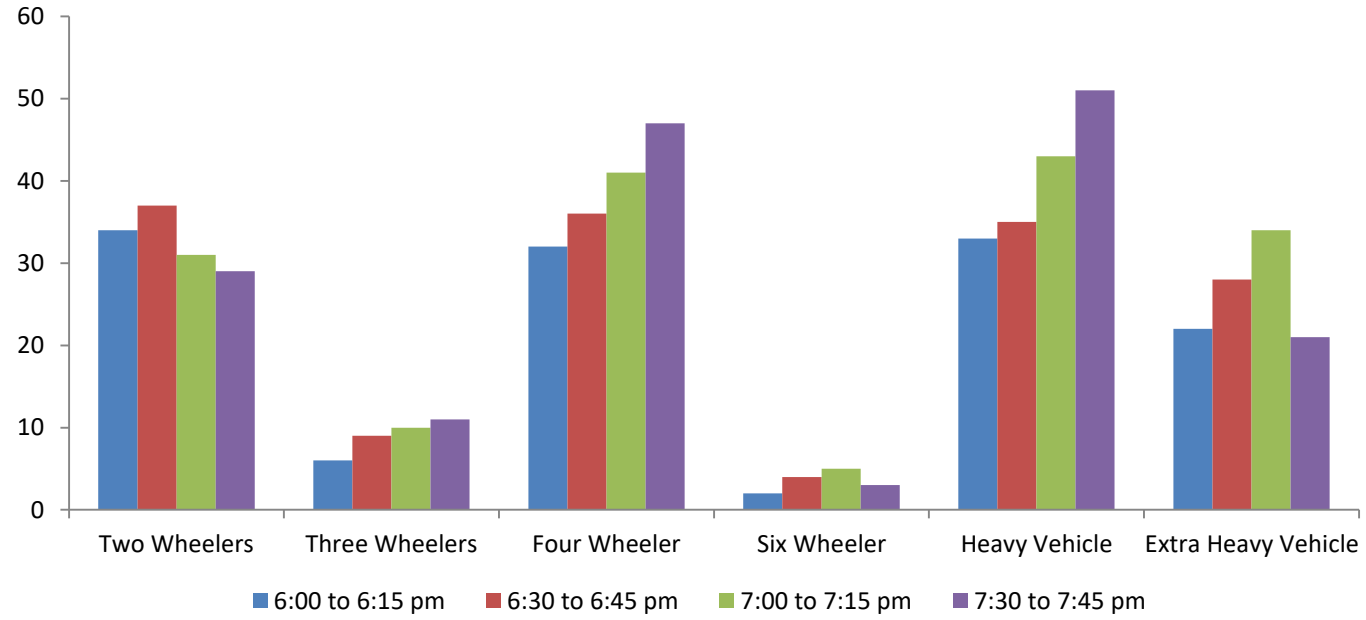

Fig- Graph between No of Vehicles Vs Time (COR TO BHL)

Table 6: Comparison of Road Traffic Between BHL TO COR and COR to BHL NH-79

Comparison of BHLTO COR and COR TO BHL NH-79, 26/03/2019 Friday Timing (10:00 AM to 11:45 AM)									
		BHL to COR				COR to BHL			
Time		10:00 to 11:15 AM	10:30 to 10:45 AM	11:00 to 11:15 AM	11:30 to 11:45 AM	10:00 to 11:15 AM	10:30 to 10:45 AM	11:00 to 11:15 AM	11:30 to 11:45 AM
No of vehicles	Two Wheelers	56	54	60	29	47	43	33	41
	Three Wheelers	9	13	3	11	7	5	6	7
	Four Wheeler	33	22	33	47	29	27	35	31
	Six Wheeler	18	15	12	3	11	16	10	12
	Heavy Vehicle	14	21	11	51	13	22	14	16
	Extra Heavy Vehicle	25	14	21	21	27	23	13	17

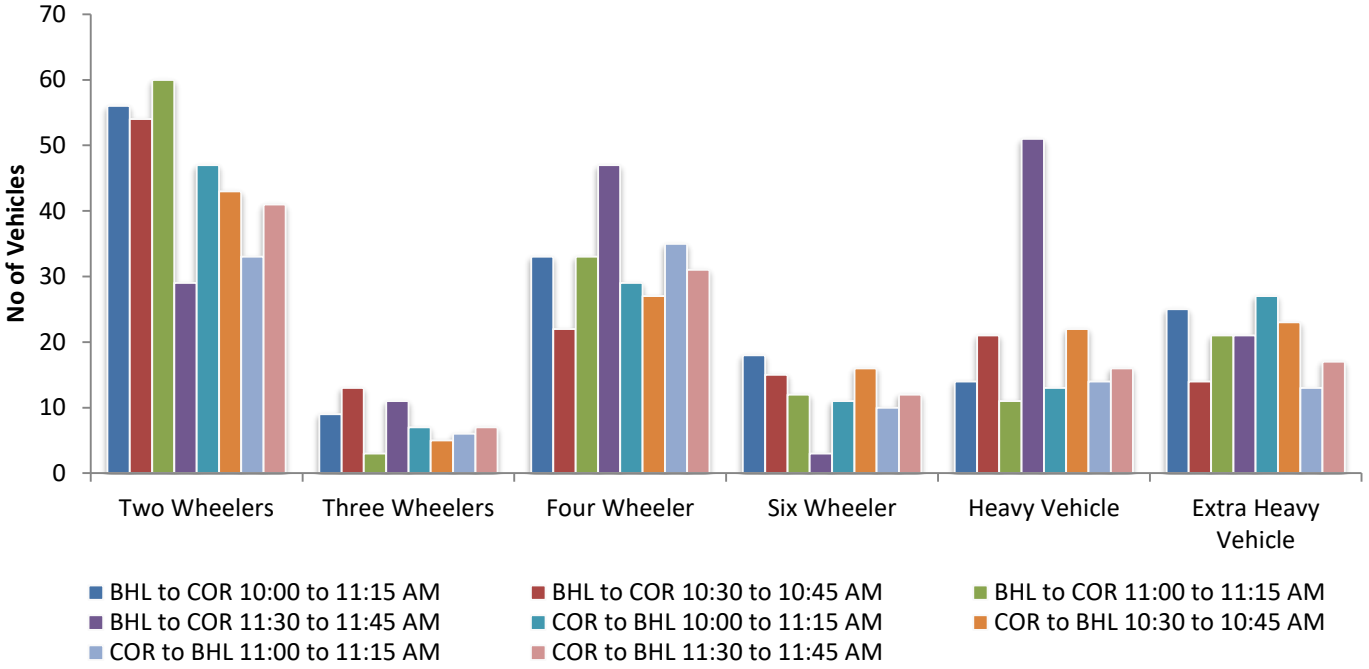

Fig- Graph between No of Vehicles Vs Time (BHL to COR and COR to BHL)

Table 7: Comparison of Road Traffic Between BHL TO COR and COR TO BHL on NH-79

Comparison of BHL TO COR and COR TO BHL NH-79, 26/03/2019 Friday Timing (06:00 PM to 07:45 PM)									
		BHLTO COR				COR TO BHL			
		6:00 to 6:15 pm	6:30 to 6:45 pm	7:00 to 7:15 pm	7:30 to 7:45 pm	6:00 to 6:15 pm	6:30 to 6:45 pm	7:00 to 7:15 pm	7:30 to 7:45 pm
No of vehicles	Two Wheelers	46	38	27	17	34	37	31	29
	Three Wheelers	9	15	12	17	6	9	10	11
	Four Wheeler	47	49	41	35	32	36	41	47
	Six Wheeler	4	2	6	3	2	4	5	3
	Heavy Vehicle	35	42	51	56	33	35	43	51
	Extra Heavy Vehicle	28	29	35	39	22	28	34	21

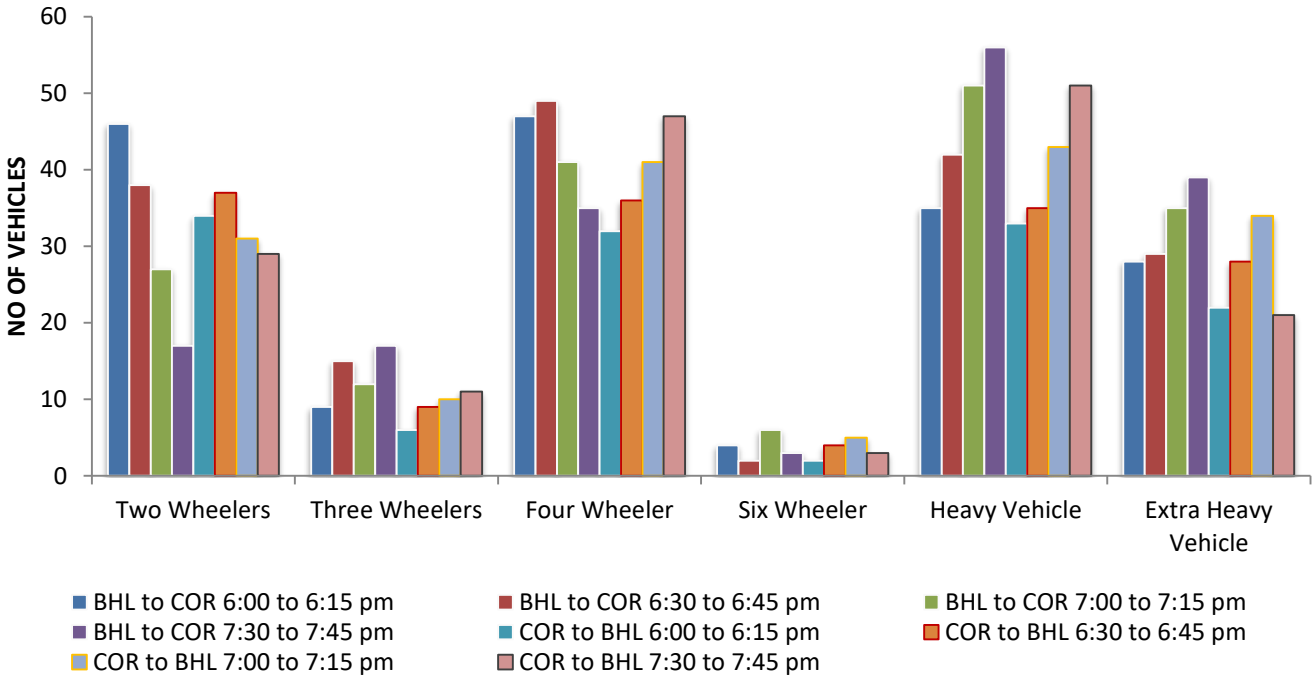

Fig- Graph between No of Vehicles Vs Time (BHL to COR and COR to BHL)

Table 8: PCU Factor for NH 79 BHL to COR in Morning Time

Types of Vehicles	No of Vehicles	PCU	Total PCU
Two Wheelers	199	99.5=100	**949**
Three Wheelers	36	36	
Four Wheeler	135	135	
Six Wheeler	48	144	
Heavy Vehicle	97	291	
Extra Heavy Vehicle	81	243	

Table 9: PCU Factor for NH 79 BHL to COR in Evening Time

Types of Vehicles	No of Vehicles	PCU	Total PCU
Two Wheelers	128	64	**1297**
Three Wheelers	53	53	
Four Wheeler	172	172	
Six Wheeler	15	45	
Heavy Vehicle	184	552	
Extra Heavy Vehicle	131	393	

Table 10: PCU Factor for NH 79 COR TO BHL in Morning Time

TYPES OF VEHICLES	No of Vehicles	PCU	Total PCU
Two Wheelers	164	82	**811**
Three Wheelers	25	25	
Four Wheeler	122	122	
Six Wheeler	49	147	
Heavy Vehicle	65	195	
Extra Heavy Vehicle	80	240	

Table 11: PCU Factor for NH 79 COR TO BHL in Evening Time

TYPES OF VEHICLES	No of Vehicles	PCU	Total PCU
Two Wheelers	131	65.5=66	**1101**
Three Wheelers	36	36	
Four Wheeler	156	156	
Six Wheeler	14	42	
Heavy Vehicle	162	486	
Extra Heavy Vehicle	105	315	

CONCLUSION

It can be concluded that vehicle composition most of the vehicle in the traffic stream were Heavy and extra heavy vehicles. BHL to COR, PCU Factor is higher than COR to BHL, PCU factor. After volume study as we observed that more traffic is in the peak hours i.e. in morning and evening.

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ABBREVIATIONS

ACRONYM	FULL FORM
BHL	Bhilwara
COR	Chittorgarh
MT	Metric Tonnes
NH	National Highway
PCU	Passenger Car Unit

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A Study on Alluvial Soil Stabilization using Bitumen Emulsion

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***Abstract*: The main objective of this study is to improve the properties of the Alluvial soil by adding bitumen emulsion. An attempt has been made to use emulsion for improving the strength of Alluvial soil expressed in terms of CBR values which may prove to be economical. In this study, the whole laboratory work revolves around the basic properties of soil and its strength in terms of CBR. A little cement added to provide better soil strength. It is observed that excellent soil strength results by using cationic bitumen emulsion (CMS) with little quantity of cement used as filler. The appropriate mixing conditions for Alluvial soil with CMS Bitumen emulsion have been first attempted. This is followed by deciding four particular material conditions to show the variation in dry density and CBR value to achieve the best possible strength properties of Alluvial soil. The most important part of a road pavement is subgrade soil and its strength. If strength of soil is poor, then stabilization is normally needed. Subgrade is sometimes stabilized or replaced with stronger soil material so as to improve the strength. Such stabilization is also suitable when the available subgrade is made up of weak soil. Increase in sub grade strength may lead to economy in the structural thicknesses of a pavement. Cement, fly ash, lime, fibers etc. are very commonly used for soil stabilization.**

Keywords: Alluvial soil, CBR, Bitumen Stabilization, bitumen emulsion

1. INTRODUCTION

Soil is the most abundant construction materials of nature. Just about all kind of construction is based with or upon the soil. Long term performance of pavement structures is altogether affected by the strength and durability of the subgrade soils. In-situ sub-grades frequently don't provide the support required to achieve acceptable performance under the traffic loading with increasing environmental demands. Despite the fact that stabilization is a well-known option for improving soil engineering properties yet the properties determined from stabilization shift broadly because of heterogeneity in soil creation, contrasts in micro and macro structure among soils, heterogeneity of geologic stores, and because of chemical contrasts in concoction interactions between the soil and utilized stabilizer.

1.2 Objective of work

The main objective of my study work is to improve the properties of the Alluvial soil by adding little bit cement as filler and bitumen emulsion as stabilizing agent. An attempt has been made to use emulsion for improving the strength and geotechnical properties of Alluvial soil. Very mostly, use of use of bitumen emulsion is environmentally accepted. The experiments which to be conducted are Specific Gravity of the soil sample, Grain size Distribution of soil sample and liquid limit plastic limit test to identify the material and Standard Proctor test to obtain maximum dry density and optimum moisture content of soil sample, CBR test of soil sample mixing with emulsion and cement. So the main objective is to maximize the CBR value by checking some conditions to increase the CBR value of soil subgrade.

2. STUDY AREA

Srinagar is the largest city and the summer capital of the Indian union territory of Jammu and Kashmir. It lies in the Kashmir Valley on the banks of the Jhelum River, a tributary of the Indus, and Dal and Anchar lakes.

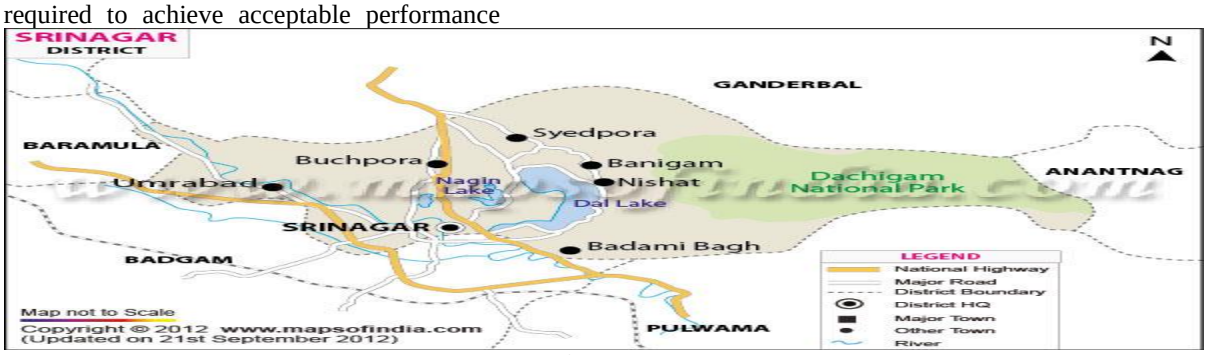

Fig 1: Map of Srinagar

3. MATERIAL AND METHODOLOGY

In my work locally available in Srinagar Alluvial soil is taken as experimenting material. Medium setting emulsion (MS) is used as stabilizing agent in this particular study. Bitumen sand stabilization is an effective process as bitumen makes soil stronger and improves resistance capacity against water and frost. Actually bitumen is a very effective agent for sand stabilization but for soil stabilization it is being very costly. There is no any particularly following process or method for soil bitumen stabilization and most importantly there is no any code for bitumen soil stabilization in Indian Standard. This experiment study deals with some specific tests like Modified Compaction Test, CBR Test and the main

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objective is to optimize the strength of Alluvial soil or improve the dry density property in this project also attempt was made to maximize optimizing stability changing the mixing process with bitumen emulsion.

Selection of material and methodology those are the first criteria for any type of experimental investigation. To know the soil physical properties following tests are conducted like specific gravity test, grain size distribution test by sieve analysis and plastic limit and liquid limit test. After that the important part is to choose mixing procedure and the cases or different conditions for conducting the next tests. To determine the maximum dry density of the material modified proctor test has been conducted. But the actual goal is to increase the strength. So CBR test are conducted in different cases and conditions and make a comparative experimental study. So the methodology is how to achieve maximum bearing capacity or maximize the CBR value.

4. RESULTS

Table 1: Specific gravity test result

Sample No	M1 (gm)	M2 (gm)	M3 (gm)	M4 (gm)	Sp. Gravity
1.	114.67	164.67	383.56	351.87	2.73
2.	113.76	163.76	384.41	352.86	2.71
3.	115.34	165.34	385.69	353.94	2.74

Here soil material is tested three times. And the average specific gravity value comes 2.726. But here no temperature correction is done. This test have been done in room temperature nearly 25*C.

Liquid limit and Plastic limit Test Results

From these experimental results a proper idea about the type of soil has been found.

Liquid Limit (WL): 28.91%

Plastic Limit (WP): 21.67%

Plasticity Index (IP): 7.24%

Grain Size distribution

Various physical and engineering properties with the help of which soil can be properly identified are called index properties

Here 2000 gm of sample soil was taken and dried in oven for 12 hours. Mostly used test for grain size distribution analysis is sieve analysis. Eleven sieves were used. And the results from sieve analysis of the soil are plotted on a semi-log graph with particle diameter or the sieve size in X axis and percentage finer in Y axis.

Table 2.: Grain Size distribution result

Sieve No. #	Sieve size	Mass of soil retained in each sieve (gm)	Percent retained (%)	Cumulative retained (%)	Percent finer (%)
1/2 Inch	12.5 mm	0	-----	0	100
3/8 Inch	9.5 mm	99.1	4.95	4.95	95.05
1/4 Inch	6.3 mm	318.8	15.94	20.84	79.16
#4	4.75 mm	397.5	19.88	40.77	59.33
#8	2.36 mm	510.2	25.51	66.28	33.72
#16	1.18 mm	255.1	12.71	79.03	20.97
#30	600 micron	166.2	8.31	87.34	12.66
#50	300 micron	132.1	6.61	93.95	6.05
#80	150 micron	48.7	2.44	96.39	3.61
Pan	-----	72.3	3.6	100	0

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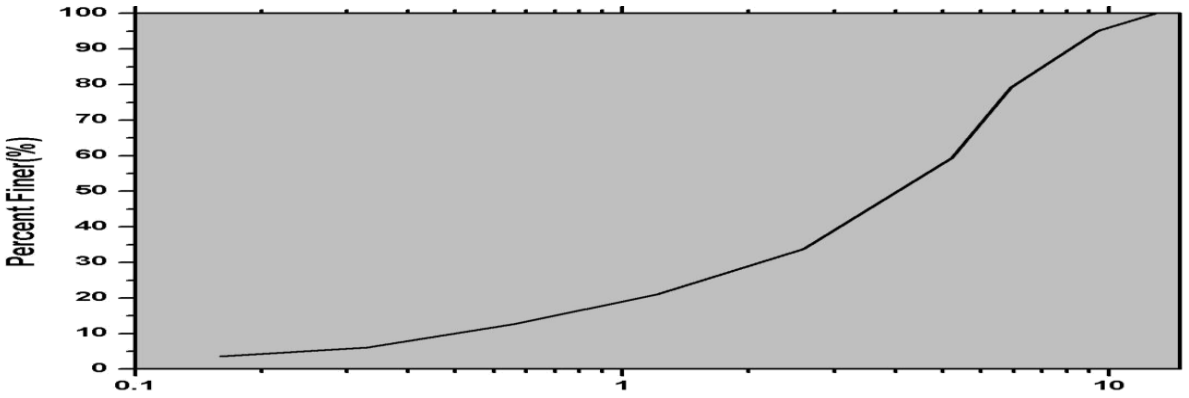


Graph 1 : Grain size distribution graph

Compaction Test Results

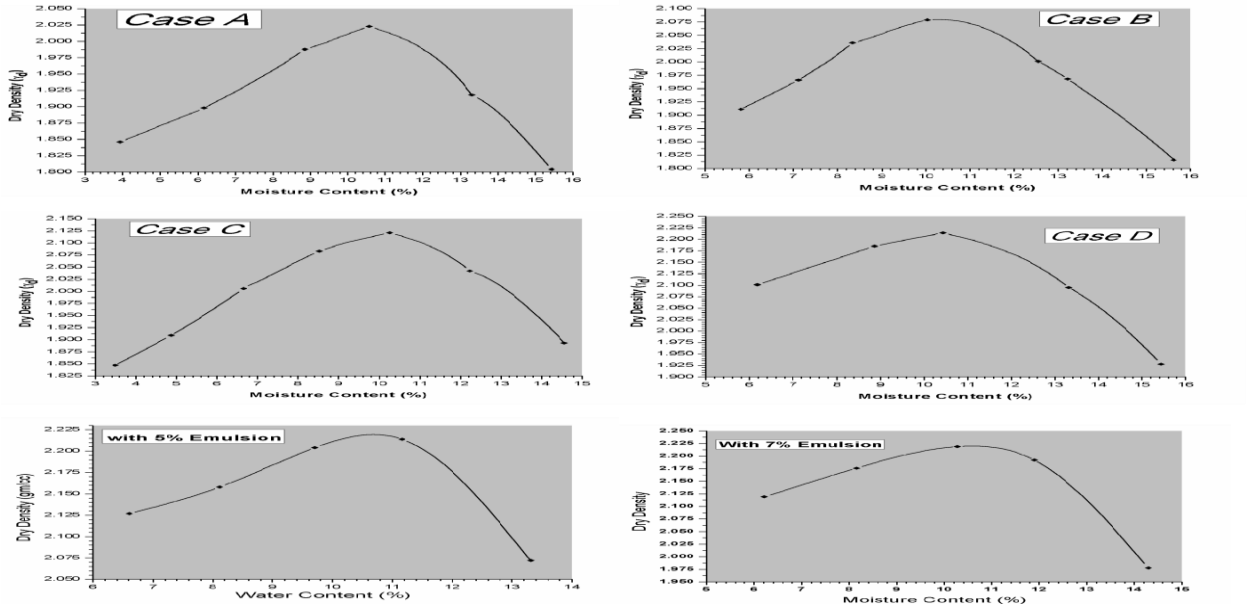
From this test, maximum dry density of the specimen was found to be 2.026gm./cc and OMC of 10.52%.The common matter on both works is to provide the optimum value on bitumen content percentage 3% to 4%. After testing in different percentage 3%, 5% and 7% it is seen that maximum dry density of this soil is not so much effectively changed. As it is used as a stabilizing agent to being applicable it should be economical. So, 3% emulsion is taken in this particular study. As I previously said very few works had done on bitumen soil stabilization. Only bitumen sand stabilization IS code is available. So, how to mix the Alluvial soil with emulsion is the main problem. Therefore four particular conditions for testing are used here to check the variation of maximum dry density of this Alluvial soil mixing with emulsion.

Condition I: Normal available tested soil is used for testing

Condition II : Normal available soil tested with 3% MS emulsion added

Condition III: Normal available soil tested with 3% MS emulsion and 2% cement added

Condition IV : Normal available soils tested mixing with 3% of emulsion and 2% of cement added and wait 5 hour before testing. In this four particular condition modified proctor test is performed and plotted with moisture content percentage in X axis and corresponding dry density value in Y axis. From carves of graphs plotted, there is a crown point where the value of dry densityis maximum. Here corresponding moisture content is optimum moisture content. In this four particular conditions tested modified proctor graph listed below. Those graphs strictly indicate that Case D gives the optimum value.



Graph 2: Modified proctor test graphs

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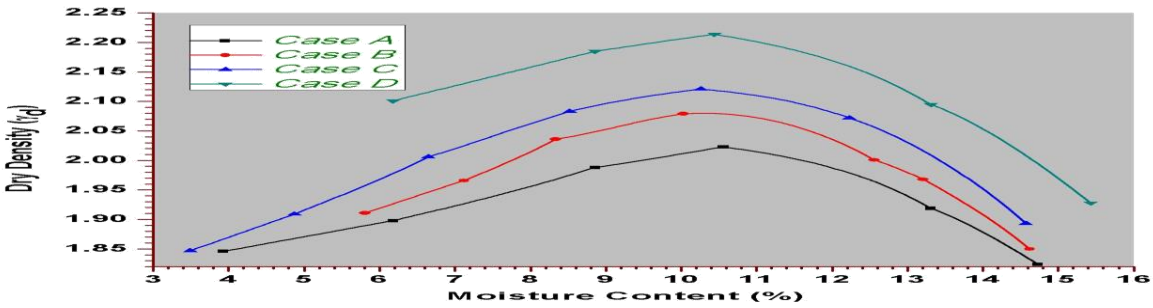
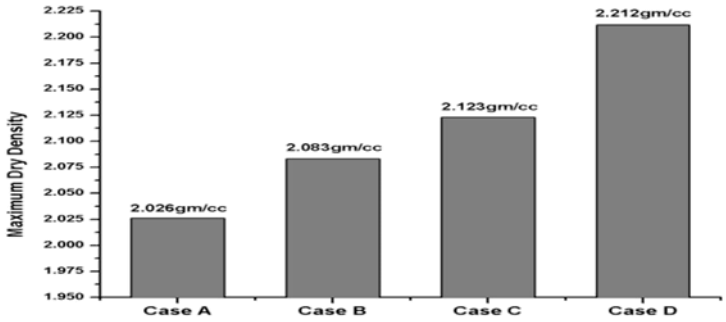


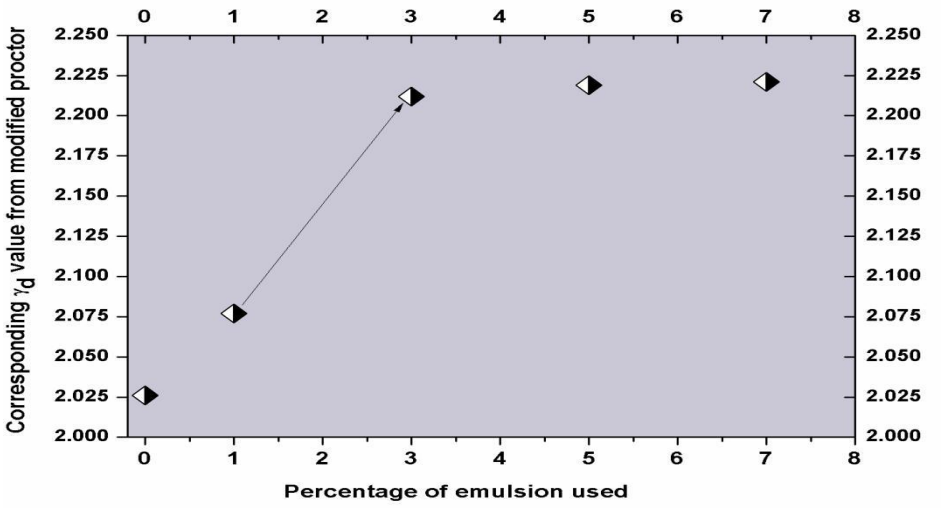
Graph 3: Modified proctor test comparison graph

From the previous modified proctor result it is strictly showing how the dry density value for the same material is going to increase from case A to case D, which is the change of maximum dry density value from 2.026 gm/cc up to 2.212 gm/cc. Little bit of fluctuation in optimum moisture content value in different cases. This Yd value is a very important physical property in case of stability of subgrade soil. Bellow the variation of maximum dry density in those special cases are shown bar wise



Graph 4: Variation of maximum dry density value

So again modified proctor test is done varying the bitumen content 1%, 3%, 5% and 7% following mixing procedure D. This result gives us a clear idea about used 3% bitumen content.



Graph 5: Variation of MDD with emulsion quantity

Cbr Test Results

Penetration in mm are plotted in X axis and load expressed in kg with corresponding points are plotted in Y axis and prepare graph for different specimen. The CBR values at 2.5mm and 5.0mm penetrations are calculated for each specimen from the corresponding graphs which is shown below. Generally the CBR value at 2.5mm penetration is higher and this value is adopted.CBR is defined as the ratio of the test load to the standard load, expressed as percentage for a given penetration of the plunger. This value is expressed in percentage. Standard load of different penetration is discussed before. Here testing is done on three different testing condition on previously four cases. So total twelve number of CBR value is measured by moulding

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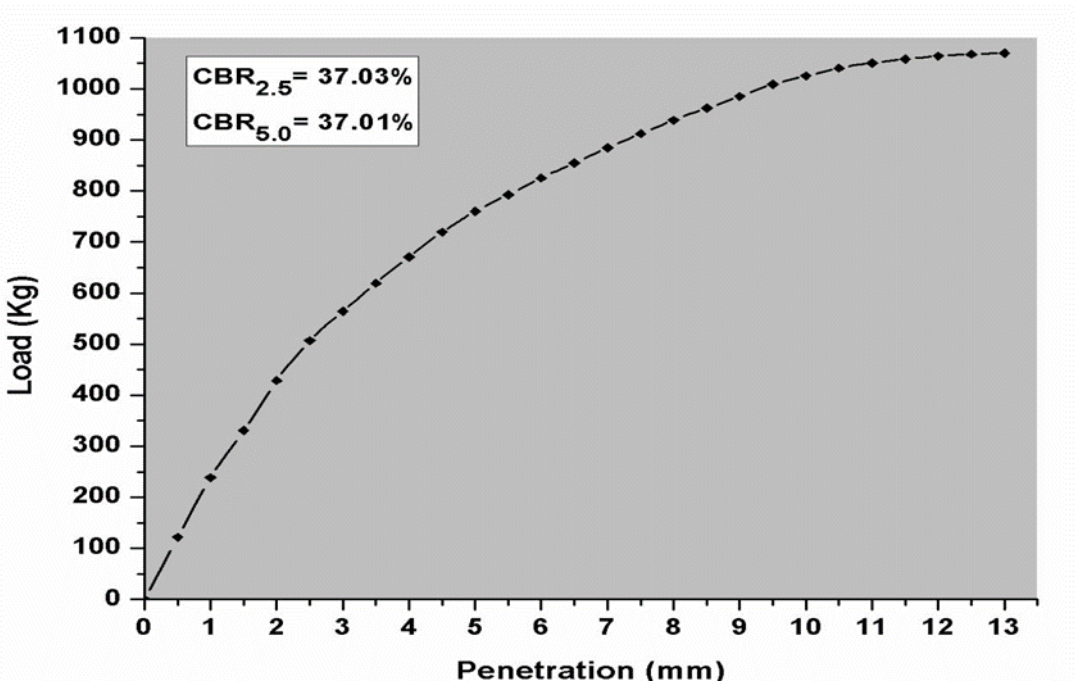
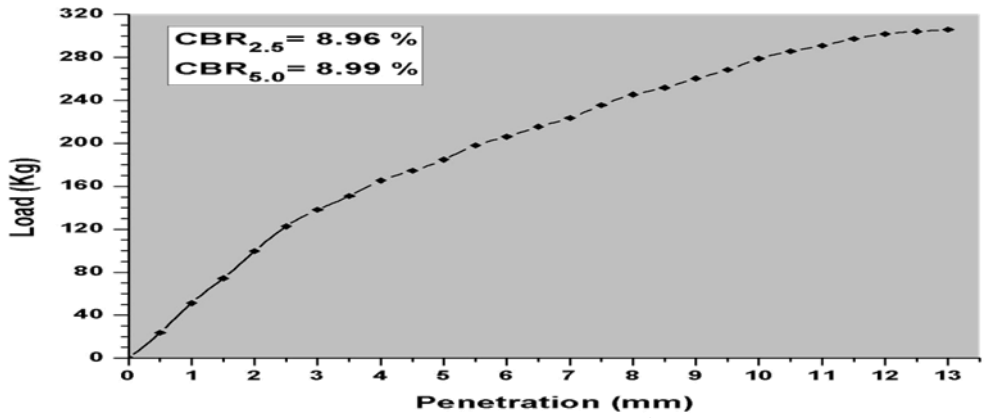
twelve different specimens, three different type of specimen for each case. The corresponding CBR value for each type of specimen is written on left above corner of each graph. In this comparative experimental study it is shown that how bitumen content and mixing procedure effect on CBR value of a particular soil. CBR value and the CBR graph is case wise shown below.

Case A:

Mould size: standard volume 2250 cc
Case A: Normal available tested soil is used for testing in this case Used proctor test result of Case A. Maximum Dry Density value: 2.026 gm./cc
Optimum Moisture Content: 10.52%
CBR test is done in three conditions. First one is in un-soaked condition, secondly in two days of soaking condition and lastly in four days of soaking condition. CBR value at 2.5mm penetration and 5mm penetration is calculated.



Graph 6 : CBR Test Result, Case A (Un-soaked)



Graph 7 : CBR Test Result, Case A (2 days of soaking)

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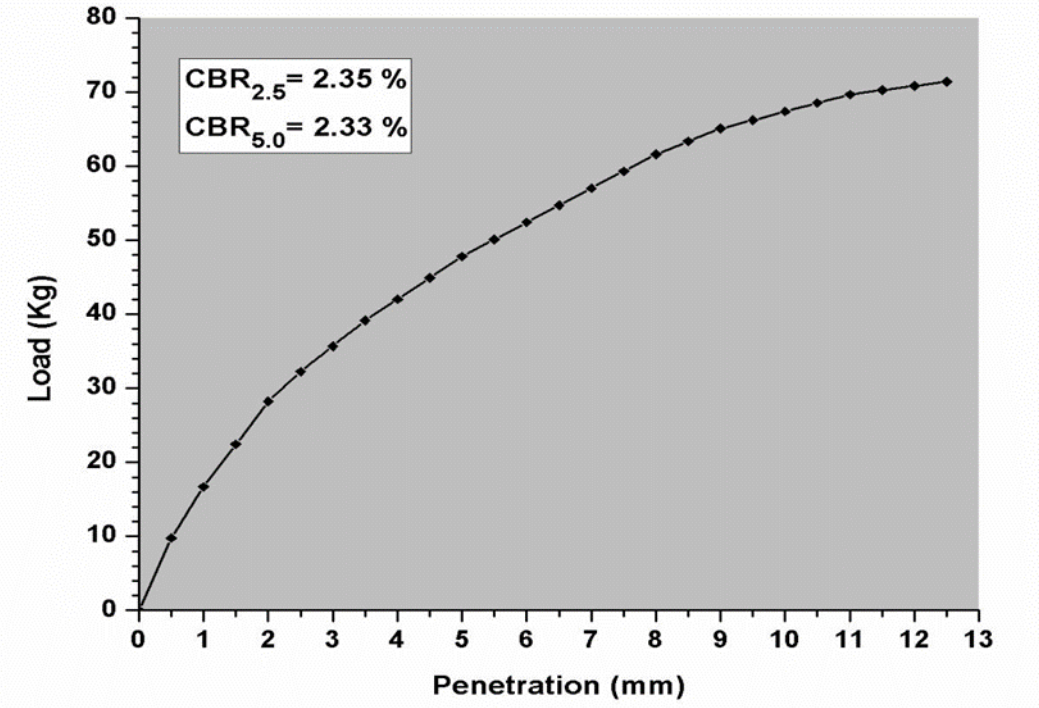
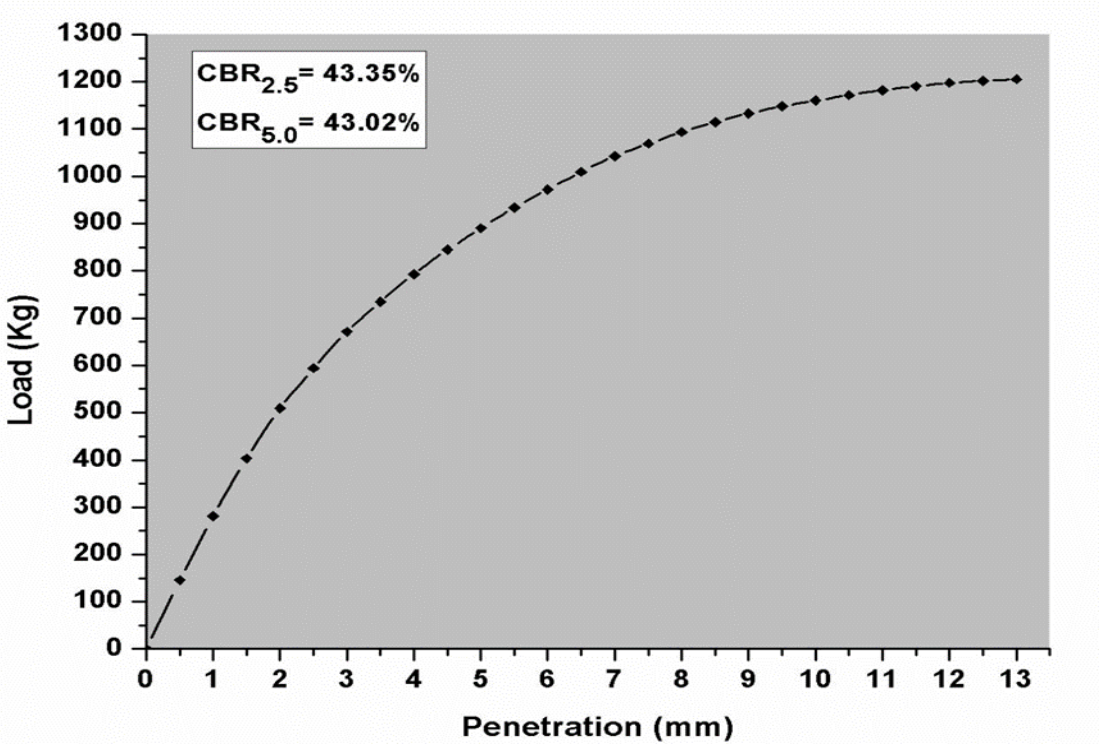


Graph 8: CBR Test Result, Case A (4 days of soaking)

Case B:
Mould size: standard volume 2250 cc
Case B: Normal available soil tested with 3% MS emulsion added Used proctor test result of Case B. Maximum Dry Density value: 2.083 gm./cc
Optimum Moisture Content: 10.45%
CBR test is done in three conditions. First one is in un-soaked condition, secondly in two days of soaking condition and lastly in four days of soaking condition. CBR value at 2.5mm penetration and 5mm penetration is calculated.



Graph 9: CBR Test Result, Case B (Un-soaked)

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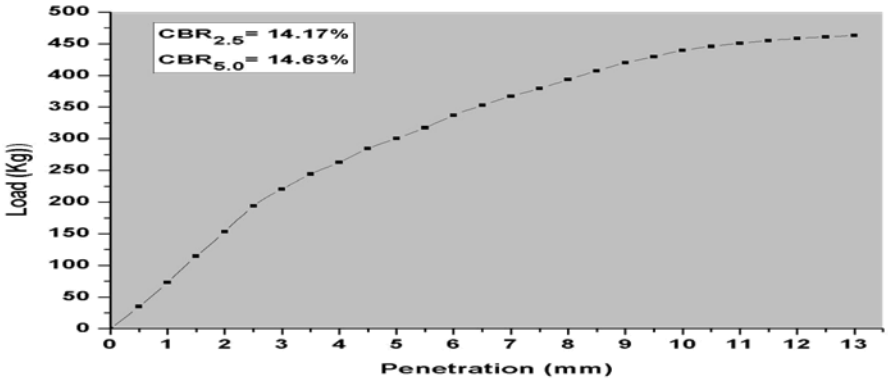
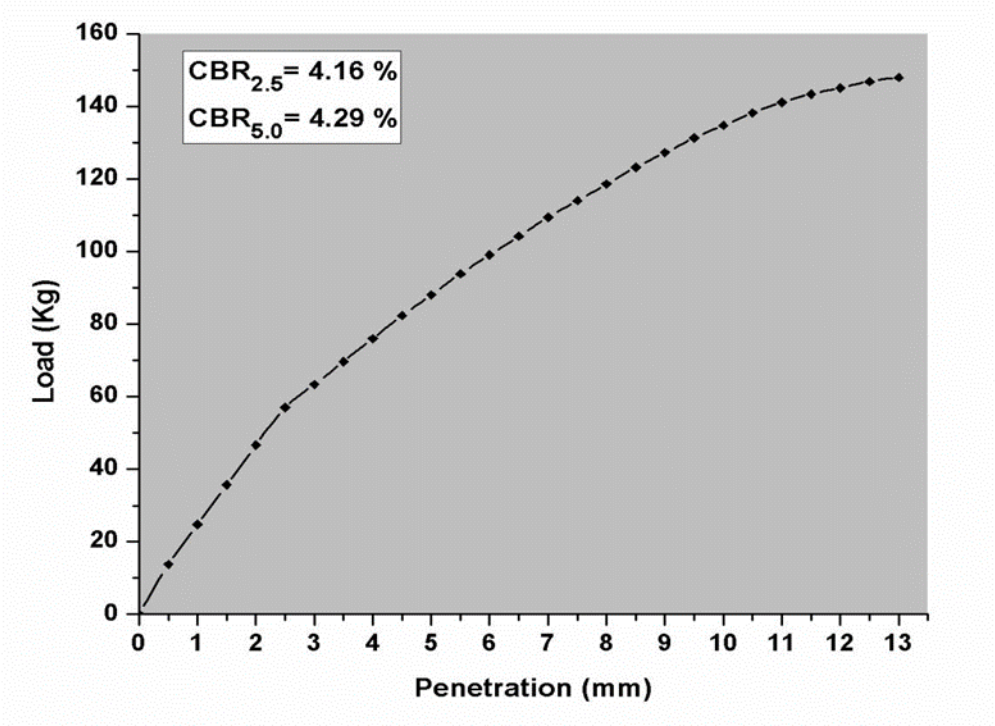


Graph 10: CBR Test Result, Case B (2 days of soaking)



Graph 11: CBR Test Result, Case B (4 days of soaking)

Case C:

Mould size: standard volume 2250 cc
Case C: Normal available soil tested with 3% MS emulsion and 2% OPC cement added
Used proctor test result of Case C.
Maximum Dry Density value: 2.123 gm./cc
Optimum Moisture Content: 10.25%
CBR test is done in three conditions. First one is in unsoaked condition, secondly in two days of soaking condition and lastly in four days of soaking condition. CBR value at 2.5mm penetration and 5mm penetration is calculated.

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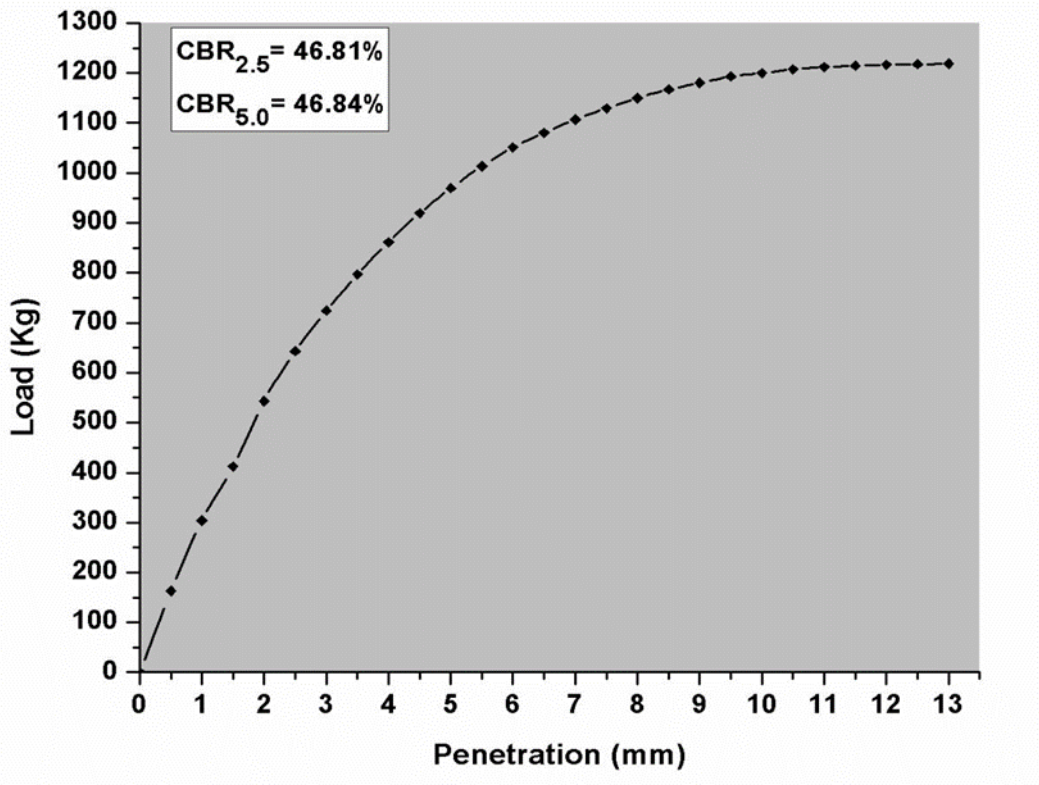
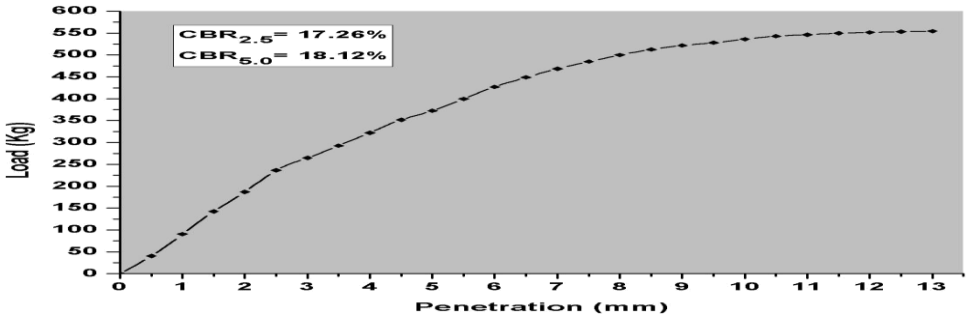
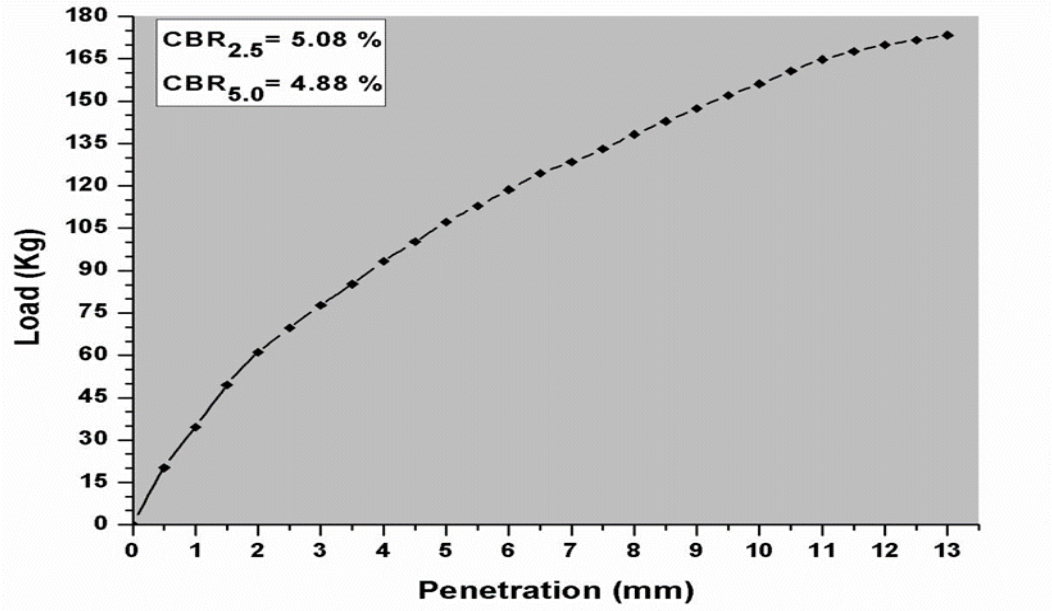


Graph 12: CBR Test Result, Case C (Un-soaked)



Graph 13: CBR Test Result, Case C (2 days of soaking)



Graph 14: CBR Test Result, Case C (4 days of soaking)

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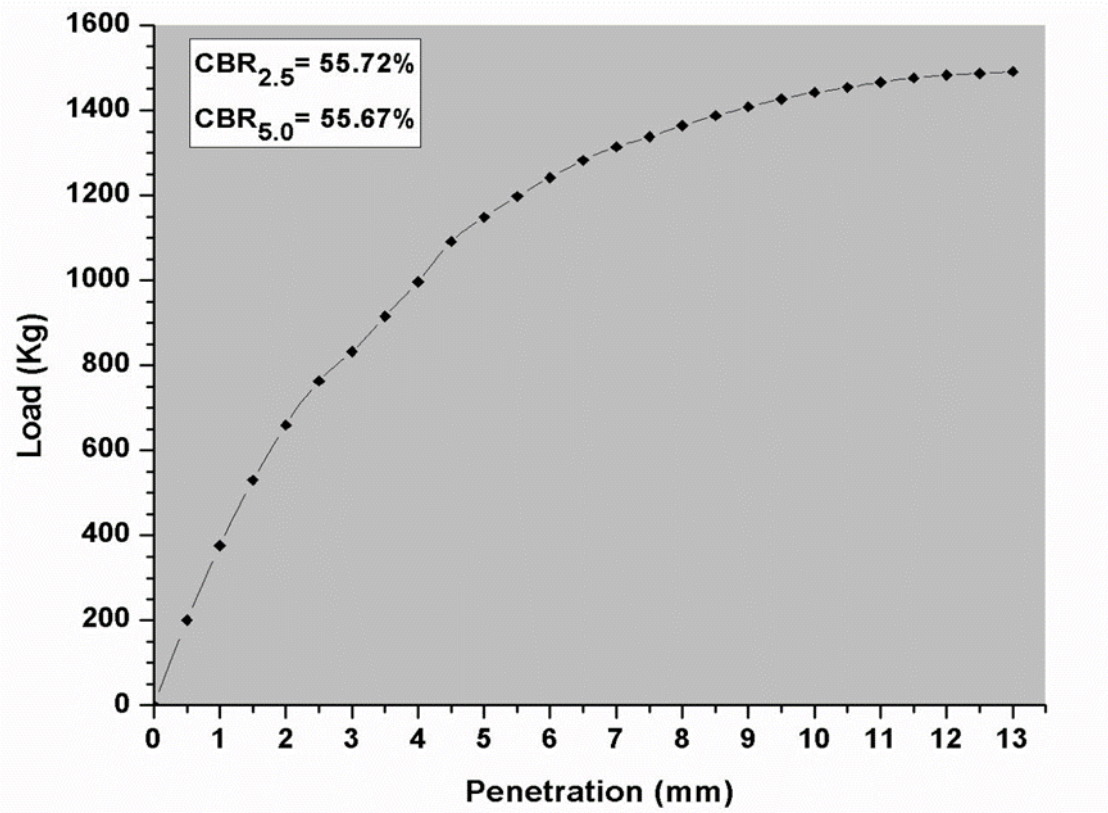
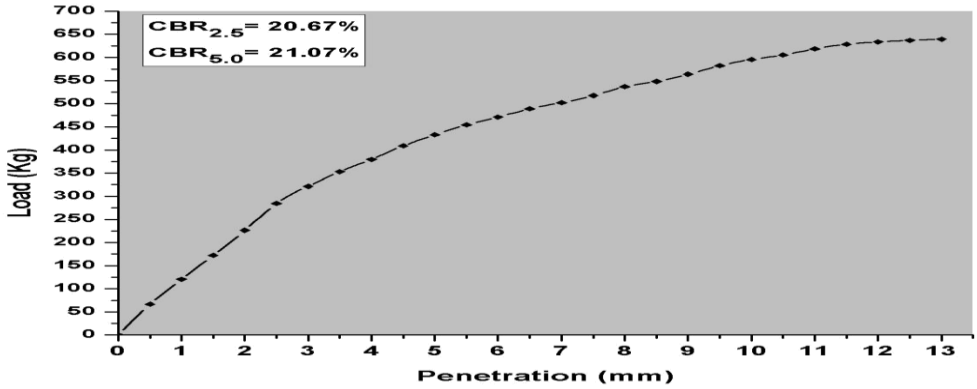
Case D:

Mould size: standard volume 2250 cc
Case D: Normal available soil tested mixing with 3% of emulsion and 2% of OPC cement added and after 5 hour testing started.
Used proctor test result of Case D.
Maximum Dry Density value: 2.212 gm./cc
Optimum Moisture Content: 10.58%
CBR test is done in three conditions. First one is in unsoaked condition, secondly in two days of soaking condition and lastly in four days of soaking condition. CBR value at 2.5mm penetration and 5mm penetration is calculated.



Graph 15: CBR Test Result, Case D (Un-soaked)



Graph 16: CBR Test Result, Case D (2 days of soaking)

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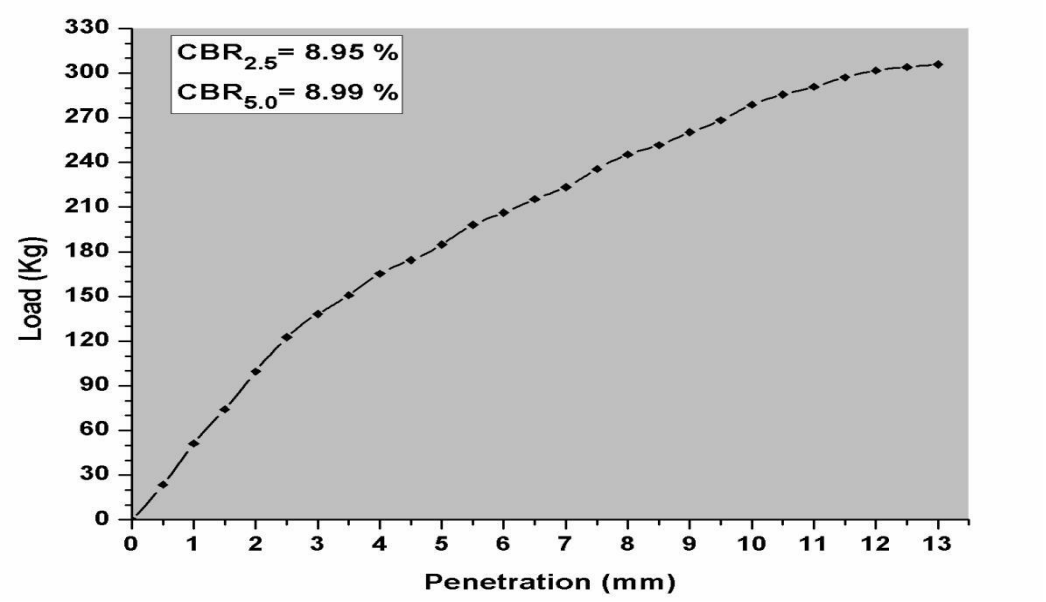
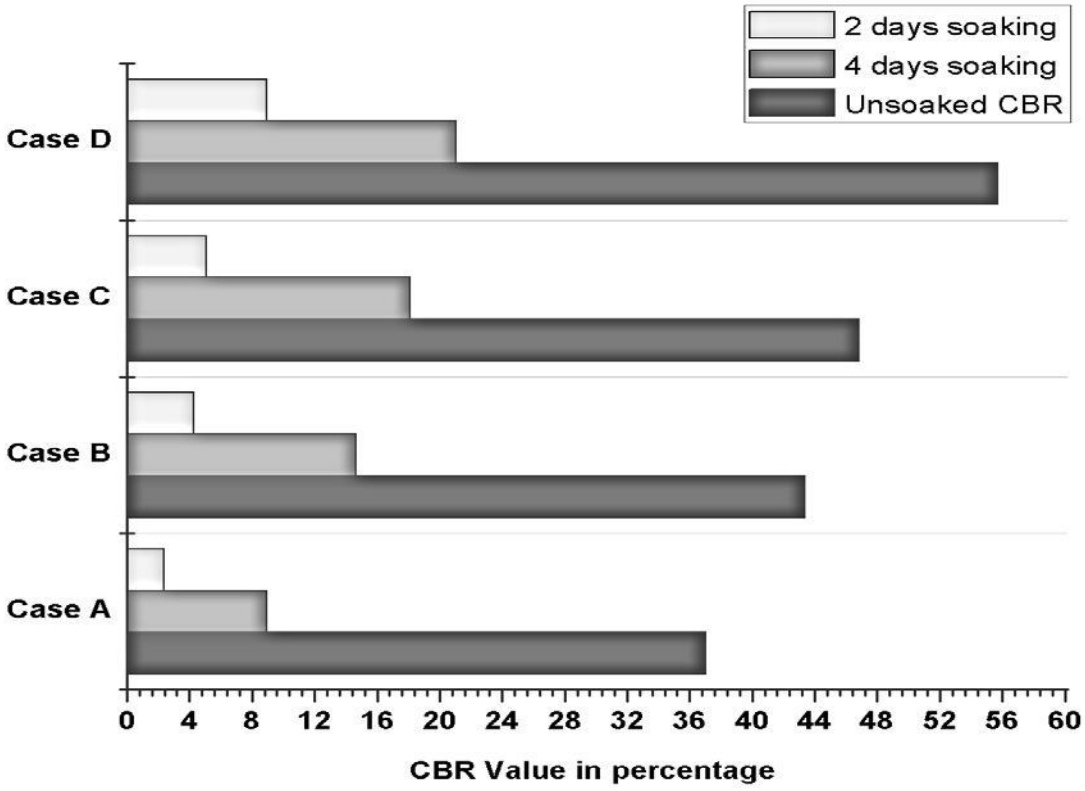


Graph 17: CBR Test Result, Case D (4 days of soaking)

5. DISCUSSION

Subgrade may be defined as a compacted soil layer, generally of naturally occurring local soil, assumed to be 300 mm in thickness, just below of the pavement crust. It provides a suitable foundation for the pavement. So it is very important to improve strength of subgrade soil, it may be by replacing good soil or by stabilization of existing soil. To check the subgrade soil stability CBR test is very commonly used test. The all CBR results are plotted in a bar to check whether the improvement of CBR is done or not and if done then what would be that condition where CBR value become maximum. Following bar gives about a clear idea on this.



Graph 18: CBR value comparison bar chart

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6. CONCLUSION

From this study it is clear that there is a considerable improvement in California Bearing Ratio (CBR) of sub-grade due to use of MS bitumen emulsion if proper mixing is done. It is seen that it best results are obtained if the soil emulsion mix is left for about five and half hours after mixing. In each state of condition it was found that CBR value has increased consecutively from Case A to Case D. In this particular experimental study CBR value has increased up to fifty percent of the unmodified soil CBR. Observing its economic cost and quality of stabilization improvement, it is clear that this type of stabilization may be applicable in Alluvial soil or in shoulder portion of highways.

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Analysis of Surface & Ground Water Quality and its Suitability for Drinking Purposes in Pulwama City

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Abstract

This study is an attempt to assess the physico-chemical characteristics of surface and sub-surface resources in Pulwama city. Water sample were collected from surface and Groundwater resources from 16 sampling locations in proximity of Pulwama for three continue month. The samplings were chosen to cover the entire radius of Pulwama and 20 km of Jhelum river and other three rivers such as ramshi, arapal and sasara river after preliminary survey of sampling area in and around Pulwama. The main focus is to assess various quality parameters like pH, DO, TDS, Turbidity, hardness, Ca2+, Mg2+ etc. In this study the value of all observed parameters shown in tables and represented in graphical format. pH, turbidity, conductivity, total dissolved solids, alkalinity, resistivity, salinity were analyzed using Systronic 9 parameter water analyzer, total hardness (TH), content of calcium (Ca2+), magnesium (Mg2+) were measured by EDTA titration method, total alkalinity (TA) was determined by titrimetric method, Fluoride (F-) was determined by using Systronic Spectrophotometer, DO, BOD and chloride (Cl-) by standard methods given by NEERI, APHA. In three months nearly 55 water samples were collected from different locations of Pulwama city. The samples were preserved in ice. It has been concluded from this dissertation work that in Pulwama city, source of surface water of Jhelum River, sasara river, arapal and romshi river water quality is suitable for drinking purpose. Similarly, groundwater quality is not suitable for drinking purpose at Town Hall, Fruit market and Railway station of Pulwama city. In this study, the Town Hall area found nitrate (55 mg/l) above the permissible limit, Fruit market area found dissolved oxygen (2.7 mg/l) below the range of permissible limit and in the railway station area found fluoride (4.30 mg/l) higher the permissible limit of IS: 10500 for the quality of drinking water.

Keywords; *EDTA, Spectrophotometer, BOD, Hardness*

I. INTRODUCTION

Water is the most precious natural resources that comprise 70% of the earth's surface. It is the most essential for everything on our planet to grow and prosper and without which life on Earth would be impossible. Although we recognize this fact, we disregard it by polluting our rivers, lakes, and oceans. Subsequently, we are slowly but surely harming our planet to the point where organisms are dying at a very alarming rate. In addition to innocent organisms dying off, our drinking water has become greatly affected as is our ability to use water for recreational purposes. The effects of water pollution are not only devastating to people but also to animals, fish and birds. Polluted water is unsuitable for drinking, recreation, agriculture, and industry. It diminishes the aesthetic quality of lakes and rivers. Water pollution has many sources. Routine uses of fertilizers and pesticides for agriculture and random disposal of industrial and domestic wastes are progressively more as significant sources of water

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pollution. .The most contaminated of them are the city sewage and industrial waste discharged into the rivers. The facilities to treat waste water are not adequate in any city in India. Currently, only about 10% of the Sewage generated is treated; the remaining is discharged as it is into our water bodies. When poisonous substances enter lakes, streams, rivers, oceans, and other water bodies, they get dissolved or lie suspended in water or get deposited on the bed. This results in the pollution of water where by the quality of the water destroys, affecting aquatic ecosystems. Pollutants can also leak down and affect the groundwater deposits.

II. STUDY AREA

Pulwama is a town and a notified area committee in Pulwama district in the Jammu and Kashmir. It is almost 28km from the Srinagar district. It is often called the Anand of Kashmir or Dudha-Kul of Kashmir because of its high milk production. The district is reported to be one of the pretty spots on the earth, because of its pleasant climate, innumerable springs, streams, waterfalls, fragrant flowers, delicious fruits and other natural sceneries. Besides district Pulwama is famous all over the world for saffron cultivation which is mainly grown in Karewa lands of Pampore, Kakapora and Pulwama.

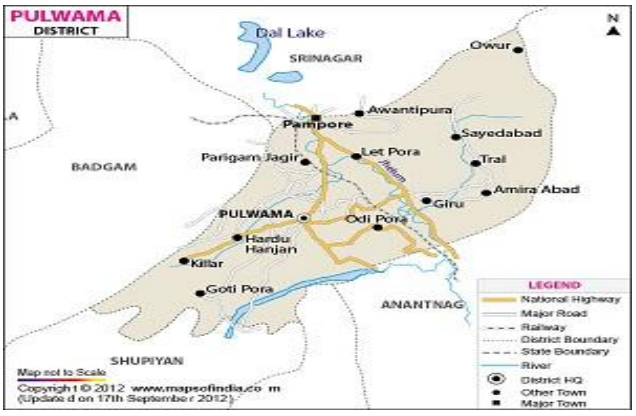

Figure 2.1: Map of Pulwama

It is centrally located in the valley of Kashmir, situated between the geographical coordinates of 33°37´- 34°06´ N latitude and 74°33´- 75°14´ E longitude. Pulwama has an average elevation of 1,630 m amsl and bounded by Srinagar in the north, in the west by Poonch and Budgam and in the east and south by Anantnag. This district was formed in 1979 by separation of Tehsil Pulwama, Shopian and Tral of the Anantnag district. This district consists of 550 villages, which until 2007 were grouped in five (5) Tehsils viz. Shopian, Pulwama, Tral, Pampore and Awantipora. In 2007, pulwama district has been divided in two parts viz. district Shopian and district Pulwama. Now there are there are eight tehsils, namely Pulwama, Tral, Awantipora, Pampore, Rajpora, Shahoora, Kakpora and Aripal. The total number of villages came down to 331 with four community block. The total area of the pulwama is 951 km2. The administrative centre of the district is to be found at Pulwama which is about 28 kilometres from the Dalgate Srinagar.

III. MATERIAL AND METHODOLOGY

In this research work, sites were selected which are present at the populated areas of Pulwama city where the water is used for drinking by living things. Peoples are using water through main sources that are surface water of Jhelum River and other water bodies and groundwater of hand pump was collected. The most populated and densely populated areas where the sites have been selected to collect from the ground sources of water are Railway station area, Town Hall, Police line area, Shaheed park, X change colony circle, Fruit market, Murran – III, Dadoora area, Khidmat, Sirnoo, Masjid area and Themna. The site of surface sources of water is Jhelum River, Ramshi River, Sasara River and Arapal River. In my dissertation work, surface water and groundwater sample has been collected, the methodology used for sampling was grab at the time of sampling the temperature was 20oC to 35oC. The samples were preserved in ice. Then I determine and analysis the various quality parameters such as, pH, turbidity, conductivity, total dissolved solids, alkalinity, resistivity, salinity were analyzed using Systronic 9 parameter water

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analyzer, total hardness (TH), content of calcium (Ca2+), magnesium (Mg2+) were measured by EDTA titration method, total alkalinity (TA) was determined by titrimetric method, Fluoride (F-) was determined by using Systronic Spectrophotometer, DO, BOD and chloride (Cl-) by standard methods given by NEERI, APHA

Figure 3.1: collection of ground water Sample

3.1 Groundwater Sampling

Sampling process of Ground water is, for water sampling one liter cane is used. At the time of water sampling it had been made sure that the cane are properly washed or rinsed to avoid contamination of dissolved as well as suspended impurities from outside. Groundwater samples have been collected from hand pumps which are used for drinking for public from twelve public places of different identified locations

3.2 Surface water Sampling

Sampling method of Surface water is, for water sampling one liter of plastic cane is used. At the time of water sampling it had been made sure that the bottle are properly washed or rinsed to avoid contamination of dissolved as well as suspended impurities from outside. Surface water samples have been collected from Jhelum River ,Arapal and other two rivers which is used for drinking for public from six points of different identified locations.

Table 1: Indian Standard Specifications of water quality for drinking water, IS: 10500

S. No.	Parameters	Desirable limit	Permissible limit
1	pH	6.5 – 8.5	No Relaxation
2	Turbidity (NTU)	5	10
3	Total Dissolved Solid (mg/l)	500	2000
4	Total Hardness (mg/l)	200	600
5	CaH (mg/l)	75	200
6	MgH (mg/l)	30	100
7	Dissolved Oxygen (mg/l)	6 - 8	4 – 5
8	Alkalinity (mg/l)	200	600
9	Chloride (mg/l)	250	1000
10	Fluoride (mg/l)	1	1.5
11	Nitrate (mg/l)	45	No Relaxation

IV. RESULT AND DISCUSSION

4.1: Graphical Representation of Ground Water Samples Analysis Result:

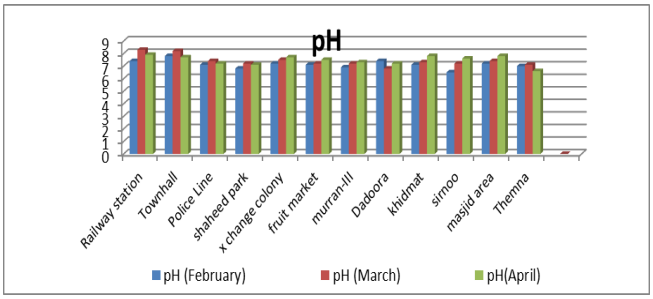

Figure 4.1: Above graph shows groundwater pH at different location of different months

The value of pH of different ground water samples lies between 6.5 to 8.3. The value of pH was found maximum in The Railway station area of pulwama where as it was minimum in sirnoo area of Pulwama city. The value of pH was measured for three months from february to april 2020. According to Indian standard the pH for drinking water lies between 6.5 to 8.5.

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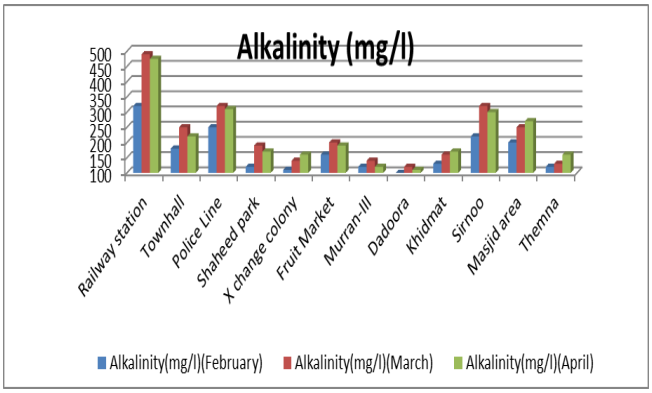

Figure 4.2: Above graph shows groundwater Alkalinity at different location of different months

The value of Alkalinity of different ground water samples lies between 100 to 490 mg/l. The value of Alkalinity was found maximum in the Railway station area of pulwama where as it was minimum in themna area of Pulwama city. The value of Alkalinity was measured for three months from february to april 2020.

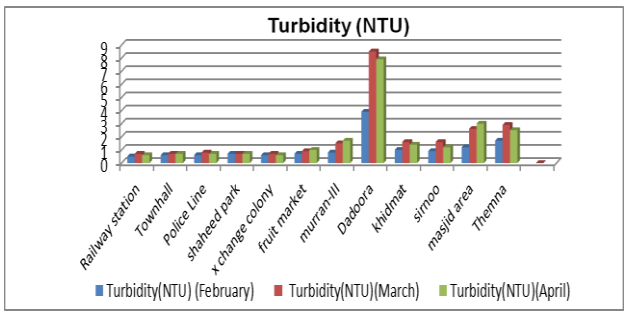

Figure 4.3: Above graph shows groundwater Turbidity at different location of different months

The value of ground water turbidity lies between 0.5 to 7.9 NTU.The value of Turbidity was found maximum in the

Dadoora area of pulwama where as it was minimum in Railway station area ,townhall area and in police line area of Pulwama city. The value of Turbidity was measured for three months from february to april 2020.

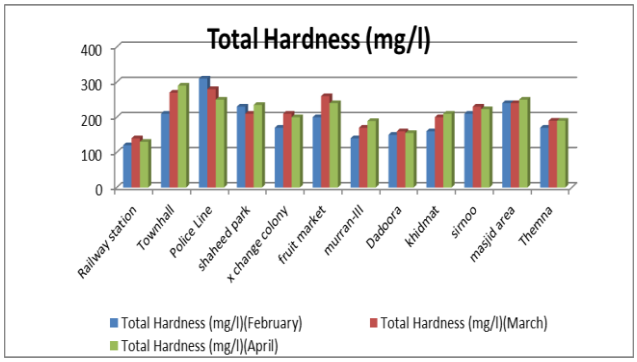

Figure 4.4: Above graph shows groundwater Total Hardness at different location of different months.

The value of Total hardness were lies between 120 to 310 mg/l. The value of Total Hardness was found maximum in the police line area of pulwama where as it was minimum in Railway station area of Pulwama city. The value of Total Hardness was measured three months from february to april 2020.

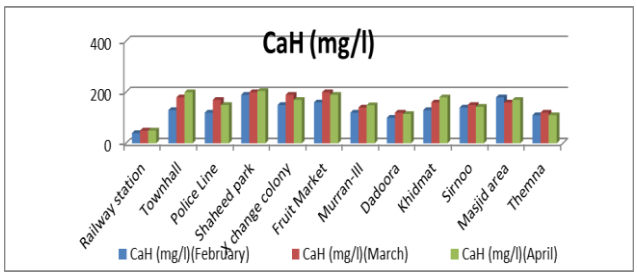

Figure 4.5: Above graph shows groundwater CaH at different location of different months

The value of calcium hardness in different area of ground water were lies between 40 to 205 mg/l. The value of calcium Hardness was found maximum in the shaheed park area of pulwama where as it was minimum in Railway station area of Pulwama city. The value of calcium Hardness was measured for three months from february to april 2020.

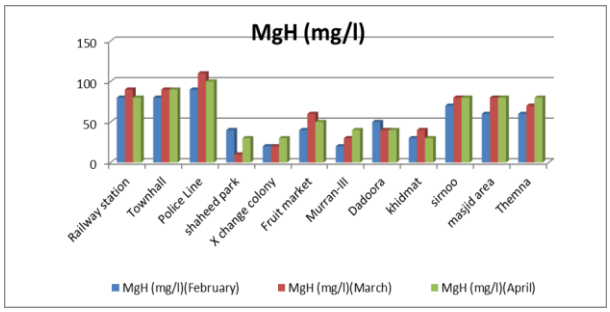

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Figure 4.6: Above graph shows groundwater MgH at different location of different months.

The value of Magnesium hardness in different area of ground water were lies between 20 to 110 mg/l. The value of magnesium Hardness was found maximum in the police line area of pulwama where as it was minimum in X change colony and in murran-III area of Pulwama city. The value of Magnesium Hardness was measured for three months from february to april 2020.

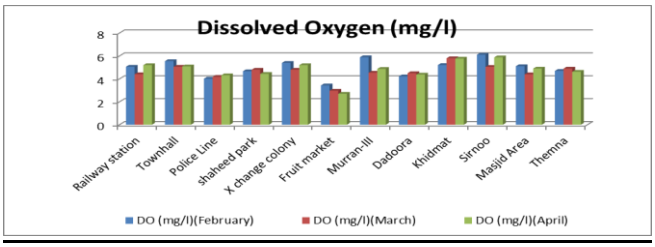

Figure 4.8: Above graph shows groundwater DO at different location of different months

The value of Dissolved oxygen in different area of ground water were lies between 2.7 to 5.88 mg/l. The value of Dissolved Oxygen was found maximum in the sirnoo area of pulwama where as it was minimum in Fruit market area ofPulwama city. The value of Dissolved Oxygen was measured for three months from february to april 2020.

The value of TDS in different area of ground water were lies between 310 to1020 mg/l. The value of TDS was found maximum in the police line area of pulwama where as it was minimum in Dadoora area of Pulwama city. The value of TDS was measured for three months from february to april 2020.

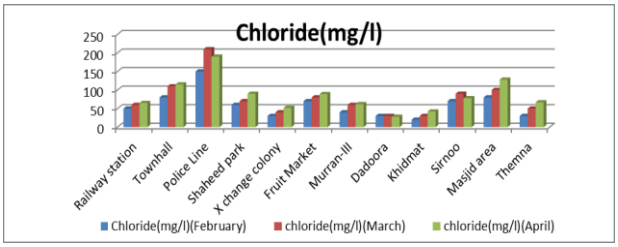

Figure 4.7: Above graph shows groundwater Chloride

The value of chloride in different area of ground water were lies between 20 to 190mg/l .the chloride was measured for threemonths

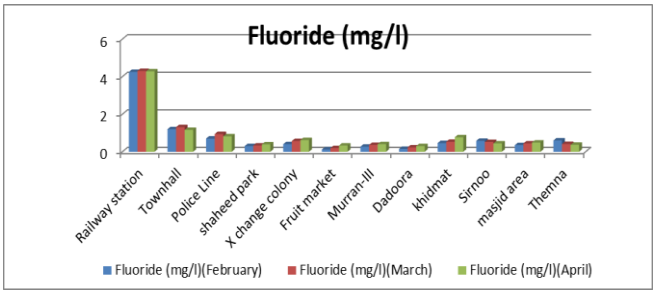

Figure 4.11: Above graph shows groundwater Fluoride at different location of different months

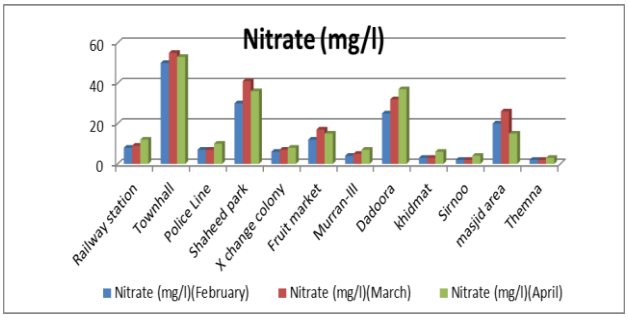

Figure 4.9: Above graph shows groundwater Nitrate at different location of different months

The value of Nitrate in different area of ground water were lies between 2 to 53 mg/l. The value of Nitrate was found maximum in the Townhall area of pulwama where as it was minimum in Sirnoo and themna area of Pulwama city. The value of Nitrate was measured for three months from february to april 2020.

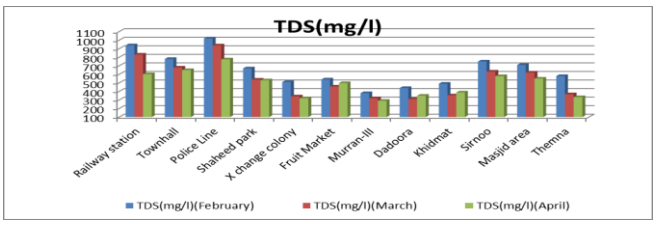

Figure 4.10: Above graph shows groundwater TDS at different location of different months

The value of Flouride in different area of ground water were lies between 0.12 to 4.30 mg/l. The value of Flouride was found maximum in the

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Railway station area of pulwama where as it was minimum in Fruit market area of Pulwama city. The value of Flouride was measured for three months from february to april 2020.

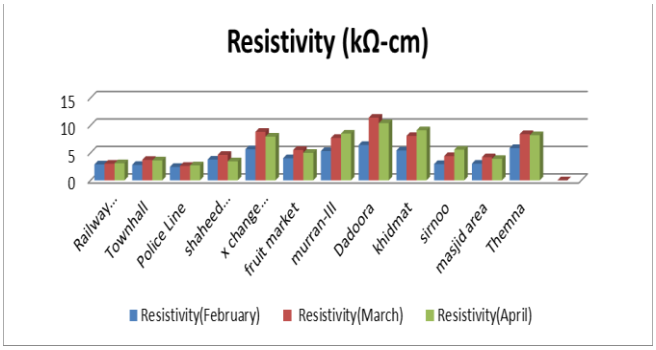

Figure 4.12: Above graph shows groundwater Resistivity at different location of different months

The value of Resistivity in different area of ground water were lies between 2.43 to 11.4 kΩ-cm. The value of Resistivity was found maximum in the Dadoora area of pulwama where as it was minimum in police line area of Pulwama city. The value of Resistivity was measured for three months from february to april 2020

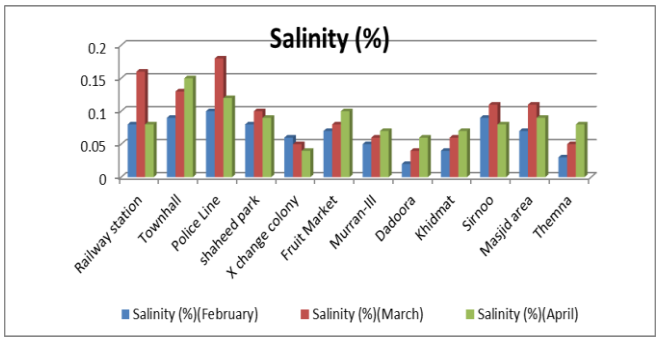

Figure 4.13: Above graph shows groundwater Salinity at different location of different months

The value of salinity in different area of ground water were lies between 0.02 to 0.18 percent. The value of salinity was found maximum in the police line area of pulwama where as it was minimum in Dadoora area of Pulwama city. The value of salinity was measured for three months from february to april 2020

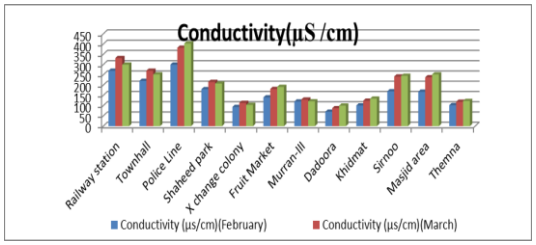

Figure 4.14: Above graph shows groundwater Conductivity at different location of different months

The value of Conductivity in different area of ground water were lies between 70.2 to 403 µS/cm. The value of conductivity was found maximum in the police line area of pulwama where as it was minimum in Dadoora area of Pulwama city. The value of Conductivity was measured for three months from february to april 2020

4.2 Graphical Representation of Surface Water Samples Analysis Result:

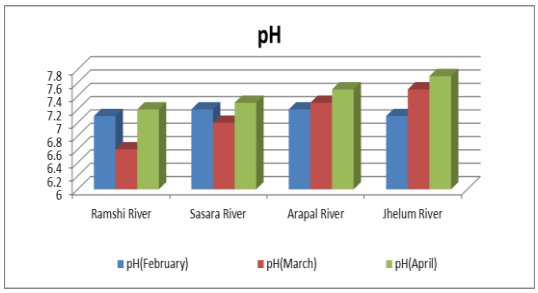

Figure 4.15: Above graph shows surface water pH at different location of different months

The pH values for different Surface water samples lies between 6.6 to 7.7. The value of pH was found maximum in the Jhelum river of pulwama where as it was minimum in Ramshi river of Pulwama city.

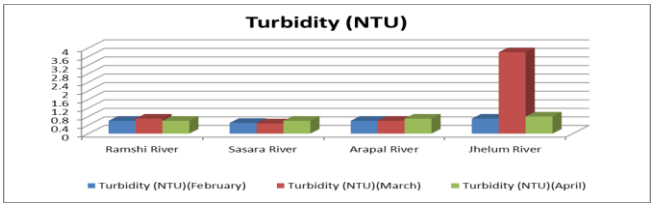

Figure 4.16: Above graph shows surface water Turbidity at different location of different months

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The value of Surface water turbidity lies between 0.48 to 3.8 NTU.The value of Turbidity was found maximum in the jhelum river of pulwama where as it was minimum in sasara river of Pulwama city.

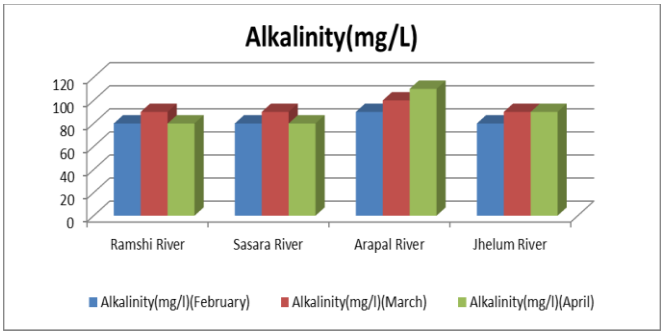

Figure 4.17: Above graph shows surface water Alkalinity at different location of different months

The value of Surface water Alkalinity were lies between 80 to 110 mg/l.The value of Alkalinity was found maximum in the Arapal river of pulwama where as it was minimum in romshi and sasara river of Pulwama city

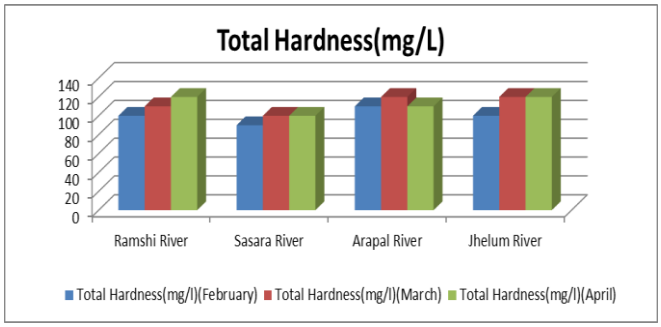

Figure 4.18: Above graph shows surface water Total Hardness at different location of different months

The value of Surface water Total hardness were lies between 80 to 110 mg/l.The value of Total Hardness was found maximum in the Jhelum river of pulwama where as it was minimum in sasara river of Pulwama city

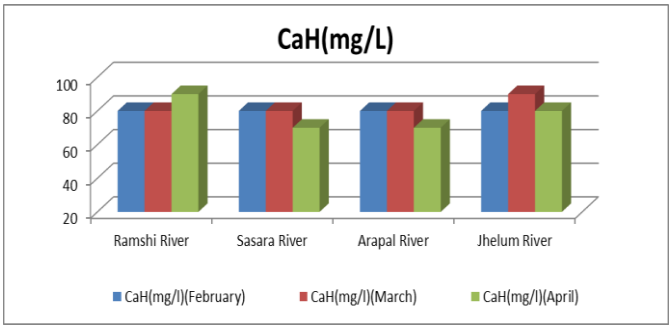

Figure 4.19: Above graph shows surface water CaH at different location of different months

The value of Surface water Calcium hardness were lies between 80 to 110 mg/l.The value of calcium hardness was found maximum in the Ramshi river of pulwama where as it was minimum in sasara river of Pulwama city.

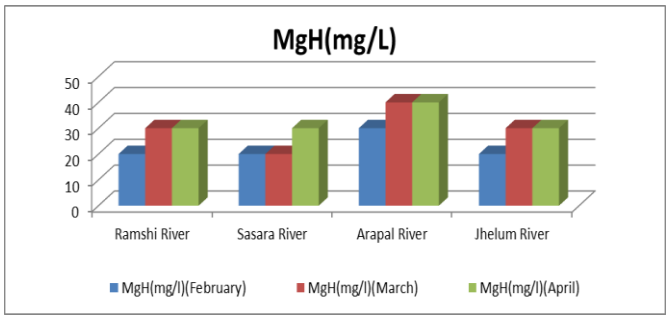

Figure 4.20: Above graph shows surface water MgH at different location of different months

The value of Surface water Magnesium hardness were lies between 80 to 110 mg/l.The value of Magnesium hardness was found maximum in the Arapal river of pulwama where as it was minimum in sasara river of Pulwama city.

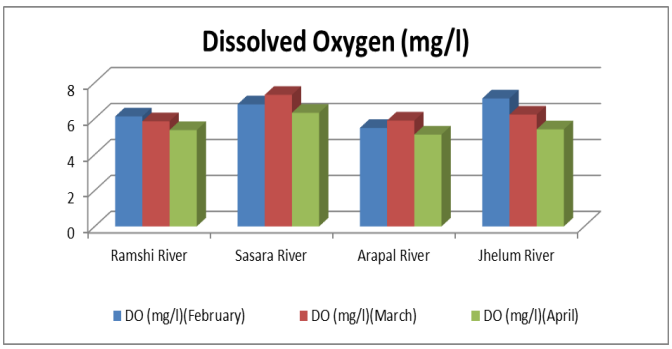

Figure 4.21: Above graph shows surface water DO at different location of different months

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The value of Dissolved oxygen were lies between 5.11to 7.32 mg/l.The value of Dissolved oxygen was found maximum in the sasara river of pulwama where as it was minimum in Arapal river of Pulwama city.

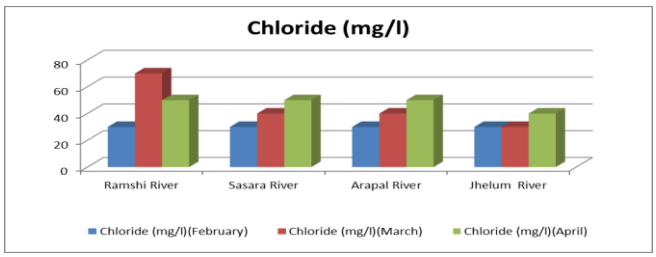

Figure 4.22: Above graph shows surface water Chloride at different location of different months

The value of chloride were lies between 30 to 70 mg/l.The value of chloride was found maximum in theRamshi river of pulwama where as it was minimum in jhelum river of Pulwama city.

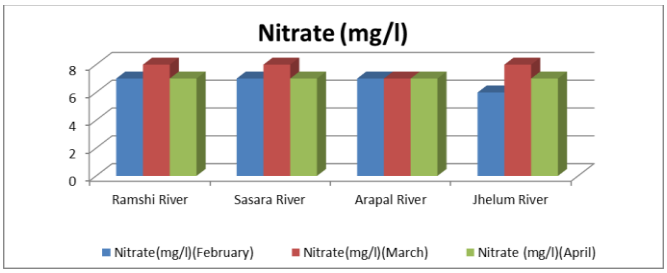

Figure 4.23: Above graph shows surface water Nitrate at different location of different months

The value of Nitrate were lies between 6 to 8 mg/l.The value of nitrate was found maximum in the Ramshi river of pulwama where as it was minimum in jhelum river of Pulwama city.

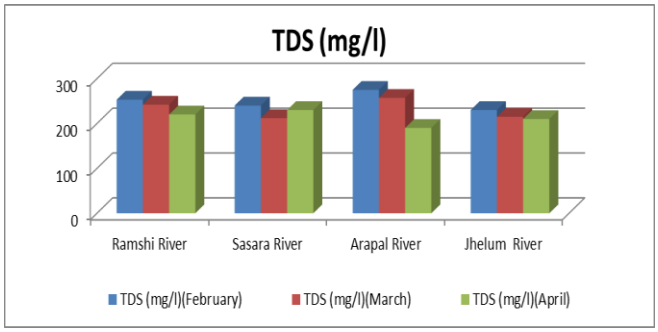

Figure 4.24: Above graph shows surface water TDS at different location of different months

The value of TDS were lies between 190 to 275 mg/l.The value of TDS was found maximum in the Arapal river of pulwama where as it was minimum in jhelum river of Pulwama city.

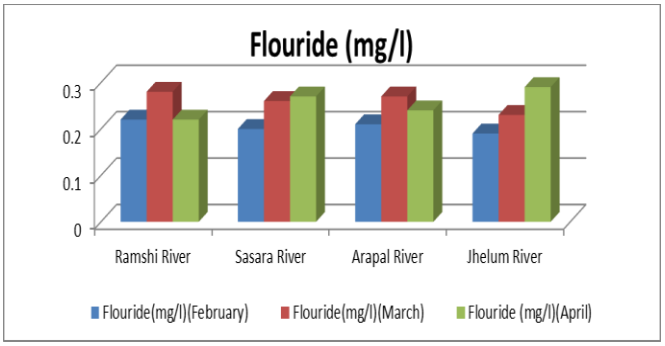

Figure 4.25: Above graph shows surface water Fluoride at different location of different months

The value of flouride were lies between 0.19 to 0.28 mg/l.The value of Flouride was found maximum in the Ramshil river of pulwama where as it was minimum in jhelum river of Pulwama city.

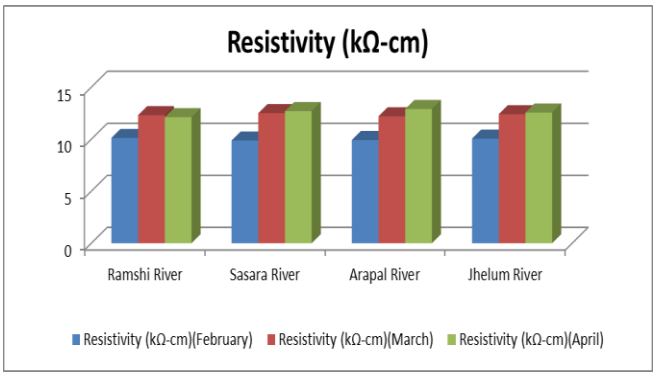

Figure 4.26: Above graph shows surface water Resistivity at different location of different months

The value of Resistivity were lies between 9.87 to 12.11 kΩ-cm.The value of Resistivity was found maximum in the Ramshil river of pulwama where as it was minimum in Sasara river of Pulwama city.

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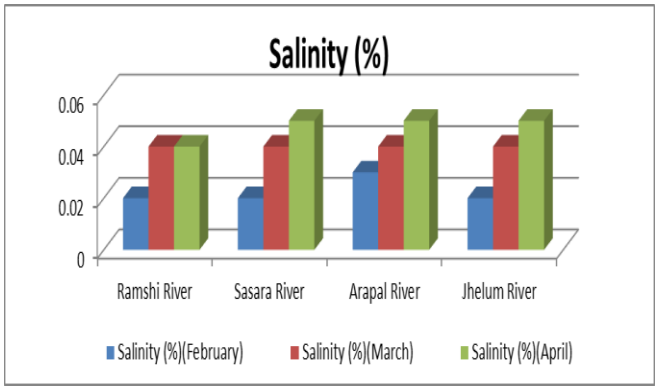

Figure 4.27: Above graph shows surface water Salinity at different location of different months

The value of Salinity were lies between 0.02 to 0.05percent.The value of salinity was found maximum in the Jhelum river of pulwama where as it was minimum in Sasara river of Pulwama city.

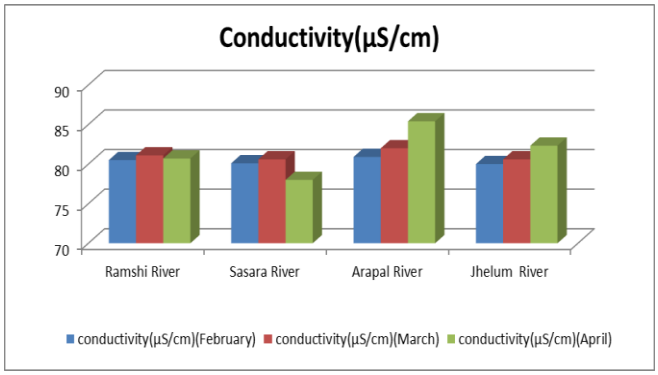

Figure 4.28: Above graph shows surface waterConductivity at different location of different months

The value of Conductivity were lies between 78 to 85.4 .The value of Conductivity was found maximum in the Arapal river of pulwama where as it was minimum in Sasara river of Pulwama city.

V. Discussion

The observation and analysis test result that has been carried out in these three months on physiochemical properties of groundwater and surface water in Pulwama city is classified below. Sample collected from Themna area is situated at the bank of Jhelum River in Pulwama city. In this area water parameters, like alkalinity, total hardness, turbidity, chloride, nitrate, TDS and fluoride is below the acceptable limit where as other parameters such as calcium hardness, magnesium hardness are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Sirnoo is situated in the Pulwama city. In this area waters parameters, like turbidity, chloride, nitrate and fluoride is below the acceptable limit where as other parameters such as alkalinity, total hardness, calcium hardness, magnesium hardness, TDS are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Khidmat is situated in the Pulwama city. In this area water parameters, like alkalinity, total hardness, TDS, turbidity, chloride, nitrate and fluoride is below the acceptable limit where as other parameters such as calcium hardness, magnesium hardness are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Murran - III is situated in the PULWAMA city. In this area water parameters, like alkalinity, total hardness, turbidity, chloride, nitrate, fluoride and TDS is below the acceptable limit where as other parameters such as calcium hardness, magnesium hardness are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Shaheed park is situated in the PULWAMA city. In this area water parameters, like alkalinity, turbidity, total

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hardness, chloride, nitrate and fluoride is below the acceptable limit where as other parameters such as magnesium hardness, TDS, calcium hardness are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from X change colony is situated in the Pulwama city. In this area water parameters, like alkalinity, turbidity, total hardness, magnesium hardness, chloride, nitrate and fluoride are below the acceptable limit where as other parameters such as calcium hardness, TDS, dissolved oxygen are below the permissible limit and pH at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Fruit market is situated in the PULWAMA city. In this area water parameters, like alkalinity, total hardness, turbidity, chloride, nitrate and fluoride is below the acceptable limit where as other parameters such as calcium hardness, magnesium hardness, TDS are below the permissible limit and pH at their permissible range but dissolved oxygen is not at the range. It is below permissible limit. The temperature and conductance do not affect water quality used for drinking purpose. So, this area groundwater is not suitable for drinking on the basis of obtained results. Fruit market area water is treating and increases dissolved oxygen before domestic use, especially for drinking. Sample collected from Town Hall is situated near to old bus stand of Pulwama city. In this area water parameters, like turbidity, chloride is below the acceptable limit where as other parameters such as alkalinity, total hardness, magnesium hardness, fluoride, calcium hardness and TDS are below the permissible limit. pH and dissolved oxygen at their permissible range. In this area nitrate found above the permissible limit. The temperature and conductance do not affect water quality used for drinking purpose. This area groundwater is not suitable for drinking without treatment on the basis of obtained results. Sample of groundwater collected from Masjid area is situated in Pulwama city. In this area water parameters, like turbidity, chloride, nitrate and fluoride is below the acceptable limit where as other parameters such as calcium hardness, magnesium hardness, alkalinity, TDS and total hardness are below the permissible limit. pH and dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Police line is situated in the Pulwama city. In this area water parameters, like turbidity, chloride, nitrate and fluoride is below the acceptable limit where as other parameters such as alkalinity, total hardness, calcium hardness, TDS, magnesium hardness are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Railway station area is situated near by railway station of the Pulwama city. In this area water parameters, like turbidity, total hardness, calcium hardness, chloride and nitrate is below the acceptable limit where as other parameters such as alkalinity, TDS, magnesium hardness are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area fluoride found beyond the permissible limit. This area groundwater is not suitable for drinking on the basis of obtained results. So, this area water is not use in drinking and food, without treated the ground water.

Sample collected from Dadoora industrial area is situated next to the Pulwama national highway. In this area water parameters, like alkalinity, total

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hardness, chloride, TDS and fluoride is below the acceptable limit where as other parameters such as turbidity, calcium hardness, magnesium hardness, nitrate are below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this area groundwater is suitable for drinking on the basis of obtained results. Sample collected from Jhelum River in the Pulwama city. In this location water parameters, like turbidity, alkalinity, total hardness, magnesium hardness, chloride, nitrate, fluoride and TDS is below the acceptable limit where as other parameters such as calcium hardness is below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this location point surface water is suitable for drinking on the basis of obtained results. Sample collected from Romshi River is situated in the Pulwama city. In this location water parameters, like turbidity, alkalinity, total hardness, magnesium hardness, chloride, nitrate, fluoride and TDS is below the acceptable limit where as other parameters such as calcium hardness is below the permissible limit. pH and dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this location point surface water is suitable for drinking on the basis of obtained results. Sample collected from Sasara river is situated in the Pulwama city. In this location water parameters, like turbidity, alkalinity, total hardness, magnesium hardness, chloride, nitrate, fluoride and TDS is below the acceptable limit where as other parameters such as calcium hardness is below the permissible limit. And pH, dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this location point surface water is suitable for drinking on the basis of obtained results. Sample collected from Arapal river is situated in the Pulwama city. In this location water parameters, like alkalinity, turbidity, total hardness, chloride, TDS, fluoride and nitrate is below the acceptable limit where as other parameters such as calcium hardness and magnesium hardness below the permissible limit. pH and dissolved oxygen at their permissible range. The temperature and conductance do not affect water quality used for drinking purpose. In this location point surface water is suitable for drinking on the basis of obtained results.

VI. CONCLUSION

It has been concluded from this dissertation work that the physiochemical property of surface water and groundwater have been checked the quality of water, whether it is suitable for drinking purpose or not. The dissertation work have been carried out at four different locations in the Pulwama city through Jhelum River, Romshi River, Sasara river, Arapal river and twelve different areas of groundwater at Pulwama city that are Railway station, Police line, Town Hall, X change colony, Fruit market, Shaheed park, Khidmat, Sirnoo, Murran, Masjid area, Themna, Dadoora industrial area. In this dissertation work, parameters like pH, turbidity, resistivity, total hardness, calcium hardness, magnesium hardness, total dissolved solid, salinity, alkalinity, conductivity, chloride, nitrate, fluoride, dissolved oxygen of water have been analyzed in laboratory. It has been concluded from this dissertation work that in Pulwama city, source of surface water of Jhelum River, sasara river, arapal and romshi river water quality is suitable for drinking purpose. In the study of the samples collected at various months from different locations of Jhelum and other three rivers are come in the range of permissible limit. That of the groundwater quality is not suitable for drinking purpose at Town Hall, Fruit market and Railway station of Pulwama city. In this study, the Town Hall area found nitrate (55 mg/l) above the permissible limit, Fruit market area found dissolved oxygen (2.7 mg/l) below the range of permissible limit and in the railway station area found fluoride (4.30 mg/l) higher the permissible limit of IS: 10500 for the

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quality of drinking water. The parameter should be in the range of permissible limit which is nitrate below 45 mg/l, dissolved oxygen is above 4 mg/l and fluoride is below 1.5 mg/l. Apart from the above listed location other than this groundwater is suitable for drinking purpose and the parameters limits are in their optimum range or within the permissible limit.

VII. SUGGESTIONS AND RECOMMENDATIONS

These days nearly 80% of diseases are water borne and it is suggested to the consumes that not to use water without treatment if the water is less or severely polluted it can cause harmful water borne diseases mostly in rainy season. Where the water is not suitable for drinking purpose we can adapt proper treatment techniques to remove impurities, if the water is severe and after treatment we are unable to remove desirable level of impurities then the water can be used for other purpose such as gardening, flushing, washing etc.It is suggested to the residents from the obtained observation to use surface water because all the parameters of surface water is in desirable limits and if there is no available source of surface then they can use ground water for their consumption because in some area groundwater is in desirable and at some places it is in permissible limit. If there is any source of pollution is accumulating in water body then proper mitigation measure should be taken and if possible, divert the source of pollution or reduce the harmful effect of the pollutants.

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Analysis of Traffic Performance of NH79 Road, Rajasthan, India

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***Abstract*:- This research focused on analyzing the traffic performance of NH79 road from Chittorgarh/Bhilwara Rajasthan India. The road is currently a 2 way-direction with 3 lane carriageways in both the direction, after closely observation the problems identified, were traffic congestion, delay, prone to accident which associated with high traffic volume and inappropriate parking facilities. The parameters considered in this research were Capacity, Density, Saturation Ratio. After analysis conducted from the data collected, it was revealed that, the road section has an average daily capacity of 12609 veh/day and average hourly traffic flow of 1261veh/hour with average speed of 54 K.P.H. the traffic density of the road is 112vs/m, therefore based on the parameters evaluated it is concluded that road belongs to level of service E, this is because all the parameter are within the range service class E in compliances with the recommendation made in the (HCM, 2000), thus it is recommended that the NH79 section shall be facilitated with proper Planning due to the fact the road is still growing and changing, resulting in a more responsive and useful transportation process, also Management and Maintenance will immensely help for the road to sustain its life span without deterioration and provision of well-integrated Traffic control system especially in Gangrar town junction will reduce the level conduction, delay prone to accident and travel time of the drivers and other road user.**

Keywords: Performance, Traffic, Volume, Parameters, Delay

1.0: INTRODUCTIONS

A times, the expressway with multiple lane was considered to be the answer to making of the traffic problems associated with road high volume. When a multiple lane is used as the form of control at road high volume, its geometric features are of great impact on its ability to properly carry out its intended function. Apart from queuing delays which occur due to heavy traffic at peak hours, the geometric features of expressway with multiple lane could cause delays at other times throughout the day, thereby affecting traffic performance significantly. Congestion, particularly on city streets and urban freeways continue to pose a serious problem to traffic engineers. However, construction of new roads or widening of existing ones may not always be the solution for relieving congestion since the capacity of urban roads are generally governed by that of their intersection; the solution might be to increase the capacity of critical intersection rather than constructing new roads or widening the entire length of the road way.

According to research by (1) on The Effect Analysis of Traffic Volume, Velocity and Density in Dr. Siwabessy Salobar Road, they found the street is considered to be one of the busy streets in ambon city with various vehicles passing by along with the crowded pedestrian activities. Especially in the morning and evening hours, the flow analysis of Dr. siwabessy road traffic is said to have not experienced saturation because the ratio of volume to capacity has a value less than 1. Based on their study it was found out that both traffic flow from ambon city to Air sabolar or vice versa shows the dominant influence of vehicles speed (Us) on traffic density(D) compared to traffic volume factor(V), (1) generated a regression model of DR. siwabessy road the formula for ambon to air salobar is $D=18.32-0.35U_s + 0.024Q$ And that of air salobar to ambon is $D=18.67-0.396U_s+0.021Q$ where both have a very high correlation value of (R_2=0.999). (2) found that the effective of management urban planning comes directly from the accurate data collections and analysis at various central business district (CBD), from the analysis of tanke-tipper intersection, they found that the existing capacity intersection is given as 4969Vph and practical capacity are Q_p=4224Vph and 6676Vph as the new propose practical capacity. Also (2), research found that the video-graphy cost ₦8,700 while the manual counting method cost ₦ 11,400, they further concluded that the tanke-tipper intersection operate level of service F which need a serious modification.

The operational performance of mengxi square rotary intersection in Zhenjiang, china was surveyed and analysed by (3) based on the following parameters which include vehicle velocity distribution, gap distribution and lane distribution which provide the basis for design and improving traffic flow on the rotary intersection, (3) concluded that the average velocity increase from lane 1, lane 2 to lane 3 also the average velocity for Light vehicles is much compared to that of Heavy vehicles for all the sections. According to Assessment study conducted by (4) at Baban Gwari roundabout a rotary intersection along katsina road in Kano metropolis of Kano state of Nigeria. it was observed that the roundabout experienced daily and frequent concurrent delay, accidents, queue built up at morning and evening peak hours.

2.0: NEED FOR THE RESEARCH

NH79 Road Chittorgarh/Bhilwara section is presently a 2-way with 3-lane carriageway in each direction in which traffic movement is very high mostly along gangrar because of a market presence. After closely observing the roads, the problems identified are high traffic volume which lead to traffic congestion because of crossing, inadequate parking facilities along gangrar market. Therefore, this study is necessary to explore the effects of the geometric features and traffic flow parameters as it

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affects the traffic performance of NH79 Road, Chittorgarh/Bhilwara's section.

3.0: AIM AND OBJECTIVES OF THE STUDY

3.1: Aim

The aim of the research work is to analyse the traffic performance of NH79 road, Chittorgarh/Bhilwara's section**.**

3.2: Objectives of the Study

The objectives of this study were

To conduct a preliminary survey on the existing features of Chittorgarh/Bhilwara's section of the NH79 road.

To Determine traffic volume of Chittorgarh/Bhilwara's section of the NH79 road.

To Determine Operational Performance most specifically on Chittorgarh/Bhilwara's section of the NH79 road.

4.0: GENERAL DESCRIPTION OF THE STUDY AREA

The NH79 is the road which links Chittorgarh and Bhilwara district within Rajasthan (India). it's also made up of rigid pavement having 2-way with 3-lane carriageway in each direction, each carriage way is 4.2m and service lane which its currently under construction. other physical features of NH79 include

- **Roadway median**: The roadway median in the NH79 has the height of 0.23m and width of 5m.
- **Drainage**: Drainage is one of the most important features in any road because it drains water from the road and discharge it to the discharging point, the drainage system along NH79 has the height of 0.6m and width of 1.43m
- **Pedestrian walkway**: The pedestrian walkways was constructed to in compliances with the IRC Provision it has width of 2m and length of 0.25
- **Flyovers**: There are currently 5 flyovers between gangrar to Chittorgarh four out of the five are fully constructed while one is under construction.
- **Service lane**: The service lane in NH79 is currently under construction about 1.5 km is completed the service lane width is 7m

Figure 5.0: Portion of NH79 Road, Chittorgarh/Bhilwara's Section.

5.0: METHODOLOGY

The methods employed to obtained the required data for this research includes; Preliminary survey on the existing features of the NH79 road section, Traffic Volume study on section of NH79 road. Which was determined manually by using the Procedures Observers were positioned at various cross section of the roadway, the number of vehicles that passes each observer was noted The vehicles timing was expressed in hourly periods and different type of vehicle was categories and record for ten hours, This was repeated for a week. The results were tabulated and from the methods employed the relevant parameters such as passenger's car unit, Capacity, Density, Saturation Ratio were determined in order to assess the performance capacity of the road section used for the research. Also, average travel speed. Was determined by Procedures followed; The chosen distance was measured, the observer was stationed at initial point of measured distance, the specimen vehicle was identified, the time taken to reached the end point was noted, Then, the speed was calculated.

6.0: ANALYSIS AND DISCUSSIONS OF RESULT

6.1: Traffic Volume Count Result

Seven consecutive days traffic volume count was conducted for 10 hours count (08:00am- 06:00pm) at the NH79 Chittorgarh/Bhilwara Road Rajasthan India. The traffic volume of the vehicle recoded during the survey was converted to passenger's car unit/equivalence using an appropriate conversion factors as stated in the Indian road congress (6). And the result was presented below.

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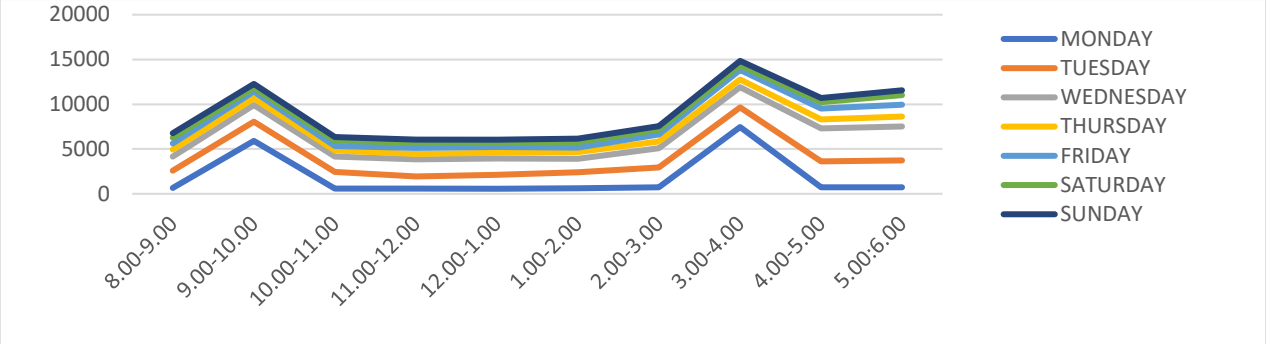

Figure 6.1.1: Traffic Volume Count of Chittorgarh/Bhilwara

The result of the Traffic Volume Count in Figure above revealed that there is increased of traffic in volume in the morning hours and with the 09:00am-10:00am as the morning peak hours and also having the 3:00pm-04:00pm as evening peak hours this shows that there is high volume of traffic in both morning and evening hours and less traffic during the mid-day hours, the average daily traffic obtained is 12609veh/day shows that the road is moderately dense in comparison with the recommendation of daily traffic volume stated Highway capacity manual (HCM 2000), therefore the road capacity can be seen as adequate.

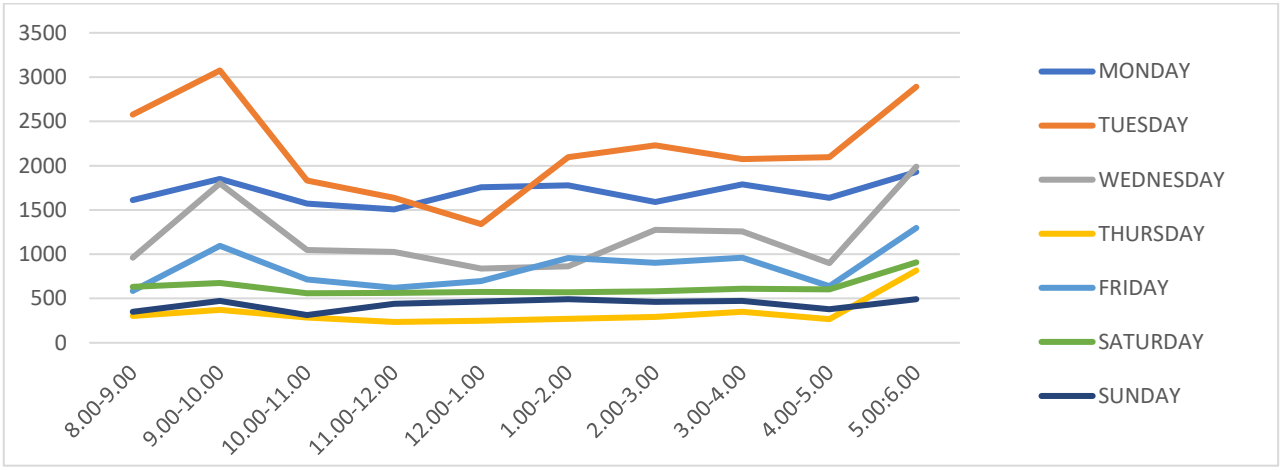

Figure 6.2: Passenger's Car Unit of Bhilwara/Chittorgarh

the result of the Traffic Volume Count of Bhilwara-Chittorgarh presented above follsow similar trend with its counter direction having morning peak hour period of 09:00am-10:00am and 05:00-06:00pm as evening hours' peak hour period, the average daily traffic obtained is 10477veh/day shows that the road is highly dense in comparison of the recommendation of daily traffic volume stated Highway capacity manual (HCM 2000), therefore the road capacity can be seen as adequate.

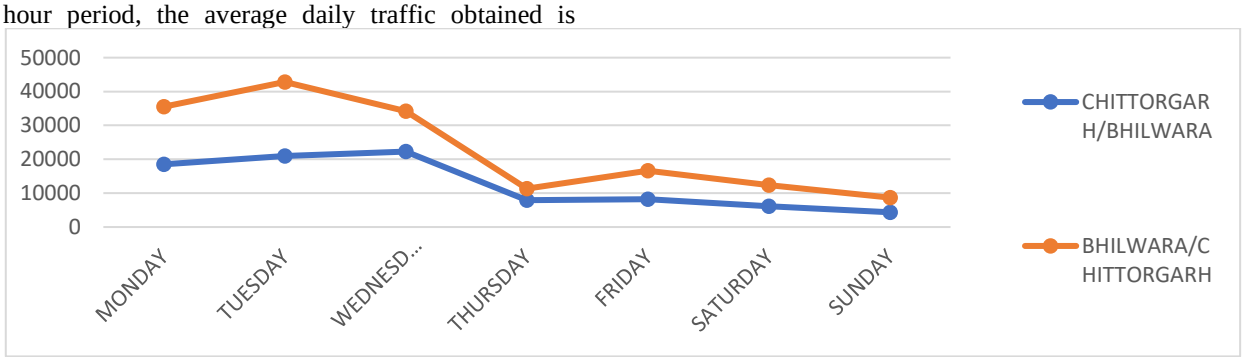

Figure 6.3: Annual Average Daily Traffic

The summary of annual average daily traffic obtained during the analysis can be seen that Bhilwara –Chittorgarh has little higher value compared with the Chittorgarh to Bhilwara. And Tuesday with the highest value while Sunday having lowest value. This may be due to higher population of people moving from the Chittorgarh to Bhilwara.

6.4: Traffic Density

Traffic density was evaluated and presented in the table and figure below

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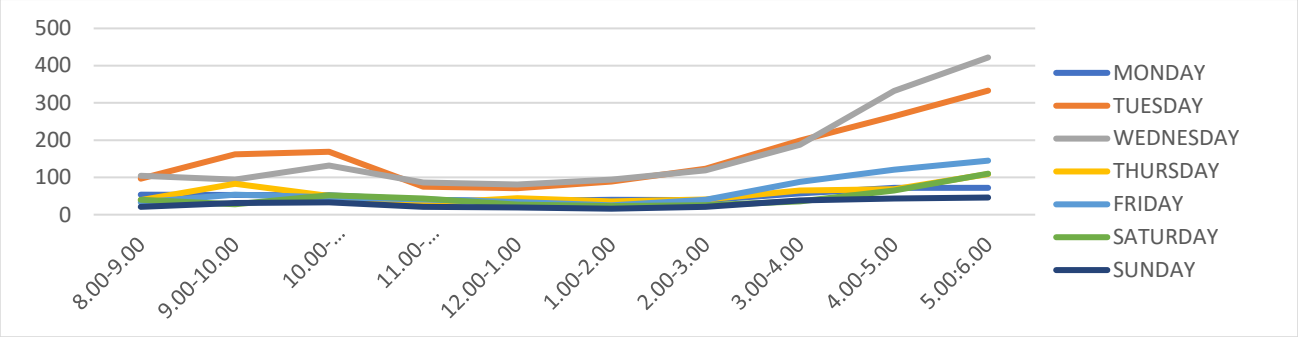

Figure 6.5: Traffic Density of Chittorgarh/Bhilwara

The result of the traffic presented above revealed that the road is highly dense in the morning hours between 08:00-11:00am which correspond to morning peak hours' while at the evening hours there it increased from 03:00-06:00pm with Wednesday having the highest value while Sunday having the lowest value as shown in the figure above this happened due to variation of vehicles movement on the road. The daily density of this direction is 116vs/m and it's within the range of the recommended value Highway capacity manual (HCM 2000),

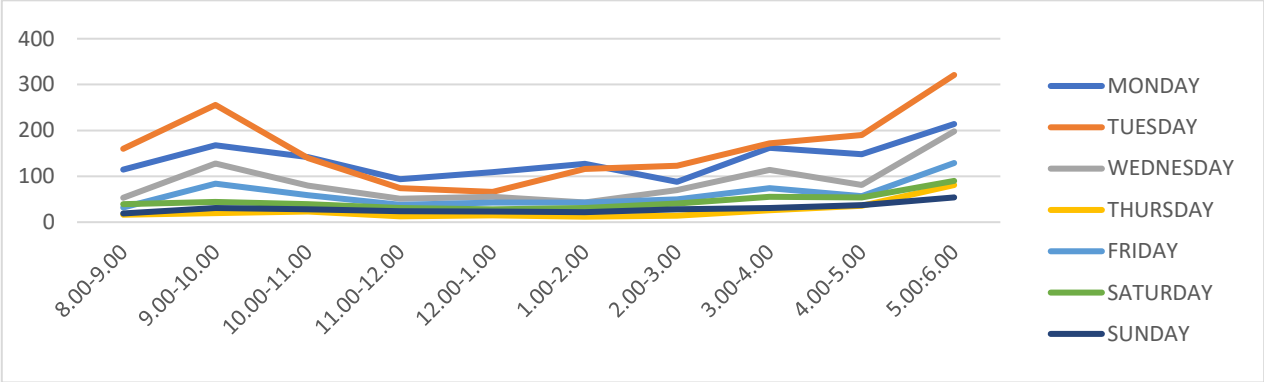

Figure 6.6: Traffic Density of Bhilwara/Chittorgarh

The same nature of traffic movement obtained along the Bhilwara/Chittorgarh when compared with the other direction but the peak hours here is 9-10am while the densely hours occurred between 04:00-06:00pm during midday hours there is less movement of traffic along the direction of the Bhilwara/Chittorgarh and the average daily density is 112vs/m and when its compared with the Highway capacity manual (HCM 2000),

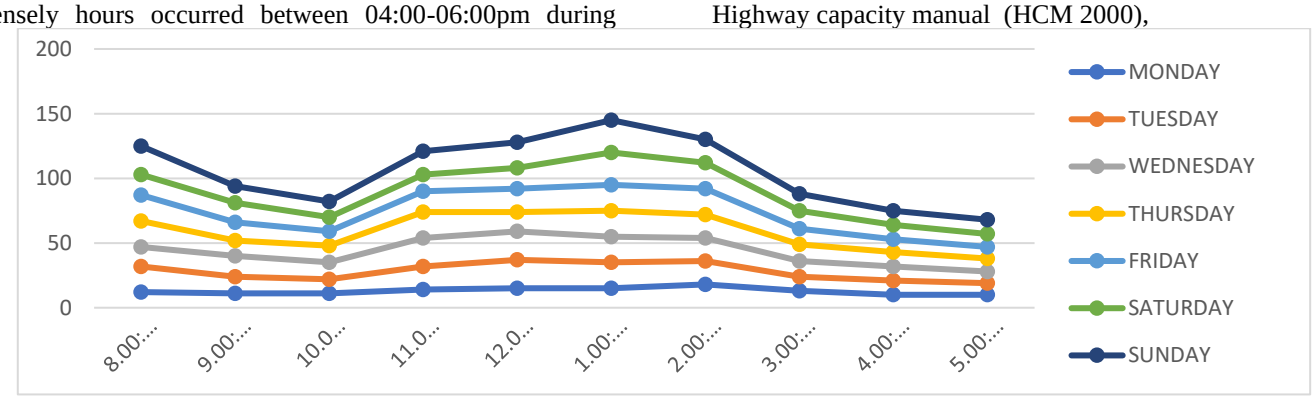

Figure 6.7: Average Hourly Speed Chittorgarh/Bhilwara

The result of vehicles speed were presented above revealed that there is less speed during both morning and evening peak hours, which resulted from the high flow traffic during morning and evening hours respectively, while the speed increases as the traffic flow decreases during mid-day (12:00pm to 03:00pm) this resulted from less movement of both commercial and private vehicle along the road.

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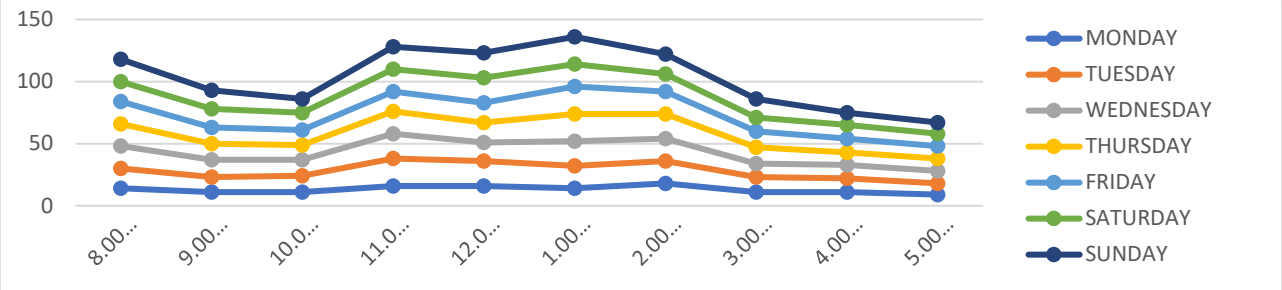

Figure 6.8: Average Hourly Speed Bhilwara/Chittorgarh

7.0: THE SPEED

The speed of the Bhilwara/Chittorgarh flow similar trend with that of Chittorgarh/Bhilwara the little difference is the average speed.

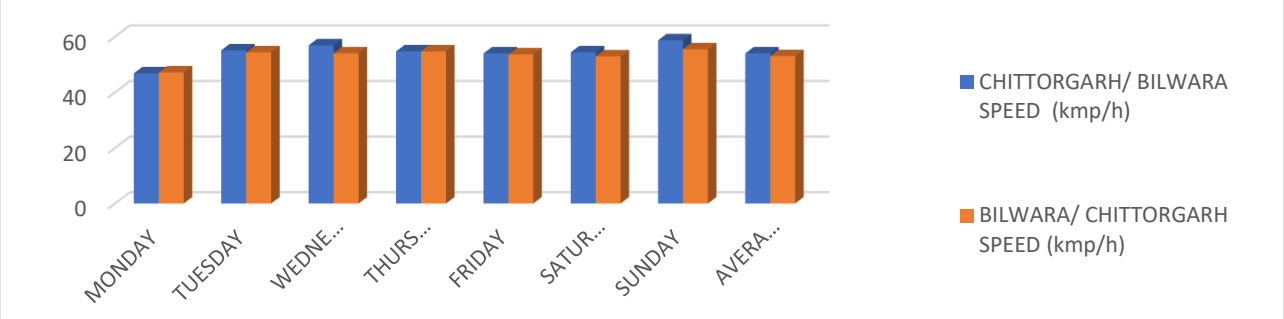

Figure 7.1: Average Speed of Moving Vehicles

The daily average speed of the vehicle which ranges from 46.8 to 54 K.P.H to conclude on the speed it can be categories as the level service E, It can be also be seen that the average speed of the vehicle is within the recommended speed of 50-60KPH Highway capacity manual (HCM 2000).

7.2: Saturation Ratio

The saturation level is very negligible having an average value of 0.1 for each hour this can be has little impact on the level of service of the road.

8.0: GENERAL DISCUSSION

The analysis preliminary conducted along the NH79 revealed that the road has high probability of accident this is because there is no any provision of traffic regulation the will guide vehicle and other road users such as pedestrian to the right path, also poor parking facilities is found to negate the smooth movement of vehicle due to rampant and irregular parking along the road side of the NH79 especially in gangrar junction market, this market proximity cause congestion, delay, and sometimes prone to accident potentialities along the road. the analysis of data of traffic volume count, traffic density, capacity, speed, level of saturation along the NH79 section revealed that the road has an average daily capacity 12609veh/day and average hourly traffic flow of 1261veh/hour with average speed of 54 K.P.H, the traffic density of the road is 112, therefore base on the parameters evaluated it can concluded that road can be level of service E this is because all the parameter are within the range with in compliances with the recommendation made in the (HCM, 2000).

8.1: CONCLUSIONS

With the result discussed above, the following conclusions were drawn.

The preliminary survey conducted on the NH79 road section revealed that it's made up of rigid pavement having 2-way with 3-lane carriageway in each direction, each carriage way is 4.2m and service lane which its currently under construction there is no any provision of parking facilities along the road especially in Rangarar town where there is tendency of high volume of daily traffic due to the presence of market and railway station.

Traffic volume study carried out along the road section revealed that the peak hour volume occurs Chittorgarh/Bhilwara in the morning (09:00am-10:00am) and evening (3:00pm-04:00pm) hours with average daily volume of 12609veh/day while Bhilwara/Chittorgarh direction has morning peak hour period between 09:00am to 10:00am and 05:00 to 06:00pm as evening hours' peak hour period with an average traffic obtained is 10477veh/day respectively and less flow of traffic is experience during midday hours due to less movement of vehicles during the period which former conditions associated with less speed of and later conditions with an incremental speed of 53.5K.P.H. all falls within the recommended range of speed limit of 50-60K.P.H Highway capacity manual (HCM 2000).

Operational Performance or level of service of NH79 road section can be categories as E this is because the average speed is 53.5K.P.H the average daily traffic volume of 11543Veh/day an average traffic density of 114 as well as the saturation capacity of 0.1 therefore the road is within its good condition of operation using Highway capacity manual (HCM 2000).

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9.0: FUTURE SCOPE/RECOMMENDATIONS

Based on survey and analysis of result, the following recommendations can be drawn from the study.

Planning: Although the **NH79** road is still growing and changing, and undoubtedly many of the methods and procedures used today will be modified in the future, resulting in a more responsive and useful transportation process such as provision of parking facilities along in Rangarar, town.

Management and Maintenance: traffic management system is also important as the design of the road facilities itself, unless the system is adequately managed so to serve its function well. Therefore, there is need for the continuous maintenance to prolong the service life of the road.

Traffic control system: regulation of traffic by provision traffic signal system along the NH79 especially in Rangarar town junction will reduce the level conduction, delay prone to accident and travel time of the drivers and other road user.

10.0: REFERENCE

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Application of Bio-Enzyme in Wastewater (Greywater) Treatment

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Abstract - *With rapid industrialization and ongoing development activities by humankind has polluted the water and reduced the quality of water at such a level that it becomes a threat to life. Since, water is an essential element for nature as well as for humans to perform various tasks to run the continuous cycle of survival. It becomes very much essential to make it pure. In past few years, researchers are working to find new techniques for reclamation of water focusing on biological or physical wastewater treatment methods rather than chemical ones. Use of bio-enzyme in biological treatment of wastewater could be a viable and eco-friendly solution. In this study bio-enzyme obtained from fermentation of flower waste was used to treat the wastewater (greywater) sample. The wastewater samples were digested for a period of 5, 15 and 25 days by mixing with 5%, 10% and 15% bio-enzyme solution. The parameters like pH, TDS, BOD_5, COD, Ammonia Nitrogen and Phosphates were analyzed for present investigation. The results showed that bio-enzyme can remove TDS, BOD_5 and COD characteristics of the wastewater; while complete removal of ammonical nitrogen and phosphate was observed with low concentration of bio-enzyme solution. No considerable variation in the characteristics pH was noted; it remains acidic. Bio-Enzyme can be used as an economic option to enhance wastewater attributes by treating it with bio-enzymes and make fit it for various purposes. Moreover, utilization of bio-enzymes can also help in checking disposal of chemicals during wastewater treatment processes making it environmentally sustainable.*

Key Words: Bio-Enzyme, Garbage Enzyme, Greywater Treatment, Waste Enzyme, Wastewater Treatment

1. INTRODUCTION

More than 70 % of the fresh water bodies carrying polluted water and ground water level have been reduced to zero at certain places[1]. The water which gets contaminated or polluted lost its usefulness and become a waste; such water generally termed as wastewater. Wastewater contains a wide range of elements that could impact environmental and public health negatively. To minimize potential harmful impacts, it is highly recommended that wastewater must be treated prior to discharge or reuse. Various treatment and purification technologies have been developed to reclaim the usefulness of wastewater. These treatment technologies are based on three basic processes i.e. Physical, chemical and biological[2]. For treatment of the wastewater which generally contains a high amount of organic content, biological treatment is most suitable option. Biological processes require an ample amount of time for treatment which cannot fulfill the daily demand of water. So, it becomes necessary to accelerate the rate of reaction by some means. For effective and efficient treatment of wastewater using biological treatment, enzymes could be the solution[3]. Enzymes not only act as catalyst moreover they increase the rate of reaction many folds with less energy in desired direction to get desired output, if properly used.

To perform various metabolic functions living cells produces biocatalyst that performs specific bio-chemical action/response very much needed for flourishing life. These biocatalysts are called as enzymes[4]. Enzyme is the natural liquid formulation extracted from fermentation of vegetable/fruits which does not catch fire/ cause corrosion and non-poisonous in nature[5]. An enzyme shows attributes that make their utilization favorable when contrasted with conventional chemical catalysts. Enzymes are particular for their substrates and catalyze just one or few bio-chemical reactions among numerous probabilities[6]. The enzymes being for the most part proteins and peptides; they are degradable by microorganisms and effortlessly expelled from adulterated streams without causing any disposal issues. Enzymes utilized in wastewater fall in the category of biological supplements[7].

Enzymes produced under anaerobic conditions from fermentation of organic waste material such as fruit/ vegetable waste along with brown sugar and water in a fixed proportion are called as Bio-Enzymes or Waste Enzyme or Garbage Enzymes[8]. Bio-Enzymes or waste enzymes or garbage enzymes are different than any other enzymes which are produced by a living cell or microorganism such as fruit enzymes[9]. Fruit enzyme can be used in edible products or is edible while on the other as bio-enzymes are not fit for human consumption. Bio-Enzyme can be utilized for natural household cleaning; as natural insecticides; replacement of chemical detergent; as body care; as natural antiseptic for houses, as organic fertilizer; removing odour and toxic air released from smoking, car exhaust, chemical resides from household products, etc., and it also prevents blockage of drainpipes, helps in purifying the water bodies when flows them. It also acts as repellent for mosquitoes, flies, rats, cockroaches and other nuisance creating organisms[10]. Effective treatment of wastewater can be done by utilizing bio-enzymes[11].

For the treatment of domestic wastewater with advanced level of degradation in a shorter span of time, bio-enzyme performs the same task as done by enzymes. In Malaysia, many researchers have performed investigation to check the bio-enzyme as viable solution for wastewater treatment[12].

In India, bio-enzyme is not much known and practiced at very low level[10]. Usage of bio-enzyme not only provides an alternative solution to biological recovery from organic waste it will also help in minimization and reduction of waste; since municipal solid waste mainly consists of organic waste. It also puts a check on greenhouse emissions, lessen the burden on landfills[13].

This paper presents the results from digestion of greywater using bio-enzymes produced from flower waste at three different concentrations i.e. 5%, 10% and 15% after 5, 10 and 25 days of digestion period. An attempt has been made to understand the effectiveness of bio-enzymes produced from organic waste material in treating wastewater specifically greywater.

2. MATERIALS AND METHODS

2.1 Materials

The materials used in this study are:

- Flower waste (fresh)
- Jaggery (chemical free)
- Water (free from any kind of impurity)
- Plastic container with screw cap (preferably)
- Aluminium foil

All the materials was collected as specified above and in sufficient quantity as per requirement

2.2 Methods

Methodology followed in the present study can be divided in two main steps:

(i) Bio-Enzyme preparation
(ii) Wastewater treatment using bio-enzyme

2.2.1 Preparation of bio-enzyme

Flower waste in required quantity was collected as organic substances to make enzymes. After the collection of waste separation is done to ensure no any chemical substance enter in to the system which can affect the process. Flower waste was then shredded in small pieces to increase surface area for reaction. It is done to increase the rate of decomposition. Jaggery, flower waste and water were mixed together in the ratio of 1:3:10 to prepare waste enzyme or bio-enzyme [14]. The mixing process was done in an air-tight plastic container which can expand and has screw bottle caps. Gases will get formed during production of waste enzyme so plastic container with screw caps such as plastic bottle is the best alternative for releasing the gases so produced. Then the container was kept at safe place so no one can disturb the digestion process; where the food waste is broken down into smaller compounds by microbes along with the release of gases under fermentation process. To release gases lid was opened once in a day, for a minute or so, then the lid was put back on, it was kept back in the dark place and the same procedure was repeated on another day (for first one month at least).

After third week onwards, the gas production was reduced a bit. In the second month, lid was opened on end of the week for first two weeks as gas release was reduced considerably and again it was kept in the dark. After completion of 45 days, the container was tightly closed and left it for another 45 days of digestion. The total duration to complete the process was 3 months, as recommended in the previous studies [15].

After 90 days of digestion a brown colored liquid along with many small particles and some undigested residue was prepared in the container. That brown colored liquid was raw enzyme and it was needed to separate it out from other solid matter left after digestion. Filtration was done to obtain the prepared bio-enzyme or waste enzyme with enhance the structural, functional properties. Filtered bio-enzyme solution was kept separately in closed container. The characterization of the bio-enzyme was done immediately, after 30 and 60 days of filtration to know the stability of the enzyme solution [16].

2.2.2 Wastewater treatment using bio-enzyme

When the characterization of bio-enzyme was over then the wastewater (greywater) sample are collected after from a drain where wastewater doesn't contain excreta. After collection of raw wastewater sample it was analyzed to know its initial characteristics. Then nine beakers was filled the wastewater sample mixed with bio-enzyme or flower waste enzyme solution in different proportion i.e. 5%, 10%, and 15%[10]. Each three beakers having wastewater sample mixed same concentration of bio-enzyme was prepared for 5, 15 and 25 days of digestion. The change in the characteristics of the treated wastewater sample after digestion period of 5, 15 and 25 days, were analyzed and noted[17].

3. RESULT & DISCUSSION

In present study, different tests were carried out in batches to determine the effective dosage of flower waste enzyme for treatment of greywater sample. The parameters like pH, TDS, BOD_5, COD, Ammonia Nitrogen and Phosphate were analyzed for all the samples as per procedures in standard methods[18]. The characteristics of flower waste enzyme solutions were analyzed immediately after filtration, 30 days after filtration and 60 days of filtration. For present study, 5%, 10% and 15% of flower waste enzyme after 60 days of filtration with wastewater (greywater) sample were selected. Total nine beakers were filled by wastewater sample along with 5%, 10% and 15% enzyme solution obtained from fermentation of flower waste. These beakers were covered with a foil of aluminium and were kept for digestion period of 5 days, 15 days and 25 days. The variations in characteristics of the wastewater sample after 5, 15 and 25 days of digestion were observed and analyzed.

3.1 Characteristics of Bio-Enzyme/Waste Enzyme

The characteristics of enzyme solution for flower waste after three months of fermentation period was noted; immediately after filtration of the enzyme solution, 30 days after filtration and 60 days after filtration. The waste enzyme solution is rich in organic content. The characteristics of the bio-enzyme extracted out of flower waste in tabulated below (Table 1).

Table -1: Characteristics of Flower Waste Enzyme

Parameter	Just after filtration	30 Days of filtration	60 days of filtration
PH	3.09	3.41	4.01
TDS (mg/L)	2012	1415	1012
BOD5(mg/L)	1252	535	83
COD(mg/L)	44620	2523	153
Ammonical Nitrogen (mg/L)	0	0	0
Phosphate (mg/L)	0	0	0

The low pH value of the bio-enzyme solution prepared from flower waste shows its acidic nature. The BOD_5 and COD values were high when the enzyme solution was analyzed immediately after filtration of the solution. But after 30 days of filtration, BOD reduced to less than half of initial concentration and COD concentration came to level of less than 10%. Moreover, After 60 day of filtration of enzyme solution, drop of more than 90% and about 99% in BOD and COD concentration respectively.

3.2 Characteristics of Raw Wastewater (Greywater) Sample

Before treating the wastewater sample with bio-enzyme, it is essential to find out the characteristics of the raw wastewater sample. The parameters like pH, TDS, BOD_5, COD, Ammonia nitrogen and Phosphates were found out. Table 2 demonstrates the raw wastewater characteristics used in present study.

Table -2: Raw wastewater (greywater) characteristics

Parameter	Units	Value
PH	--	6.16
TDS (mg/L)	mg/L	563
BOD5(mg/L)	mg/L	192
COD(mg/L)	mg/L	290
Ammonical Nitrogen (mg/L)	mg/L	9.6
Phosphate (mg/L)	mg/L	110

3.3 Characteristics of the Wastewater Sample after Treatment with Bio-Enzyme

The raw greywater sample was treated using 5%, 10% and 15% bio-enzyme solution obtained from flower waste. These samples were then left for 5, 15 and 25 days. The variations of phosphate, ammonical nitrogen, COD, BOD5, TDS and pH with time for different concentrations of bio-enzyme solution were analyzed and discussed below:

- ***pH***

After treatment with bio-enzyme the variations was observed in pH value of the effluent and the corresponding variation in the characteristic of treated wastewater sample after 5, 15 & 25 days of digestion are shown in figure 1.

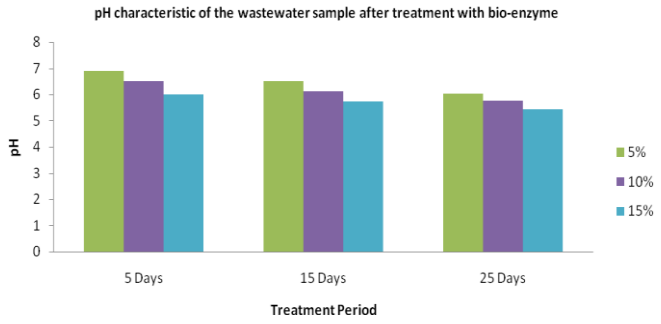

Fig -1: Variation in pH characteristic of the treated wastewater sample

The filtered bio-enzyme obtained from flower waste was found acidic in nature as indicated by low its pH value (see Table 1). When it get mixed with greywater, the pH of wastewater sample having 5% bio-enzyme for digestion of 5 days, increased to nearly neutral range due to enzymatic reactions but slowly get reduced at constant rate with increase in digestion period. Similar variation is also noted for wastewater samples having 10% and 15% bio-enzyme mixed.

- ***TDS***

After treatment with bio-enzyme the variations was observed in TDS content of the effluent and the corresponding variation in the characteristic of treated wastewater sample after 5, 15 & 25 days of digestion are shown in figure 2.

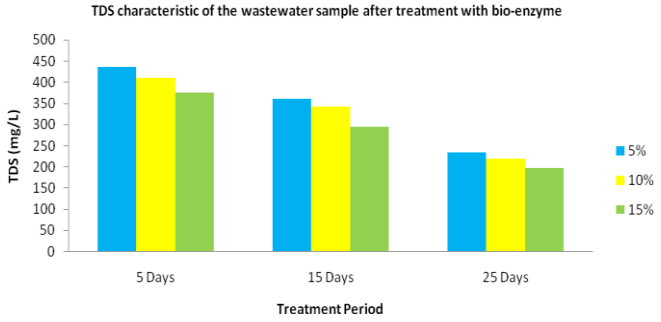

Fig -2: Variation in TDS characteristic of the treated wastewater sample

TDS characteristic of wastewater sample mixed with 5% bio-enzyme for digestion of 5 days, 15 days and 25 days was noted with decrement at constant rate; When compared with initial TDS of raw wastewater sample (see Table 2) more than 50% TDS got removed after 25 days of digestion due to enzymatic reactions. Similar, variation is also noted for wastewater samples having 10% and 15% bio-enzyme mixed.

➢ *BOD_5*

After treatment with bio-enzyme the variations was in the BOD_5 characteristic of treated wastewater sample after 5, 15 & 25 days of digestion are shown in figure 3.

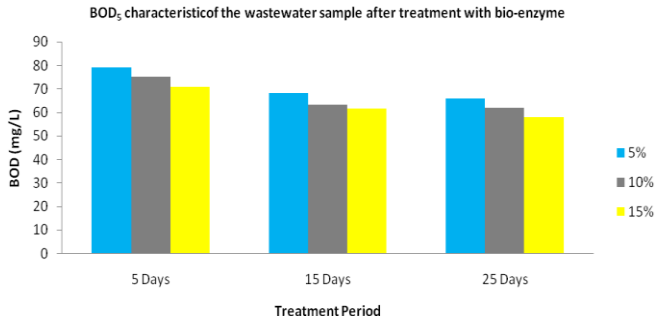

Fig -3: Variation in BOD_5 characteristic of the treated wastewater sample

In BOD_5 characteristic of wastewater sample with all three concentrations (i.e. 5%, 10% and 15%) of bio-enzyme, a constant rate of reduction in BOD_5 was noted for digestion of 5 days, 15 days and 25 days. Reduction was more than 50% for digestion period of initial 5 days. While this rate falls down below less than 10% for next 10 and 20 days.

➢ *COD*

The variations in COD characteristic of the treated wastewater sample after 5, 15 & 25 days of digestion with bio-enzyme are shown in figure 4.

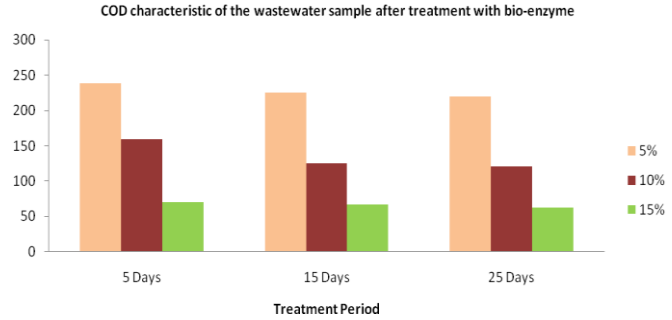

Fig -4: Variation in COD characteristic of the treated wastewater sample

A decrease of about 20% can be observed in COD characteristic of wastewater sample (see Figure 3.4) mixed with 5% of bio-enzyme for 5 days, 15 days and 25 days of digestion. While on mixing 10% and 15% bio-enzyme solution with wastewater sample a sharp removal rate was observed.

➢ *Ammonical Nitrogen*

The variations in ammonical nitrogen characteristic of the treated wastewater sample after 5, 15 & 25 days of digestion with bio-enzyme are shown in figure 5.

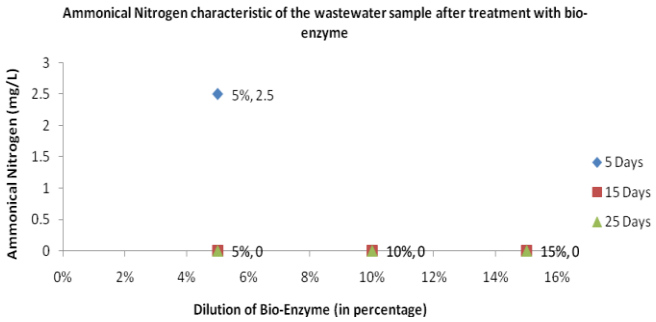

Fig -5: Variation in ammonical nitrogen characteristic of the treated wastewater sample

More than 70% of the ammonical nitrogen was removed of the wastewater sample mixed with 5% bio-enzyme for digestion of first 5 days. While 100% removal rate was observed for wastewater sample mixed with 10% and 15% bio-enzyme solution for first 5 days of digestion.

➢ *Phosphate*

The variations in phosphate characteristic of the treated wastewater sample after 5, 15 & 25 days of digestion with bio-enzyme are shown in figure 6.

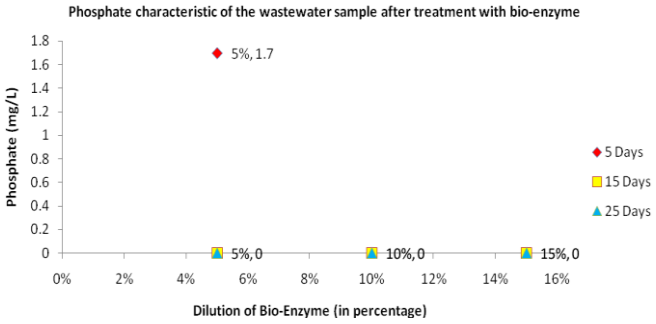

Fig -6: Variation in phosphate characteristic of the treated wastewater sample

In case of phosphate characteristic, more than 95% removal was observed for wastewater sample mixed with 5% bio-enzyme solution for digestion of first 5 days. While 100% removal rate was observed for wastewater sample mixed with 10% and 15% bio-enzyme solution for the first 5 days of digestion.

4. CONCLUSIONS

In present study, the bio-enzyme was produced from organic waste material i.e., flower waste. The bio-enzyme showed acidic character and high initial BOD due to the presence of high amount of organic content. The results indicate that the 10% bio-enzyme solution may effectively remove ammonical nitrogen, phosphate, TDS, BOD_5 and COD characteristics of greywater. Bio-Enzyme is cheap and cost effective as it is

obtained from waste material. Moreover, it reduces the burden on planet by utilizing the waste as resources. Hence, Bio-Enzyme can be can be used as an economic option to enhance wastewater attributes to make it fit for further utilization.

Furthermore investigations can be done to find out the suitable additives or activators or enhancer on enzyme action. Investigation on pre-treatment for the reduction of high initial BOD and COD prior to action of enzymes can also be studied. The utilization of bio-enzymes in treating all types of wastewaters under different physico-chemical conditions can also be explored. The effect of bio-enzymes on characteristics of wastewater other than or along with the parameters discussed in present study can also be investigated.

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Assessment of Fiber Reinforced Concrete (FRC) with Industrial Wastage Material for Rigid Pavements

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Abstract

In a made nation relating India, road frameworks structure the techniques for the nation. Strands can be as steel fibers, glass strands, trademark strands, produced fibers, etc. The adding of fibers to solid makes it a consistent and isotropic material. Roadways are used for generous traffic stacks all through the world remaining to its better and monetarily getting execution. Steel fiber strengthened black-tops are the new kind of pavements that are expanding a huge amount of importance in current events. These black-tops use fibers in the covering of pavements. The use of fibers in pavements has various inclinations. Steel strands decline pollution and are furthermore monetarily smart. The use of fibers constructs durability and improves strong pavements. Beside steel fibers, these strands can in like manner be made of steel and ordinary materials. Steel strands are an instance of fiber used truly coming to fruition of such black-tops. Steel strands are known to be serious and impenetrable to atmosphere conditions. These properties make steel strands significant in the improvement of structures. This paper deals with an exploratory assessment on the properties of concrete by solidifying FRC materials in the strong mix. The nature of the black-top can be extended while advancement by including more steel strands. The modifications in properties of strong when steel strands are used in concrete in its common structure and in the wake of changing its properties by displaced by steel fibers and adjusted steel fibers by 1 to 4 % in M40 assessment of concrete. Test results on Compressive Strength, Split Tensile Strength, and Flexural Strength.

Keywords; *Fiber Reinforced Concrete (FRC), Rigid Pavement, Steel Fibers, Compressive Strength, Split Tensile Strength, Flexural Strength.*

I. INTRODUCTION

Concrete through from Portland concrete, is similarly extreme in pressure yet frail in strain and will in general be hard. The delicateness in pressure can be suspicious by the utilization of unsurprising steel bars fortification and somewhat by the blending of an adequate volume of specific strands. To convey data on the possessions and entries of the more typically accessible filaments and their uses to deliver concrete with positive qualities. An imaginative liberal of fiber strengthened cement is propelled which is produced using cellulose strands. A fiber is a little independent strengthening material delivered from numerous materials like steel, plastic, glass, carbon and characteristic materials in numerous shapes and size. A numerical parameter depicting a fiber as its perspective proportion, which is characterized as the fiber length, apportioned by a reporter fiber breadth. The plain solid tumbles quickly when the diversion steady to the inevitable flexural quality is surpassed, then again fiber strengthened solid carry on to support significant loads even at avoidances considerably in extra of the break redirection of the solid. Solid asphalts are utilized for thruways, air terminals, avenues, neighborhood streets, parking garages, modern

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offices, and extra sorts of association. When suitably arranged and worked out of extreme materials, solid asphalts can convey a few times of arrangement with slight or no support. "Concrete for the most part has a higher unique expense than black-top yet takes lengthier and has lower preservation costs" at times, in any case, structure or development blunders or inadequately chose materials have extensively diminished asphalt lifetime. It is so primary for asphalt specialists to comprehend materials choice, blend proportioning, plan and specifying, waste, development procedures, and asphalt execution. It is likewise critical to comprehend the theoretical system essential normally utilized plan activities, and to know the limitations of relevance of the procedures

1.2 ADVANTAGESOFFIBER-REINFORCEDCONCRETE

- Usefulness
- Adaptability
- Rigidity
- Malleability
- Protection from plastic shrinkage while relieving
- Protection from splitting
- Shrinkage at an early age
- Imperiousness to fire

1.3APPLICATIONS

- Ground-level applications, for example, walkways and building floors
- Cellar establishments
- Building columns
- Bolster bars
- Scaffolds
- Internment vaults
- Roadways
- Seepage pipes
- Septic tanks
- Vaults and safes.

II. LITERATURE REVIEW

Ramakrishnan V., Wu G.Y., and Hosalli G.: Decide the conduct and execution qualities of the most ordinarily utilized fiber-strengthened cements (FRC) for potential runway asphalts and overlay applications.

G.M. Chena,(2014) a concentrated on compressive conduct of steel fiber fortified reused total cement after introduction to raised temperatures utilizing the Layered steel strands and the filaments had a length of 32 mm with a viewpoint proportion of 40 and reasoned that the incorporation of steel strands is compelling in controlling the advancement of break width, an expansion of steel fiber content prompted essentially littler split width.

SemsiYazıcı and Hasansahanare (2013) concentrated on the impact of steel fiber on the security among concrete and disfigured steel bar in SFRC utilizing steel filaments with two diverse l/d proportions of 40 and 80 are utilized. In view of their examination the pullout loads are seen as expanded by 7–16% when the measure of steel filaments and perspective proportion in the steel fiber cements delivered increment when contrasted with cements without steel fiber. It is seen that there are increments in the compressive and parting elastic qualities of the steel fiber cements containing steel strands of 40 and 80 l/d proportions utilized in the sum varying from 0 to 80 kg/m3 when contrasted with cements without filaments. H.T Wang and L.C Wang (2013) have decided the static and dynamic mechanical properties of the steel fiber fortified light weight total cement. The consolidation of steel fiber into network serves to build a definitive compressive quality by the resultant capturing development of splits dependent on the obligation of steel fiber and concrete glue. As the expansion in the level of steel fiber flexural and split rigidity increments.

K.E. Caballero-Morrison (2012) concentrated on the Conduct of steel-fiber-strengthened typical quality cement thin sections under cyclic stacking utilizing steel filaments, with perspective proportion l/d =

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35/0.55 = 63.63 and performed 3-point twisting test and lingering flexural quality at various volume portion rates. In view of their outcomes the consideration of steel strands into the solid blend postpones solid spread spalling and clasping of the longitudinal support bars in pressure, decreases the basic area length.

R.S. Olivito and F.A. Zuccarello , (2010) concentrated on trial examination on the elasticity of steel fiber strengthened solid utilizing various sorts of steel strands, Their viewpoint proportion l/d was equivalent to 50 and their length equivalent to 22, 30 and 44 mm at various volume parts of 1% and 2%.They led uni-hub pressure tests, direct ductile tests and four-point-twisting tests which reasoned that compressive quality of the material is less influenced by the nearness of filaments because of filaments connecting impact, cubic example didn't pound yet they held their uprightness up to finish of the test. The malleability and relentlessness increment of SFRC when fiber content in volume increments and, at a similar fiber content, when fiber length expands SFRC shows a higher twisting firmness and an unexpected breaking design in comparison to ordinary cement. Test results demonstrated an addition for the most extreme elasticity for short filaments examples a definitive strain was higher for long fiber ones.

M.C. Nataraja (2000) the heap avoidance bend is acquired with exact diversion estimation utilizing burden. By finding the pinnacle load the bends are isolated in to two areas for deciding the pre top durability and post top strength. It has been presumed that as increment in the perspective proportion of fiber flexural sturdiness increments. Thus its pliability increments with expansion of steel fiber.

III. MATERIALS

3.1.Cement:

Concrete is a folio, a fixing utilized for development that gatherings, toughens, and notification to different materials to fix them created. Concrete is every so often utilized on its individual, yet tolerably to tie sand and rock together. Concrete blended in with fine total produces mortar for stone work, or with sand and rock, items concrete.

TestParticulars	ResultObtained	RequirementsasperIS:122691987
Specificgravity	3.13	3.10-3.15
Normalconsistency (%)	31	30-35
Initialsettingtime(minutes)	37	30minimum
Finalsettingtime(minutes)	570	600maximum

3.2FineAggregate

Fineaggregatesare consistently sand or squashed stone that are a littler sum than 9.55mm in width. Normally the most aggregate size of total utilized in development is 20mm. A bigger size, 40mm, is increasingly partaken in mass cement. Prevalent total distances across decline the limit of concrete and water required.

S.No	Particulars	Value
1	Specificgravity	2.66
2	bulkDensity	15.13Kn/m^3
3	Waterabsorption	2.81%
4	Voidsinaggregate	36.25%
5	SiltContent	4.87%
6	MoistureContent	3.62%
7	FineModulus	2.40

3.3CoarseAggregates.

Coarseaggregateis the portion of the solid which is done up of the prevalent stones fixed in the blend. Solid spreads three components; Water, concrete, and total. That total is set up of fine sand and coarse rock.

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S.No	Particulars	Value
1	Specificgravity	2.70
2	BulkDensity	16.00Kn/m^3
3	Waterabsorption	0.66%
4	FranknessIndex	13.88
5	ElongationIndex	21.24
6	CrushingValue	2.42
7	ImpactValue	16.1

Table2:-PropertiesofCoarseAggregates.

3.4STEELFIBERS

Steel fiber fortified cement is a cast able or spray able compound material of water driven concrete, fine, or fine and coarse totals with isolated steel strands of quadrilateral cross-segment calmly scattered through the framework. Steel filaments reinforce concrete by assaulting elastic splitting.

S.NO	Properties	Quantity
1	AverageLength(mm)	30
2	AverageWidth(mm)	0.56
3	AspectRatio(l/d)	54
4	TensileLength	>1100
5	UltimateLength	<2
6	SpecificGravity	7.85

3.5 MIX DESIGN PROCEDURE (IS 10262-2009)

3.5.1 REQUIRED DATA

Grade of concrete = M40

Type of cement= OPC 53 grade

Specific gravity of Cement = 3.13

Specific gravity of F.A= 2.66

Specific gravity of C.A = 2.70

Bulk density of C.A= 1600kg/m^3

Fineness modulus of F.A = 2.79

Minimum cement content = 360 Kg /m^3

3.5.2 MATERIALS REQUIRED FOR M40 GRADE OF CONCRETE

Cement	394.32 kg
Fine aggregate	680 kg
Coarse aggregate	1226.88 kg
Water	157.72 lit

The Mix proportion = cement: Fine aggregate: Coarse aggregate: Water

= 394.32: 680: 1226.88:157.72

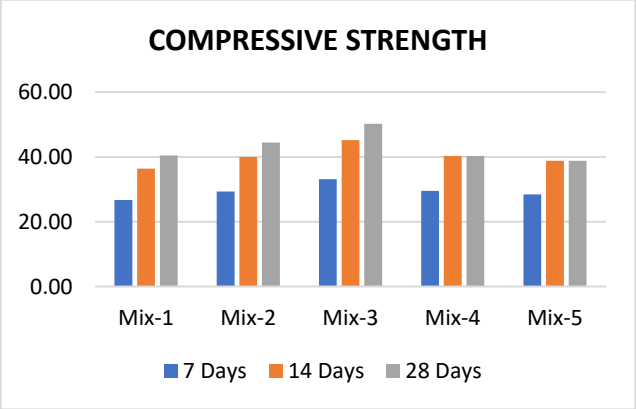
= 1: 1.724: 3.11: 0.4

3.5.3 TYPES OF PROPORTIONS

S.NO	MIXES SPECIMENS	PROPORTIONS
1	Mix-1	0% Steel Fiber
2	Mix-2	1 %Steel Fiber
3	Mix-3	2% Steel Fiber
4	Mix-4	3% Steel Fiber
5	Mix-5	4% Steel Fiber

IV. RESULTS AND DISCUSSION

4.4.1 COMPRESSIVE STRENGTH



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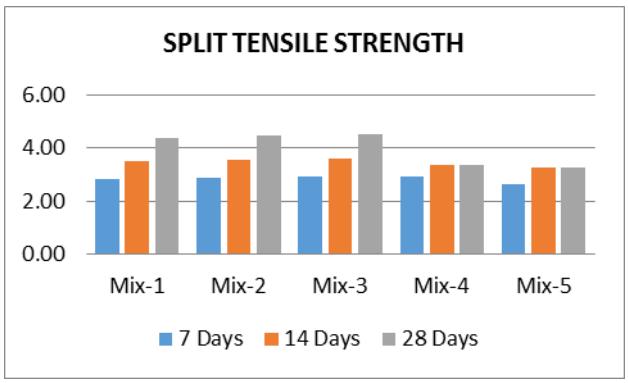
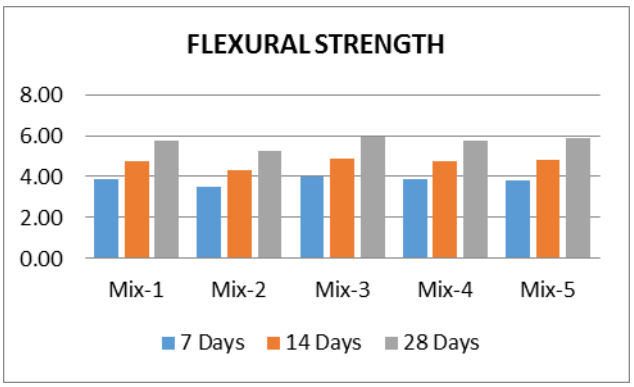
4.4.2 SPLIT TENSILE STRENGTH



4.4.3 FLEXURAL STRENGTH



V. CONCLUSION AND FUTURE SCOPE

- For the inflexible asphalts the general quality and the lifetime of a specific asphalt relies upon the flexural quality of the solid and the protection from the splitting created because of surface loads over some stretch of time.
- In this venture both the flexural and compressive quality has been improved by the expansion of steel fiber which will in the long run bring about the lessening of the asphalt thickness just as the lifetime of the asphalt.
- Adding of steel filaments to solid expands the compressive quality of cement imperceptibly.
- The expansion of steel filaments expands the rigidity. The elasticity was seen as most extreme with volume portion of 2%.
- By the expansion of steel filaments the flexure quality was found to diminish barely.
- The expansion of filaments to concrete expressively expands its durability and makes the solid progressively pliable as saw by the methods of disappointment of examples.
- The solidness of pillars was examined and was seen as most extreme for snared end fiber with 2% volume part.
- The observational conditions created in this analysis can be utilized for ascertaining the durability files or level of fiber whichever is required.
- The malleability of steel fiber strengthened cement was found to increment with increment in volume division of filaments and the greatest increment was watched for snared strands with 2%volume part.
- The improvement in the vitality retention limit of steel fiber fortified solid boards with expanding level of steel filaments.

VI. FUTURE SCOPE OF THE STUDY:

- Further research should be possible by contemplating the impact of steel fiber by putting at various profundities in the solid asphalt.
- Also by shifting the angle proportion just as the breadth of the steel strands tests should be possible to see the impact of these qualities on the flexural quality.

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Assessment of Rajasthan Surface Water Quality During Covid19 Pandemic Lockdown

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***Abstract*: This research paper aimed at investigating the effect of the covid19 pandemic lockdown on the surface water (rivers, canals, dams and lakes) quality of Rajasthan state of India.The data was collected from sixty independent monitoring stations control by the State Pollution Control Board;and was analyzed and compared with the result of April of 2019 using the Indian standardfor water quality recommendations (IS: 2296:1992). The result shows that lockdown has contributed immensely to the improvement of the surface water quality.This was due to the reduction of industrials, transportationand other anthropogenic activities that mostly contributed to the release of toxic effluents and gases which lead to the surface water contamination.Therefore, a periodic based assessment should be employed so that the quality level of surface water can be monitored and controlled as well as enforcing laws to both industries, and general public regarding refuse dumping.**

Keywords*:- *Lockdown, quality, improvement, surface-water,level

1.0 INTRODUCTION

Water is an indispensable part of human lives as it's variously involves in our daily activities from drinking, cooking and other house chores to agricultural and recreational purposes. Surface water constitute of the streams and rivers that collect water during rainfall and empty it into oceans, seas and lakes. These surface water have been the only sources of water especially during the dry season in many parts of the world. However, they in many times contain various organic and chemical constituents which render them unfit to serve their purposes (Simeonov et al., 2003; Neale et al., 2017) as they are known to transport waste waters from the municipal and industrial layouts; and agricultural runoffs containing pesticides and other chemicals. Therefore, the needs to scientifically access their quality and provide user-friendly results to environmental management agencies and general public; cannot be over emphasized as it immeasurably affect human health and rate of agricultural production. This involves assessment of physico-chemical, micro-pollutants and biological contents of the surface water which are affected by rock constituents of the river basin, atmospheric input, climatic settings and human activities. The results of the assessment are then compared with the standard values for drinking and irrigation; given by regulating bodies like the World Health Organization (WHO), United Nation International Children Emergency Fund (UNICEF) and United State Salinity Laboratory among others.

physio-chemical and biological parameters to assess the of ground water quality of the Indore city and its industrial area using water quality index which revealed that the periodic assessment on the water quality of area should be conducted and compared with the relevant standard for drinking water such as Indian standard, WHO standard; in order to have a reliable and controllable source of water supply. The work on water quality indices found that there is no any water quality index that is universally accepted for the surface water assessment. However, there are ongoing discoveries about other parameters by policymakers that can be used to increase the level of dependency on the indices. They further stated that most of indices across the world utilizes the physio-chemical and biological parameters for the quality assessment.

2.0 PROBLEM STATERMENT

The lockdown imposed by the government to tackle the spread of the noble covid-19 has led to limited industrial activities. This has considerably affected the rate of water pollution by industrial effluents hence the quality of surface water. Therefore, this research paper aim at comparatively studying the quality of the surface water before and during the lockdown in Rajasthan State.

3.0 STUDY AREA

Rajasthan occupies the northwestern part of India and is the largest state (about 10.74% of the Indian Territory) with a total area of 342, 239 sq. km bounded between latitude 23 03'-30 12'N andlongitude 69 29'-78 17'E. It's bordered in the north and northeast by Haryanaand Uttar Pradesh, in the west and northwest by Pakistan, and in the south-southeast and southwest by Madhya Pradesh and Gujarat States respectively(Zo, 2011). The state is economically thriving on agriculture and mineral resources; remarkably marble and cement. For details see (Chauhan et al., 2020).

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Figure 1: Map of Rajasthan state (Adopted from Chauhan et al., 2020).

4.0METHODOLOGY

The methodology employed in this research involves a comprehensivecomparative analysis madefrom the data collected from the sixty Rajasthan network monitoring stations controlled by the Central Pollution Control Board (CPCB)of the state.The data of water samples were collected and analyzed during the last week of April, 2020.The samples were collected from 14 rivers, 4 canals, 16 lakes and 11 dams, sum up to a total of 45 sources across the state.The analyzed data was compared with the result obtained last year in the same month of April to know the impact of lockdown on surface water quality in the state. The parameters used for this research includes BiochemicalOxygenDemand (BOD), ChemicalOxygenDemand (COD), DissolvedOxygen (DO), Total Coliform andConductivity and the result was compared with the CPCB Water Quality Criteria for Designated Best Use. In order to simplify the work, the analysiswas categorized into two part viz: flowing surface water (Rivers and Canals) and stored surface water (dams and lakes).

For this research work, the codes assigned to each respective water source will be used during the discussion as nomenclature to represent them while the actual names of the sources can be obtained from the Central Pollution Control Board (CPCB)database.

The recommendations made by the Central Pollution Control Board (CPCB)based on bureau of Indian standard (IS 2296:1992)on the quality of surface water were tabulated below:

Table 1:CPCB Water Quality Criteria for Designated Best Use

Designated-Best-Use	Class of Water	Criteria
Drinking Water Source without conventional treatment but after disinfection	A	Total Coliforms Organism MPN/100ml shall be 50 or less pH between 6.5 and 8.5 Dissolved Oxygen 6mg/l or more Biochemical Oxygen Demand 5 days 20C 2mg/l or less
Outdoorbathing (Organised)	B	Total Coliforms Organism MPN/100ml shall be 500 or less pH between 6.5 and 8.5 Dissolved Oxygen 5mg/l or more Biochemical Oxygen Demand 5 days 20C 3mg/l or less
Drinking water source after conventional treatment and disinfection	C	Total Coliforms Organism MPN/100ml shall be 5000 or less pH between 6 to 9 Dissolved Oxygen 4mg/l or more Biochemical Oxygen Demand 5 days 20C 3mg/l or less
Propagation of Wild life and Fisheries	D	pH between 6.5 to 8.5 Dissolved Oxygen 4mg/l or more Free Ammonia (as N) 1.2 mg/l or less
Irrigation, Industrial Cooling, Controlled Waste disposal	E	pH between 6.0 to 8.5 Electrical Conductivity at 25C micro mhos/cm Max.2250 Sodium absorption Ratio Max. 26 Boron Max. 2mg/l

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Retrieved from Central Pollution Control Board, (CPCB) and Bureau of Indian standard (**IS:2296:1992**) Ministry of Environment, Forestand Climate Change).

5.0 RESULTS AND DISCUSSION

5.1 The Result of the Flowing Surface Water (Rivers and Canals)

5.1.1 Biochemical Oxygen Demand (BOD)

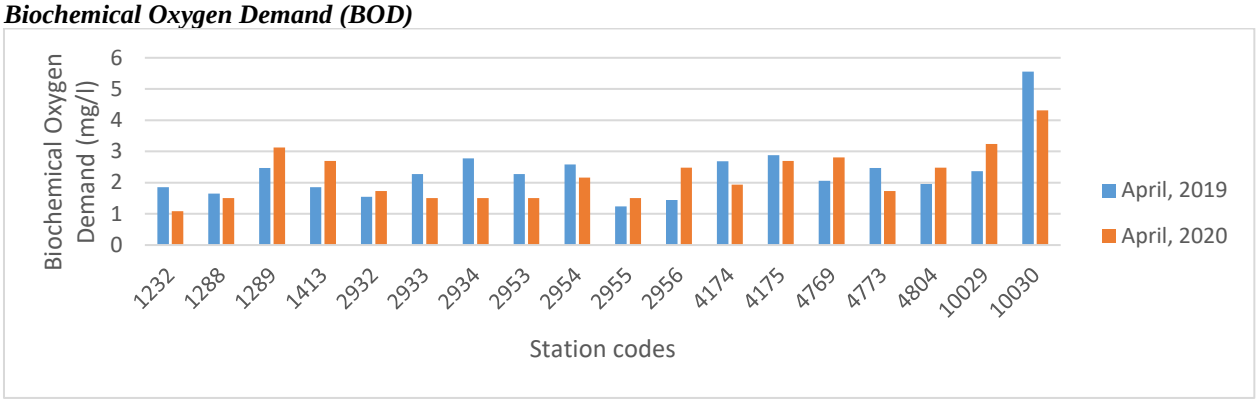

Figure 2: BiochemicalOxygen Demand (BOD)

Results of the assessed BOD in the surface waters (Rivers and Canals) of Rajasthan State before and during the lockdown due to the covid-19 is processed and presented above (Figure 2). It indicated that the BOD ranges between 1.24 mg/l to 5.56 mg/l before the lockdown; whereas it ranges between 1.08 mg/l to 4.32 mg/l during the lockdown. Generally, there is a considerable decrease in the BOD content except at 1289, 1413, 2932, 2955, 2956, 4769, 4804 and 10029 stations all of which are rivers around Chambal area except 2932 which happened to be Narmada main canal. However, the BOD content at 10030 are exceptionally high both before and during the covid-19 lockdown.Still during the lockdown Using the (IS:2296:1992)recommendations stations 1232, 1288, 2932, 2933, 2934, 2953, 2955, 4174 and 4733, belong to class A, while stations 1413, 2954, 2956, 4175, 4769 and 4804, can be categorized in class B and C. but station 1289, 10029 and 10030 belong to class D.

5.1.2Chemical Oxygen Demand (COD)

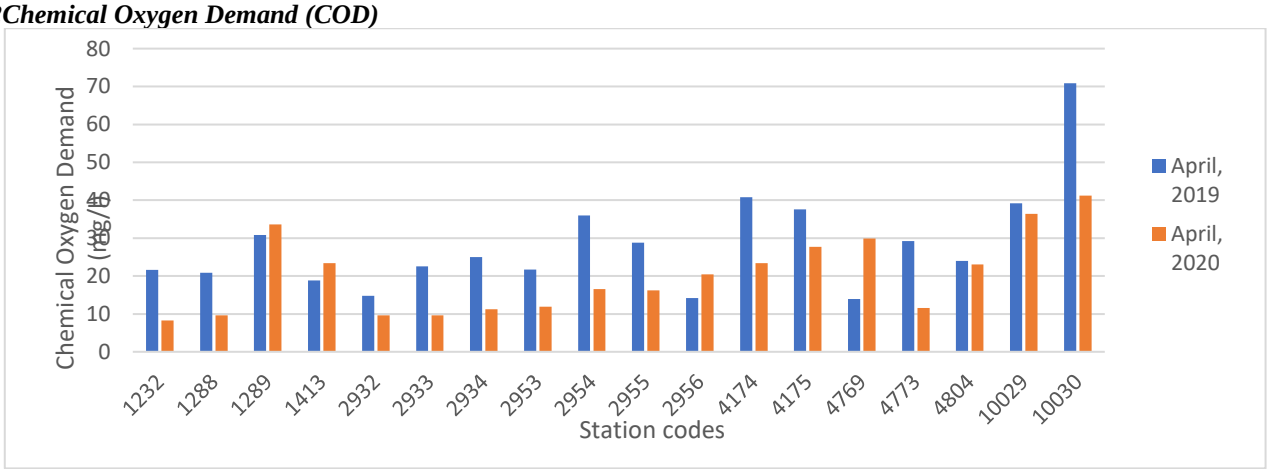

Figure 3: ChemicalOxygen Demand (COD)

Results of the COD contents of the Rivers and Canals in Rajasthan State before and during the lockdown due to the covid-19 pandemic were compared and presented above (Figure 2). It indicated a general decrease in the COD content except at 1289, 1413 and 2956 stations. Similar to the BOD, the highest COD content both before and during the lockdown was recorded at station 10030 whereas the lowest COD contents were recorded at stations 4769 and 1232; before and after the lockdown respectively.No recommendation giving by (IS: 2296:1992)regarding the content of (COD).

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5.1.3Dissolved Oxygen (DO)

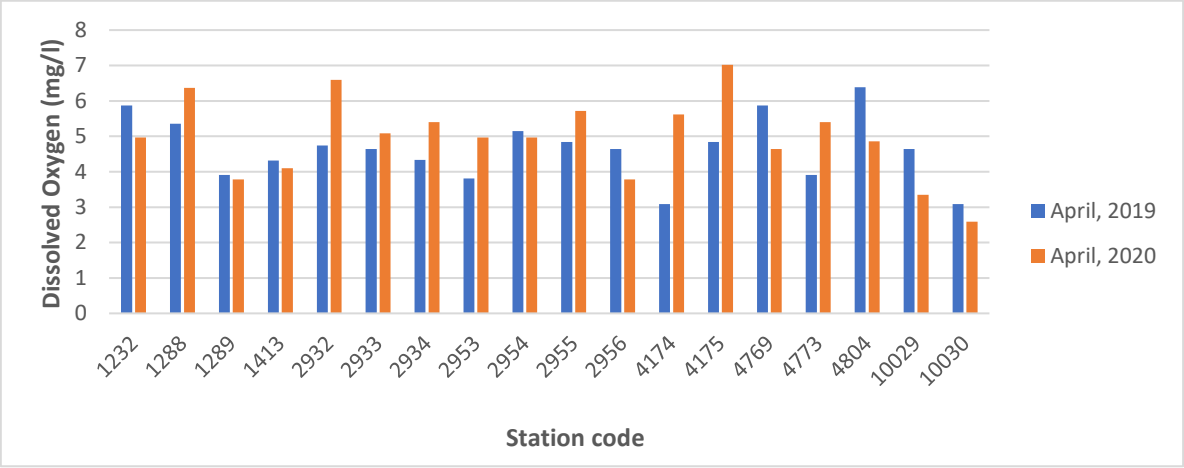

Figure 4: Dissolved Oxygen (DO)

The DO contents of the Rivers and Canalsin Rajasthan before and during the covid-19 lockdown is shown above (Figure 3). Highest DO values were recorded at 10029 and 4175 stations before and during the lockdown respectively; whereas lowest DO values were recorded at 4174 and 10030 before the lockdown and at 10030 during the lockdown. The highest percentage increase was recorded at station 4174 (82%) while the highest percentage decrease was recorded at station 10029. In general, decrease in DO was recorded in nine (9) station while increase in the other nine (9). Considering the (IS: 2296:1992) recommendations during lockdown station 1288, 2932, and 4175 belong to class A, while station 2933, 2934, 2955, 4174, 4773, belong to class B and stations 1232, 1413, 2953, 2954, 4769, 4804. However, the remaining stations of 1289, 2956, 10029, 10030 are of class D.

5.1.4Total Coliform

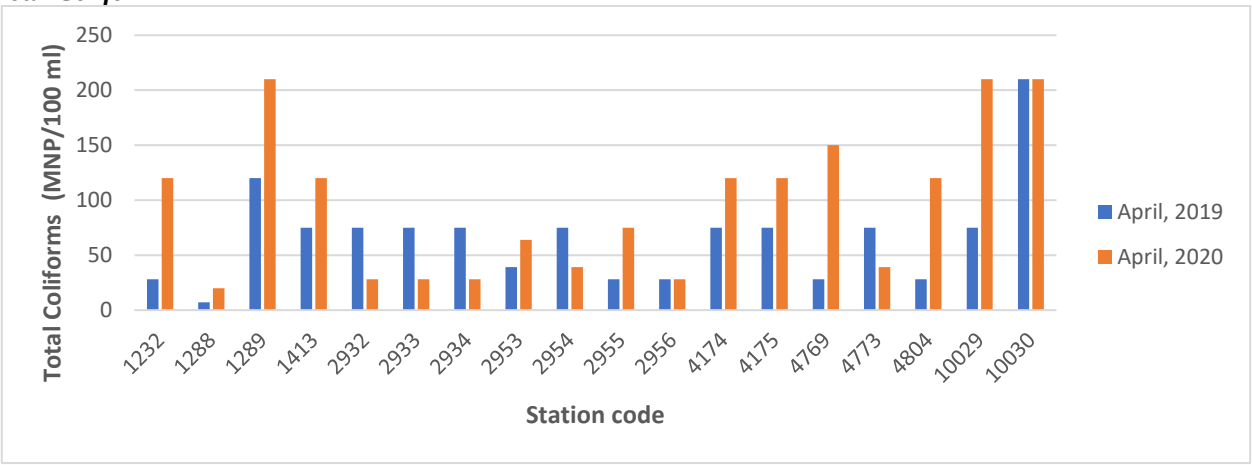

Figure 5: Total Coliforms

The total coliform present in the water bodiesof Rajasthan state before and during the lockdown are compared above (Figure 4). It ranges between 7 to 210 mg/l before the lockdown and 20 to 210 mg/l during the lockdown. Before the lockdown, the highest total coliform content was recorded at station 10030 (210 mg/l) while the lowest was at station 1288 (7mg/l). During the lockdown, the highest total coliform content was recorded at the stations 1289, 10029 and 10030 (210 mg/l) while the lowest was recorded at station 1288 (20 mg/l). It should be noted that the two lowest values before and during the lockdown were recorded at the same station (1288) and that the total coliform content at station 10030 was the same before and during the lockdown. The value coliform based on the IS recommendationsduring the lockdown of stations 1288, 2932, 2933, 2934, 2954, 2956, 4773, are in class A while all the remaining stations are in class B.

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5.1.5Conductivity

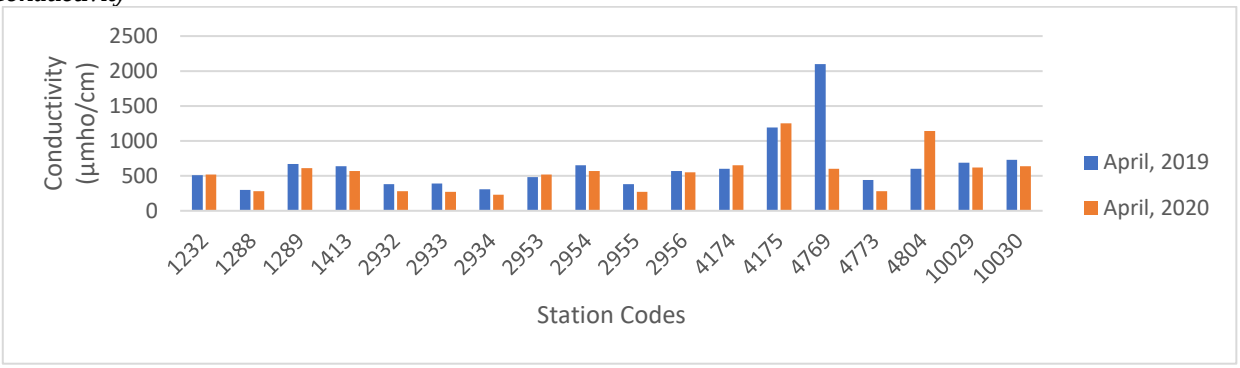

Figure 6: Conductivity

The results of conductivity assessedfromRivers and Canalsof Rajasthan state before and during the covid-19 lockdown were compared above (Figure 5). The conductivity values ranged between 300 to 2100 µmho/cm before the lockdown and between 230 to 1250 µmho/cm during the lockdown. There has generally been a decrease in the conductivity values across all the stations except at 1232, 2953, 4174 and 4804. The decrease in the conductivity values can be attributed to the decrease in the rate of discharge of industrial effluents into the waterways due to the halt in or extremely reduced industrial activities as a result of covid-19 lockdown. The exceptionally high percentage increase recorded at station 4804 (90%) may be due to the non-stop of industrial activities in the area or other local factors.

5.2 RESULT OF THE STORED SURFACE WATER (DAMS AND LAKES)

5.2.1 Biochemical Oxygen Demand (BOD)

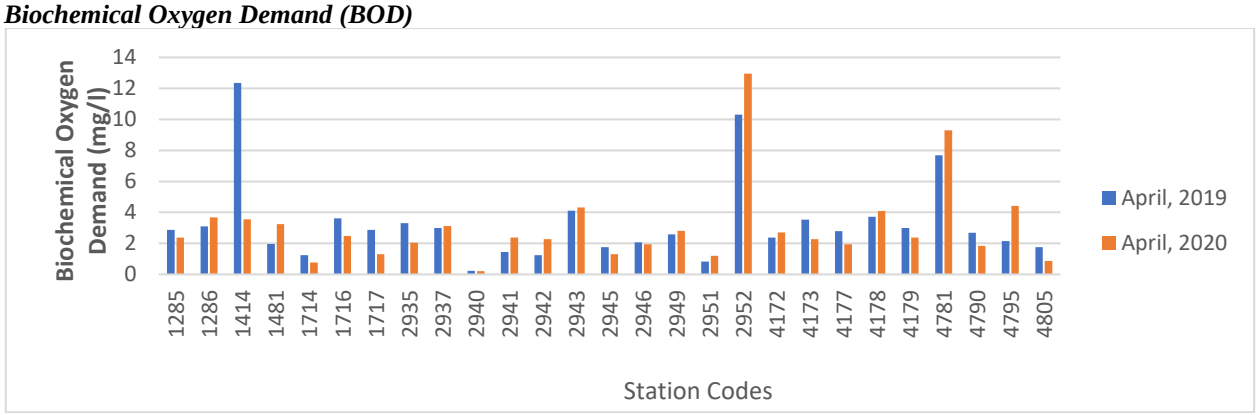

Figure 7: BiochemicalOxygen Demand (BOD)

From the result presented above it can be seen that some stations'BODhave increased while some have decreasedduring the lockdown.The following stations showed decrease in biological oxygen demand 1285, 1414, 1714, 1716, 1717, 2935, 2945, 2946, 4173, 4177, 4179, 4790, 4805.While the remaining stations showed an increase in the biological oxygen demand. Also considering therecommendation made by the bureau of Indianstandard of water qualitystations 1714, 1717, 2940, 2945, 2946, 2951, 4177, 4790 and 4805 are within class A while, 1285,1716, 2935, 2941, 2942, 2949, 4172, 4173, 4179 are within the class B.However, the remaining stations need a series of disinfection and treatment before they can be regarded suitable for human consumption. As they fell within the D class and only 2952 and 4781 belong to group E as their content reaches 12.96 and 9.29mg/**l** respectively.

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5.2.2 Chemical Oxygen Demand (COD)

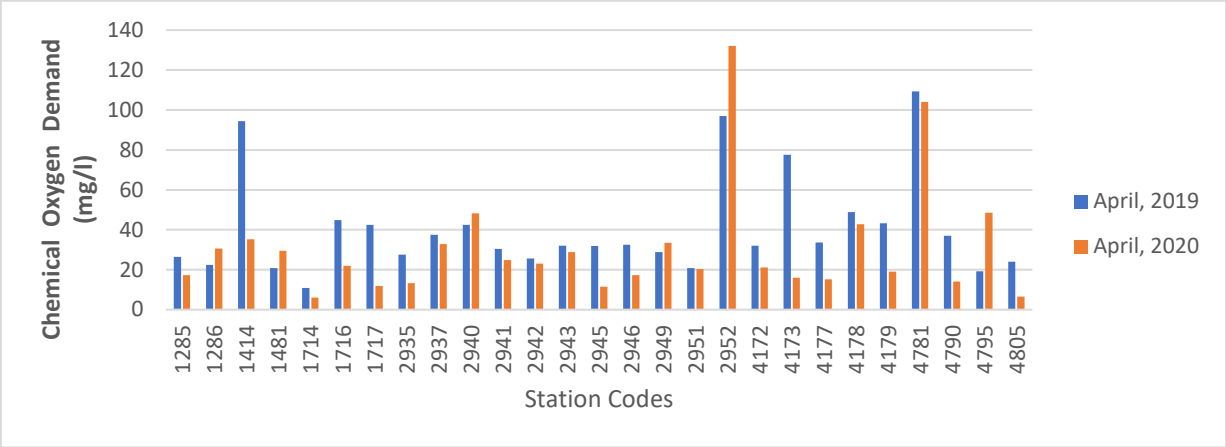

Figure 8: ChemicalOxygen Demand (COD)

With regard to the chemical oxygen demand of Dams and Lakesin Rajasthan statewhich was presented above it can be seen thatStations 1285, 1414, 1714, 1716, 1717, 2935, 2937, 2941, 2942, 2943, 2945, 2946, 2951, 4172,4173, 4177, 4178, 4179, 4781, 4790 and 4805 experienced decrease in chemical oxygendemand while the remaining station shows increases.Although no recommendation made by the IS about the chemical oxygen demand its value can be related to (BOD).

5.2.3 Dissolved Oxygen (DO)

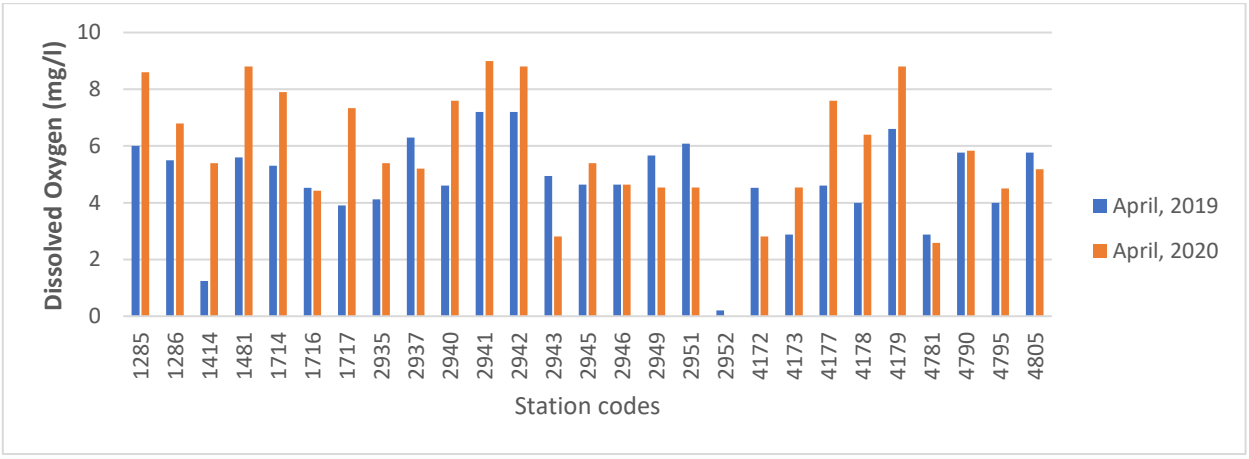

Figure 9: Dissolved Oxygen (DO)

The dissolved oxygen of 1716, 2937, 2943, 2949, 2951, 2952, 4172, 4781 and 4805 stationsdecrease during the lockdown period while all remaining stations show an increase in the dissolved oxygen. the content of the dissolved oxygen of 1285, 1286, 1481, 1714, 1717, 2940, 2941, 2942, 4177, 4178, 4179 are within the class A, while the content of 1414, 2935, 2937, 2945, 4790, and 4805 belong to class B. the content of 1716, 2946, 2949, 2951, 4173, 4795 are within class C and the remaining station sample belong to classE.

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5.2.4 Total Coliform

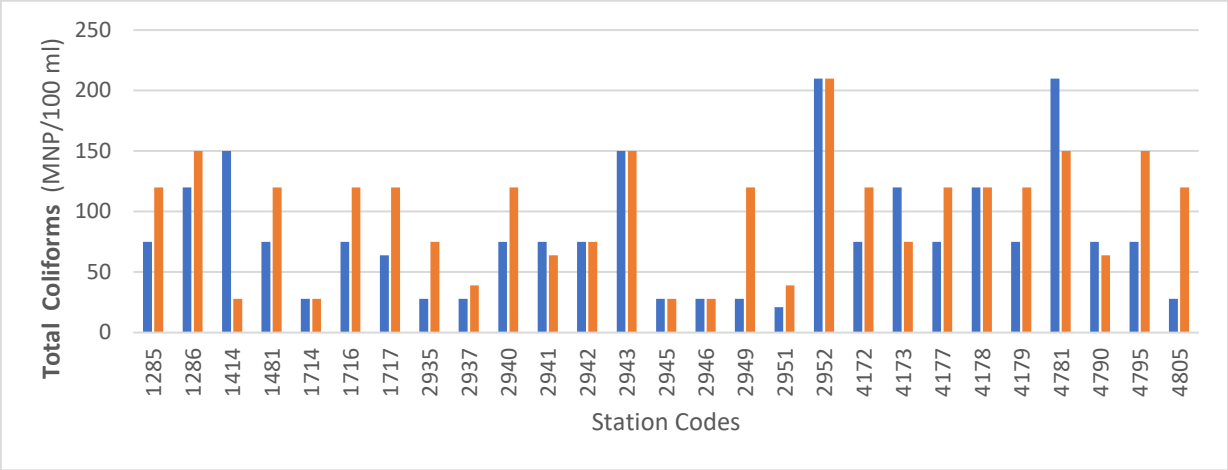

Figure 10: Total Coliforms

The Total Coliforms of stations 1414, 1714, 2937, 2927, 2945, 2946, 2951 belong to class A during lock down which shows an improvement based on IS recommendation while the remaining belong to class B of the Indian Standard of water quality though there is a significant increase of the total coliforms in the following stations 1285, 1286, 1481, 1716, 1717, 2935, 2937 2940, 2949, 2952, 4172, 4177, 4179, 4975, and 4805.Stations 1714, 2942, 2943, 2946, 2952, and 4178 have the same value of total coliformsbefore and during the lockdown while the remaining stations showed decrease in the total coliform values.

5.2.5 Conductivity

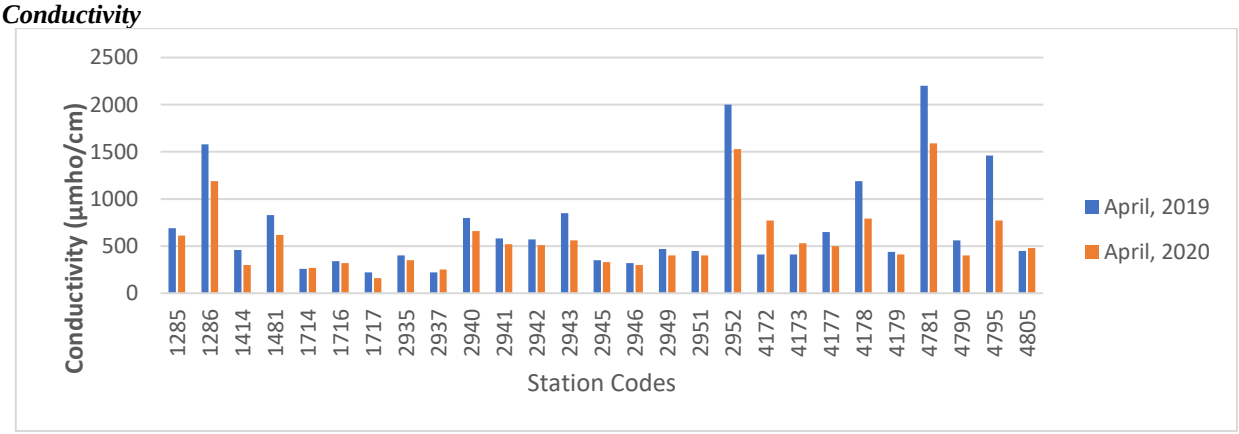

Figure 11: Conductivity

The recommendationsmade by Indian standard of water quality about conductivity were just based on class E for irrigation and other purposes, while the other classes have no any recommendation.All the conductivityvalues recorded before and during the lockdown are within the range prescribed by the Indian standard.However, there are certain variations noticed among the stations surveyed in which stations 1714, 2937, 4172, 4173, and 4805 have an increased value of conductivity while the remaining stations have decreased values.

6.0 CONCLUSIONS

Investigating the quality level of water sources based on certain parameters prescribed byperiodically is of outmost importance. Therefore, based on the above analysis made; the following conclusions were drawn:

1. The quality level of mostof the surface water bodies;both the flowing and stored sources wereremarkablyimproved during the lock down and are within the permissible levels based on the recommendation of Indian standard of water quality. This might be due to the absence or limited industrial and transportation activities which leads to the decrease of industrialeffluentsrelease into the waterways, smoke and gases release from chimneys and combusting engines; hence decrease or increase of the content of these parameters analyzed.Moreover, the lockdown has stopped some anthropogenic activities such as bathing at the river sides, tourist activities at dams and local fishing using chemicals; which considerably lead to increase or decrease of the parameters.
2. Based on the CPCB recommendations, someof the surface water can be used for drinking and other human purposes without any further treatments,while other categories need an additional treatment before used for public purposes.The remaining sources with less qualityi.e. having high contentof contaminants can serve the purposes of irrigation and industries.

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7.0 RECOMMENDATIONS

The need fora continuous monitoring of the level of surface water quality is of paramount importance as it has a direct relationship with human health, rate of crops production and other public activities.Therefore,in order to maintain the optimized level of water quality; the following recommendations can be employed by the government agency concerned with the water quality regulation in the state:

1. The release of the toxic effluents and other related pollutants direct to the water bodies especially surface water should be carefully monitoredby the CPCB team.This can be achieved by reducing the level of pollutant concentration before they are release to the waterways from the industrial area.
2. Public enlightment should be made on the dangers associated with inappropriate dumping of refuse and release of waste from household activities to the river or other sources of water; as they lead to the polluting of the surface water and the environment in general.
3. Legislature should be made to ensure strict adherence to the environment rules and regulations.
4. To haveconsistent, reliable and high-quality level of water, the sessional changes i.e. post and pre monsoon seasons, assessment of water quality in the state should be conducted in the state and the CPCB should provide periodic update about it.

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ASSESSMENT OF WATER QUALITY PARAMETRS FOR GOVERDHAN SAGAR LAKE OF UDAIPUR, RAJASTHAN

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Abstract - *The current research work was conducted to find out the water quality status of Goverdhan Sagar Lake of Udaipur (Rajasthan). An attempt has been made to assess the current physico-chemical and biological status of the lake. The physico-chemical and biological parameters of the lake have been studied at three locations for a period of six months from October'19 to March'20 and June'20. Physico-chemical parameters of lake were found to be moderate throughout the study period as compared to the Drinking water standards. The average water quality parameters of the lake during the study period were found to be, Temperature 28.6 ^{0}C, Colour and odour disagreeable, pH 9.0, EC 735 ppm, BOD 3.8 ppm, COD 42.3 ppm, DO 5.3 ppm, nitrogen content 7.1 ppm, Alkalinity 245.9 ppm, Total hardness 30.9 ppm, Calcium hardness 7.9 ppm, Magnesium hardness 23.0 ppm, Chloride content 161.7 ppm, Fluoride content 0.5 ppm, MPN coliform 350 MPN/100ml.*

Key Words: Goverdhan Sagar Lake, Water Quality, Pollution, Physico-Chemical Parameters, Biological Status

1. INTRODUCTION:

Water is found everywhere on Earth, from the polar ice caps to steamy geysers and wherever water flows on this planet, you can be sure to find life. Human realised that water is essential for the survival and hence early civilizations started near great rivers –e.g. Tigris and Euphrates in Mesopotamia, Nile in Egypt, Indus in India and Huang ho in China (Bairwa, 2008). Our earth surface has 71% of water and 29% land. Out of total water on earth 96.5% is in ocean which is salty and not useful for drinking, growing crops. Only 2.5% water is fresh water in which nearly 70% locked up in ice and rest is in the ground. Only 1.3 % fresh water is present on surface, mostly in lake and about 1% is salty water is in ground (Shiklomanov, 1993).

India accounts for about 2.45 percent of world's surface area, 4 percent of the world's water resources and about 16 percent of world's population. The total water available from precipitation in the country in a year is about 4000 cubic km. The availability from surface water and replenishable groundwater is 1,869 cubic km. Out of this only 60 percent can be put to beneficial uses. Thus, the total utilisable water resources in country are only 1,122 cubic km.

Central Pollution Control Board of India estimates that 75-80% of water pollution by volume is from domestic sewerage, while untreated sewerage flowing into water bodies including rivers have almost doubled in recent years. Inadequate sanitation facilities and waste water policy framework are primary reason responsible for the groundwater and surface water pollution in the country (Dey, 2015).

Aquatic life depends on the Physico-chemical and Biological characteristics of water and Industrialization, urbanization and discharge from human activities can produce undesirable change in Physico-chemical and Biological characteristics of water. As Udaipur is blessed with the good number of lakes and it is also known as 'The city of lake'. Every year numbers of tourist come from all around the world to visit Udaipur city and the lakes of Udaipur are the major source of drinking water. Therefore, it is important to asses and monitors the water quality of the lakes and its significant values provided information about the problems related with public health.

The objective of present paper is to investigate the Physico-Chemical and Biological parameters of water for Goverdhan Sagar Lake. Scope of this study is to check the compliance of selected parameters with the permissible limit recommended under various standards.

2. METHODOLOGY:

2.1 Study Area:

Goverdhan Sagar Lake is located 2.5 km away from the south-west of Udaipur at 74^{0}42' E Longitude and 24^{0}34' N latitude. It has an overall length of 1.97 km, covering a total water spread area of 30.81 hectares. The lake is rain-fed and receives water from Pichhola Lake via the connecting canal. The catchment area is approximately 2.56 square meters. The capacity at maximum lake level is 9 million cubic metres. The deeper position of the lake lies towards the north-east which has a steep slope, while the field and farmland lie towards the south-west (Mehta, 2009).

The details of morphometric features of the Goverdhan Sagar Lake are given in Table-1.

Table -1: Morphomitric features of Goverdhan Sagar Lake

Latitude	24°32'N
Longitude	73°41'E
Altitude	582 m (MSL)

Average rainfall	670 mm
Water spread area	Over 17.97 ha.
Weed choked marginal area	Over 12.83 ha.
Total area	30.81 ha.
Catchment area	2.56 sq.km.
Maximum depth (Zm)	25 ft.
Maximum length (L)	1.97 km
Maximum width (bx)	0.72 km
km Length of shoreline (L)	3888.8 m
Capacity of F.T.L.	9 million cubic meter
Type of dam	Masonry
District	Udaipur
Accesses	2.5 km away from Udaipur.

(Source: Mishara et al.,2016)

2.2 Sampling station

For present study, the following three sampling station was selected in Goverdhan Sagar Lake for the collection of water sample:

1) Near Goverdhan sagar pal side (Eastern shore of lake)
2) Near Smart city park (Western shore of lake)
3) Near Pashupatheshwar Temple (Northern shore of lake)

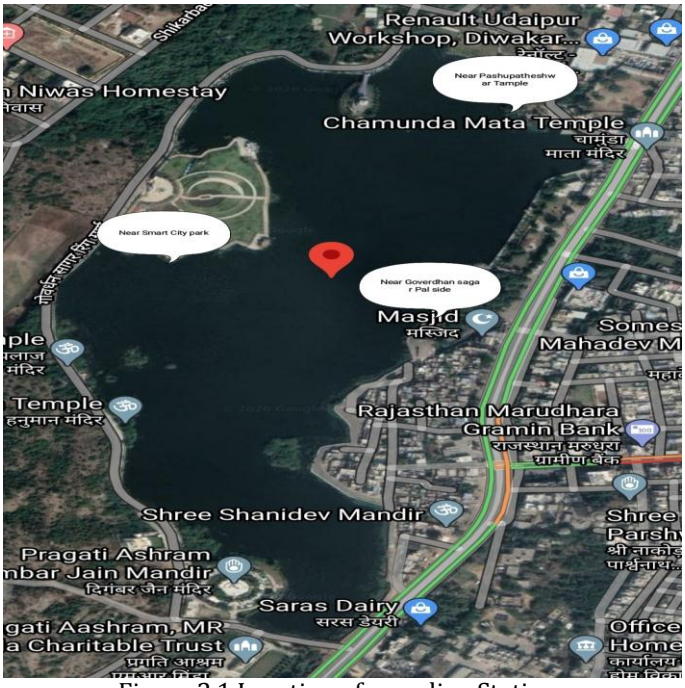

Figure 2.1 Location of sampling Station

2.3 Sampling Method and Collection

Grab or Catch sampling method is used for the present study. A grab sample is an individual sample collected without compositing or adding other samples (NEERI, 2011).

During the study period, sample was collected from all three sampling stations manually using grab method of sampling.

2.4 Testing

The water quality of Goverdhan Sagar Lake was analysed using standard methods as mentioned in the Manual on Water and Wastewater analysis (NEERI, 2011; Trivedy & Goel, 1984; and APHA, 2005).

In this study, Physico-Chemical parameters like water temperature, pH, TDS, BOD, COD, DO, Total alkalinity, Total nitrogen content, Total hardness, Calcium Hardness, Magnesium Hardness, Fluoride Content and Biological Parameter like MPN Coliform were analysed using standard method mentioned in the manual. These parameters give a brief knowledge about water quality and pollution status of Goverdhan Sagar Lake.

3. RESULT & DISCUSSION:

Table -2: Average water quality parameters of Goverdhan Sagar Lake

S. No.	Parameters	Average value
1	Temperature	27.3^{0}C - 30.2^{0}C
2	pH	8.4 - 9.4
3	EC	772 – 839mS/cm
4	TDS	509 – 550 ppm
5	BOD	3- 4.13 ppm
6	COD	20.4- 47.84 ppm
7	DO	4.70- 6.20 ppm
8	Total nitrogen content	7 - 7.3 ppm
9	Alkalinity	200 - 280 ppm
10	Total hardness	28-32.9 ppm
11	Calcium hardness	6.6 -9.8 ppm
12	Magnesium hardness	20.4-24.2 ppm
13	Chloride content	149.9-170.4 ppm
14	Fluoride content	0.416-0.578 ppm
15	MPN Coliform	350.0 MPN/100ml

❖ ***Temperature***

Temperature plays an important in influencing the characteristics of water. When temperature gets high it reduces the solubility characteristic of water which in turn affects the quality of water and shows the level of contamination/pollution. In present study the water temperature were recorded with care as per the sampling procedure and it was found between 27.3^{0}C - 30.2^{0}C at all three sampling stations (See Table 2). Mishara *et al.* (2016) also observed an average water temperature of 28.57^{0}C for Goverdhan Sagar Lake. A similar range of water temperature is commonly found to prevail in water bodies of arid and semi-arid regions of Rajasthan (Sarang, 2001; Rajkumar, 2005; and Balai, 2007). However, in some typical areas of arid and semi-arid regions the surface water temperature showed a wide annual fluctuation as per the investigations conducted by Rawat (2002) and Balai (2007). These findings are very much in consonance with the findings of past research.

❖ ***Hydrogen-ion concentration (pH)***

pH is an important factor of freshwater bodies deciding fish health as well as the productivity of water. Slightly alkaline pH has been considered as most suitable for fish culture while pH above 9 is unsuitable (Swingle, 1967; Jhingran, 1977). In present study, the pH of lake water was found between 8.4 - 9.4 at all three sampling stations (See Table 2). The pH of Goverdhan sagar lake was found to be alkaline which is suitable for supporting good aquatic productivity but if the average value increases beyond recorded values then it will not suitable for aquatic productivity. Mishara *et al.*, 2016) reported an average pH of 7.18 for Goverdhan Sagar Lake earlier. Such alkaline pH for lakes has also been found in other research work (Dangi and Sharma, 2017).

❖ ***Electrical conductivity (EC)***

The electrical conductivity represent total ionic load in water due to dissolved substance. In present study the EC of water was recorded between 772 – 839 mS/cm at all three sampling stations (See Table 2). This observation is supported by the study of Sarang (2001) where the similar range of EC values were found in the Jaisamand lake Udaipur, Rajkumar (2005) found values of EC 630 mS/cm in the Daya reservoir.

❖ ***Total dissolved solids (TDS)***

Indian Standards prescribed the desirable limit of TDS as 500 ppm in drinking water; presence of excess TDS may cause gastrointestinal irritation when consumed. TDS analysis also has great involvement in the control of biological and physical waste water treatment processes (Thirupathaiah *et al*., 2012). In present study, the TDS content of lake water sample was recorded slightly above the permissible limit i.e. 509 – 550 ppm at all three sampling stations (See Table 2). Rajkumar (2005) found values of TDS 406.21ppm in the Daya reservoir, Dangi and Sharma (2017) found TDS 230.4 ppm - 428.8 ppm of Picchola lake.

❖ ***Dissolved Oxygen (DO)***

Dissolved oxygen is the most critical water quality variable in aquatic ecosystem. It is of primary importance both as regulator of metabolism of plant and animal communities and as an indicator of water condition. In present study the values of DO were recorded with care as per the sampling procedure and it was found between 4.70 - 6.20 ppm at all three sampling stations (See Table 2). Mishara *et al.* (2016) observed DO content as 3.80 ppm -7.80 ppm for Goverdhan Sagar Lake.

❖ ***Chemical Oxygen Demand (COD)***

COD gives a measure of organic strength of domestic and industrial wastes. The higher value of COD indicates the presence of undesirable organic matter, demanding investigation of the cause before the water is pronounced potable. In present study the values of COD were recorded with care as per the sampling procedure and it was found between 20.4 - 47.84 ppm at all three sampling stations (See Table 2). COD has indicating the pollution level due to oxidisable organic matter present in water.

❖ ***Bio-chemical oxygen demand (BOD)***

BOD is a measure of quantity of oxygen required by bacteria and other micro-organisms under aerobic condition in order to biochemically degrade and transform organic matter present in the water body. High BOD is considered as a limiting factor for the living organisms, it is an indirect indicator of organic pollution of water body. In present study the values of BOD were recorded with care as per the sampling procedure and it was found between 3 - 4.13 ppm at all three sampling stations (See Table 2). Similar readings were also observed in other lakes of Rajasthan region (Rawal *et al.*, 2014; Choubisa and Dubey, 2017).

❖ ***Alkalinity***

Natural water bodies show a wide range of fluctuation in total alkalinity values depending upon the location, season, plankton population and nature of bottom deposits. It is a measure of buffering capacity of the water and is important for aquatic life in a fresh water system because it acting as a stabilizer for pH. In present study the Alkalinity of water was found between 200 - 280 ppm at all three sampling stations (See Table 2). Mishra *et al.* (2012) also found the similar value of alkalinity for Goverdhan Sagar Lake. Higher range Alkalinity was reported in different water bodies of Udaipur by Rajkumar (2005) & Balai (2007). Alkalinity above 40 ppm has been considered as good sign of productivity, further total alkalinity above 60 ppm are indication of nutrient rich condition, which is good for the production of fish food organisms.

❖ ***Hardness***

Klein (1956) and Sawyer (1960) classified water on the basis of hardness as:

Water Type	Harness
Soft water	upto 75 ppm
Moderately hard	75 to 150 ppm
Hard water	150 to 300 ppm
Very hard water	above 300 ppm

Hardness of water hinders the lather forming action and also responsible for scaling in the water carrying systems. The quantity of total hardness, calcium hardness and magnesium hardness for Goverdhan Sagar Lake were found as 28 - 32.9 ppm, 6.6 - 9.8 ppm, and 20.4 - 24.2 ppm respectively (See Table 2). These values of hardness indicated that the water of Goverdhan Sagar Lake can be considered as soft water as per the classification explained above.

❖ ***Chloride content***

Chloride in water is derived from natural mineral deposit, agriculture or irrigation discharge and industrial water. Presence of chloride content in high quantity indicated pollution of water due to sewage or industrial water. In present study, chloride content of the water was found between 149.9 - 170.4 ppm at all three sampling stations (See

Table 2). Choudhary and Ahi (2015) recorded 55.27 - 134.86 ppm of chloride content for Sagar Lake.

❖ ***Fluoride content***

Fluoride content upto 1 ppm will helps to prevent dental cavities and during formation of permanent teeth it combines chemically with tooth enamel, resulting in harder, stronger teeth that are more resistant to decay and excess value of fluoride cause bone fluorisis and other skeleton abnormalities. In present study the Fluoride content of water were found between 0.416-0.578 ppm at all three sampling stations (See Table 2). Very less fluoride content also affects bone density, so for healthy bones an adequate quantity of fluoride is essential.

❖ ***Total Nitrogen content***

In the ecosystem of lake the major input of nitrogen is through run off, but this may also be contributed from the decomposition of nitrogenous matter and its further oxidation (Goldman and Horne, 1993). Nitrogen is essential for many photosynthetic autotrophs. Presence of Nitrogen in water indicates presence of organic matter. Nitrogen present in water on four forms which are as: Free ammonia; Indicates recent pollution, Organic ammonia; Indicates quantity of nitrogen before decomposition has started, Nitrite (NO_2^-); Indicates partly decomposed condition, Nitrate (NO_3^-); Indicates old pollution (fully oxidised). In the present study the total nitrogen content varied from 7 - 7.3 ppm in Goverdhan Sagar Lake. Mishra *et al.* (2012) found nitrate-nitrogen as 0.46 mg/l for Goverdhan Sagar Lake.

❖ ***MPN Coliform***

Coliform bacteria are described and grouped, based on their common origin or characteristics such as Escherichia coli (E. Coli), as well as other type of coliforms bacteria that are naturally found in polluted water. The presence of faecal coliform bacteria in aquatic environment indicates that the water has been contaminated with the faecal material of man or other animals. The presence of coliform which themselves are harmless aerobic lactose fermented organisms but their presence or absence indicates the presence and absence of pathogenic bacteria. Coliform are (B-coli, E-coli) important harmless aerobic microorganisms which are found residing in the intestine of all warm blooded animals and excreted with their faces. These bacteria live longer in water than pathogenic bacteria. Hence if coliforms are absent pathogens would be absent. Colifoem indicate the degree of pollution and their high density shows the difference between clean and polluted waters (Ray and Hill, 1978). Coliform will be used as indicator of pollution in water due to the potential for introducing pathogens and other pollutants along with these bacteria (McMath et al. 1999, Perkins and Hunter, 2000). In the present study, MPN Coliform was found only in the month of June and the value was recorded as 350 MPN/100 ml (Table 2). MPN value shows high pollution level of the water present in Goverdhan Sagar Lake, which in turn makes it unfit for human consumption.

4. CONCLUSION

Goverdhan Sagar Lake is nutrient rich and alkaline water body. The water quality indicated that the water of lake is suitable for the fishery purpose. The bacterial load of lake water is very high as the values of bio-chemical oxygen demand, Chemical oxygen demand and MPN show its high pollution status and the water of lake is highly contaminated. If the similar condition continue for the longer period, lake may soon become ecological inactive. However, water of the lake was not found suitable for drinking and domestic uses. Suitable restoration program should be initiated for the sustainable use of lake.

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Effect of Polypropylene Fiber for Cement Concrete Based on Rigid Pavement

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Abstract— ***Concrete has the largest volume in present time construction and it is expected that there will be no other substitute for concrete in the upcoming time. Since such as high volumes of concrete are being used for newly construction work, it is peremptory to produce better quality of concrete that will be long lasting with increase mechanical properties to boost the service life of any structure. However fine concrete can generate using automation and controlled environment. It is not feasible to alter its inherent breakable essence and the need of any tensile strength. In this condition, fibre reinforced concrete (FRC) look to be a feasible alternative. In this research study main focus on the practicability of using polypropylene fibers as subordinate reinforcement to concrete to change its brittle nature. Accordingly, various percentages of polypropylene fibers were put into concrete and a sequence of lab experiments were control to explore the use of polypropylene FRC in rigid pavements. Automatic properties of concrete such as compressive strength, flexural strength and the ability to withstand wear, pressure, or damage, property such as abrasion resistance. In this study fibre dose of 0.1% - 0.3% by volume was introduced to the concrete. Fibre content 0.2% - 0.3% was found significant to enhance the property of concrete.***

Keywords: ***Polypropylene fibres, Compressive Strength, Flexural Strength, Rigid Pavement.***

INTRODUCTION

1.1 GENERAL

Concrete is a vast material using worldwide. Concrete is using in manufacturing of infrastructure such as bridges, roads, buildings etc. by use of concrete on a vast scale; we are reducing our natural minerals. There is no other substitute by which we can replace concrete. Now days for new constructions we produce high volume of concrete. Then it is compulsory that we produce such concrete that is more durable and have enhanced mechanical properties of concrete, which will maximize the service life. Concrete has its brittle nature and does not possess any tensile strength. Fibre reinforced can be an alternative that will modify its brittle nature. Rigid pavement resists all the loading through slab action. In slab action there is tension force generated at the bottom of rigid pavement. Due to tension at bottom concrete slab may crack because concrete provides only 10% tensile strength as compare to its compressive strength. To overcome this effect we can use different available fibre such as glass fibre, polypropylene fibre, steel fibre etc as secondary reinforcement. The present study focuses on the utilize of using Polypropylene Fibre that will act as secondary reinforcement and will improve brittle nature of concrete. Various fractions were considered for study and different tests carried out in laboratory. Various properties such as compressive strength, flexural strength, abrasion resistance and impact resistance were determined. All mechanical properties of concrete increases with varying % of fibre dose. The present study at different fibre content carried out to check that at how much extent the mechanical properties of concrete will vary as compare to its original mechanical property.

1.2 POLYPROPYLENE FIBRE

Polypropylene fibre was first suggested by 1965 as a blend to concrete for construction of blast resistant structures for the US Corps of Engineers. The fibre enhances additionally according to the various studies, now it is used as small, discontinuous fibrillation material for production of fiber reinforced concrete. Since the use of polypropylene fiber has expanded tremendously in the construction of various structures because inclusion of fibers in concrete enhance the toughness, flexural strength, tensile strength and impact strength further failure mode of concrete. Polypropylene fibre is economical, abundantly available, and like all artificial fibres of a consistent quality. Polypropylene fibre is shown in figure 1.1

1.2.1 Properties of Polypropylene Fibre

The raw material for polypropylene fibre is purely coal. Its method of polymerization, its excessive molecular weight and the way it is take care of into fibres combine to give polypropylene fibres very useful properties as describe below:

- Polypropylene Fibre is chemically inert. It does not react with any chemical inside the concrete. In contact with most aggressive chemicals only the concrete will always deteriorate first.

Figure 1.1 Polypropylene Fibre

- The hydrophobic surface not being moist by a cement paste helps to stop chopping fibres from balling outcome throughout mixing like other fibres.
- The water request is nil for polypropylene fibre.
- Polypropylene Fibre oriented randomly in the concrete, which provides strength in all directions.
- It is very light more material rather than cement ingredients, so it does not increase the dead load of the structure.

1.2.2 Role of Fibre

- In initial stage when concrete converts from plastic stage to harden stage minor cracks are developed due to hydration of water. These cracks remain permanently even after hardening of concrete. Through these cracks, water enters into a concrete structure and durability of concrete get reduced. Polypropylene fibre reduces these cracks by bridging action across the crack as shown in figure 1.2. Polypropylene fibre increases durability by reducing crack width.
- Concrete is weak in tension and brittle in nature. This property of concrete is improved by addition of Polypropylene fibre to the concrete. Concrete is powerful only in compression along with Polypropylene fibre possessing only tensile strength. By addition of these two materials we can manufacture a concrete that not only provides compressive strength, but also provides tensile strength to concrete. Polypropylene fibre works as secondary reinforced in concrete. These fibres are randomly oriented in concrete. This increases mechanical property of concrete. Polypropylene fibre plays important role in concrete to make less permeable and high strength concrete.

The major causes for crack evolution are Plastic shrinkage, Plastic settlement, Freeze thaw damage, Fire damage etc.

1.2.3 Advantage of Polypropylene Fibre

Polypropylene Fibre has following advantages:

- it is relatively inexpensive material
- it has low coefficient of friction.
- It provides resistance to moisture.
- It has good chemical resistance.
- It possesses flexural strength, fatigue resistance and impact resistance.

2.0 METHODOLOGY ADOPTED FOR MIX DESIGN

Concrete mix design is the process of selecting suitable elements of concrete and decided their relative quantity to make a concrete of required power, durability, and feasible as economical as viable is known as concrete mix design. Mix design is done in two steps. In first step components of material is selected and in the second step mix is designed by doing trials with the right combination of different ingredients according to IRC: 44-2008.

2.1 Design of Concrete Mix

Compressive strength of concrete is considered as an index for mix design. Therefore mix design is generally brought out for a certain compressive strength of concrete along with adequate workability required for pavement concrete.

2.1.2 Mix Composition

The concrete mix was designed for varying percentages of polypropylene fibre, with a constant quantity of cement, sand, coarse aggregate and super plasticizer. The polypropylene fibre percentage taken as 0.1%, 0.2%, 0.3% by volume. The quantities of different ingredients are given in Table 2.1.2 and Table 2.1.3

Table 2.1.2 Composition of Mix (Saturated Surface Dry Aggregate)

Cement (kg/m^3)	Sand (Kg/m^3)	Coarse Aggregate (kg/m^3)	Water (kg/m^3)	Admixture (kg/m^3)	w/c Ratio
388	773	1256	124	3.49	0.32
1	2	3.24	0.32		

Table 2.1.3 Composition of Mix (Dry Aggregate)

Cement (kg/m^3)	Sand (kg/m^3)	Coarse Aggregate (kg/m^3)	Water (kg/m^3)	Admixture (kg/m^3)	w/c Ratio
388	766	1249	137.8	3.49	0.32
1	1.97	3.22	0.35		

2.2 CASTING OF SPECIMEN

Proportion in the Table 3.9 was used for casting the specimens. Only fibre content varied for casting different mixes. Casting of specimens is shown in figure 2.2. Quantities of ingredients weighed as per table, and mixing procedure adopted is as follow:

1. Weighed quantities of coarse aggregate and fine aggregate mixed in dry state.
2. Required quantities of cement and fibre added to mix of coarse aggregate and sand.
3. Now water added as given below:
    a) Add approximate 50% of total water to the dry mix.
    b) Add about 40% of water mixed with admixture.
    c) Now add remaining water and mix it well.

Figure 2.2 Casting of Specimens

All moulds properly oiled before casting the specimen. After mixing workability determined by Slump test, and the entire specimen casted with proper compaction and smooth finishing. After 24 hours all specimen removed from moulds and submerged in water for curing at room temperature.

2.3 TESTING PROCEDURE

Testing is done on fresh concrete and after curing. For fresh concrete slump was determined to control workability of concrete. For testing of the specimen, the specimen withdraws out from the tank and surface is wiped out. The various performed is shown below:

1. Compressive Strength of cubes after 7 and 28 days.
2. Flexural Strength and Modulus of Rupture of concrete after 7 and 28 days.
3. Abrasion test at 28 day

3.0 CONCRETE MIX PROPORTIONING

3.1 MIX DESIGN

As per IRC-58, M-40 grade is recommended to be used in pavement construction for major roads. M-40 grade concrete was used for carrying out various investigations for this study. The mix design of M-40 grade concrete has been done using the guideline of IRC: 44-2008 and IS: 10269-2009.

3.1.1 Mix Proportioning for Trial Mix Based on Aggregate in SSD Condition

1. Cement = 388 kg/m^3
2. Water = 124 kg/m^3
3. Fine Aggregate = 773 kg/m^3
4. Coarse aggregate = 1256 kg/m^3
5. Chemical-Admixture = 3.49 kg/m^3
6. Water/Cement ratio = 0.32
7. The various mix proportions used for study of concrete are given in Table 3.1.1.

Table 3.1.1 Mix Proportion for Various Mix

Mix	Cement kg/m^3	Water kg/m^3	Fine Aggregate kg/m^3	Coarse Aggregate kg/m^3	Super plasticizer kg/m^3	Polypropyene Fibre Kg/m^3
Control mix (N)	388	124	773	1256	3.49	0 (0%)
Mix 1	388	124	773	1256	3.49	0.910 (0.1%)
Mix 2	388	124	773	1256	3.49	1.82 (0.2%)
Mix 3	388	124	773	1256	3.49	2.73 (0.3%)

Quantities of all ingredients are kept constant except polypropylene fiber content.

Control mix does not have any fiber content. Further fibre content taken in increasing order from Mix 1 to Mix 3. Fiber content is taken in % by volume of concrete varying from 0.1% to 0.3% as shown in Table 4.2.

4.0 RESULTS AND DISCUSSION

4.1 Compressive Strength of Concrete

It is the characteristic strength of concrete. It is the most important aspect of concrete to withstand in compressive force. Cubes of M-40 grade concrete of size 150mm were casted and tested after curing. This test was performed on compression testing machine.

Concrete cubes for compressive strength trail at 7 days and 28 days.

4.2 Flexural Strength of Concrete

Rigid pavement resists the entire load due to flexural action of slab. So this flexural strength is very important aspect. M-40 grade concrete specimen was casted as a beam for testing of flexural strength of concrete, and trail at 7 day and 28 day.

Figure 4.1 Graphical Arrangement of Compressive Strength at 7 & 28 day

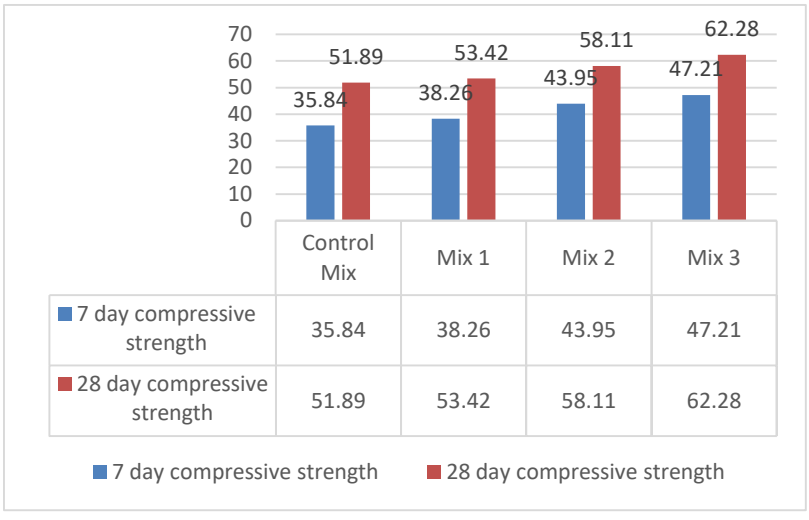
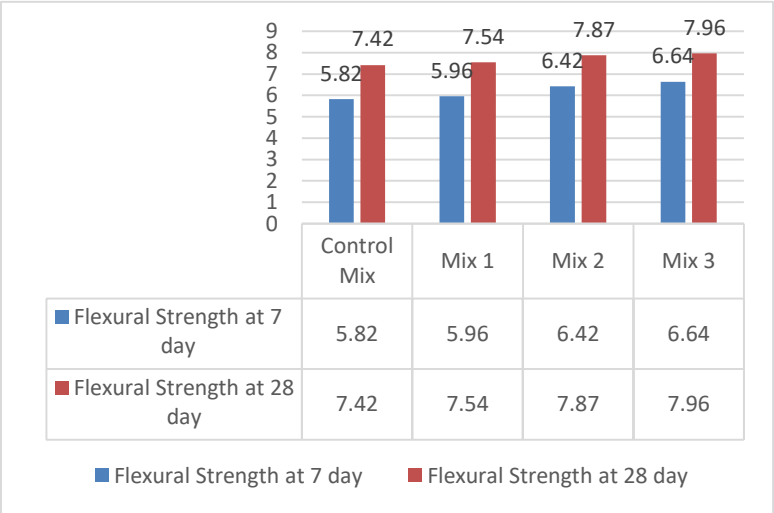


Figure 4.2 Graphical Comparison of Flexural Strength at 7 & 28 day



For 7 day flexural strength test result the rate of gain of strength decreases after Mix 2. Up to Mix 2 the gain increases faster and decreases slightly after Mix 2.

5.0 CONCLUSIONS

The present study "Effect of Polypropylene Fibre Based on Cement Concrete for Rigid Pavement" has been done successfully to assess the addition of polypropylene fibre on various things of concrete used in the rigid pavement construction. The main conclusions drawn from the study are as given below:

1. It is noticeable that grow in polypropylene fibre content in concrete increase compressive strength.
2. Polypropylene fibre content in the concrete also increases flexural strength.
3. The increase in above strength is due to the fact that the polypropylene fibre arrests the cracks developed in concrete, this grow the strength of concrete.
4. Grow in compressive along with flexural strength up to 0.20% by volume fibre content rapidly and strength increment decreases after 0.20% fibre content. It shows that fibre content between 0.20%-0.30 percent is beneficial to use.
5. The mechanical properties of polypropylene fibre reinforced concrete are superior to plain reinforced concrete.
6. There is the small increment in abrasion resistance of concrete due to polypropylene fibre.

Overall there is an increment in mechanical properties and durability properties of concrete.

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A Review on Alopecia Areata

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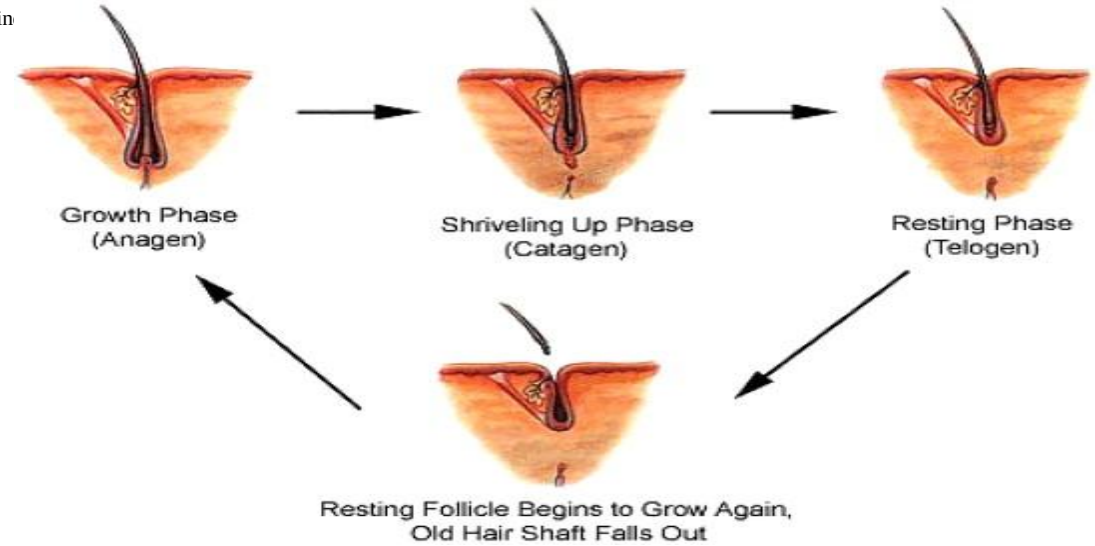
ABSTRACT

Alopecia areata is a complicated genetic, immune-mediated unwellness that targets anagen hair follicles. The unwellness affects youngsters and adults and is characterized by spherical or oval patches of hair loss, loss of all scalp hair (alopecia totalis), hair (alopecia universalis), or ophiasis pattern hair loss. Patients might also gift with uneven loss in multiple hair-bearing areas. ordinarily associated diseases embody respiratory disorder, rhinitis, atopic eczema, thyroid unwellness, and autoimmune diseases, like inflammation and skin condition. Nail abnormalities could precede, follow, or occur at the same time with hair loss activity. alopecia has no far-famed age, race, or ethnic preponderance and in distinction to different response diseases like inflammation or lupus, the follicle doesn't typically sustain permanent injury and maintains its potential to acquire hair. it's calculable that alopecia affects between 6 and 7 million people within the U.S . Genes, the immune and nervous systems have all been concerned within the pathological process of alopecia. though several treatments ar obtainable, there's still no cure. Bolstered by new scientific and translational opportunities from recently revealed genome-wide association studies, AN bold treatment development program has recently been initiated by the National alopecia Foundation

Keywords :-Causes and Symptoms of alopecia areata , its diagnosis , potential treatments and conclusion.

Introduction of Alopecia Areata :-

Alopecia areata is a common autoimmune disorder that often results in unpredictable hair loss.It affects roughly 6.8 million people in the United States and 147 million people worldwide.In most cases, hair falls out in small patches around the size of a quarter. There may be only a few patches, but alopecia areata can affect wider areas of the scalp.If there is a complete loss of hair on the scalp, doctors diagnose alopecia totalis. If there is hair loss throughout the entire body, the condition is called alopecia universalis. Alopecia can affect anyone, regardless of age, gender, or race, though most cases develop before the age of 30.In this article, we look at the causes and symptoms of alopecia areata, its diagnosis, and potential treatments.Alopecia areata may be a malady that happens once the system attacks hair follicles and causes hair loss. Hair follicles square measure the structures in skin that type hair. whereas hair may be lost from any a part of the body, alopecia sometimes affects the pinnacle and face. Hair usually falls go into tiny, spherical patches regarding the dimensions of 1 / 4, however in some cases, hair loss is additional intensive. the general public with the malady square measure healthy and haven't any alternative symptoms.The course of alopecia varies from person to person. Some have bouts of hair loss throughout their lives, whereas others solely have one episode. Recovery is unpredictable too, with hair regrowing absolutely in some individuals however not others.There is no cure for alopecia, however there square measure treatments that facilitate hair grow back additional quickly. There are resources to assist in



TYPES OF ALOPECIA AREATA:-

There are three main types of alopecia areata:

- **Patchy alopecia areata.** In this type, which is the most common, hair loss happens in one or more coin-sized patches on the scalp or other parts of the body.
- **Alopecia totalis.** People with this type lose all or nearly all of the hair on their scalp.
- **Alopecia universalis.** In this type, which is rare, there is a complete or nearly complete loss of hair on the scalp, face, and rest of the body.

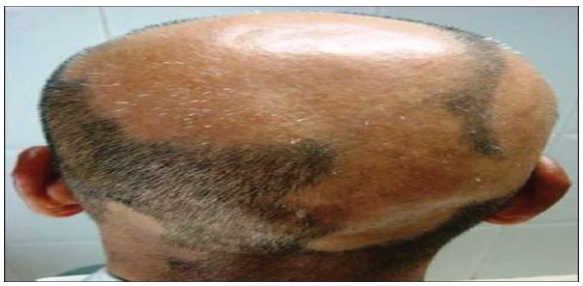
Other forms of Alopecia:-

Diffuse alopecia ends up in sharp and sudden cutting of the hair everywhere the scalp. It will be arduous to diagnose as a result of it's a great deal like different types of hair loss like telogen emission or male or feminine pattern hair loss.

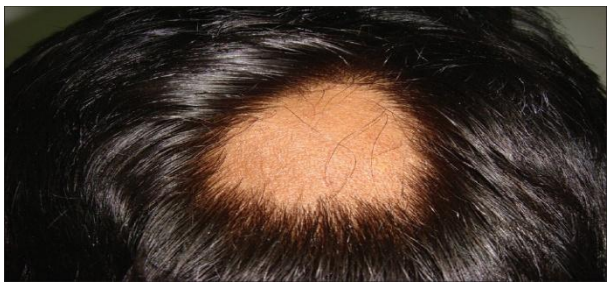
Ophiasis phalacrosis includes a distinctive pattern of hair loss, which has the edges and lower back of the scalp (called the os region) within the form of a band. Ophiasis alopecia will be tougher to treat, as a result of it doesn't respond as quickly to medication.

With every type of alopecia, hair loss and regrowth will be terribly unpredictable and alternating (happen over and over), for several years. tho' for a few individuals, hair might grow and not fall out once more. presently there's no cure for alopecia. However, your hair follicles stay alive in spite of what sort you've got. this implies that hair regrowth will happen once a few years of severe or widespread hair loss.

There are many treatment choices accessible for these completely different types of alopecia. the sole thanks to make sure what sort of alopecia you'll have, and also the best course for treatment, is to create an arrangement along with your doctor.



Localized patch of alopecia areata



Small patches, merging and forming larger patch

Causes:-

- The condition happens once white blood cells attack the cells in hair follicles, inflicting them to shrink and dramatically hamper hair production. it's unknown exactly what causes the body's system to focus on hair follicles during this means.While scientists ar unsure why these changes occur, it appears that biology ar concerned as alopecia is a lot of possible to occur in an exceedingly one who incorporates a shut friend with the illness. One in 5 individuals with the illness incorporates a friend WHO has conjointly developed alopecia.Other analysis has found that a lot of individuals with a case history of alopecia even have a private or case history of alternative reaction disorders, like immediate allergy, a disorder characterised by a bent to be hyper allergic, redness, and skin disease.

Despite what many of us assume, there's little or no scientific proof to support the read that alopecia is caused by stress. Extreme cases of stress may probably trigger the condition, however most up-to-date analysis points toward a genetic cause.

.

Multifactorial etiology of alopecia areata.(fig)

Symptoms:-

The most outstanding symptom of alopecia is uneven hair loss. Coin-sized patches of hair begin to fall out, chiefly from the scalp. Any website of hair growth is also affected, though, together with the beard and eyelashes.The loss of hair are often fast, developing in barely a couple of days or over a amount of a couple of weeks. There is also skin sensation or burning within the space before hair loss. The hair follicles don't seem to be destroyed so hair will re-grow if the inflammation of the follicles subsides. those who expertise simply a couple of patches of hair loss typically have a spontaneous, full recovery with none style of treatment.

About thirty p.c of people United Nations agency develop alopecia notice that their condition either becomes additional intensive or becomes a continual cycle of hair loss and regrowth.

About 1/2 patients pass though alopecia among one year, however several can expertise over one episode. Around ten p.c of individuals can prolong to develop phalacrosis totalis or phalacrosis universalis.Alopecia areata also can have an effect on the fingernails and toenails, and generally these changes ar the primary sign that the condition is developing.

There are variety of tiny changes which will occur to nails:

- pinpoint dents seem
- white spots and features seem
- nails become rough
- nails lose their shine
- nails become skinny and split

Additional clinical signs include

- Exclamation mark hairs: this happens once few short hairs that get narrower at their bottom and grow in or round the edges of bald spots.
- Cadaver hairs: this can be wherever hairs break before reaching the skin surface.
- White hair: this could grow in areas full of hair loss.

Alopecia areata primarily affects hair, however in some cases, there ar nail changes moreover. folks with the sickness ar sometimes healthy and haven't any different symptoms.

Hair Changes Alopecia areata usually begins with unforeseen loss of spherical or oval patches of hair on the scalp, however any a part of the body is also affected, like the beard space in men, or the eyebrows or eyelashes. round the edges of the patch, there ar typically short broken hairs or "exclamation point" hairs that ar narrower at their base than their tip. there's sometimes no sign of a rash, redness, or scarring on the clean patches. Some folks say they feel tingling, burning, or cutaneous sensation on patches of skin right before the hair falls out.

When a clean patch develops, it's exhausting to predict what is going to happen next. the probabilities include

- The hair regrows at intervals a number of months. could|it's going to|it should} look white or grey initially however may regain its natural color over time.
- Additional clean patches develop. generally hair regrows within the initial patch whereas new clean patches ar forming.
- Small patches be a part of to make larger ones. In rare cases, hair is eventually lost from the whole scalp, known as phalacrosis totalis.
- There is a progression to complete loss of hair, a kind of the sickness known as phalacrosis universalis. this is often rare.

In most cases, the hair regrows, however there is also sequent episodes of hair loss.The hair tends to acquire on its own additional totally in folks with:

- Less intensive hair loss.
- Later age of onset.
- No nail changes.
- No case history of the sickness.
- Nail Changes

Nail changes like ridges and pits occur in some folks, particularly people who have additional intensive hair loss.

❖ **Diagnosis:**

Doctors area unit sometimes able to diagnose alopecia fairly simply by examining symptoms. they could investigate the degree of hair loss and examine hairs from affected areas underneath a magnifier.

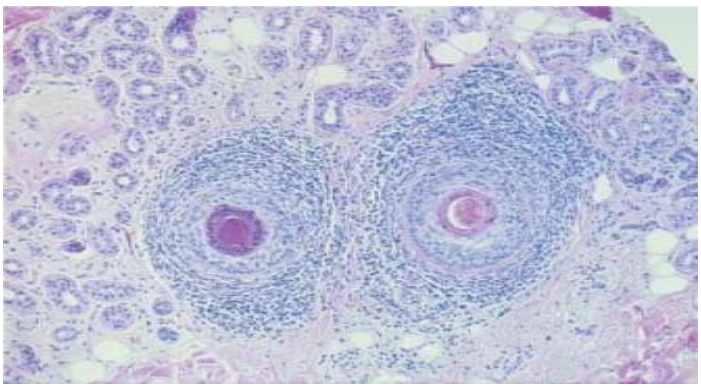
Doctors typically diagnose alopecia by:

- Examining the areas wherever the hair has been lost and looking out at your nails.
- Examining your hair and follicle openings employing a hand-held magnifying device.
- Asking regarding your medical and case history.

Other health conditions will cause hair to fall go into identical pattern as alopecia. to work out if another condition is inflicting the hair loss, your doctor might order blood tests or a skin diagnostic test

Histopathology:-

The histopathologic options of alopecia rely on the stage of the present episode and don't vary with the age, sex or race of the patient (Igarashi et al., 1981). within the acute stage, terminal hairs area unit encircled by neural structure lymphocytes ('swarm of bees'). within the acute stage, faded anagen and enhanced catagen and telogen hairs area unit characteristically found. within the chronic stage, faded terminal and enhanced miniaturized hairs area unit found, with variable inflammation. technique studies have shown deposits of C3, IgG, and immune gamma globulin on the basement membrane of the inferior a part of the follicle (Shimmer and Parker, 2001). throughout recovery, increasing numbers of terminal anagen hairs from regrowth of miniaturized hairs and a scarcity of inflammation area unit noted. {alopecia area unitata|alopecia} ought to histologically be suspected once high percentages of telogen hair or miniaturized hair are gift, even within the absence of a peribulbar leucocyte infiltrate. The histopathology of the lesion in ADTA reveals infiltration of mononuclear cells round the hair follicles and distinguished pigment incontinence (Garcia-Hernandez, 2000).



Swarm of bees' appearance of the inflammatory infiltrate around terminal hair follicles in alopecia areata. (H&E stain).

Testing

The **pull test** helps evaluate diffuse scalp hair loss. Gentle traction is exerted on a bunch of hairs (about 40) on at least 3 different areas of the scalp, and the number of extracted hairs is then counted and examined microscopically. Normally, < 3 telogen-phase hairs should come out with each pull. If > 4 to 6 hairs come out with each pull, the pull test is positive and is suggestive of telogen effluvium.

The **pluck test** involves sequentially pulling out about 50 individual hairs abruptly ("by the roots"). The roots of the plucked hairs are examined microscopically to determine the phase of growth and thus help diagnose a defect of telogen or anagen or an occult systemic disease. Anagen hairs have sheaths attached to their roots; telogen hairs have tiny bulbs without sheaths at their roots. Normally, 85 to 90% of hairs are in the anagen phase, about 10 to 15% are in telogen phase, and < 1% are in catagen phase. Telogen effluvium shows an increased percentage of telogen-phase hairs on microscopic examination (typically > 20%), whereas anagen effluvium shows a decrease in telogen-phase hairs and an increased number of broken hairs. Primary hair shaft abnormalities are usually obvious on microscopic examination of the hair shaft.

Scalp biopsy is indicated when alopecia persists and diagnosis is in doubt. Biopsy may differentiate scarring from nonscarring forms. Specimens should be taken from areas of active inflammation, ideally at the border of a bald patch. Fungal and bacterial cultures may be useful.

Daily hair counts can be done by the patient to quantify hair loss when the pull test is negative. Hairs lost during the first morning combing or during washing are collected in clear plastic bags daily for 14 days. The number of hairs in each bag is then recorded. Scalp hair counts of > 100/day are abnormal except after shampooing, when hair counts of up to 250 may be normal. Hairs may be brought in by the patient for microscopic examination.

- **Treatment**

There is presently no cure for alopecia, though there area unit some types of treatment that may be steered by doctors to assist hair re-grow additional quickly.

Treatments for gentle alopecia

INTRALESIONAL adrenal cortical steroid INJECTIONS

This methodology of treatment — the foremost common sort of treatment for arata|alopecia} — uses corticosteroids that are injected into vacant patches of skin with a little needle. These injections square measure perennial regarding each four to 6 weeks and square measure sometimes given by a specialist.

TOPICAL Rogaine

With this type of treatment, a five-hitter topical Rogaine resolution is applied once or doubly daily to assist stimulate hair on the scalp, eyebrows and beard to grow. 2 and five-hitter topical Rogaine solutions square measure obtainable however aren't sometimes effective for alopecia once used alone, however once applied together with topical adrenal cortical steroid medications, some individuals see improved results.

ANTHRALIN CREAM OR OINTMENT

This artificial, tar-like substance — conjointly wide used for skin disease — may be a common sort of treatment for alopecia. Anthralin is applied to the smooth-faced patches once daily and so washed off usually when a brief time (usually 30-60 minutes later) or in some cases, when many hours

TOPICAL CORTICOSTEROIDS

In alopecia, corticosteroids square measure thought to decrease the inflammation round the follicle. Topical steroids will are available in totally different brands, strengths and preparations, like solutions, lotions, foams, creams, or ointments.

Treatments for in depth alopecia, baldness totalis and baldness universalis

ORAL CORTICOSTEROIDS

Corticosteroids taken within the sort of a pill area unit typically prescribed for in depth scalp hair loss to do to suppress sickness activity and acquire hair.

TOPICAL therapy

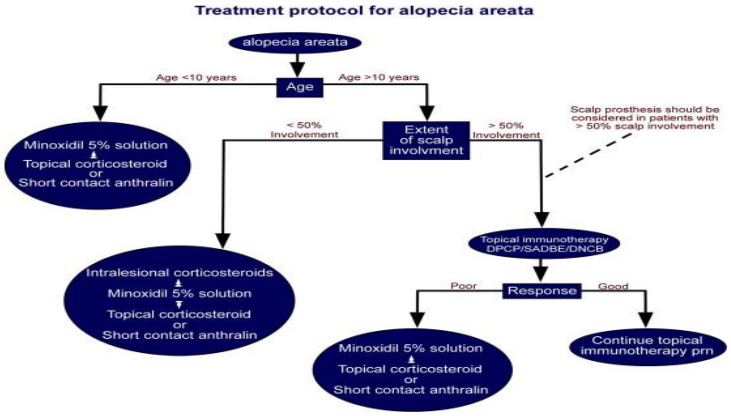
Topical therapy is employed to treat in depth alopecia, baldness totalis and baldness universalis. this type of treatment involves applying chemicals like diphencyprone (DPCP), dinitrochlorobenzene (DNCB) or squaric acid dibutyl organic compound (SADBE) to the scalp. This causes associate degree allergic rash (allergic contact dermatitis) that appears like poison oak or Hedera helix, that alters the immune reaction.

IMMUNOMODULATORS: medication to block THE immune reaction

Immunomodulatory medication — specifically, Roman deity enzyme (JAK) inhibitors — like tofacitinib (Xeljanz) and ruxolitinib (Jakafi), area unit a brand new sort of medical aid being tested for alopecia. These medications were originally approved to treat bound blood disorders and atrophic arthritis. they're not approved by the agency for alopecia however, associate degreed area unit solely out there right away within the sort of an oral medication. A topical formulation is presently in clinical trials within the us.

Biological medical care

These medications synthesized from recombinant proteins cut back the unhealthful T cells, inhibit T-cell activation and inhibit inflammatory cytokines, suggesting a possible role within the treatment of AA. Enbrel may be a agent and a fusion macromolecule receptor consisting of 2 human TNF receptors and Fc domain of human human gamma globulin G1. Strober et al. administered fifty mg of Enbrel double weekly to patients with moderate to severe AA. They but discovered no vital hair regrowth once twenty four weeks of treatment (Strober et al., 2005). Studies with alternative biological agents within the treatment of AA ar still current. In cases wherever all the treatments fail, alternative choices that are reported for AA ar hair transplant, however recently it's solely been performed in eyebrows with sensible results. Another various is micropigmentation, conjointly called tattoo; it's been used aesthetically to camouflage varied medical conditions associated with medicine.



*Algorithm for management of Alopecia areata in different age groups. (*Adapted with permission from the Editor, J. Am. Acad. Dermatol. 2010;62:191–202).*

CONCLUSION

Alopecia areata encompasses a nice impact on the looks and psyche of the afflicted individual. Moreover, no uniformly dependable treatment is thought. Corticosteroids have shown promising results and ar time tested medication in management over the years. different treatments that are used with some success include: Rogaine, anthralin, DNCB, SADBE, PUVA, cyclosporine. With every treatment, facet effects and cosmetically acceptable improvement should be thought of. Support mechanisms within the type of native support teams ought to be shaped so as to produce content for the affected patients and allay their psychiatrical comorbiditie

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Gene Therapy used in Cancer Treatment

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ABSTRACT:

Cancer has been, from the beginning, a goal of severe studies for gene remedy approaches. Currently, extra than 60% of all on-going scientific gene remedy trials global are focused on most cancers. Indeed, there's a clean unmet scientific want for novel treatments. This is in addition entreated with the aid of using the truth that contemporary traditional most cancers treatments are regularly bothered with the aid of using their toxicities. Different gene remedy techniques had been employed for most cancers, which includes pro-drug activating suicide gene remedy, anti-angiogenic gene remedy, oncolytic virotherapy, gene remedy-primarily based totally immune modulation, correction/repayment of gene defects, genetic manipulation of apoptotic and tumor invasion pathways, antisense, and RNAi techniques. Cancer types, that have been focused with gene remedy, include brain, lung, breast, pancreatic, liver, colorectal, prostate, bladder, head and neck, skin, ovarian, and renal most cancers. Currently, most cancers gene remedy merchandise have received marketplace approval, each of which might be in China. In addition, the stimulation of the host`s immune system, the usage of gene healing approaches, has received widespread interest. The intention of this evaluate is to factor out the maximum normally viral and non-viral vectors and methods utilized in most cancers gene remedy, in addition to spotlight a few key effects finished in scientific trials.

Keywords: most cancers; glioma; gene remedy; gene transfer; viral vectors; non-viral vectors; safety; scientific trials

1. Introduction

Cancer is a main worldwide fitness hassle accounting, annually, for extra than 8 million deaths globally. It is a complex, multifactorial sickness concerning adjustments with inside the genome, that's orchestrated via way of means of host and environmental interactions [1]. The hallmarks of most cancers are self-sufficiency in boom signals, insensitivity to anti-boom signals, cappotential for tissue invasion and metastasis, limitless replicative potential, sustained angiogenesis, and evasion of apoptosis [1]. The tumor microenvironment, which consists of diverse non-malignant cells expressing diverse regulatory proteins, as nicely as the extracellular matrix, performs a pivotal position with inside the initiation and development of cancers [2]. Gene remedy objectives at handing over genetic fabric into goal cells or tissue and to explicit it with the intention to advantage a healing effect. It has the benefit over traditional cures because of the truth that it can be administered locally, thereby handing over, locally, a excessive healing dose without risking systemic detrimental effects. Furthermore, seeing that maximum gene cures are unmarried time applications, they may be cost powerful with inside the lengthy run.

2. Gene Therapy for Cancer: An Overview

Rogers et al. became one of the first to illustrate an preliminary proof-of-idea of virus mediated gene transfer. What he confirmed became that overseas genetic fabric may be transferred to cells of hobby via way of means of making use of viruses [3]. Motivated via way of means of the outcomes he went even similarly and examined it in humans. With this experiment, Rogers have become the primary to carry out a human gene remedy trial. In that examine, Rogers used a wild-kind Shope papilloma virus that allows you to introduce the gene for arginase into girls laid low with a urea cycle disorder (i.e., hyperargininemias) [4,5]. He hypothesized that the Shope papilloma virus could certainly encode the gene for arginase interest and that this gene should be transferred via way of means of introducing the virus to the sufferers. Unfortunately, the final results of the trial became negative. There became no alternate withinside the arginine levels, nor became there a alternate withinside the scientific route of the sickness in those sufferers. Even aleven though Rogers “out of the box” wondering became intriguing, it became doomed to fail because it later grew to become out that the Shope papilloma virus genome does now no longer encode the arginase gene.

The US Food and Drug Administration (FDA) permitted the primary gene remedy protocol, which became performed in 1989. Therein, tumor infiltrating lymphocytes accumulated from superior cancer sufferers have been ex vivo transduced with a marker gene (i.e., now no longer a healing gene), increased in vitro, and re-infused to the sufferers [6]. The first scientific trial on most cancers with an healing intend became commenced withinside the following year, in which sufferers with superior cancer have been dealt with with tumor infiltrating lymphocytes genetically changed ex vivo to explicit tumor necrosis factor [6].

Another crucial milestone withinside the records of gene remedy became the examine performed via way of means of Cline et al. Cline dealt with thalassaemia sufferers, in which he extracted bone marrow cells from those sufferers and transfected ex vivo with plasmids containing the human globulin

gene. After cells have been transfected they have been administered again to the sufferers [7,8]. The purpose why this examine affords a milestone withinside the records of gene remedy isn't always due to the failure of the examine itself, however due to the fact the examine became done with out the consent to carry out those research from the University of California, Los Angeles (UCLA) Institutional Review Board. This case proven that expertise became very confined and that human gene remedy might be technically, in addition to ethically lots greater complicated than expected.

3. Gene Transfer Methods and Vectors Used for Gene Therapy

The venture in gene remedy is to supply an good enough quantity of genetic fabric into goal cells or tissues and to hold gene expression for a preferred duration of time. Genetic fabric may be brought to their goal cells or tissues through distinctive strategies of shipping. In principle, we will group them into

(1) bodily
(2) viral
(3) non-viral strategies; and
(4) bacterial or yeast.

Electroporation, ultrasound, and gene gun deliveries are examples of bodily strategies that have been used. As the call already implies, with viral vectors a biological (i.e., virus) vector is used as a automobile to supply the genetic fabric into the cells, while with non-viral gene switch strategies a artificial carrier (liposomes or nanoparticles) is used. Different vectors have distinctive houses in relation to their transduction performance and their efficacy to specific the brought genes. In addition, they range in appreciate of the period of expression of the transgene, in addition to their protection profile. Depending at the requirements, distinctive vectors may be used for distinctive healing purposes.

Currently, viral vectors are taken into consideration because the only of all gene shipping strategies for in vivo gene switch. Ideally, the gene switch vector have to be capable of goal a selected tissue with high transduction performance and maintain a stable, regulated gene expression with none facet outcomes or immunogenic responses. Unfortunately, not one of the presently used gene shipping vectors fulfil all these criteria. Local injection of a vector usually effects in a limited, however correct impact area. On the contrary, systemic management of a vector can bring about a machine extensive expression. Consequently, vectors and their management strategies were changed so as to gain centered shipping, as nicely as to boom transduction performance [9]. Most viral vectors have, however, already natural tropism to positive mobileular sorts or tissues, which may be applied for healing approaches [10].

3.1. Viral Vectors

The maximum generally used viral vectors used for gene switch are adenoviruses, lenti- and retroviruses (inclusive of the human immunodeficiency virus (HIV)), vaccinia viruses, adeno associated viruses (AAV), and baculoviruses. These vectors range from every different concerning their mobileular tropisms, expression profiles, transgene capacities, immunogenicity, in addition to distinctive period of transgene expression.

In addition to their origin, viral vectors may be divided into integrating and non-integrating vectors. Adenoviruses and baculoviruses are examples of non-integrating vectors. They lack the capacity to combine their genome (and, hence, with it additionally the transgene) into the host genome. Lenti-and retroviruses, in addition to AAVs, at the contrary, are examples of vectors that do combine into the host genome. While the expression of the transgene is brief in case of non-integrating viral vectors (diminishing in some weeks), integrating vectors generally effects in long-term [removed]months, as much as years). This integration of the transgene into the host genome has raised issues approximately the protection of those vectors. This is because of the truth that integration has been located with retroviral vectors to arise every now and then in actively expressed sites (i.e., insertional mutagenesis) [11–13].

Genetic fabric may be brought additionally via way of means of ex vivo gene switch approach. Therein, the genetic fabric is delivered to the cellular out of doors the patient (i.e., ex vivo), into formerly remoted autologous cells, which then are re-delivered again to the patient.

Currently, adenoviruses are the maximum dominant gene shipping vectors utilized in gene remedy. More than 50 exceptional serotypes had been recognized for adenoviruses, which may be divided similarly into six subgroups (A–F) [14]. Of the ones, the serotypes 2 and five are the maximum usually used ones in gene remedy. A restricting issue with adenoviruses is the truth that detectable stages of pre-present antibodies may be discovered in 97% of individuals, which doubtlessly might also additionally have an effect on transduction performance and healing outcome.

3.2. Non-Viral Vectors

Viral vectors had been proven to be green gene switch tools. Nevertheless, drawbacks such as fast clearance of viral vectors from the bloodstream (while injected systemically), their immunogenic and inflammatory potential, has advised the improvement of recent artificial gene shipping vectors. In truth, non-viral gene shipping structures are a subject this is presently being studied notably as alternatives for viral shipping structures. The most effective shape of a non-viral machine is bare plasmid DNA. The gain of bare plasmid is that it poses the bottom shape of toxicity or different undesirable reactions. In addition, it is straightforward to formulate and cheaper to produce. However, its drawback is the low transfection performance in comparison to viral-mediated gene switch [15]. As a result, to enhance transfection performance, cationic polymers, or lipids formulations had been evolved to condense plasmid DNA to shield the degradation of DNA and to decorate uptake and transfection of plasmids [15]. The gain with the ones formulations is that polymers or lipids can relatively effortlessly be designed to gain positive properties. For example, non-viral vectors can effortlessly be centered to a goal

tissue or cellular via way of means of coupling of cellular- or tissue-precise concentrated on moieties at the carrier. Furthermore, via way of means of determining the dimensions of the micro- or nanoparticle the biodistribution, mobile internalization, and intracellular trafficking of the micro- or nanoparticle may be influenced [16]. Unfortunately, the fulfillment of non-viral shipping structures in scientific packages in gene remedy has been limited. Compared to viral vectors, non-viral vectors have now no longer long gone thru the evolutionary method of time that viruses have, which commonly may be visible as low transduction efficiencies in vivo.

The fulfillment of the non-viral gene remedy is depending on the diverse extra- and intracellular limitations that have an effect on the efficacy of all gene shipping structures, inclusive of mobile uptake, endosomal escape, nuclear uptake, and gene expression [16–18].

4. Clinical Efficacy of Gene Therapy

Different gene remedy techniques the usage of exceptional gene switch vectors had been studied for most cancers gene remedy. These consist of induction of apoptosis, oncolytic virotherapy, immune modulation, anti-angiogenic gene remedy, correction of gene defects, inhibition of tumor invasion, gene remedy to decorate chemo- and radiotherapy, myeloprotective gene remedy, antisense and RNA interference (RNAi) primarily based totally techniques, and pro-drug activation/suicide gene remedy. Unfortunately, most effective few of those techniques have made it honestly to the clinic. One usually used method in most cancers gene remedy has been the usage of a usually taking place mutation withinside the p53 protein. In 2003, Lang et al. defined a section I medical trial the use of an adenoviral vector encoding for the tumor suppressor gene TP53 to deal with sufferers with recurrent malignant gliomas, in which 15 sufferers need to go through intratumoral stereotactic injection of the adenoviral vector through an implanted catheter, accompanied via way of means of en bloc resection of the tumor and remedy of the post-resection hollow space [19]. Due to the layout of the take a look at, tumor reaction couldn't be assessed, however the take a look at confirmed minimum toxicity. No systemic viral dissemination turned into found and a most tolerated dose turned into now no longer reached on this take a look at. Furthermore, evaluation of tumor specimens confirmed limited transgene expression near the injection webweb page. Another take a look at, and much like the virus utilized by Lang et al. is Gendicine™. Gendicine™ is a replication-incompetent adenovirus encoding for the TP53 gene (in region of the viral E1 gene) used for the remedy of loads of cancers. What makes Gendicine™ thrilling is the truth that it have become the first gene remedy product that has been accepted for medical use [20]. In a section I medical trial, with 12 laryngeal most cancers sufferers, Gendicine™ confirmed healing potential, as not one of the sufferers dealt with with Gendicine™ had tumor relapse for the duration of the five-yr follow-up after the remedy [21] Additionally, Gendicine™ confirmed correct protection profile, exemplified via way of means of a section II/III trials with 132 head and neck squamous mobileular carcinoma sufferers. Therein, 32% confirmed fever because the simplest side-impact of the remedy [22]. When Gendicine™ turned into utilized in aggregate with radiotherapy, 64% of the sufferers answered with a entire regression and 29% with a partial regression whilst with radiotherapy alone, 19% confirmed a entire regression and 60% a partial regression, suggesting synergistic impact of the aggregate remedy [22].

A 2nd gene remedy product that obtained marketplace approval via way of means of the Chinese SFDA is Oncorine™, evolved via way of means of Chinese Shanghai Sunway Biotech. Oncorine™ is a conditionally replicative adenovirus, that is produced via way of means of deleting the adenoviral E1B 55K gene. The deletion of this gene prevents the virus to bind and inactivate the wild-kind p53 protein, that is an critical self-defence mechanism of the host towards virus infection [23]. When E1B 55K interest is removed, the replication in normal cells is blocked, permitting simplest replication in p53-poor cells. In malignant cells the viral proliferation results in oncolysis, used as a most cancers remedy to deal with strong tumors. Interesting to this product is the truth that ONYX-1/2 (evolved via way of means of Onyx Pharmaceutical`s), which is similar to Oncorine™, in no way obtained marketplace approval. Compared to Oncorine™ ONYX-1/2 turned into now no longer capin a position to exhibit healing gain in medical settings. For instance, in a section I dose-escalation trial posted via way of means of Chiocca et al., 24 sufferers with recurrent malignant glioma have been injected with the oncolytic virus in a complete of 10 injections into 10 unique webweb sites of the hollow space of resected tumors [24]. Even aleven though the take a look at confirmed that ONYX-1/2 turned into secure and that not one of the sufferers skilled critical negative occasions that would be attributed to the virus, all sufferers confirmed tumor progression. One affected person with anaplastic astrocytoma had solid sickness and sufferers who underwent a 2nd resection had lymphocytic and plasmacytoid mobileular infiltration on the webweb page of injection. Oncorine™ and ONYX-1/2 have collectively furnished a huge quantity of protection information for diverse types of most cancers, inclusive of glioma, head and neck, pancreatic, and ovarian cancers, demonstrating an suited protection profile [20]. Typical headaches covered fever, injection webweb page pain, nausea, alopecia, leucopenia, and flu-like symptoms [25].

In order to enhance efficacy of oncolytic viruses, extra healing proteins had been introduced to the viruses. An instance for that is Onco VEXGM-CSF, that is a 2nd-technology oncolytic herpes simplex virus (HSV), moreover coding for the healing protein granulocyte macrophage Colony-stimulating factor. A segment I protection take a look at confirmed that Onco VEXGM-CSF turned into properly tolerated and secure whilst administered with the aid of using intratumoral injection in sufferers with cutaneous or subcutaneous deposits of breast, head and neck and gastrointestinal cancers, and malignant cancer who had failed previous remedy [26]. In addition, proof of an antitumor impact turned into visible in that take a look at, which turned into further supported with the aid of using a Phase I/II, wherein Onco VEXGM-CSF turned into given in aggregate with radiotherapy and cisplatin to sufferers with untreated level III/IV squamous mobileular most cancers of the pinnacle and neck [27].

4.1. Gene Therapeutic Approaches to Stimulate the Immune System

Immunotherapy is a subject that has received a good deal interest recently. Typically, in immunotherapy the goal is to decorate both the popularity or presentation of tumor-related antigens (TAA`s). Unfortunately, there are not unusualplace demanding situations which have been confronted with the aid of using immunotherapies, along with the herbal tolerance in the direction of TAAs and the strongly immunosuppressive tumor microenvironment. Particularly, the genetic engineering of T cells has been of extreme research [28]. An instance for genetic engineering of T cells is the creation of a T mobileular receptor (TCR) towards a regarded TAA. An instance of such an technique is the scientific file with the aid of using Morgan et al., in which they transduced regular peripheral blood lymphocytes (PBLs) the use of retroviral vectors with an anti-MART1 TCR transgene that turned into remoted from tumor infiltrating lymphocytes (TILs) of sufferers with cancer [29]. Therein, they established long lasting engraftment of the T cells in 15 sufferers at tiers exceeding 10% of peripheral blood lymphocytes for at the least months after mobileular infusion. Furthermore, they determined excessive sustained tiers of circulating, engineered PBLs at 365 days after infusion in sufferers who each established goal regression of metastatic cancer lesions.

In some other scientific trial T cells have been transduced with a TCR towards the antigen NY-ESO-1, a most cancers/testis (CT) antigen expressed in diverse cancers [30]. In addition, on this trial, an goal scientific reaction in sufferers turned into determined, presenting proof that creation of a TCR concentrated on a TAA represents a viable choice for the remedy of most cancers.

Similarly to introducing a TCR an synthetic T mobileular receptor (normally known as a chimeric antigen receptor; CAR) may be brought to T cells. Utilizing CAR to goal T cells to most cancers cells has ended in surprising reaction quotes withinside the sanatorium towards haematological malignancies [31]. An instance is the take a look at done with the aid of using Kochenderfer et al., who assessed in a scientific segment I trial the capability and protection of adoptive switch of genetically changed T cells expressing CAR towards CD19 [32].

Another manner to enhance an anti-tumoral immune reaction turned into evaluated with the aid of using Herman et al. in a randomized segment III scientific trial amongst sufferers with regionally superior pancreatic most cancers [33]. A 2nd era replication-poor adenovirus of the serotype five containing the TNF-α Cdna below the early boom reaction protein 1 (Egr-1) promoter turned into assessed for this purpose. The Egr-1 is a promoter, that is prompted with the aid of using ionizing radiation, hence limiting the expression of the transgene to the radiation field. In that take a look at, 304 sufferers have been randomly assigned 2:1 to conventional of care plus gene remedy (i.e., adenovirus encoding for TNF-α) as opposed to general of care alone. The outcomes discovered that despite the fact that general of care plus gene remedy turned into secure it did now no longer bring about a survival advantage in sufferers with regionally superior pancreatic most cancers [33]. A greater promising result, in contrast, turned into supplied in a take a look at with the aid of using Malmström et al., in which they studied the immunostimulating consequences of gene remedy with adenoviral vectors expressing CD40 ligand [34]. CD40L belongs to the TNF gene Superfamily and is understood to be a strong immune stimulator of T helper 1 cells. This take a look at recruited 8 sufferers with invasive bladder most cancers for a segment I/IIa trial comparing the safety, efficacy of gene transfer, immune effects, and antitumor responses [34]. The outcomes confirmed that the presence of IFN-γ turned into improved withinside the biopsies of tumors, while stages of circulating T regulatory cells have been decreased. Further histologic assessment indicated that adenoviral CD40L gene remedy decreased the load of malignant cells withinside the bladder. In any other take a look at accomplished via way of means of Chiocca et al., eleven sufferers have been injected with unique doses of interferon-β-expressing adenoviruses starting from 2 × 1010 to 2 × 1011 viral debris stereotactically into the tumor [35]. This turned into accompanied via way of means of surgical elimination of the tumor 4 to 8 days later with extra injections of the adenovirus into the tumor bed. Unfortunately, all sufferers had disease development and/or recurrence inside 4 months of the remedy. The median time to tumor development turned into nine.three weeks and the median normal survival turned into 17.9 weeks.

In addition to the above noted strategies, the utilisation of a seasoned-drug activating suicide gene remedy is an method that has been notably explored pre-clinically and withinside the medical institution for most cancers remedy, with a purpose to be mentioned in greater element below.

4.2. Pro-Drug Activating Suicide Gene Therapy

The precept of seasoned drug activating suicide gene remedy is to introduce a transgene encoding for an enzyme this is both absent in mammalian cells or found in a totally inactive form, into the tumor. The enzyme produced via way of means of the transduced cells will convert the ultimately administered inactive seasoned drug into its lively form, evoking the demise of cells expressing the healing gene. Therein, the bystander effect (a phenomenon in which additionally the neighboring non-transduced cells are killed) is essential for the healing success [36]. In this concept, mind tumors undergo numerous capabilities that make them specially amenable to seasoned-drug activating gene remedy. First of all, mind tumors are usually single, localized lesions of unexpectedly dividing cells in a historical past of non-dividing cells. Furthermore, recurrence usually occurs withinside the near area of the authentic lesion. Unfortunately, the primary outcomes have been now no longer very promising. Transduction performance turned into a first-rate trouble ensuing in a negative healing efficacy. The use of retroviral vectors in the ones early research turned into maximum possibly a first-rate cause for negative transduction performance. In evaluation to retroviral vectors, adenoviral vectors have proven to have a great deal better transduction efficacy in addition to transgene expression [37]. One of the motives is that in evaluation to retroviruses, adenoviruses transduce each dividing and quiescent cells. This characteristic may offer an essential advantage, as now no longer all most cancers cells proliferate withinside the tumor at a given time point. In 1996, Eck et al. posted the primary segment I scientific trial, wherein the seasoned-drug activating enzyme Herpes simplex virus—thymidine kinase (HSV-tk) packed into an adenovirus turned into used with the aim to deal with sufferers with recurrent gliomas [38]. The first finished trial the usage of adenovirus HSV-tk in sufferers with malignant glioma, however, turned into posted via way of means of Sandmair et al. in 2000 [37]. In that take a look at, Sandmair

et al. in comparison the efficacy of each the retrovirus-packaging cells for HSV-tk and the adenovirus mediated HSV-tk gene remedy for the remedy of number one or recurrent gliomas. Twenty-one sufferers have been enrolled in that take a look at. The suggest survival time withinside the adenovirus HSV-tk institution turned into 15 months and appreciably longer while in comparison to a 7.four months survival time withinside the retrovirus-packaging mobileular institution. The manage institution, which obtained adenovirus LacZ had a suggest Survival time of 8.three months. Although the retrovirus-packaging mobileular techniques had been discovered safe, no efficacy become observed. The low gene switch efficacy with retrovirus and the dearth of the treatment reaction indicated that retroviral HSV-tk gene remedy might not be green sufficient in human scientific settings. The loss of efficacy become similarly showed withinside the first randomized, open-label, parallel organization section III scientific trial of 248 sufferers, wherein HSV-tk become produced with the aid of using retroviral generating cells. The examine did now no longer display any development of survival [39]. The scientific efficacy of HSV-tk gene remedy become first proven in separate section II scientific trials; a section IIa trial and a randomized and managed section IIb trial [37,40]. Therein, 17 sufferers with operable or recurrent malignant gliomas receiving HSV-tk gene remedy out of 36 sufferers implicated a survival gain over manipulate sufferers, who did now no longer obtain HSV-tk gene remedy [40]. The suggest survival of the sufferers handled with HSV-tk gene remedy become substantially longer ($p < 0.0095$) while in comparison to the same old care organization or a historic manipulate organization ($p < 0.0017$). This examine become additionally traditionally the primary randomized, managed trial with an adenoviral vector the use of the HSV-tk pro-drug activating suicide gene, wherein survival advantage might be proven. Encouraged with the aid of using those results, a multicenter, widespread care managed, randomized scientific section III trial become commenced. Therein, 250 sufferers had been recruited and randomly allotted, whereof 124 had been allotted to the experimental organization and 126 to the same old care organization.

The median time to loss of life or re-intervention become longer withinside the experimental organization (308 days) than in the manipulate organization (268 days). Interestingly, in a subgroup of sufferers with non-methylated repute of the DNA restore gene MGMT (O6-alkylguanine DNA alkyltransferase), the chance ratio (HR) become 1.72 ($p = 0{\cdot}008$). However, no statistical distinction withinside the ordinary survival among the organizations become observed [41]. Although the examine did now no longer reveal development of ordinary survival, the findings counseled that the usage of HSV-tk gene remedy after tumor resection can boom time to loss of life or re-intervention in sufferers with newly identified supratentorial glioblastoma multiforme. Furthermore, this examine demonstrates that domestically added gene remedy for glioblastoma need to be similarly developed, in particular for sufferers who're not going to reply to conventional chemotherapy. This examine is, as a consequence far, the handiest adenoviral vector examine that has finished a section III scientific trial, that's primarily based totally on the suicide gene remedy with HSV-tk.

5. Safety of Gene Therapy

Despite the tragic case of Jesse Gelsinger, who died because of gene remedy the use of adenoviral vectors, the protection statistics accrued from one-of-a-kind human gene remedy trials had been uniformly satisfactory. However, it need to be mentioned that viral vectors utilized in gene remedy are typically human pathogens, and hence, pre-present antibodies in opposition to the viral vector can be present, which may bring about an undesirable immune reaction. For example, an injection of adenoviral vectors will bring about an preliminary non-unique immune reaction withinside the host, i.e., launch of a number of cytokines accompanied with the aid of using a particular antibody and mobileular-mediated immune reaction directed in opposition to transduced cells. However, the reaction in the direction of adenoviruses is serotype dependent. For example, a examine with the aid of using Thoma et al. proven that the on the spot cytokine reaction of macrophages following adenovirus stimulation differs among adenovirus serotypes, hence, is serotype-unique. Particularly, in a long-time period examine, in which both adenovirus of the serotype 11 (Ad11) or 5 (Ad5) become administered intra peritoneally, Ad11 brought about no/moderate and Ad5 moderate/excessive toxicity [42].

Generally, there may be nevertheless now no longer tons long-time period protection statistics the usage of viral vectors in humans. Nevertheless, numerous meta-evaluation exist already for adenoviruses demonstrating an good enough protection profile in humans [41,43]. The tolerability in the direction of adenoviral vectors has been ideal and the facet results have by and large been slight with none critical negative occasions associated with gene remedy.

Different method with the purpose of enhancing the protection of gene remedy had been implemented. One technique is to increase focused on techniques with a view to beautify the transport of gene transfer vectors, and hence, to enhance the period and efficacy of gene expression. Generally, one in every of the predominant shortcomings with gene remedy is their loss of specificity to their goal cells and their low transduction efficiency. Improving specificity and/or transduction efficacy in the long run might end result also in a higher protection profile. Consequently, the development of transduction efficacy of gene transfer vectors has come along side the improvement of vector technologies, consisting of re-engineering of viral vectors the usage of epitope insertion, chemical modification, and molecular evolution [44]. An instance for this changed into tested in a segment I medical trial through Kim et al., in which they changed the RGD fiber knob on adenoviruses, thereby improving viral infectivity of most cancers cells [45].

The position of innate immunity, in addition to the activation of T and B cells in reaction to the vector and its transgene product is a subject of severe research. Particularly, the feasible results of gene transfer vectors and/or their expressed proteins on nearby lymph nodes are subjects that require similarly evaluation. The pre-life of neutralizing antibodies (e.g., in opposition to numerous adenovirus serotypes or AAVs) has been recounted already for pretty a while and it's miles regarded that those pre-present neutralizing antibodies can significantly lessen transduction efficiency [46].

In order to enhance specificity, in addition to transduction efficiency, viral floor proteins had been changed, eliminated or replaced. For instance, lentiviral vectors had been generated, in which a cell kind particular ligand or antibody has been fused to the viral envelope (i.e., pseudotyping) [47]. The drawback of this has been that unique adjustments led to low vector titers during lentivirus production [13]. Furthermore, it's been proven that focused

on may doubtlessly compromise the access of the vector into the cell [13,47]. On the opposite to focused on viral vectors to particular cells, pseudotyping also can be used to develop tropism of the viral vector to different cells. For instance, retroviruses and lentiviruses are regularly pseudotyped with the Vesicular Stomatitis virus G-protein (VSV-G) to widen their tropism and to boom their yield in production [48].

Another technique to boom specificity of viral vectors to their goal cells is the use of tissue-particular or conditional promoters. An instance for conditional structured gene expression is the use of hypoxia-particular regulatory structures, in which gene expression is aimed to be prompted and confined to ischemic tissues [49]. Commonly, those hypoxia-particular regulatory structures had been carried out to numerous ischemic sickness models, consisting of ischemic myocardium, stroke, and injured spinal cord, however can also be utilized in most cancers gene remedy [50]. Gene expression also can be regulated based on a genotypic feature (e.g., a mutated TP53 gene in most cancers cells), which has been mentioned already above in case of Oncorine™.

The danger of insertional mutagenesis with integrating vectors is a protection danger. Retroviruses, lentiviruses and AAVs are examples of viruses that combine their genome into their host chromosomes. By doing so, there may be a hazard that those vectors might also additionally combine into gene regulatory regions or into transcriptionally lively regions, respectively, which doubtlessly can adversely end result in insertional mutagenesis and oncogenesis. Several procedures had been advanced to bypass those Problems. Therefore, centered integration of transgenes to predetermined genomic webweb sites has been one of the maximum vital subjects in cutting-edge vector improvement. One of the maximum green strategies to achieve centered integration into human cells is primarily based totally on DNA double-strand break-better homologous recombination [51]. In addition, lentivirus/transposon hybrids had been advanced to be able to reduce the chance of insertional mutagenesis [52]. For example, the Sleeping Beauty transposon machine is an appealing technique permitting strong integration of the transgene via transposition into the target mobileular genome [53,54]. The benefit of the Sleeping Beauty transposon machine is that it does now no longer showcase a desire for integration inside lively genes and the inverted repeats have simplest very low residual promoter/enhancer activity. The chance of genotoxicity/mutagenesis because of gene remedy has been one of the predominant arguments towards human gene remedy is. However, the reality, that traditional most cancers therapies (i.e., radiation remedy and chemotherapy) can also motive genetic changes is often disregarded. It is reality that many chemotherapeutic drugs, in addition to radiation remedy, might also additionally motive genetic changes and oncogenesis in patients [55–57].

In addition, with the aid of using growing the producing of gene switch vectors (i.e., improvement of manufacturing mobileular lines, manufacturing strategies, in addition to the purification steps) the protection profile of gene switch vectors may be improved. For example, gutless adenoviral vectors are vectors, in which all different genes however the ones crucial for virus manufacturing are eliminated and changed with the gene of interest, pushed with the aid of using a appropriate promoter. As a end result, gutless adenoviruses nevertheless showcase excessive transduction performance and comparable tropism to preceding vectors, however are much less immunogenic than the primary generation adenoviral vectors. However, due to the fact that gutless vectors are without all viral genes, co-contamination with a helper adenovirus is needed that gives proteins wanted for its genome replication, packaging, and capsid formation. As each helper and gutless vectors have the equal viral capsid, separation ought to be addressed earlier than purification, that is exhausting and has now no longer been with out demanding situations [58].

6. Conclusions

Gene remedy is an fascinating and capacity technique to deal with diverse diseases, consisting of most cancers.Currently maximum gene remedy protocols are confined to the nearby management of the gene switch vector, or to ex vivo gene switch approaches. One of the demanding situations in gene remedy remains the low transduction performance and its minimum distribution of the vector inside the tissue. However, it must be emphasised that consciousness must now no longer simplest be directed closer to vector improvement itself, however also closer to the producing of those vectors. The excessive price worried in viral vector manufacturing, that is the end result of tedious downstream purifications steps, has been challenging. In addition, the idea of the use of gene remedy as a unmarried agent remedy has now no longer been as a success as being hoped. Consequently, aggregate remedy with current traditional modalities or different new therapies must be taken into consideration and can provide extra gain in most cancers gene remedy.

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"A Review Article on Diabetes Treated by Ayurveda"

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ABSTRACT: -

Type 1 diabetes mellitus (T1DM), also known as autoimmune diabetes, is a continual disease characterised through insulin deficiency due to pancreatic β-mobile loss and leads to hyperglycaemia. Although the age of symptomatic onset is normally during childhood or youth, signs and symptoms can now and again develop much later. Although the aetiology of T1DM is not completely understood, the pathogenesis of the disorder is concept to involve T mobile-mediated destruction of β-cells. Islet-concentrated on autoantibodies that focus on insulin, 65 kDa glutamic acid decarboxylase, insulinoma-associated protein 2 and zinc transporter eight — all of which might be proteins associated with secretory granules in β-cells — are biomarkers of T1DM-related autoimmunity which are observed months to years before symptom onset, and can be used to identify and take a look at people who are liable to developing T1DM. The kind of autoantibody that looks first relies upon at the environmental cause and on genetic elements. The pathogenesis of T1DM may be divided into three tiers relying on the absence or presence of hyperglycaemia and hyperglycaemia- associated symptoms (such as polyuria and thirst). A remedy isn't always available, and patients depend upon lifelong insulin injections; novel processes to insulin remedy, together with insulin pumps, non-stop glucose monitoring and hybrid closed-loop systems, are in development. Although extensive glycaemic manipulate has decreased the incidence of microvascular and macrovascular complications, most of the people of patients with T1DM are still developing these headaches. Major research efforts are had to reap early prognosis, prevent β-mobile loss and broaden higher remedy alternatives to improve the pleasant of life and analysis of these affected.

1. Introduction: -

Diabetes mellitus (DM) might be one of the oldest illnesses recognised to guy. It was first said in Egyptian manuscript about 3000 years ago.1 In 1936, the difference among type 1 and kind 2 DM turned into genuinely made.2 Type 2 DM was first defined as a factor of metabolic syndrome in 1988.Three Type 2 DM (previously known as non-insulin structured DM) is the maximum not unusual form of DM characterised through hyperglycemia, insulin resistance, and relative insulin deficiency.4 Type 2 DM consequences from interaction between genetic, environmental and behavioral risk elements. People residing with kind 2 DM are extra susceptible to diverse styles of each brief- and lengthy-term complications, which frequently result in their premature dying. This tendency of elevated morbidity and mortality is visible in sufferers with kind 2 DM because of the commonness of this kind of DM, its insidious onset and overdue popularity, mainly in resource-bad developing nations like Africa.

Epidemiology

It is estimated that 366 million people had DM in 2011; by 2030 this would have risen to 552 million.8 The quantity of human beings with type 2 DM is growing in each united states with 80% of human beings with DM dwelling in low- and center-earnings nations. DM prompted 4.6 million deaths in 2011.Eight It is expected that 439 million people could have kind 2 DM with the aid of the yr 2030.9 The incidence of kind 2 DM varies considerably from one geographical area to the alternative due to environmental and life-style risk factors. Literature search has shown that there are few information available on the superiority of kind 2 DM in Africa as a whole. Studies examining information tendencies inside Africa factor to proof of a dramatic growth in occurrence in each rural and concrete putting, and affecting both gender equally. The majority of the DM burden in Africa seems to be type 2 DM, with much less than 10% of DM instances being kind 1 DM.11 A 2011 Centre for Disease Control and Prevention (CDC) report estimates that DM influences about 25.Eight million people in the US (7.8% of the population) in 2010 with 90% to 95% of them being kind 2 DM.12 It is predicted that the superiority of DM in adults of which type 2 DM is becoming outstanding will growth in the subsequent a long time and lots of the increase will arise in developing nations wherein the general public of patients are aged between 45 and sixty four years. It is projected that the latter will same or maybe exceed the previous in growing international locations, thus culminating in a double burden due to the modern fashion of transition from communicable to non-communicable diseases.

Lifestyle, Genetics, and Medical Conditions

Type 2 DM is due in the main to life-style factors and genetics.15 A wide variety of way of life factors are recognised to be important to the development of kind 2 DM. These are physical inactivity, sedentary life-style, cigarette smoking and generous consumption of alcohol.Sixteen Obesity has been discovered to make contributions to approximately fifty five% of cases of type 2 DM.17 The expanded rate of childhood weight problems among the Nineteen Sixties and 2000s is thought to have brought about the growth in type 2 DM in children and children.18 Environmental pollutants may

additionally make a contribution to the current increases in the price of type 2 DM. A susceptible wonderful correlation has been determined between the concentration in the urine of bisphenol A, a constituent of a few plastics, and the prevalence of kind 2 DM.19

There is a robust inheritable genetic connection in kind 2 DM, having loved ones (specifically first diploma) with type 2 DM increases the dangers of growing type 2 DM significantly. Concordance among monozygotic twins is near one hundred%, and about 25% of these with the sickness have a circle of relatives records of DM.20 Recently, genes observed to be appreciably related to developing kind 2 DM, include TCF7L2, PPARG, FTO, KCNJ11, NOTCH2, WFS1, CDKAL1, IGF2BP2, SLC30A8, JAZ F1, and HHEX. KCNJ11 (potassium inwardly rectifying channel, subfamily J, member 11), encodes the islet ATP-touchy potassium channel Kir6.2, and TCF7L2 (transcription aspect 7- like 2) regulates proglucagon gene expression and consequently the manufacturing of glucagon-like peptide-

1.21 Moreover, obesity (which is an unbiased threat element for type 2 DM) is strongly inherited.22 Monogenic bureaucracy like Maturity-onset diabetes of the younger (MODY), constitutes up to 5% of instances.23 There are many clinical situations which could probably supply upward push to, or exacerbate kind 2 DM. These encompass weight problems, hypertension, improved ldl cholesterol (blended hyperlipidemia), and with the situation frequently termed metabolic syndrome (it's also called Syndrome X, Reaven's syndrome).24 Other reasons encompass acromegaly, Cushing's syndrome, thyrotoxicosis, pheochromocytoma, persistent pancreatitis, cancer, and pills.25 Additional factors found to growth the risk of type 2 DM consist of getting older,26 high-fats diets, and a less energetic life-style.

Pathophysiology

Type 2 DM is characterised by using insulin insensitivity due to insulin resistance, declining insulin manufacturing, and eventual pancreatic beta-cell failure.28,29 This results in a decrease in glucose delivery into the liver, muscle cells, and fats cells. There is an boom inside the breakdown of fat with hyperglycemia. The involvement of impaired alpha-cell feature has these days been identified inside the pathophysiology of type 2 DM.30 As a end result of this dysfunction, glucagon and hepatic glucose levels that rise for the duration of fasting aren't suppressed with a meal. Given insufficient ranges of insulin and elevated insulin resistance, hyperglycemia consequences. The incretins are essential intestine mediators of insulin launch, and inside the case of GLP-1, of glucagon suppression. Although GIP interest is impaired in people with type 2 DM, GLP-1 insulinotropic effects are preserved, and accordingly GLP-1 represents a doubtlessly beneficial healing option.30 However, like GIP; GLP-1 is swiftly inactivated by way of DPP-IV in vivo. Two healing tactics to this trouble were advanced: GLP-1 analogues with improved 1/2-lives, and DPP-IV inhibitors, which prevent the breakdown of endogenous GLP-1 in addition to GIP.30 Both training of retailers have shown promise, with capacity not handiest to normalize fasting and postprandial glucose tiers but also to improve beta-mobile functioning and mass. Studies are ongoing on the function of mitochondrial disorder in the development of insulin resistance and etiology of kind 2 DM.31 Also very important is adipose tissue, as endocrine organ speculation (secretion of numerous adipocytokines, i.E., leptin, TNF-alpha, resistin, and adiponectin implicated in insulin resistance and possibly beta-cell disorder).30

A majority of individuals laid low with kind 2 DM are obese, with crucial visceral adiposity. Therefore, the adipose tissue performs a vital role within the pathogenesis of kind 2 DM. Although the foremost idea used to provide an explanation for this link is the portal/visceral hypothesis giving a key position in improved non-esterified fatty acid concentrations, new rising theories are the ectopic fats storage syndrome (deposition of triglycerides in muscle, liver and pancreatic cells). These hypotheses represent the framework for the examine of the interaction among insulin resistance and beta-cellular dysfunction in kind 2 DM in addition to between our obesogenic surroundings and DM hazard in the next decade.30

Diabetes mellitus

usually called diabetes, is a metabolic disorder that reasons excessive blood sugar. The hormone insulin transports sugar from the blood into your cells to be stored or used for electricity.

Without looking after proper food regimen, diabetes can cause a construct-up of sugars in the blood, that could increase the chance of dangerous complications along with stroke and heart diseases. Gradual increase in Diabetes can cause diabetic complications like blindness, kidney failure, and nerve damage. These damages are the end result of harm to small vessels, called microvascular disease. Hyperglycemia, causes to spillage of glucose into the urine, as a result the time period candy urine.

3. Types of Diabetes

Three foremost diabetes can increase TYPE 1, TYPE 2 and GESTATIONAL diabetes.

Type 1 Diabetes

Type 1 is likewise referred to as juvenile diabetes occurs while the frame fails to provide insulin. People affected with type 1 diabetes are insulin-established, which means that they have to take synthetic insulin daily to live alive.

Type 2 Diabetes

Type 2 diabetes influences the manner the frame makes use of insulin, the cells inside the frame do not react to it as effectively as they once did. This is the maximum communal sort of diabetes which has strong links with obesity.

Gestational Diabetes

During being pregnant, girls will be laid low with Gestational Diabetes whilst the frame can become less sensitive to insulin. However, this form of diabetes does no longer arise in all women and usually resolves after giving start.

4. Ayurvedic Diabetes Treatments :

Ayurvedic treatments for diabetes range from internal, herbal medications to purifying panchkarma procedures such as vanamaVirechana, Vasti etc., based on the severity of the condition. These natural remedies are intended to enhance insulin sensitivity of type – 4 glucose receptors thus reducing insulin resistance, and also to enhance nsulin secretion and regeneration of beta cells.

Yoga for Diabetes:

Yoga helps in controlling diabetes. This is mainly because Yoga keeps a check on the causes of Diabetes. Stress and obesity are main causes that can lead to Diabetes. Regular yoga practice with meditation reduces stress and slows down the fat accumulation in the body. Pranayama, surya namesake, Bal asana, Vajras Ana, sarvangasana, Hal asana, dhanurasna are few of the postures that are effective.

5. Ayurvedic Treatment for Diabetes at Ayurvedagram:

Customized Kerala therapies as prescribed by our doctors, regular yoga and physical exercise, individually tailored low carbohydrate diet and low stress level in day-to-day life goes a long way in maintaining normal blood glucose level.
The treatment of diabetes in Ayurveda calls for dietary changes that can help control blood glucose levels. The dietary recommendations suggested for the Ayurvedic treatment for diabetic patients include:

- The food consumed should be astringent or bitter. Bitter gourd, moong, barley are recommended to be included in the diet.
- The diet should include plenty of fruits and vegetables that have rich fiber content.
- Spices like turmeric, cumin, coriander, and cardamom should be used while cooking.
- Instead of eating three heavy meals, 5 or 6 small meals can be eaten to prevent blood sugar level spikes.

The Ayurvedic treatment for Type II Diabetes involves the use of herbal remedies that can help control blood glucose levels. Some of the popular herbs used in diabetes treatment in Ayurveda include:

- **Gymnema** or **Gurmar** is one of the main herbs used to treat diabetes as it has the property of ‘destroying sugar’ by curbing the craving for sugar.
- **Fenugreek** or **Methi seeds** have high fiber content and it regulates blood sugar levels.
- **Jamun** is a fruit that helps to reduce blood sugar levels. It is one of the potent medicines used in Ayurveda.
- **Neem** and **Tulsi** are two other common herbs that are helpful in treating diabetes as they help to improve insulin management by the body.
- **Giloy** or **Guduchi** is yet another powerful herb that helps manage blood sugar levels and helps to improve general immunity.

There are a variety of tried and tested classical formulations as well as proprietary formulas that can help reverse this metabolic disorder if discovered early. Ayurvedagram offers an authentic ayurvedic approach to help manage diabetes with a dedicated team of ayurvedic experts and counsellors. Reach out to us to know more.

Can diabetes be cured by Ayurveda?

Diabetes is described in Ayurveda as Prameha, and it is essentially a metabolic disorder that is caused by the body's inability to break down glucose. Even though the complete cure of diabetes is debatable, treatment of diabetes in Ayurveda by maintaining healthy blood glucose levels is feasible. Ayurvedic supplements, holistic purification treatments, and remedial massages are given by expert Ayurvedic practitioners to help you lead a healthy lifestyle and control diabetes.

How can I get rid of diabetes permanently?

There is no permanent cure for diabetes but you can control high blood sugar levels by using Ayurvedic remedies. It is recommended by Ayurvedic practitioners to take Ayurvedic tablets and herbal supplements to maintain the body. You can also incorporate healthy practices like avoiding alcohol and smoking, reducing carbohydrates, avoiding consumption of excess oil, and regular exercise to keep diabetes in check.

What is the best treatment for diabetes?

Customized Ayurvedic therapies by Ayuvedagram are great for the treatment of diabetes as they involve herbal supplements, and Panchakarma procedures help in enhancing insulin sensitivity, reduce insulin resistance, and boosts insulin secretion to regenerate beta cells. Treatment of Diabetes in Ayurveda also involves a diet of fruits and vegetables rich in fiber, spices like cumin, coriander, turmeric, and cardamom, eating small meals throughout the day, and consuming herbs like Gymnema to curb sugar cravings, Fenugreek to regular blood sugar levels, neem and Tulsi to enhance insulin management, and Guduchi to manage blood sugar levels by boosting immunity.

Can prediabetes be cured by Ayurveda?

According to Ayurveda, pre-diabetes symptoms include Dantaadeenam malaadhyatwam (decreasing oral hygiene), Paani paadayoho daaha (a burning sensation in the feet and palms), and Chikkanata dehe (a sticky feeling in the whole body). Pre-diabetes symptoms can be controlled through herbal supplements like Tumeric, Amla, neem leaves, curry leaves, and natural Ayurvedic remedies prescribed by your Ayurvedic practitioner.

Which foods are safe for diabetes?

Certain vegetables like cabbage, carrot, broccoli, spinach, onion, garlic, cucumber, lettuce, tomato, radish, and beetroot, and citrus fruits are great for diabetics. You can also consume whole grains, sprouts, chickpeas, and herbal dietary supplements like alma, cinnamon, turmeric, fenugreek, neem, green tea, and aloe Vera to keep blood sugar levels under control. Nevertheless, you are always welcome at Ayurveadagram to consult the experts and get proper and the best treatment of diabetes in Ayurveda

Management Approaches

a. Prevention

1. Use of various preparations made from yava (barley), mudga (green gram), old rice,bitter gourd, drum-stick, methi(fenugreek), patola (snake gourd), pumpkin, cucumber, bimbi,watermelon, buttermilk, triphala etc. are beneficial as preventive measures for borderline diabetic patients
2. Dinacharya (daily regimen) and ritucary! (seasonal regimen)
3. Regular exercise/ increase in calorie consuming activities (Brisk walking, swimming,etc.)
4. Regular use of rasayana drugs (Amalaki ras!yana etc.)
5. Restriction in intake of sugar/ sugar products, fried food and dairy products
6. Restriction in the use of different types of wine, excess use of oil, clarified butter, milk,sugarcane products, cakes and the meat of domestic and aquatic animals
7. Avoidance of day sleep and laziness

6. Conclusions

Type 2 DM is a metabolic disease that can be averted through life-style amendment, weight loss program manipulate, and manage of obese and obesity. Education of the population remains key to the manage of this rising epidemic. Novel drugs are being evolved, but no remedy is to be had in sight for the disease, in spite of new perception into the pathophysiology of the ailment. Management should be tailor-made to enhance the satisfactory of lifestyles of people with kind 2 DM.

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Diabetes Mellitus: Review Article

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ABSTRACT

One of the most prevalent non-communicable diseases in the world is diabetes mellitus. India faces a number of difficulties in managing diabetes, including a rising prevalence of the disease in both urban and rural areas, a lack of public awareness of the disease, a lack of adequate medical facilities, a high cost of treatment, subpar glycaemic control, and an increase in the frequency of diabetic complications. Subcutaneous injections can be used to administer insulin therapy for diabetes up to four times per day. Long-term insulin therapy has a negative impact on patient outcomes because of issues with patient compliance and the invasiveness of its administration. Type 1 diabetes is becoming more common, but type 2 diabetes mellitus, which accounts for more than 90% of all instances of diabetes, is the main cause of the epidemic. Obesity and a sedentary lifestyle are two additional risk factors for type 2 diabetes, which is a serious and prevalent chronic illness caused by a complicated interaction between genes and the environment.

Keywords: Diabetes, Medical Education, , Genetics, Genomics , Obesity

INTRODUCTION

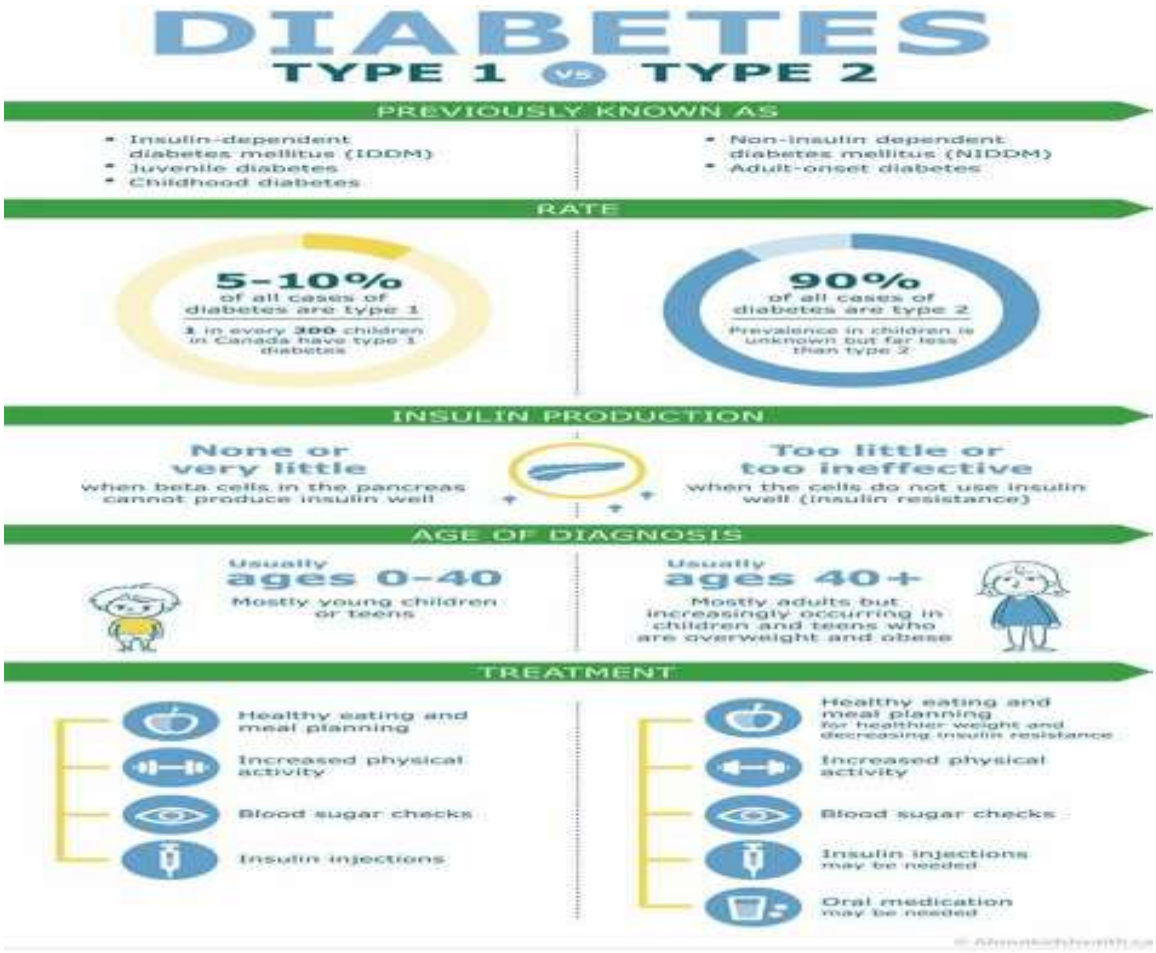
Diabetes mellitus, commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level (hyperglycemia) over a prolonged period of time. Symptoms often include frequent urination, increased thirst and increased appetite. If left untreated, diabetes can cause many health complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, damage to the nerves, damage to the eyes and cognitive impairment. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. Insulin is a hormone which is responsible for helping glucose from food get into cells to be used for energy.

Type 1 diabetes

Type 1 Diabetes results from failure of the pancreas to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" or "juvenile diabetes". The loss of beta cells is caused by an autoimmune response. The cause of this autoimmune response is unknown. Although Type 1 diabetes usually appears during childhood or adolescence, it can also develop in adults.

Type 2 diabetes

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" or "adult-onset diabetes". Type 2 diabetes is more common in older adults, but a significant increase in the prevalence of obesity among children has led to more cases of type 2 diabetes in younger people. The most common cause is a combination of excessive body weight and insufficient exercise.



Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels. In women with gestational diabetes, blood sugar usually returns to normal soon after delivery. However, women who had gestational diabetes during pregnancy have a higher risk of developing type 2 diabetes later in life.

Type 1 diabetes must be managed with insulin injections. Prevention and treatment of type 2 diabetes involves maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Type 2 diabetes may be treated with oral antidiabetic medications, with or without insulin. Control of blood pressure and maintaining proper foot and eye care are important for people with the disease. Insulin and some oral medications can cause low blood sugar (hypoglycemia). Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes. Gestational diabetes usually resolves after the birth of the baby.

As of 2019, an estimated 463 million people had diabetes worldwide (8.8% of the adult population), with type 2 diabetes making up about 90% of the cases. Rates are similar in women and men. Trends suggest that rates will continue to rise. Diabetes at least doubles a person's risk of early death. In 2019, diabetes resulted in approximately 4.2 million deaths. It is the 7th leading cause of death globally. The global economic cost of diabetes-related health expenditure in 2017 was estimated at US$727 billion. In the United States, diabetes cost nearly US$327 billion in 2017. Average medical expenditures among people with diabetes are about 2.3 times higher.

signs and symptoms

Objective evidence of a disease such as a rash or cough is a sign. Doctors, family members, and anyone experiencing signs can identify them.

However, less noticeable disruption of normal functioning, such as abdominal pain, back pain, and malaise, is a symptom and can only be recognized by the affected individual. Symptoms are subjective. That is, others can only know the symptoms when told by the affected person.

This MNT Knowledge Center article describes the effects of signs and symptoms, and their history. The play also introduces different types of signs and symptoms, as well as their medical use.

Simple facts about signs and symptoms

Mild headaches can be a symptom because no one else can observe them. Medical symptoms are divided into chronic, recurrent, and remission symptoms. An example of a medical sign is high blood pressure that can be measured and observed by others. Anthony van Leuwenhoek invented the microscope in 1674 and changed the face of diagnostic tools.

Symptoms

There are three main types of symptoms.

Remission Symptoms:

When symptoms improve or disappear completely, they are called remission symptoms. For example, the symptoms of a cold may last for several days and then disappear without treatment.

Chronic Symptoms:

These are long-term or recurrent symptoms. Chronic symptoms are common in ongoing conditions such as diabetes, asthma, and cancer.

Recurrence Symptoms:

These are symptoms that have appeared in the past, resolved, and then returned. For example, the symptoms of depression may not appear for years, but may recur afterwards. In some cases, there are no symptoms at all. For example, a person can unknowingly suffer from high blood pressure for years, and some cancers are asymptomatic until later, more aggressive stages.

These are known as asymptomatic conditions, and the onset of symptoms is often associated with discomfort and dysfunction, but asymptomatic conditions can be fatal.

Many types of infections are asymptomatic. These are called asymptomatic infections and can be transmitted, but they do not cause any noticeable symptoms in people with the infection. The infection can be transmitted to others during the latency period or while the infectious agent has invaded the body. Another risk of asymptomatic infection is that it can cause complications that are not related to the infection itself. For example, untreated urinary tract infections (UTIs) can lead to preterm birth. Many infectious diseases, such as

HPV, are asymptomatic and can infect others. Examples of infections that initially cause no symptoms include HIV, human papillomavirus (HPV), herpes simplex virus (HSV), syphilis, hepatitis B and C. Usually talk to your doctor about another problem. It is important to have regular health checks to identify underlying problems that may not be obvious. Many cancers are asymptomatic in the early stages. Prostate cancer, for example, does not show symptoms until it has progressed to a certain point in time. This is why some cancers are so dangerous, as early treatment is often important in the treatment of cancer. For this reason, regular health checks are important for people at risk.

Sign

Medical signs are medical facts or features related to physical reactions that are confirmed by a doctor, nurse, or medical device during a patient's examination. They can often be measured, and this measurement can be central to diagnosing medical problems. Patients may be unaware of the signs and may appear irrelevant. But in the hands of doctors who know how these signs relate to other parts of the body, the same signs can hold the key to treating the underlying medical problem. ..

Some examples of signs that a doctor may be associated with a disease:

Hypertension:

This may indicate cardiovascular problems, side effects to medication, allergies, or many other possible conditions or disorders. There is sex. This is often combined with other signs to reach a diagnosis.

Fingerbeat:

This can be a sign of lung disease or many hereditary disorders. Doctors are trained to find signs that untrained people may not consider important Signs fall into the following categories:

- **Prognostic Signs:** These are signs of the future. Instead of identifying the nature of the disease, they predict the outcome of the patient. B. What is likely to happen to him and how serious the illness is likely to be.
- **Medical History Signs:** These signs indicate part of a person's medical history. For example, skin scars may indicate a history of severe acne.

Diagnostic Signs:

These signs help doctors recognize and identify their current health problems. For example, high levels of prostate-specific antigen (PSA) in men's blood can be a sign of prostate cancer or prostate problems.

Pathological Signs:

This means that the doctor can assign the signs to the condition with absolute certainty. For example, the presence of a particular microbe in a blood sample may indicate a particular viral infection.

Diabetic emergencies

People with diabetes (usually but not exclusively in type 1 diabetes) may also experience diabetic ketoacidosis (DKA), a metabolic disturbance characterized by nausea, vomiting and abdominal pain, the smell of acetone on the breath, deep breathing known as Kussmaul breathing, and in severe cases a decreased level of consciousness. DKA requires emergency treatment in hospital.

A rarer but more dangerous condition is hyperosmolar hyperglycemic state (HHS), which is more common in type 2 diabetes and is mainly the result of dehydration caused by high blood sugars. Treatment-related low blood sugar (hypoglycemia) is common in people with type 1 and also type 2 diabetes depending on the medication being used. Most cases are mild and are not considered medical emergencies.

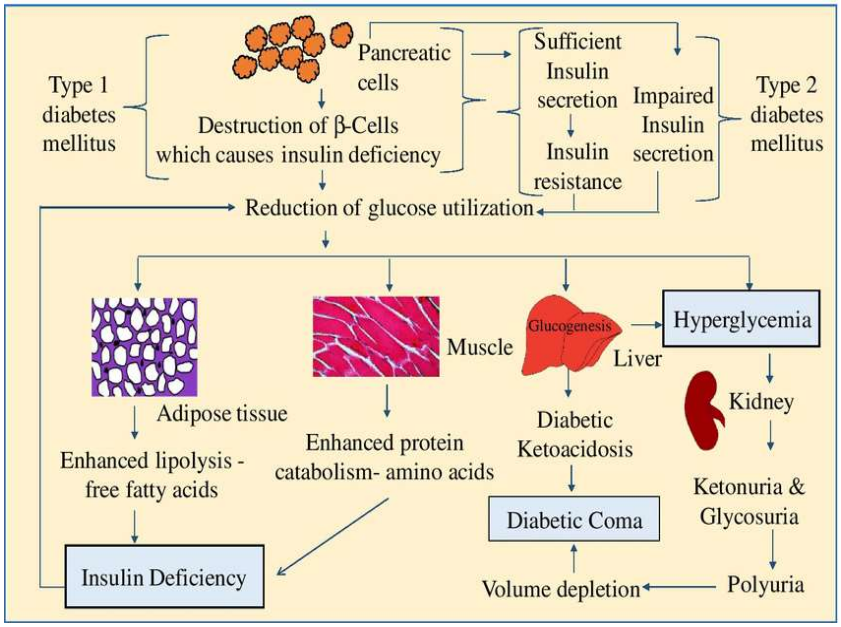
fects can range from feelings of unease, sweating, trembling, and increased appetite in mild cases to more serious effects such as confusion, changes in behavior such as aggressiveness, seizures, unconsciousness, and rarely permanent brain damage or death in severe cases. Rapid breathing, sweating, and cold, pale skin are characteristic of low blood sugar but not definitive. Mild to moderate cases are self-treated by eating or drinking something high in rapidly absorbed carbohydrates. Severe cases can lead to unconsciousness and must be treated with intravenous glucose or injections with glucagon.

Pathophysiology

A patient with DM has the potential for hyperglycemia. The pathology of DM can be unclear since several factors can often contribute to the disease. Hyperglycemia alone can impair pancreatic beta-cell function and contributes to impaired insulin secretion. Consequentially, there is a vicious cycle of hyperglycemia leading to an impaired metabolic state. Blood glucose levels above 180 mg/dL are often considered hyperglycemic in this context, though because of the variety of mechanisms, there is no clear cutoff point. Patients experience osmotic diuresis due to saturation of the glucose transporters in the nephron at higher blood glucose levels. Although the effect is variable, serum glucose levels above 250 mg/dL are likely to cause symptoms of polyuria and polydipsia.

Insulin resistance is attributable to excess fatty acids and proinflammatory cytokines, which leads to impaired glucose transport and increases fat breakdown. Since there is an inadequate response or production of insulin, the body responds by inappropriately increasing glucagon, thus further contributing to hyperglycemia. While insulin resistance is a component of T2DM, the full extent of the disease results when the patient has inadequate production of insulin to compensate for their insulin resistance.

Chronic hyperglycemia also causes nonenzymatic glycation of proteins and lipids. The extent of this is measurable via the glycation hemoglobin (HbA1c) test. Glycation leads to damage in small blood vessels in the retina, kidney, and peripheral nerves. Higher glucose levels hasten the process. This damage leads to the classic diabetic complications of diabetic retinopathy, nephropathy, and neuropathy and the preventable outcomes of blindness, dialysis, and amputation, respectively.



Treatment / administration

The physiology and management of diabetes is complex and requires a variety of interventions for successful disease management. Diabetes awareness and patient involvement are important for management. Patients will get better results if they can independently monitor their diet (carbohydrates and general calorie restriction), regular exercise (more than 150 minutes a week), and blood glucose. [28]

Lifelong treatment is often required to avoid unwanted complications. Ideally, blood glucose should be maintained at 90-130 mg / dL and HbA1c should be maintained below 7%. Glucose management is important, but overly aggressive management can lead to hypoglycemia, which can have harmful or fatal consequences. Since T1DM is a disease primarily due to insulin deficiency, daily injections or insulin pump delivery is central to treatment. Diet and exercise may be appropriate treatments, especially for early-stage type 2 diabetes. Other treatments may target insulin sensitivity or increase insulin secretion by the pancreas. Specific drug subclasses include biguanide (metformin), sulfonylurea, meglitinide, α-glucosidase inhibitor, thiazolidinedione, glucagon-like peptide-1 agonist, dipeptidyl peptidase IV inhibitor (DPP-4), selective, amilinomi. Peptides, and sodium-glucose transporter-2 (SGLT-2) inhibitors. Metformin is a front-line prescription diabetes drug that works by lowering basal and postprandial plasma glucose. Insulin may also be needed for patients with type 2 diabetes, especially those with inadequate glucose management at an advanced stage of the disease. In patients with morbid obesity, obesity surgery is a possible means of normalizing blood sugar levels. Recommended for people who have failed other treatments and have serious comorbidity. [29] The GLP-1 agonists liraglutide and semaglutide correlate with improved cardiovascular outcomes. The SGLT-2 inhibitors empagliflozin and canagliflozin have been shown to not only prevent the development of heart failure, but also improve cardiovascular outcomes with potential renal protection.

Microvascular complications are a risky complication of diabetes and require regular examination. To diagnose diabetic retinopathy, qualified medical personnel should perform regular diabetic retinopathy tests. Neurological examinations using the monofilament test can identify patients with neuropathy who are at risk of amputation. Doctors may also advise patients to have a daily foot examination to identify foot lesions that may be overlooked due to neuropathy. Low-dose tricyclic antidepressants, duloxetine, anticonvulsants, topical capsaicin, and analgesics may be needed to treat neuropathic pain in diabetes. Urinary microalbumin testing can also assess early renal changes due to diabetes with albuminuria above 30 mg / g creatinine, along with an estimated GFR. The antiproteinuria effect of angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) reverses the progression from microalbuminuria to macroalbuminuria in patients with delayed type 1 or type 2 diabetes. It will be the best drug for.

The FDA has approved pregabalin and duloxetine for the treatment of diabetic peripheral neuropathy. Tricyclic antidepressants and anticonvulsants have also been used to manage the pain of diabetic neuropathies, with varying successes.

ADA also recommends regular blood pressure screening for diabetics with a goal of systolic blood pressure of 130 mmHg and diastolic blood pressure of 85 mmHg. [30] Pharmacological treatment of hypertensive diabetic patients usually includes angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics, beta blockers, and / or calcium channel blockers. ADA is diabetic so that low-density lipoprotein cholesterol (LDL-C) is less than 100 mg / dL in the absence of cardiovascular disease (CVD) and less than 70 mg / dL in the case of atherosclerotic cardiovascular disease. There is a recommendation for patient lipid monitoring (ASCVD). Statins are the first-line therapy for the treatment of dyslipidemia in diabetic patients. ADA

suggests that low doses of aspirin may also be beneficial for diabetics at high risk of cardiovascular events. However, the role of aspirin in reducing cardiovascular events in diabetic patients remains unclear ….

Complications

Regardless of the specific type of diabetes, complications involve microvascular, macrovascular, and neuropathic issues. Microvascular and macrovascular complications vary according to the degree and the duration of poorly control diabetes and include nephropathy, retinopathy, neuropathy, and ASCVD events, especially if it is associated with other comorbidities like dyslipidemia and hypertension.[45] One of the most devastating consequences of DM is its effect on cardiovascular disease (ASCVD). Approximately two-thirds of those with DM will die from a myocardial infarction or stroke.[46] In T2DM, fasting glucose of more than 100 mg/dL significantly contributes to the risk of ASCVD, and cardiovascular risk can develop before frank hyperglycemia.[47][48]

DM is also a common cause of blindness in adults aged 20 to 74 years in the United States. Diabetic retinopathy contributes to 12000 to 24000 new cases of blindness annually, and treatments generally consist of laser surgery and glucose control.[49]

Renal disease is another significant cause of morbidity and mortality in DM patients. It is the leading contributor to end-stage renal disease (ESRD) in the United States, and many patients with ESRD will need to start dialysis or receive a kidney transplant.[49] If the albuminuria persists in the range of 30 to 300 mg/day (microalbuminuria), it seems to be a predictable earliest marker for the onset of diabetic neuropathy. When macroalbuminuria (300 mg / 24 h or more) begins, the progression to ESRD accelerates. Random spot urine samples for measuring the ratio of albumin to creatinine are the most widely used and preferred methods for detecting microalbuminuria, a rapid, easy, and predictable method. Two of the three tests performed over a 6-month period showing sustained levels of creatinine above 30 mcg / mg confirm the diagnosis of microalbuminuria.

DM is also the leading cause of limb amputation in the United States. This is primarily due to DM-related angiopathy and neuropathy. [49] Many patients who develop neuropathy require regular foot examinations to prevent infection from overlooked wounds. The duration of diabetes is the most important risk factor for the development of diabetic retinopathy. In people with type 1 diabetes, it usually develops about 5 years after the onset. Therefore, it is recommended that retinal examinations in these patients be started approximately 5 years after diagnosis. In patients with type 2 diabetes, many patients may already have retinal changes at the time of diagnosis. By the age of 10, about 10%, by the age of 15, 40%, and by the age of 20, 60% will have nonproliferative retinal disease. For these patients, it is advisable to start an annual retinal screening at the time of diagnosis. Post-study studies have shown that proper glycemic control has a positive effect on the onset and progression of diabetic retinopathy. Uncontrolled blood pressure is an additional risk factor for macular edema. Therefore, lowering blood pressure in diabetics also affects the risk of developing retinopathy.

]The most acute complication of DM is diabetic ketoacidosis (DKA), which typically presents in T1DM. This condition is usually either due to inadequate dosing, missed doses, or ongoing infection.[53] In this condition, the lack of insulin means that tissues are unable to obtain glucose from the bloodstream. Compensation for this causes the metabolism of lipids into ketones as a substitute energy source, which causes systemic acidosis, and can be calculated as a high anion-gap metabolic acidosis. The combination of hyperglycemia and ketosis causes diuresis, acidemia, and vomiting leading to dehydration and electrolyte abnormalities, which can be life-threatening. In T2DM, hyperosmolar hyperglycemic syndrome (HHS) is an emergent concern. It presents similarly to DKA with excessive thirst, elevated blood glucose, dry mouth, polyuria, tachypnea, and tachycardia. However, unlike DKA, HHS typically does not present with excessive urinary ketones since insulin still gets produced by pancreatic beta cells. Treatment for DKA or HHS involves insulin administration and aggressive intravenous hydration. Careful management of electrolytes, particularly potassium, is critical in the management of these emergent conditions.

Conclusion

Diabetes is a late murderer for whom no cure is known. However, with proper awareness and timely treatment, complications can be reduced. The three main complications are associated with blindness, kidney damage and heart attack. Strict control of a patient's blood glucose is important to avoid complications. One of the difficulties of tightly controlling blood sugar levels is that such attempts can lead to hypoglycemia. This causes far more serious complications than elevated blood sugar levels. Researchers are currently looking for alternative ways to treat diabetes. The purpose of this study is to give an overview of the current state of diabetes research. The author believes that diabetes is one of the most challenging research topics of the new century and wants to encourage new researchers to take on the challenge.]

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Quality Management System

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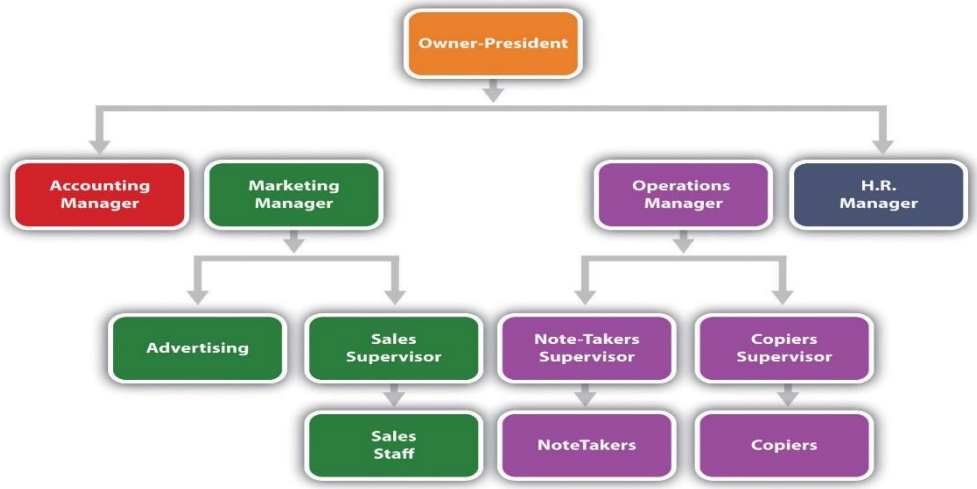
QUALITY ???

- How properly does product layout meet client perception?
- Does dosage shape supply the favored safety, efficacy and stability?
- Does it fulfill Provider- Controller- Consumer?



QMS model – Customer-to-customer for customer

TOTAL QUALITY MANAGEMENT

QMS principles

1. Customer focus
2. Leadership
3. Process method
4. Involvement of people
5. System method to management
6. Continual improvement
7. Factual method to decision-making
8. Mutually useful provider relationship

12 Steps

1. Assure guide of key energy group
2. Use chief behaviour to generate electricity for extrade
3. Use symbol & language to sell effort
4. Build in stability
5. Surface dissatisfaction with gift state
6. Ensure complete participation in extrade process
7. Give praise for accomplishment
8. Allow time to disengage from gift state

9. Project & conversation a clean photo of future
10.Use a couple of motivation
11.Develop organizational crew for transition to TQM
12.Builds-in systematic remarks for preserving TQM

Six Pillar

1. Commitment of pinnacle management
2. Organizational structure & Roles
3. Education & Training
4. Transparent & powerful communication
5. Recognition & Rewards
6. Customer focus & satisfaction

PDCA Cycle

Level of QMS

1. Customer focus
2. Organizational management
3. Process control
4. Inspection & Audit
5. Market sound

Organizational Management

Personnel

1. Training & ability development
2. Change control
3. Health & hygiene
4. Performance competency

Management

1. Policy making
2. Decision making
3. Pilot plan scale up & maintenance
4. Implementation of regulations

Process Control

Control

1. Entry level
2. Production level
3. QC Lab
4. Sampling & documentation
5. Release management & marketplace survey

Inspection:

1. Internal inspection
2. External inspection

a. Routine
b. Concise
c. Follow up
d. Special
e. QS review
f. Problem dealing

Regulation

For pleasant control on Global level:

1. ISO
2. WHO
3. ICH
4. Regional Legislation

ISO (International Organization for Standardization)

Federation of 156 countries.
ISO/TS 16949 – Tech. specification at improvement of QMS aimed disorder prevention, discount in variants, persistent improvement.
First drafted as ISO 16949:2002 (March 2002)
ISO 9000 series – QMS (Published in 1987)
ISO 9000:2005 – Cover primary concept & Vocabulary used
ISO 9001:2008 – Set requirement of QMS
ISO 9004:2009 – How to make QMS extra efficient & effective
ISO 9011:2011 – Set guiding principle on Int. & Ext. audit of QMS
ISO 10005 – Prepare excellent plan for projects
ISO 10011 - 1/2/3 - Guideline for auditing a excellent system
ISO 10012 – Caliberation system & size control
ISO 10013- Quality guide for precise excellent need

Popular standard
ISO 9000 Quality management
ISO 14000 Environment management
ISO 3166 Country codes
ISO 26000 Social responsibility
ISO 50001 Energy management
ISO 31000 Risk management
ISO 22000 Food safety management
ISO 27001 Information security management
ISO 20121 Sustainable events

ICH (International convention on Harmonization)
ICH Q-Documents
Q1 Stability
Q2 Analytical Validation
Q3 Impurities
Q4 Pharmacopoeias
Q5 Quality of Biotechnological Products
Q6 Specifications
Q7 Good Manufacturing Practice
Q8 Pharmaceutical Development
Q9 Quality Risk Management
Q10 Pharmaceutical Quality Systems

Q10 = ICH Q7 + ISO GMP guideline
Objective of Q10 –
1. To acquire product realization
2. Establish & keep nation of control
3. Facilitate improvement

ICH Q10 Pharmaceutical Quality System
ICH Q10 demonstrates enterprise and regulatory authorities` assist of an effectivepharmaceutical exceptional gadget to decorate the exceptional and availability of drugs round theglobal withinside the hobby of public health. Implementation of ICH Q10 at some point of the productlifecycle need tofacilitate innovation and persistent development and fortify the hyperlink betweenpharmaceutical improvement and production activities.
FDA`s steering documents, which include this steering, do now no longer set up legally enforceableresponsibilities. Instead, guidances describe the Agency`s cutting-edge wondering on a subject and need tobe regarded most effective as recommendations, until particular regulatory or statutorynecessities arecited. The use of the phrase need to in Agency guidances manner that some thing is usually recommended orrecommended, however now no longer required.

Quality regulation in Ayurveda
1. Government of India
2. AYUSH Ministry
3. India Quality Council (QCI)
4. State legislature and committee
5.5. CCRAS (Gives a protocol for research)

6. ICMR
7. Faculty of Science and Technology
8. Ministry of Chemicals and Fertilizer
9.PLIM

AYUSH Mark for Quality

• AYUSH Meet with QCI for pleasant trouble in Dec 2008, and signal an aggrement to to help in accredation to ayurvedic product in July 2009 and released AYUSH mark in Aug 2009.
• QCI Gives accredation
1. NABL offers accredation to the labotatories (Should meet std. of ISO17025)
2. NABCB offers Ayush mark on requirements of ISO manual 65.
• Logo of NABCB emerge as obligatory considering the fact that June 2011.

AYUSH Mark

1. Premiun- In compliance to International regulatory requirements.
2. Standard- In compliance to home regulatory requirements.

Summary in terms of Ayurveda

• 1920 & 1940 in adhiveshana, government says that when freedom Ayurveda could be countrywide scientific pathy.
• The D&C act 1920 framed while quinine great become compromised.
• In 1940, D&C act become framed apart from law for TM.
• In 1964 law for ASU medication become introduced to D&C act, with attempt of Pt. Shiv Sharma & Pt. Anant Sharma and CCIM become constituted.
• APC become constitutes to assess and submit great standards.
• ASUDTAB become set up below sec.33C.
• Dept. of ISM&H become set up in 1995 which become renamed as Dept. of AYUSH and once more it have become Ministry of AYUSH in Nov. 2014.
• CCRAS watch great in studies in Ayurveda.
• PLIM to broaden and compare laboratory protocol for testing.
• Ayurveda now ruled below D&C act 1940 via way of means of DCG of India via country government.
• 2008 Pharmacovigilence application become released.
• AYUSH mark released in 2009.
• ASIIA become released in 2007 (GoI & DST) - to restore early omission)
• WHO realize TM in 2000.
• WHO has released method for TM 2002-2007 and 2014-2023.

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ASTHMA: AN OVERVIEW

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ABSTRACT
Asthma is a long-term lung condition. People with asthma have sensitive airways in their lungs which react to triggers, causing a 'flare-up'. In a flare-up, the muscles around the airway squeeze tight, the airways swell and become narrow and there is more mucus. These things make it harder to breathe. An asthma flare-up can come on slowly (over hours, days or even weeks) or very quickly (over minutes). A sudden or severe asthma flare-up is sometimes called an asthma attack. Asthma cannot be cured, but for most people it can be well controlled by following a daily management plan. Symptoms often vary from person to person, but they are most commonly breathlessness, wheezing, tight feeling in the chest and continuing cough. Symptoms often occur at night, early in the morning or during/just after activity. The causes of asthma are not fully understood, although people with asthma often have a family history of asthma, eczema and hay fever. Research has shown that exposure to tobacco smoke (especially as a baby or young child), obesity and some workplace chemicals can increase the risk of developing asthma.

KEYWORDS: Asthma is a long-term risk of developing asthma.

INTRODUCTION
Previous studies have shown that there is considerable roomfor improvement in adherence to asthma medication treatment.[1,2] Because poor adherence may reduce the likelihood of achieving and maintaining good asthma control, it isimportant that adherence to prescribed asthma medication be addressed by the health-care provider during regularfollow-up consultations.[3] Adherence may be regardedas a multifaceted behaviour that is influenced by a variety of factors, one of which is the health-care provider.[4] Asthma clinics led by specially trained asthma nurses have been shown to be effective in asthma management, for instance, in relation to adherence.[5] Moreover, the interaction between the health-care professional and the patient regarding joint treatment decisions, taken by the asthmapatient and the clinician together, seems to have a positive effect on adherence as well.[6] Another factor affectingadherence is beliefs about the asthma medication.[7,9] Individuals with asthma who, for instance, believe that their medication is necessary for their present and future health or that it prevents exacerbation of their disease are more likely to be adherent. In contrast, individuals who are concerned about their asthma medication are more inclined to deviate from the prescribed treatment.[7,8] It has also been reported that individualswith uncontrolled asthma tend to be sceptical about their asthma medication, which may cause them to choose symptom management strategies other than the medication.[10] Asthma is often studied in clinical settings, where the population of patients does not necessarily reflect individuals with asthma in general. Additionally, few studies have addressed treatment adherence, medication beliefs, and asthma control in relation to reported asthma followup consultations in individuals with asthma in the general population. It could be hypothesised that asthma follow-up consultations may have a positive influence on adherence to asthma medication treatment and medication beliefs and that adherence, medication beliefs, and asthma controlwould be associated. The aim of the present study was to investigate adherence to asthma medication treatment, medication beliefs, and asthma control in relation to asthma followup consultations in individuals with asthma in the general population. A further aim was to describe associations between adherence, medication beliefs, and asthma control.

Definition
Asthma is defined as a chronic inflammatory disease of the airways. The chronic inflammation is associated with airway hyperresponsiveness (an exaggerated airwaynarrowing response to triggers, such as allergens and exercise), that leads to recurrent symptoms such as wheezing, dyspnea (shortness of breath), chest tightness and coughing. Symptom episodes are generally

associated with widespread, but variable, airflow obstruction within the lungs that is usually reversible either spontaneously or with appropriate asthma treatment.[11]

Sigs and symptom

Asthma is characterized by recurrent episodes of wheezing, shortness of breath, chest tightness, and coughing.[19] Sputum may be produced from the lung by coughing but is often hard to bring up.[27] During recovery from an attack, it may appear pus-like due to high levels of white blood cells called eosinophils.[28] Symptoms are usually worse at night and in the early morning or in response to exercise or cold air.[29] Some people with asthma rarely experience symptoms, usually in response to triggers, whereas others may have marked and persistent symptoms.[30]

Causes

Asthma is caused by a combination of complex and incompletely understood environmental and genetic interactions.[13,14] These factors influence both its severity and its responsiveness to treatment.[15] It is believed that the recent increased rates of asthma are due to changing epigenetics (heritable factors other than those related to the DNA sequence) and a changing living environment.[16] Onset before age 12 is more likely due to genetic influence, while onset after 12 is more likely due to environmental influence.[17]

Pathophysiology

Asthma is associated with T helper cell type-2 (Th2) immune responses, which are typical of other atopic conditions. Various allergic (e.g., dust mites, cockroach residue, furred animals, moulds, pollens) and non-allergic (e.g., infections, tobacco smoke, cold air, exercise) triggers produce a cascade of immune-mediated events leading to chronic airway inflammation. Elevated levels of Th2 cells in the airways release specific cytokines, including interleukin (IL)-4, IL-5, IL-9 and IL-13, that promote eosinophilic inflammation and immunoglobulin E (IgE) production by mast cells. IgE production, in turn, triggers the release of inflammatory mediators, such as histamine and cysteinyl leukotrienes, that cause bronchospasm (contraction of the smooth muscle in the airways), edema (swelling) and increased mucous secretion (mucous hypersecretion), which lead to the characteristic symptoms of asthma.[11,12] The mediators and cytokines released during the early phase of an immune response to an inciting allergen, trigger a further inflammatory response (late-phase asthmatic response) that leads to further airway inflammation and bronchial hyperreactivity.[12] Evidence suggests that there may be a genetic predisposition for the development of asthma. A number of chromosomal regions associated with asthma susceptibility have been identified, such as those related to the production of IgE antibodies, expression of airway hyperresponsiveness, and the production of inflammatory mediators. However, further study is required to determine specific genes involved in asthma as well as the gene-environment interactions that may lead to expression of the disease.[11]

Diagnosis

While asthma is a well-recognized condition, there is not one universal agreed upon definition.[18] It is defined by the Global Initiative for Asthma as "a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction within the lung that is often reversible either spontaneously or with treatment".[19]

There is currently no precise test for the diagnosis, which is typically based on the pattern of symptoms and response to therapy over time.[20,18] A diagnosis of asthma should be suspected if there is a history of recurrent wheezing, coughing or difficulty breathing and these symptoms occur or worsen due to exercise, viral infections, allergens or air pollution.[21] Spirometry is then used to confirm the diagnosis.[21] In children under the age of six the diagnosis is more difficult as they are too young for spirometry.[22]

Spirometry

Spirometry is recommended to aid in diagnosis and management.[23,24] It is the single best test for asthma. If the FEV1 measured by this technique improves more than 12% and increases by at least 200 milliliters following administration of a bronchodilator such as salbutamol, this is supportive of the diagnosis. It however may be normal in those with a history of mild asthma, not currently acting up.[18] As caffeine is a bronchodilator in people with asthma, the use of caffeine before a lung function test may interfere with the results.[25] Single-breath diffusing capacity can help differentiate asthma from COPD.[21] It is reasonable to perform spirometry every one or two years to follow how well a person's asthma is controlled.[26]

Classification

Asthma is clinically classified according to the frequency of symptoms, forced expiratory volume in one second (FEV1), and peak expiratory flow rate.[31] Asthma may also be classified as atopic (extrinsic) or non-atopic (intrinsic), based on whether symptoms are precipitated by allergens (atopic) or not (non-atopic).[32] While asthma is classified based on severity, at the moment there is no clear method for classifying different subgroups of asthma beyond this system.[33] Finding ways to identify subgroups that respond well to different types of treatments is a current critical goal of asthma research.[33]

Although asthma is a chronic obstructive condition, it is not considered as a part of chronic obstructive

pulmonary disease, as this term refers specifically to combinations of disease that are irreversible such as bronchiectasis, chronic bronchitis, and emphysema.[34] Unlike these diseases, the airway obstruction in asthma is usually reversible; however, if left untreated, the chronic inflammation from asthma can lead the lungs to become irreversibly obstructed due to airway remodeling.[35] In contrast to emphysema, asthma affects the bronchi, not the alveoli.[36]

Medications

Medications used to treat asthma are divided into two general classes: quick-relief medications used to treat acute symptoms; and long-term control medications used to prevent further exacerbation.[37] Antibiotics are generally not needed for sudden worsening of symptoms.[38]

Fast–acting

- Short-acting beta2-adrenoceptor agonists (SABA), such as salbutamol (*albuterol* USAN) are the first line treatment for asthma symptoms.[39] They are recommended before exercise in those with exercise induced symptoms.[40]
- Anticholinergic medications, such as ipratropium bromide, provide additional benefit when used in combination with SABA in those with moderate or severe symptoms.[39] Anticholinergic bronchodilators can also be used if a person cannot tolerate a SABA.[34] If a child requires admission to hospital additional ipratropium does not appear to help over a SABA.[41]
- Older, less selective adrenergic agonists, such as inhaled epinephrine, have similar efficacy to SABAs.[42] They are however not recommended due to concerns regarding excessive cardiac stimulation.[43]

Long–term control

- Corticosteroids are generally considered the most effective treatment available for long-term control.[37] Inhaled forms such as beclomethasone are usually used except in the case of severe persistent disease, in which oral corticosteroids may be needed.[37] It is usually recommended that inhaled formulations be used once or twice daily, depending on the severity of symptoms.[44]
- Long-acting beta-adrenoceptor agonists (LABA) such as salmeterol and formoterol can improve asthma control, at least in adults, when given in combination with inhaled corticosteroids.[45][46] In children this benefit is uncertain.[45][46] When used without steroids they increase the risk of severe side-effects,[47] and with corticosteroids they may slightly increase the risk.[48][49] Evidence suggests that for children who have persistent asthma, a treatment regime that includes LABA added to inhaled corticosteroids may improve lung function but does not reduce the amount of serious exacerbations.[50] Children who require LABA as part of their asthma treatment may need to go to the hospital more frequently.[50]
- Leukotriene receptor antagonists (such as montelukast and zafirlukast) may be used in addition to inhaled corticosteroids, typically also in conjunction with a LABA.[37][52] Evidence is insufficient to support use in acute exacerbations.[53][54] In children they appear to be of little benefit when added to inhaled steroids,[55] and the same applies in adolescents and adults.[56] They are useful by themselves.[57] In those under five years of age, they were the preferred add-on therapy after inhaled corticosteroids by the British Thoracic Society in 2009.[58] A similar class of drugs, 5-LOX inhibitors, may be used as an alternative in the chronic treatment of mild to moderate asthma among older children and adults.[59][51] As of 2013 there is one medication in this family known as zileuton.[59]
- Intravenous administration of the drug aminophylline does not provide an improvement in bronchodilation when compared to standard inhaled beta-2 agonist treatment.[60] Aminophylline treatment is associated with more adverse effects compared to inhaled beta-2 agonist treatment.[60]
- Mast cell stabilizers (such as cromolyn sodium) are another non-preferred alternative to corticosteroids.[37]

Delivery method

Medications are typically provided as metered-dose inhalers (MDIs) in combination with an asthma spacer or as a dry powder inhaler. The spacer is a plastic cylinder that mixes the medication with air, making it easier to receive a full dose of the drug. A nebulizer may also be used. Nebulizers and spacers are equally effective in those with mild to moderate symptoms. However, insufficient evidence is available to determine whether a difference exists in those with severe disease.[61] There is no strong evidence for the use of intravenous LABA for adults or children who have acute asthma.[62]

Adverse effects

Long-term use of inhaled corticosteroids at conventional doses carries a minor risk of adverse effects.[63] Risks include thrush, the development of cataracts, and a slightly slowed rate of growth.[63][64][65] Higher doses of inhaled steroids may result in lower bone mineral density.[66]

CONCLUSION

If anyone recurrently experience shortness of breath or you hear a whistling or wheezy sound in your chest when you breathe, you may have asthma - a chronic condition that reasons inflammation and narrowing of the bronchial tubes (the passage ways that allow air to enter and leave the lungs). If people with asthma are exposed to a substance to which they are sensitive or a situation that changes their regular breathing patterns, the symptoms can become further severe. Asthma symptoms affect an

estimated 26 million Americans - 19 million adults and 7 million children — and are one of the chief causes of absences from work and school. Asthma often runs in families; according to the World Health Organization, about half the cases are due to genetic susceptibility and half result from environmental factors. Though there is no cure for asthma, effective treatments are available. Asthma can be finest managed by seeing an allergist. There are two types of asthma: allergic (begun by exposure to an allergen) and nonallergic (triggered or started by stress, exercise, illnesses like a cold or the flu, or exposure to extreme weather, irritants in the air or some medications).

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Phacormacognosy in Various Systems Medicine

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ABSTRACT
Medicinal plants based traditional systems of medicines are playing important role in providing health care to large section of population, especially in developing countries. Interest in medicinal plants as a re-emerging health aid has been fuelled by the rising costs of prescription drugs in the maintenance of personal health and well-being, and the bio prospecting of new plant-derived drugs. Medicinal plants are an integral component of ethno veterinary medicine. Farmers and pastoralists in several countries use medicinal plants in the maintenance and conservation of the healthcare of livestock. About 90% of the marketed plant drugs are obtained from wild resources. Today, traditional drugs are used as a starting point for the development of novelties in drugs. The practice of traditional medicine is widespread in China, India, Japan, Pakistan, Sri Lanka and Thailand. The Indian traditional medicines can be classified into two groups. In the first group are the medicinal preparations belonging to the Ayurvedic, Siddha, & the Unani systems while the folk medicines belong to the second group.

Key words: role of pharmacognosy in allopathy and traditional systems of medicine namely, Ayurveda, Unani, Siddha, Homeopathy and Chinese systems of medicine.

I. INTRODUCTION

1.1 Role of pharmacognosy in allopathy

Pharmacognosy is a branch of applied science, which has developed immensely in the recent years and represents one of the major subjects in the field of pharmacy[2]. Its scope includes the study of physical and chemical characteristics as well as therapeutic properties of crude drugs of biological origin. It has also led to the development of novel drugs and nutraceuticals. Research work in pharmacognosy is done in the areas of botany, zoology, phytochemistry, chemistry of natural products, biosynthesis, biotransformation etc. Medicinal plants possess diverse chemical compounds that can elicit different pharmacological actions. Therefore, they often serve as chemical models or templates of new drug leads and new chemical entities. According to a latest research, about 80% of the existing drugs during the period of 1994-2007 were based on natural products. Today, the discovery of allopathic drugs from medicinal plants have become more advanced process involving the arc of techniques like mass spectrometry, NMR spectroscopy etc. These techniques have markedly reduced the effort and time required for the structural elucidation of crude extracts, Moreover, they require very little quantities of plant extract analysis[9]. Medicinal plants that serve as a source of different leads for several allopathic drugs have been mentioned in the following table.

Table 1: Medicinal Plants as a Source of Lead for Drugs

Category	Plant source	Active compound

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1.	Antidiabetic	Karela (Momordica charantia)	Charantin Gymnemic acid IV
2.	Anti-inflammatory	Gurmar (Gymnema sylvestre)	Boswellic acid Curcumin
3.	Cardiovascular	Guggul (Boswellia serrata)	Withanolides Reserpine
4.	Anti-leishmanial	Turmeric (Curcuma longa)	Arjunolic acid Diospyrin
5.	Anti-malarial	Aswagandha (Withania somnifera)	Plumbagin Biflavonoids
6.	Anti-obesity	Rauwolfia (Rauwolfia serpentina)	Nimbolide Tea polyphenolides
7.	Antiviral	Terminalia arjuna Diospyros species	Gallic acid, chebulagic acid and other galloyl glucose.
8.	Anti-neoplastic	Plumbago species Selaginella bryopteris Neem (Azadiracha indica) Alpinia officinarum Terminalia bellerica Combretaceae family members	Combretastatins

The isolated active molecules from traditional medicinal plants, other than serving as valuable traditional drugs are also used as lead molecules. These molecules upon chemical modification or as such serves as template for the designing of synthetic molecules that hold the pharmacologically active agents eliciting the desired activity [1]. Certain examples of such drugs are represented in the following table allopathic drugs have been mentioned in the following table.

Table 2: Allopathic Drugs Developed from Traditional Medicinal Plants

Drug	**Template**	**Plant source**	**Uses**
Verapantil	Papaverine	Papaver somniferum	Clinical Use**:** Angina and cardiac arrhythmias. Traditional Use: As analgestic and soporific in
Sodium cromoglycate	Khellin	Ammi visnaga	Mediterranean region. Clinical Use: Antiasthmatic
Neostigmine	Physostigmine		Traditional Use: To treat
Metformin	Galegine	Physostigma venenosum	bronchial disorders in Egypt.
Etoposide	Podophyllotoxin	Galega officinalis	Clinical Use: To treat myasthenia gravis
		Podophyllum peltatum	Clinical Use: To treat type-2 diabetes Traditional Use: To treat diabetes in Europe
Bromocriptine	Ergotamine		
		Claviceps purpurea	Clinical Use: Anticancer agent Traditional Uses: Purgative and in wort treatment in
Atracurium	Tubocurarine		

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		Chondodendron tomentosum	North America. Clinical Use: Antiparkinsonian agent Traditional Use: As an oxytocic in Central Europe. Clinical Use: Muscle relaxant

1.2 Traditional systems of Medicine

For more than a century the conventional or allopathic system of medicine has dominated the picture all over the world as the standard system of medicine. Highly advanced technology and drugs based on chemical compounds instead of natural therapies and herbal medicines are used to research, diagnose, and treat diseases. The ever-increasing rate and range of technology and therapeutic advancements in the conventional medicine has raised the expectations of the general population of curing all their illness. Despite these advancements, the fact that there remain many limitations to the treatment of diseases that fails to guarantee 100% curative results has brought disillusionment among the public. This has led to an increasing search for traditional panacea particularly by those who have not benefitted from the previous treatment, those who have apprehensions concerning the toxicity and safety of modern drugs and by those who cannot meet the extraordinary expenses in most of the countries [10].

Since many patients are left dissatisfied and finding it difficult to continue, it is obvious that traditional medicines are required, expected, demanded, and accepted.

Traditional medicine is a term employed for all the healing practices that do not fall within the realm of conventional medicine. It includes a variety of therapeutic and preventive health care practices such as Ayurveda, Homeopathy, naturopathy, chiropractic, aromatherapy, acupuncture, rei-koi, magnetotherapy, yoga and herbal medicine that do not follow generally accepted medical methods and may not have a scientific explanation for their effectiveness. Traditional systems of medicine also referred to as complementary, supporting or assisting medicine are not part of the standard conventional medicine but are the ones that are used along with or instead of the standard care provided by doctors or allied health professionals such as nurses, pharmacists, physical therapists. Traditional medicine has been prevalent in various countries like India and China much before the development of present-day medical science. For example, in India, Ayurveda, meditation, yoga, Unani herbal medicine and siddha have been used since ancient period to heal the body.

In contrast to the conventional health care practitioners who are primarily concerned with identifying the symptoms and treating the disease in the affected part of the body only, the complementary and traditional medicine practitioners take a holistic approach to patient care. They treat the patient as a whole person but not just a set of symptoms. They tend to be strongly prevention oriented and regard a high value to the body's natural ability to heal itself. They employ certain low-tech, hands-on techniques and principles many of which can be traced to long-established ancient traditions in treating patients.

Few of the basic principles followed by traditional medicine practitioners are:

They rely on the intrinsic ability of the body to heal itself and focus on strengthening the immune system. They do not rely on prescription drugs, surgery, and other conventional medical procedures, rather they use natural methods and remedies. They look at the whole person, and take into consideration the mind, body and spirit when diagnosing and treating a patient. They focus not just at the symptoms and the disease but also at the underlying causes.

The goal of the treatment is not just to cure or fix a symptom but to create and restore optimum mental, physical, and spiritual health in the person. They promote on-going care to prevent disease.

The claims made by traditional medicine practitioners are not accepted by conventional medical practitioners because of lack evidence-based assessment of safety and efficacy. Still now-a-days many people are turning gradually towards traditional therapies as these are safe, have no side effects, expenses are reasonable, and these are equally effective in the treatment of patients with

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diseases which the conventional medicine cannot cure.

II. AYUSH

AYUSH or the department of Ayurveda, yoga and Naturopathy, Unani, Siddha and Homeopathy was established in the year 1995. It was formerly known as department of Indian systems of Medicine and Homeopathy (ISMH).the establishment of ISMH was the collective result of research and coordination carried out by central council for Ayurvedic Research in Indian Medicine and Homeopathy (CCRIMH).The ISMH was renamed as Ayush in November 2003. It plays a key role in revival of traditional medicine in our country [12-14].

2.1. Plans of AYUSH

The main agenda of AYUSH is to develop and promote the practise of traditional medicine in India. The following are the plans for this purpose.

1.Elevation of research as well as cultivation and regeneration of medicinal plants.

2.Regularization of educational standards and laying down of pharmacopoeia standards for improvement of quality of medicinal products by complying with Good Manufacturing Practices (GMP) and Good Laboratory practices (GLP).

3.Appreciation of traditional systems of medicine by establishing AYUSH clinics in district allopathic hospitals and spreading knowledge and effectiveness of AYUSH among people for its integration in health care.

2.3. Ayurvedic system of Medicine

The term Ayurveda is derived from the Sanskrit words Ayur meaning "life" and Veda meaning "knowledge or science" ie,"science of life". It is the most ancient original system of Indian medicine believed to have evolved over 5000 years ago in the far reaches of the majestic Himalayas, presumably from the deep wisdom of spiritually enlightened rishis or sages [12].

Ayurveda was first perceived by Brahma who taught this science to Daksha Prajapati who taught it to Aswani Kumars and so on. The Hindu mythology described in the four spiritual texts called Vedas Viz,,Rigveda,Yajurveda,Samaveda and Atharvaveda. They were compiled 5000 years ago by the Aryans during the vedic age of the prominent Indian sage Srila Vyasadeva. Ayurveda is said to be an Upaveda (part) of Atharvaveda. It is the science of health and healing practised by ancient Aryans based on the principle "maintaining the health of a relieving the diseased from the disease condition" [14].

Around 900 BC, Charaka, a great sage and a physician of atreya school(school of physicians) wrote "Charaka Samhita" describing 341 medicinal plants and gave a comprehensive illustration of human anatomy,growth of foetus within the womb, etiology of physical and spiritual illness, their treatment and preventive measures. The next landmark in Ayurveda was around 600 BC when Sushruta a surgeon from the Dhanvantari school (school of surgeons) wrote "Sushruta Samhita" mentioning 395 medicinal plants and described the physiology of joints, nerves, and organs. His manuscript also included the list of medicinal agents derived from animals, minerals and metals and provided the description of well-developed surgical equipments employed to perform plastic surgery and amputation. It also described the method to perform massage as performed by the Chinese acupuncturists using major nerve intersections described as marma points.

"Asthang Hridaya" which originated in the 7th century AD is the best book highlighting the principles and practice of nedicine by Vagbhatta.

Charaka,Sushruta and Vagbhatta are regarded as the "powerful traid"(Vrihat Traya) of the golden period of Ayurveda extending from 900 BC to 1000 AD.

In about 9th century,Madhava wrote "Madhava Nidana Samhita" which exclusively deals with the diagnosis of a disease. In 14th century, Sarangdhara in his Materia Medica entiled "Sarangdhara Samhita" has emphasized on the principles of Ayurveda. The last authoritative writing on Ayurveda was "Bhava Prakasha"by Bhava Mishra of Magadha who described the preparations of numerous medicinal compounds.

According to Charaka Samhita Ayurveda is defined as the knowledge that indicates the appropriate and inapproprite,happy and sorrowful conditions of living, what is auspicious or inauspicious for longevity of life. It is a traditional and natural healing system based on the interaction of body, mind, and soul. yurveda includes herbal medicine, dietetics, body work,surgery,psychology and spirituality hence treats each person in a holistic approach.

Ayurveda is based on the hypothesis that all the objects in the universe including the human

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body are composed of five basic elements called panchamahabhutas namely uhva(earth),jal(water),teja(fire),akash(vacuum space or ether). These elements exist in the human body in different proportions in a balanced state as per the needs and requirements of different structures and functions of the tissues.

The growth and development of the body depends on its nutrition i.e,on food ,which again is composed of the panchamahabhutas that replenish and nourish like elements of the body. The panchamahabhutas are represented in the human body as dashas, dhatus and malas.

The humours or fluids called doshas are the physiological entities that are derived from the different combinations and permutations of these five elements. The doshas namely wind or vata(vacuum and air),bile or pitta(fire and water),phlegm or kapha (water and earth)are present all through the human body.

Ayurveda is largely based on the important principle that these doshas,together called as tridosha exist in human body in harmony and influence all mental and physical processes. As long as these remain in balance,the body remains healthy and any derangement in their proportion subjects the body to all sorts of disordered conditions. The tissues or dhatus are the basic structural entities of the body each one having its own function.

The dhatus are seven in number collectively called saptadhatus viz rasa(lymph), rakta (blood), meda (adipose tissue), mamsa (flesh), asthi (bones), majja(nervous tissue) and shukra(reproductive tissue). The saptadhatu are subjected to wear and tear and results in the formation of mala(excretory material). The chief malas are mutra(urine),shakrit(faeces)and sweda(perspiration). When tridosha,saptadhatus and malas are in balance with each other,it is called a healthy condition while imbalance results in pathological conditions.

The science of Ayurveda is divided into eight branches:kaya chikitsa(general medicine), Balachikitsa (paediatric treatment),Salakyachikitsa (ENT treatment),Vishachikitsa(toxicology),Jarachikitsa(treatment releated to genetics),Shalya chikitsa(surgery),Vajikarama chikitsa(treatment with rejuvenation and aphrodisiacs) and Graham chikitsa (mental treatment with planetary effects).

Each branch is again divided into two departments and three sections, the departments are Swastha Vrittam which deals with promotion of positive healthy and Abura Vrittam which deals with prevention and treatment of a disease. The three sections are etiology,diagnosis and treatment.

In Ayurveda, the diagnosis of disease is considered more important than the treatment. A disease is attributed to the ineffectiveness of tridoshas. For example, pain or loss of function indicates aggravated state of vata, burning sensation or loss of appetite is indicative of high pitta and vitiation or ineffectiveness of kapha is known by heaviness or accumulation of fluid.

The classical clinical diagnosis in Ayurveda is called astha sthana pariksha (eight-point diagnosis) that includes assessment of the state of the doshas as well as the physical signs. The eight point diagnosis are nadi pariksha (pulse diagnosis), mutra pariksha (urine examination), mala pariksha (stool examination),jihva pariksha (tangue examination), shabda pariksha (examination of body sounds), Vata/sparsha (nervous system assessment),pitta/drik (assessment of digestive fire and metabolic secretions).

Treatment directs avoiding causative factors responsible for setting in disequilibrium between the structural (dhatus)and physiological(doshas)entities of the body through the use of panchakarma, medicines, suitable diet,activity and regimen for restoring the balance and strengthening the body functions and to prevent or minimize the future occurrence of the disease. It is hypothesized that various pathological conditions can be treated by applying the five characteristic properties of the medicinal herbs i.e,rasa(taste),guna(physicochemical properties), virya(potency), vipak(post digestive effects) and prabhava (therapeutic effect).

Examples of some important drugs used in Ayurveda are Rauwolfia serpentina, Withania somnifera, Piper nigrum, Shilajit, Gandhak etc.

Preparation of Ayurvedic Dosage

Ayurveda literally means science of life. It comprises of the knowledge of medicines and the art of healing. A variety of Ayurvedic dosage forms have been used since ancient times and some of them are used even to this date. Ayurvedic pharmacy (Bhaishajya vigyan) proposes five basic dosage forms like swarasa, kalka, kwatha, hima and phanta. Present day Ayurvedic dosage forms includes tablets, creams, ointments and even injections. All the Ayurvedic preparations are mostly polyherbal preparations prepared by employing various pharmaceutical processes like

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size reduction and separation, extraction, fermentation, distillation, evaporation etc.

The various methods of preparing ayurvedic dosage forms are discussed below,

1.Simple Expression/Extraction

In this method, fresh vegetable drugs are pounded in a mortar with a pestle. The juice is expressed out and strained through a muslin cloth.

2.Infusion

Cold infusion (shita kasaya) is prepared by infusing the drug with 8 parts of cold water for 12 hours and then straining through a muslin cloth. Hot infusion (phanta kasaya) is prepared by infusing the drug with hot water.

3.Maceration

This process called bhawana is similar to the modern maceration process. The powdered drug is macerated with either fresh juice of a drug or its decoration or decoction of polyherbs till the solid is completely soaked. This method is usually employed for mineral drugs.

4.Decoction

Kwatha or decoction is prepared by boiling 1 part of the drug with 16 parts of water (8 parts for dry drugs) until the quantity is reduced to one-fourth of its bulk.

5.Digestion

This process is similar to decoction process but continued for a much longer time. It is called pachana.

6. Hot Extraction

In this process, the drug is made into a pulp and wrapped inside the leaves of jambolan or palasha. The leaves are sealed with a thick layer of clay which are then roasted into fire of crow-dung cakes until the upper layer of clay turns brick red in colour. The clay and the leaves are removed, and the partially dried pulp is expressed out for juice. Thus, hot extraction or putapaka process is an extraction process by a unique method of roasting.

7. Soft Extract

It is a process of concentration of the decoction until an extract of soft consistency (avalcha) is obtained.

8. Milk decoction

It is prepared by boiling 1 part of the drug with 8 parts of milk and 32 parts of water till the water evaporates. Milk decoction is called kshirapaka.

9.Medicated Oils and Clarified Butter

These oily, liquid preparations are prepared by digesting the drugs or their juices or decoctions with oil or ghee.

10.Spiritous Fermentation

This process is employed for the preparation of alcohol of varying degrees of strength. The powdered drugs or their decoctions are fermented in water or honey or kept in earthen pots for a long time. The fermented mixture is then clarified by straining through a muslin cloth. If decoction of the drug is used, then the fermented liquor obtained is called arista and if powdered drug is used then the preparation is called asava. Different kinds wines(suras)are prepared by distillation of asavas and aristas.

11.Acetous Fermentation

This method is used for the preparation of kanjika (vinegar).1 part of paddy is steeped in 4 parts of water and set aside for a formight in an earthern pot. The clear, transparent liquid is strained through a muslin cloth and preserved as vinegar. Kanjika is used as such or as a vehicle in other preparations. It can also be used as menstrum for the extraction of drugs.

12.Confection (Kandapaka) Making

It is the process of digesting powdered drugs with syrup till the right consistency is obtained. Required quantity of honey is added at the end. Sugar syrup can be prepared by dissolving it in water or milk or in some drug decoction.

Classification of Ayurveda Dosage Forms

The various Ayurvedic dosage forms recognized in the Ayurvedic Formulary of India are as follows,

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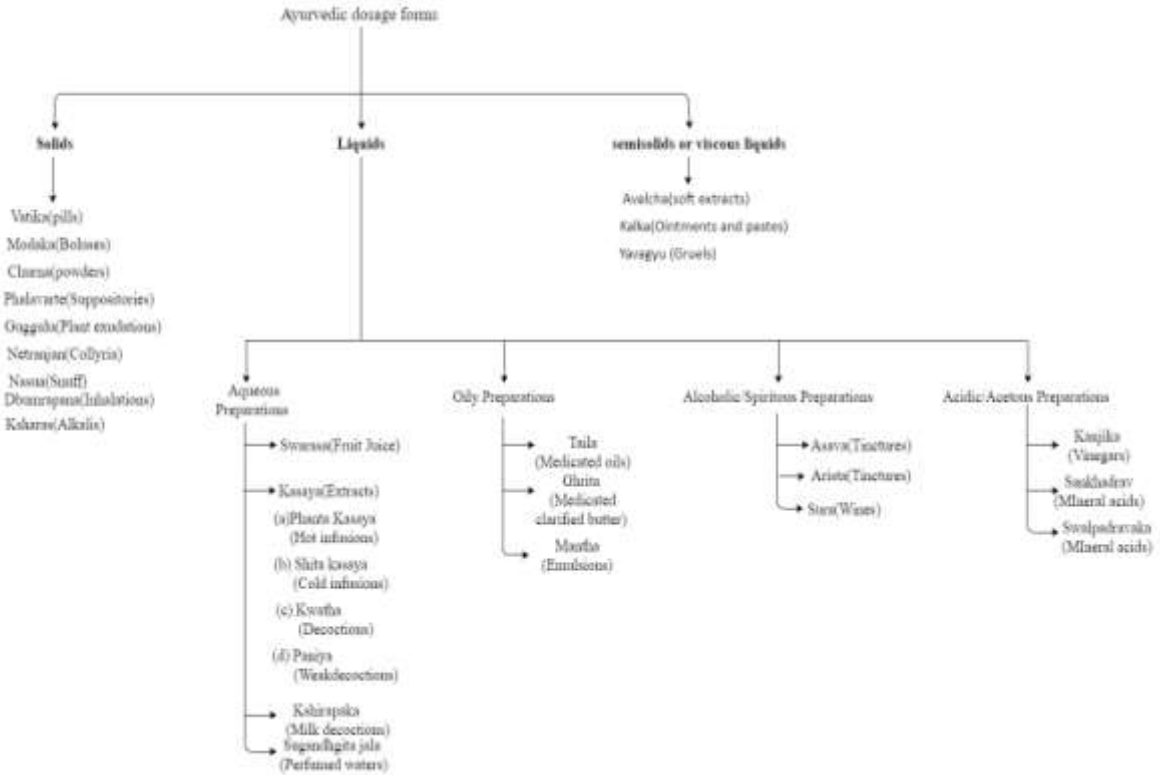

III. CHURNA

It is an ultrafine powder of drug or drugs.

Method of Preparation

The drugs prescribed in the formula (patha) are cleaned and dried properly, each drug is powdered separately and sieved through mechanical sifters or hand sieves of about 80 mesh size. The required proportion of each powdered drug is weighed accurately and then mixed. The finer the powder, the better is its therapeutic value due to better absorption[5]. Churnas when stored properly protected from moisture retain their potency for one year. Churnas are one of the most popular herbal mixtures in Ayurveda due to the following advantages,

1.Churnas are highly beneficial in improving digestion and other digestive problems.
2.They act as laxatives and hence are useful in treating constipation.
3.They enhance blood circulation throughout the body and treat hypertension, liver disorders and other stress-induced disorders.
4.Additionally, they protect the body against bacteria, viruses, mutagens, and carcinogens. The only disadvantage of these preparations is their taste. Churna of bitter drugs are difficult to swallow because of their abnoxious taste since taste masking cannot be done. Also, they absorb moisture and form lumps hence should be stored carefully in air-tight containers. E.g: Narayana churna, Eladi churna, Sitopaladi churna.

IV. AVALCHA (LEBYA)

It is a semisolid Ayurvedic dosage form prepared by adding jaggery,sugar or sugar-candy (mishri) to the prescribed drug juice or decoction and then boiling it until the mixture becomes a party mass. It is also known as guida, madaca, lcha, khanda, rasayana etc.

Method of Preparation

The essential components in the preparation of avalchas are,
1.Kasaya or swarasa or any other liquids.
2.Jaggery, sugar-candy or sugar
3.Powders or pulps of the prescribed drugs
4.Ghee or oil
5.Honey

Jaggery, sugar-candy or sugar is dissolved in a liquid vehicle and strained through a muslim

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cloth to remove the foreign particles. The paka or syrup is prepared by boiling the solution over a moderate fire until it attains one thread consistency (should form a sticky thread when pressed between two fingers) or if it sinks in water without getting easily dissolved.

The powders or pulps of the prescribed drugs are then added in small quantities and stirred continuously and vigorously until a homogenous mixture is formed. Ghee or oil is added if required while the preparation is still hot and mixed thoroughly. Finally, honey is added when the preparation is cool and mixed well. The colour and smell of avalcha depends on the drugs used.

The consistency of avalcha should neither be too dense nor too viscous. When rolled between the fingers, it should form a pill without sticking. Avalehas should be stored in glass or porcelain jars. They should be used within one year. Growth of fungus indicates deterioration.

E.g: Draksavaleha, Kutjavaleha, Suranavaleha [6].

V. TAILA

Tailas are viscous oily preparations in which tail (fixed oil) is boiled with the prescribed kasayas and kalkas of drugs according to the formula. This process ensures absorption of the active therapeutic constituents of the ingredients used.

Method of Preparation

The three essential components required for the preparation of medicated oils are, Kalka: Fine paste of the recommended drug(s) Drava-dravaiga: A liquid which may be one or more as swarasa, Kasaya, dugdha, mastu etc.

Sncha dravya : Taila or ghrita (ghee).

I part drava-dravaiga are taken. The kalka and drava are mixed together, sncha is added and the mixture is boiled. The mixture is continuous stirred to avoid kalka sticking to the vessel. When all the drava-dravyas get evaporate and the mixture in the kalka begins to evaporate, the mixture is stirred vigorously and carefully so that it does not adhere to the bottom of the vessel. The consistency of the kalka is checked from time to time to know the condition and stage of the paka. If considerable quantity of milk is added to the preparations, the oil becomes thick due to formation of ghrita.

The consistency, colour, taste and smell of tailas depend on the drugs used. Tailas may condense in cold season hence should be warmed before use.

E.gs: Narayana taila, Bhringaraja taila, Pinda taila.

VI. BHASMA

Bhasmas are powdered Ayurvedic preparations of metals, minerals, marine and animal products prepared by the process of calcination.

6.1. Method of Preparation

Bhasmas are prepared in two stages,

Stage I

The first stage is the purification process called sodhana, which is of two types.

1.Samanya Sodhana: This process is applicable to a large number of metals and mineral agents. Thin sheets of metals are heated and immersed in taila, gomutra, takra etc.,for removing the toxicity.

2. Visesa Sodhana: This process is performed over certain drugs and for certain preparations.

Stage II

This stage is called marana. The purified drug is grounded in a khalva (mortar and pestle) with juices of the specified herbs or kasayas of the drugs recommended for a particular mineral or metal for a specified period of time. Small cakes or cakrikas are made from the grounded material. These are placed in a single layer in a shallow earthen plate (sarava) and closed with another plate. The edges of the plates are scaled with a clay-smeared cloth in seven consecutive layers and dried well under sunlight.

A pit is dug in an open space and is half-filled with cow dung cakes (putas). The scaled sarava is placed in the pit and the remaining space is filled with more judas. Fire is lighted from all the sides and in the middle of the pit and allowed to burn for a specified time. When the burning is complete, the sarava is allowed to cool completely. The seal is opened, and the contents are taken out. The medicine is again made into a fine powder by grinding in a khalva. This process of triturating with the juices or kasayas, making cakrikas and giving putas is repeated as many times as prescribed in the yoga.

Bhasmas are stored in air-tight glass or earthern containers. They maintain their potency indefinitely. These are generally black, grey, dark white, yellowish or reddish in colour depending upon the drugs used in the process of marana. They are usually testeless.

E.gs: Abhraka bhasma, Tamra bhasma, Svarna bhasma.

VII. ASAVAS

Asava is the spiritous liquor obtained by the fermentation of powdered drugs in a solution of sugar or jaggery for a specified period. During the fermentation process, alcohol is produced which

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facilitates the extraction of active principles present in the drugs. The alcohol produced also serves as a preservative.

7.1. Method of Preparation

Jaggery or sugar is dissolved in the required quantity of water, boiled, and cooled. The syrup is transferred into a fermentation vessel. Fine powder of the prescribed drugs is added into the fermentation vessel, covered with a lid and the edges are sealed with clay-smeared cloth wound in seven consecutive layers. The container is kept in a special room or underground cellar or in a heap of paddy to provide a constant temperature to facilitate the fermentation process (sandhana).

After a specified period, the lid is removed, and the contents are examined to check the fermented liquor. The liquid is decanted and allowed to stand for two to three days. When the fine suspended particles settle down, it is strained and bottled.

The product should be free of froth and should not become sour (cukra). When stored in well-stoppered bottles or jars, they maintain potency indefinitely. These preparations have characteristic aromatic alcoholic odour.

E.gs: Arvindasava, Kumaryasava, Vasakasava.

VIII. ARISTA

Similar to asava, arista is also spiritous fermentation product but prepared from kasaya instead of powdered drug.

8.1. Method of preparation

The drugs mentioned in the yoga are coarsely powdered and kasaya is prepared. The decoction is strained and transferred into a fermentation vessel. Required quantity of jaggery, sugar or honey is dissolved, boiled and added. The vessel is sealed by wounding a clay-meared cloth in seven consecutive layers. The vessel is left for fermentation like for asava. After the specified period, the liquor is decanted and allowed to stand for two to three days following which it is strained and bottled. Like asava, arista also possesses a characteristic aromatic alcoholic odour and maintains potency indefinitely, if stored in well-closed containers. The preparation should not turn sour or produce froth on the top.

E.gs: Khadirarista, Balarista, Vidangarista.

IX. UNANI SYSTEM OF MEDICINE

The theory and practice of Unani medicine is also referred to as Tibb-c-Unani, Greek medicine.Arab medicine, Greco-Arab medicine, Islamic medicine and Oriental medicine. It is a natural process of treatment originated in Greece (Unani in Arabic) during the times of the legendery Greek philosopher-physician Hippocrates or Buqarat (460-377 BC). This system of medicine had evolved in Greece, since the Greeks had accumulated a great wealth of knowledge on maintaining health by freeing medicine from the shackles of superstitious beliefs and magic. A great number of Greek philosophers, scholars and physicians like Galen or Jalinous (131-210 BC), Aristotle (384-322 BC) improved and expanded the scope of the existing medical knowledge based on experiment evidences.

From Greece, Rome and Iran, Unani medicine spread its roots to the Arab world where almost all of the Greek, Roman and Latin medical and scientific works were translated into Arabic by the great Arab scholars of that time. Rhazes (850-925 AD),Abdul Quasim Zahrawi (946 AD) and lion Sina (980-1037 AD) were the legendery Arab physicians who imbibed the best from the contemporary systems of traditional medicines in Eugypt, Syria, Persia, Iraq, China and other middle Eastern countries and further refined the concepts of Unani medicine from a clinical point of view and developed surgery to high sophistication.

Thus, Unani medicine shaped into a complete and unique system of medicine during its reign in the Arab world. It was introduced into India during the 14th century by the Arab scholars who fled from Persia following invasion by Mongols. Under the patronage of the Mughal emperors, the Arab physicinas were inducted as state employers and court physicians. With time, the Unani medicine gained popularity among the Indians and it soon succeeded in establishing a strong hold in the country which continued even after the downfall of the Mughal empire. Like any other form of medicine, the Unani medicine aims to find the best possible ways by which a person can lead a healthy life. This discipline is based on two theories.

The Hippocratic theory of four humours (akhlat) according to which the human body contains four humours-blood (dum), phlegm (balgam), yellow bile (safra) and black bile (sauda). As long as these humours are present in the right proportions, a person remains healthy otherwise disease sets in. Most of the unani physicians (Hakims) believe that these humours play an important role in the creation of human temperament (mizaj). If each human being has a

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unique humoural constitution, then the people can be categorized under four basic temperaments-sanguine, bilious, phlegmatic and melancholic.

The Pythagorian theory of four elements (arkan) viz, earth (khak), fire (aatish), air (bad), water (aab). These are the constituents of matter from which all the universal animate and inanimate things are produced. These arkans represent the four qualities of the states of living human body i.e, hot, (nar), cold (barid), moist (ratab) and dry (yabis).

A perfect balance of arkan, mizaj and akhlat helps to keep the body and mind healthy so that the metabolic processes can take place easily and the body waste be evacuated. Tibb-e-Unani also maintains the view that the human body is composed of seven natural principles or components known as Umur-e-Tibbia that include,

Arkan or anasir (Elements)
Mizaj (Temperament)
Akhlat (Humours)
Aaza (Organs)
Arwah (Vital spirit)
Quwa (Power)
Afaal (Functions)

They believed that these principles constitute the body and its health. The loss of any of these components may lead to diseased conditions or even death.

The logic of maintaining a good health and keeping the diseases at bay is based on the concept of hygiene or Hifzan-e-sehat. It emphasizes on keeping food, water, and air free from pollution. By using clean and fresh water, breathing clean and fresh air and consuming clean and fresh food, diseases can be prevented. It also lays down the six essential prerequisites for the prevention of diseases and to maintain health.

These essentials known as Arab-e-sittab-zaruriah are air, food and drinks, sleep and wakefulness, excretion and retention, physical activity and rest, mental activity, and rest.

Unani medicine emphasizes on retaining the natural compounds of the body and hence prescribe drugs which are natural in their sources and forms.

Diagnosis of the disease is done based on three important aspects, pulse (nabz), urine (boul) and stool (baraz) [15-16].

X. SIDDHA SYSTEM OF MEDICINE

The Siddha system of medicine is associated with prevedic period based on the Dravidian culture and is largely therapeutic in nature. The term Siddha means achievement and Siddhars were saintly people who attained excellence in medicine through practice of bhakti and yoga. Traditionally, it is believed that this system of medicine descended from Lord Shiva who revealed the knowledge of medicine to his wife Parvati who in turn passed it to Siddhars.

Siddha is extensively practised in Tamil Nadu and in the neighbouring Tamil speaking parts. The literature relating to it of which there are at least 500 texts and more than 3000 formulae are mostly in Tamil initially written on palm leaves. It is one of the oldest medical system of India that existed from the early times. It is also called the Agasthyar system after its famous exponent saint Agasthya.

Like Ayurveda, this system of medicine believes in the role of tridoshas-vatham, pitham and karpam and that all obejcts in the universe including human body is made up of five basic elements (the panchamahabhutas) viz munn (earth), vayu (air), neer (water), aakasam (space or sky) and thee (fire) in different combinations.

The tissues are called dhatus which are seven in number: Rasa (lymph), Kurudhi (blood), Tasai (muscle), Kozhuppu (adipose tissue), Majjai (marrow), Elambu (bone), Sukkilam and artavam (male and female hormones). Unlike Ayurveda, Siddha lays important on usage of metals and minerals rather than herbs. Herbs are used only to triturate and calcinate the metals into their bhasma and sindooram forms.

Since this system of medicine believes in the concept of panchamahabhutas, the medicine meant for the human body are prepared from the five dhatus or metals like gold, lead, copper, zinc and iron after proper detoxification. Gold and lead are used for the maintenance of the body, iron and zinc for the extension of life and copper for the preservation of heat in the body.

A Siddhar approaches the medical problem in terms of the three-elemental theory. Thus, while considering the causative factors and treatment of disease, he gives more attention to the disorders of the elements of the intrinsic factors of the body than to the extrinsic factors. Identification of the causative factors of the diseases is done through pulse reading, urine and tangue examination, colour of the body, study of voice, status of digestive system etc.

The Materia Medica of Siddha science contains drugs from vegetable, mineral, metal and

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marine sources. A few drugs of animal origin are also under frequent use. Examples of few natural drugs used in Siddha system of medicine are, Ratha polam (Aloe barbadensis), Gomathaic (Datura stramonium). Ethis (Strychnos nuxvomica), Abini (Papaver somniferum), gold, silver, copper, iron, tin, lead, mercury, sulphur, pearls, diamonds, jade, coral, ruby, emerald, opal, sapphire, lapiz-lazuli, valkrantham, rajavantham etc [12-14].

XI. HOMEOPATHIC SYSTEM OF MEDICINE

Homeopathy system of medicine was found by a German physician and chemist Dr. Christian Frederick Samuel Hahnemann (1755-1843). The experimental and practical foundation for homeopathy was carried out between 1790 to 1810. Hahnemann believed that symptoms are not manifestation of the illness itself but an outward reflection of the body's defence mechanism to overcome the illness. He further stated that the medicines given for treatment should produce these symptoms instead of antagonizing them [17]. In 1790, he observed that real cures were affected by drugs which reinforce similar symptoms in healthy human subjects. Homeopathy is therefore based on the Law of Cure: Similia: similibus curantur which translates to" like are cured by like". This is the single most belief and foundation of homeopathic practice, which derives its name from the Greek words homois (like) and pathos (treatment).

With the concept of Law of similar in mind, Dr. Hanemann set about examining the effects produced by ingestion of various extracts. He started with cinchoma and to his surprise found that it produced symptoms similar to malaria. These symptoms persisted as long as the treatment was continued. With the help of his colleagues and friends, he examined the effects of a wide range of plant, animal and mineral extracts and succeeded in getting relevant results which were published in the definitive text of homeopathy The Organon of Medicine.

In contrast to other alternative therapies, in homeopathy, the drug treatment is not specified but the choice of drug depends on the individual and his symptoms rather than the clinical condition of the patient. By administering a drug that is tailored to the symptoms and complaints specific to each patient, the homeopathy encourages the body's intrinsic healing process. Drug tailoring is based on the concept of proving and prover. The process of administering doses of an extract in a healthy individual (called prover) to assess the symptoms it induces is called as proving.

The prover specifically maintains a record of the physical, mental and emotional changes induced by various doses of the extract over a period of time. Consequently, this builds up a drug picture of an extract which is compared precisely to similar symptoms produced by an illness in a patient.

For example,one patient suffering from depression may feel tired and listless (lack of energy) while another may feel agitated and irritable. Based on different symptoms shown by different patients to the same clinical conditions, different remedies would be tailored. Similarly, different conditions presenting similar symptoms can be treated with the same remedy. For example, treatment for inflammation due to a burn and due to a skin rash is designed to fit the patient's symptoms but not the aetiology [17].

During the treatment it was found that the drug extracts at normal doses aggravated the symptoms for which they were used. This led to the second feature of homeopathy-potentization, according to which the more the drug is diluted or potentized, the greater is its curative effect.

The mother tincture which is prepared by macerating the fresh drug in pure alcohol is diluted according to various scales of serial dilutions to increase the healing power of the drug. Centesimal scale involves a serial dilution of 1 in 100 and decimal scale involves dilution series of 1 to 10. One drop of mother tincture when added to 99 drops of an inert solvent (like water, alcohol or lactose) gives the first centesimal potency denoted by IC.

The solution is then shaken vigorously and tapped on a resilient surface, a process called succussion, an important part of the preparation of a homeopathic drug that claims to release the power to heal. Further dilution of 1 drop of IC to 99 drops of solvent and succussed produces the second centesimal, the process can be repeated up to 10,000 C (10M). Alternatively, 1 drop diluted to 9 parts gives the first decimal potency denoted by 1 D or 1 X. Such extreme dilutions have led to strict precautions so as to avoid contamination of the potency. The preparations should not be stored near pungent materials like perfumes, soaps and toothpastes as any strong odour will negate the potency [17].

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XII. CHINESE SYSTEM OF MEDICINE

12.1. Introduction

Traditional Chinese Medicine (TCM) originated in ancient China about 2500 years ago. The TCM practitioners uses various techniques like acupuncture, medicinal herbs etc., to promote health and/or treat diseases. The basis on which these practitioners work has been listed below. The human body represents a miniature version of the larger, surrounding universe. A person is considered to be healthy when harmony exists between two opposing yet complementary forces i.e,Yin (Passive) and Yang (active). On the other hand, diseases or illness results due to a breakdown in the equilibrium between these two forces. Enormous functions in maintaining health are performed by Qi (a vital energy that flows through the body) [1].

12.2 Yin and Yung Theory

Yin and Yung theory is the mostly accepted theory on which the TCM are based upon. As already discussed, Yin and Yung are opposing yet complementary forces whom harmony helps to maintain health whereas imbalance between there causes diseases [14].

12.2.1. Cause of Disease

According to TCM, disease or an ailment is caused due to any imbalance in the body, especially due to excess of Yin and deficiency of Yang or vice-versa. For instance, a person may experience cold due to excess of Yin (an external factor) whereas Yung (endogenous factors in the body) may cause fever.

12.2.2 Disease prevention

One of the main functions of TCM practitioners is to keep their patients healthy and strong. Over the centuries, they have learned to do this by advising their patients to stay away from alcohol, avoid smoking, minimize stress in their lives, do regular exercises etc.

12.2.3. Treatment

Today, the priority of most of the modern medicine practitioners is to keep their patients alive by managing the symptoms of the diseases rather than curing the underlying cause.

For instance, hypercholesterolaemia, diabetes, hypertension etc., are usually managed with drugs like statins, pioglitazone, and calcium channel blockers respectively. These drugs although are able to cure the symptoms, but during the rest of the patient's life have proved to cause muscle toxicity (by certain statins), congestive cardiac failure and kidney cancer (by pioglitazone) and bradycardia (by certain calcium channel blockers).

In contrast to modern medicine practitioners, the TCM practitioner's approach is pragmatic, experimental and is based on the techniques that can help the patient to get back to productive life. For instance, a person effected with stroke will be treated for up to 6 months with proper mixtures of plant medicines to achieve adequate balance in the body. This is a very tough job as each disease in each person requires an individualized therapy. Besides plant extracts, Tai Qi, yoga, prayers, meditation etc., are also included in the therapy to maintain the balance of Yin and Yang (to support health), treat the underlying cause of the disease and prevent is progression.

Techniques

To restore the harmony between Yin and Yang, the TCM practitioner may use one or more of the following several methods.

Acupuncture

Acupuncture involves a group of procedures/techniques that stimulate the specific points on the body. The commonly practised acupuncture technique involves penetrating the thin, solid metal needles into the superficial skin, subcutaneous tissue and muscles and manipulating by hand or electrical stimulation. There exists about 2000 acupuncture points on the human body that are interconnected by 12 main meridians or channels. It is through these channels, that the Qi (energy) flows between the skin surface and its internal organs. Hence acupuncture helps to maintain a balance between Yin and Yang, thereby allowing for the normal flow of QI throughout the body to restore health to mind and body.

Chinese Herbs

Thousands of medicinal plant/herbs find a mention in the Chinese Medica (a standard reference book). The commonly used parts of the herbs include leaves, roots, stems, flowers, and seeds. In TCM herbology treatment, the herbs are combined into a formula that is dispensed as tears, capsules, powders, liquid extracts, granules etc.

Every herb used has its own energy, flavour, movements in the body as well as its related meridians to which it is connected to. Usually four types of energies have been found in herbs i.e, cold, cool, warm, and hot. Herbs possessing first two types of energies are used in

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the treatment of fever, thirst, sore throat etc. whereas the latter two energy possessing herbs are used to treat cold, paints and similar other conditions.

Five types of flavours in herbs include sweet, salt, sour, bitter and pungent, sweet herbs are used to nourish deficiencies, reduce toxicities, relieve pain and slow down the progression of acute diseases. Salt herbs finds use in the treatment of severe constipation and swelling due to goitre, sour herbs are good at stopping leucorrhoea, seminal emission, diarrhoea and perspiration. Bitter herbs are used in the treatment of fever, hot sensations and damp diseases. Pungent herbs are good at promoting circulation of blood and Qi at promoting perspiration.

After administration of herbs they undergo absorption and then move in one of the four directions.

Upward towards the head. Such herbs are used for falling symptoms like prolapsed organs. Downwards towards the stomach. Such herbs are used for up-surging symptoms like coughing and vomiting. Inward towards the digestive organs. Such herbs are used to induce bowel movements and promote digestion. Outwards towards the superficial body regions. Such herbs are used to treat superficial symptoms that travel towards the internal organs.

Every herb used in TCM has its own meridian or meridians to which it will correspond to. For instance, the herbs used in the treatment of respiratory tract disorders move towards lungs and hence can be used to treat cough or asthma.

Maxibustion

This theory involves burning of moxa (roots of dried Artemisia vulgaris). The smoke and the pungent Adour produced due to burning of moxa is used to warm up blood, strengthen the kidney (Yang), stimulate the flow of Qi, dissolve stagnation, disperse cold and expel wind.

Tui Na Body Therapy

This therapy includes message, acupressure and acupuncture. The TCM practitioner may use herbal compresses, ointments and heat to enhance this therapy. It is commonly used to treat chronic pains related to skeletomuscular system.

All the important phenomena taking place in human body for example, changes occurring during different stages of life, functioning of body, changes during diseased conditions etc., are explained by the five elements i.e, fire, earth, wood, metal, and water [14].

XIII. CONCLUSION

Pharmacognosy is a scientific discipline, which is primarily concerned with the study of crude drugs obtained from natural sources, such as plants, animals, and minerals. It has also led to the development of novel drugs and nutraceuticals. Traditional systems of medicine also referred to as complementary, supporting or assisting medicine are not part of the standard conventional medicine but are the ones that are used along with or instead of the standard care provided by doctors or allied health professionals such as nurses, pharmacists, physical therapists. Traditional medicine has been prevalent in various countries like India and China much before the development of present-day medical science. For example, in India ,Ayurveda, meditation, yoga, Unani herbal medicine and siddha have been used since ancient period to heal the body.The complementary and traditional medicine practitioners take a holistic approach to patient care. They treat the patient as a whole person but not just a set of symptoms. They tend to be strongly prevention oriented and regard a high value to the body's natural ability to heal itself. Still now-a-days many people are turning gradually towards traditional therapies as these are safe, have no side effects, expenses are reasonable, and these are equally effective in the treatment of patients with diseases which the conventional medicine cannot cure.

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HIGH PERFORMANCE LIQUID CHROMATOGRAPHY AND DEVELOPMENT TECHNIQUES; A SHORT REVIEW

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ABSTRACT

High-performance liquid chromatography (HPLC) is a specific form of column chromatography which is generally used in biochemistry and analysis to separate, identify, and quantify the various drugs, drug active compound and drug related substance. The main intend of this article is to review and analyse the HPLC and its method of development techniques. High-performance liquid chromatography is generally depending on various factors such as synthetic route, solubility, polarity, pH and pKa values and most importantly chemical structures of the molecules and functional group activity etc.

1.0 INTRODUCTION

High-performance liquid chromatography (or High-pressure liquid chromatography, HPLC) is a specific form of column chromatography generally used in biochemistry and analysis to separate, identify, and quantify the active compounds.[1] The enormous success of HPLC can be attributed to a number of inherent features associated with reproducibility, ease of selectivity manipulation, and generally high recoveries. The most significant feature is the excellent resolution that can be achieved under a wide range of conditions for very closely related molecules, as well as structurally quite distinct molecules.[2] HPLC mainly utilizes a column that holds packing material (stationary phase), a pump that moves the mobile phase(s) through the column, and a detector that shows the retention times of the molecules. Retention time varies depending on the interactions

between the stationary phase, the molecules being analysed, and the solvent(s) used.[3] The separation of sample is based on the differences in the rates of migration through the column arising from different partition of the sample between the stationary and mobile phase. Depending upon the partition behaviour of different components, elution at different time takes place.[4] The sample compound with the greater affinity to the stationary layer will travel slower and for a shorter distance in comparison to compounds with 3less affinity which travel faster and for a longer distance.[5]

HPLC has numerous advantages like

1) Simultaneous Analysis
2) High Resolution
3) High Sensitivity
4) Good repeatability
5) Small sample size
6) Moderate analysis condition.
7) Easy to fractionate the sample and purify.[6]

2.0 Types of HPLC

❖ Depending on the substrate used i.e., stationary phase used, the HPLC is divided into following types

2.1 Normal Phase HPLC-This method separates analytes on the basis of polarity. NP-HPLC uses polar stationary phase and non-polar mobile phase. Therefore, the stationary phase is usually silica and typical mobile phases are hexane, methylene chloride, chloroform, diethyl ether, and mixtures of these. Polar samples are thus retained on the polar surface of the column packing longer than less polar materials.[7]

2.2 Reverse Phase HPLC- It is reverse to normal phase HPLC. The mobile phase is polar and the stationary phase is non polar or hydrophobic. The more is the non-polar nature the more it will be retained.

2.3 Size-exclusion HPLC- The column will be incorporating with precisely controlled substrate molecules. Based on the difference in molecular sizes the separation of constituents will occur.

2.4 Ion-exchange HPLC- The stationary phase is having ionically charged surface opposite to the sample charge. The mobile phase used is aqueous buffer which will control pH and ionic strength.[8]

2.5 Bio-affinity chromatography- Separation based on specific reversible interaction of proteins with ligands. Ligands are covalently attached to solid support on a bio-affinity matrix, retains proteins with interaction to the column-bound ligands. Proteins bound to a bio affinity column can be eluted in two ways:

Bispecific elution: inclusion of free ligand in elution buffer which competes with column bound ligand.

Aspecific elution: change in pH, salt, etc. which weakens interaction protein with column-bound substrate.

Because of specificity of the interaction, bio affinity chromatography can result in very high purification in a single step (10 - 1000-fold).[9]

3.0 Instrumentation of HPLC

The most important components of the HPLC instrument are: mobile phase/solvent reservoir, solvent delivery system, sample introduction device, column, detectors, data collection and output.[10] (Figure 1)

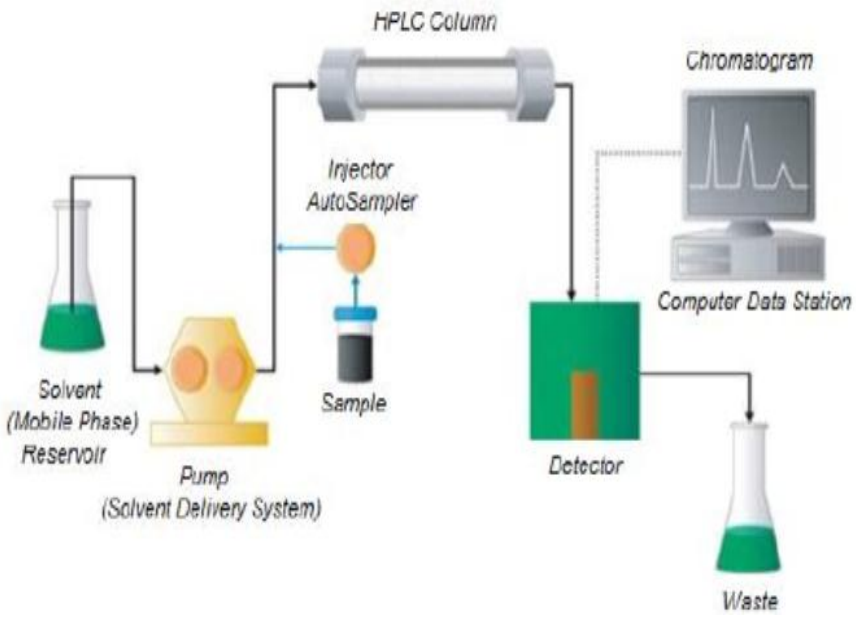

Fig. 1: High-Performance Liquid Chromatography HPLC System.

3.1 Mobile phase/solvent reservoir

The reservoir that holds the mobile phase is often no more than a glass bottle. Often, the reagent bottle that holds our HPLC solvent can be used as a reservoir. Solvent is delivered from the reservoir to the pump by means of Teflon tubing called the "inlet line" to the pump. Some HPLC systems like the Agilent 1100 shown at the right have special compartments to hold one or more mobile phase reservoirs. The reservoirs in these systems may have additional features that allow the mobile phase to be degassed and isolated from contact with air.

3.2. Solvent delivery system

The solvent delivery system is described like a deliver system of continuous pulse free flow of mobile phase to the HPLC regardless of the system back pressure.

3.3. Injection of the sample

The injection of a sample at atmospheric pressure into the system, at high pressure, represents a critical step in the chromatographic process. Sample injection valves, or switching valves, are used to introduce reproducible amounts of sample into the HPLC eluent stream without causing changes in pressure or flow.

3.4. Column

The column is the heart of a HPLC system, there are several types of matrices for support of the stationary phase, including silica, polymers, and alumina. Silica is the most common matrix for HPLC columns. Silica matrices are robust, easily derivatized, manufactured to consistent sphere size, and does not tend to compress under pressure. Silica is chemically stable to most organic solvents and to low pH systems.

3.5. Detector

An overview of various HPLC detectors is provided with discussion of unique detector characteristics and a comparison of advantages and drawbacks between them. Focus is placed on the most common detectors, including UV absorbance, fluorescence, electrochemical, conductivity, refractive index, and mass spectrometry detectors.

3.6. Data collection and Output

The output is recorded as a series of peaks, each one representing a compound in the mixture passing through the detector and absorbing UV light (in the case of HPLC-UV/Vis). The area

under the peak is proportional to the amount of substance, which is passed through detector, and this area can be calculated automatically by the computer linked to the display.

4.0 HPLC development method

There are many factors to consider when developing methods. The initially collect the information about the analyte's physiochemical properties (pKa, log P, solubility) and determining which mode of detection would be suitable for analysis. The majority of the analytical development effort goes into validating a stability indicating HPLC–method. The goal of the HPLC-method is to try & separate quantify the main active compound, any reaction impurities, all available synthetic inter-mediates and any degradants.[11]

4.1. Physicochemical properties of the active compound

Physicochemical properties of the active compound play an important role in method development. For method development one has to study the physical properties like solubility, polarity, pKa and pH of the molecule. Polarity is a physical property of a compound. It helps an analyst, to decide the solvent and composition of the mobile phase. Selection of diluents is based on the solubility of analyte. The analyte must be soluble in the diluents and must not react with any of the diluent components. The diluent should match to the starting eluent composition of the assay to ensure that no peak distortion will occur, especially for early eluting components.

The acidity or basicity of a substance is defined most typically by the pH value. The pH value is defined as the negative of the logarithm to base 10 of the concentration of the hydrogen ion, pH = - log10 [H3O+]. Selecting a proper pH for ionizable analytes often leads to symmetrical and sharp peaks in HPLC. Sharp, symmetrical peaks are necessary in quantitative analysis in order to achieve low detection limits, low relative standard deviations between injections, and reproducible retention times. The pKa is characteristic of a particular compound, and it tells how readily the compound gives up a proton. An acid dissociation constant is a particular example of equilibrium constant. For the specific equilibrium between a monoprotic acid HA. and its conjugate base A−.

It turns that the pKa of an acid is the pH at which it is exactly half dissociated. This can be shown by rearranging the expression for Ka: pH = pKa – log10([AH]/[A-])

At half-neutralization the pH is numerically equal to pKa. Conversely, when pH = pKa, the concentration of HA is equal to the concentrationtration of A−.

The buffer region extends over the approximate range pKa ± 2, though buffering is weak outside the range pKa ± 1. At pKa ± 1, acid.
[A−]/[HA] = 10 or 1/10. If the pH is known, the ratio may be calculated. This ratio is independent of the analytical concentration of the

When the pKa and analytical concentration of the acid are known, the extent of dissociation and pH of a solution of a monoprotic acid can be easily calculated.[12-15]

4.2. Column selection

The heart of a HPLC system is the column. Changing a column will have the greatest effect on the resolution of analytes during method development. Generally, modern reverse phase HPLC columns are made by packing the column housing with spherical silica gel beads which are coated with the hydrophobic stationary phase. The stationary phase is introduced to the matrix by reacted a chlorosilane with the hydroxyl groups present on the silica gel surface.

There are several types of matrices for support of the stationary phase, including silica, polymers, and alumina. Silica is the most common matrix for HPLC columns. Silica matrices are robust, easily derivatized, manufactured to consistent sphere size, and does not tend to compress under pressure. Silica is chemically stable to most organic solvents and to low pH systems. One shortcoming of a silica solid support is that it will dissolve above pH 7. In recent years, silica supported columns have been developed for use at high pH.[16]

4.3. Shape and Particle size effect

Generally, Smaller particle results in a greater number of theoretical plates, or increased separation efficiency. However, the use of smaller particles also results in increased backpressure during chromatography and the column more easily becomes plugged.[17]

4.4 Buffer selection

Choice of buffer is governed by the pH that is desired. The typical pH range for reversed phase on silica-based packing is pH 2 to 8. It is important that the buffer has a pKa close to the desired pH since buffer controls pH best at their pKa. A rule is to choose a buffer with a

pKa value <2 units of the desired mobile phase pH. General consideration for buffer selection:

1. Phosphate is more soluble in methanol/water than in acetonitrile/water or THF/water.
2. Some salt buffers are hygroscopic and this may lead to changes in the chromatography like increased tailing of basic compounds and possibly selectivity differences.
3. Ammonium salts are generally more soluble in organic/water mobile phases·
4. Trifluoroacetic acid can degrade with time. It is volatile and absorbs at low UV wavelengths.
5. Microbial growth can quickly occur in buffered mobile phases that contain little or no organic modifier at all. The growth accumulates on column inlets and can damage chromatographic performance.
6. At pH greater than 7, phosphate buffer accelerates the dissolution of silica and severely shortens the lifetime of silica-based HPLC columns. If possible, organic buffers should be used at pH greater than 7.
7. Ammonium bicarbonate buffers usually are prone to pH changes and are usually stable for only 24 - 48 hrs. The pH of this mobile phase tends to become more basic due to the release of carbon dioxide.
8. After buffers are prepared, they should be filtered through a 0.2-µm filter.
9. Mobile phases should be degassed.[18]

4.5 Buffer concentration

Generally, a buffer concentration of 10-50 mM is adequate for small molecules. Generally, no more than 50% organic should be used with a buffer. This will depend on the specific buffer as well as its concentration. Phosphoric acid and its sodium or potassium salts are the most common buffer systems for reversed-phase HPLC. Sulfonate buffers can replace phosphonate buffers when analysing organophosphate compounds.[19]

Selection of detector

Detector is a very important part of HPLC. Selection of detector depends on the chemical nature of analytes, potential interference, limit of detection required, availability and/or cost of detector. UV-Visible detector is versatile, dual-wavelength absorbance detector for HPLC. This detector offers the high sensitivity required for routine UV-based applications to low-level impurity identification and quantitative analysis. Photodiode Array (PDA) Detector offers advanced optical detection for Waters analytical HPLC, preparative HPLC, or LC/MS

system solutions. Its integrated software and optics innovations deliver high chromatographic and spectral sensitivity. Refractive Index (RI) Detector offers high sensitivity, stability and reproducibility, which make this detector the ideal solution for analysis of components with limited or no UV absorption. Multi-Wavelength Fluorescence Detector offers high sensitivity and selectivity fluorescence detection for quantitating low concentrations of target compounds.[20]

Developing the approach for analysis: While developing the analytical method on RP-HPLC the first step which is followed is the selections of various chromatographic parameters like selection of mobile phase, selection of column, selection of flow rate of mobile phase, selection of pH of mobile phase. All of these parameters are selected on the basis of trials and followed by considering the system suitability parameters. Typical parameters of system suitability are e.g., retention time should Yadav and Bhartiya RJLBPCS 2017 www.rjlbpcs.com Life Science Informatics Publications be more than 5 min, the theoretical plates should be more than 2000, the tailing factor should be less than 2, resolution between 2 peaks should be more than 5, % R.S.D. of the area of analyte peaks in standard chromatograms should not be more than 2.0 %. like other. Detection wavelength is usually isosbestic point in the case of simultaneous estimation of 2 components. After this the linearity of the drug is studied in order to know the range of concentrations up to which the drug follows the linear pattern. Analysis of the laboratory mixture is also carried out in order to know practicability of developed method for simultaneous estimation. After that analysis of marketed formulation is carried out by diluting the marketed formulation up to concentration range of linearity.[21-22]

Mobile phase

Mobile phase reservoirs

Inert container with inert lines leading to the pump are required. Reservoir filters (2-10 mm) at reservoir end of solvent delivery lines

Degassed solvent

Vacuum filtration

Sparge with inert gas (N_2 or He)

Ultrasonic under vacuum

Isocratic elution

A separation that employs a single solvent or solvent mixture of constant composition.

Gradient elution

Here two or more solvent systems that differ significantly in polarity are employed. After elution is begun; the ratio of the solvents is varied in a programmed way, sometimes continuously and sometimes in a series of steps. Separation efficiency is greatly enhanced by gradient elution.

Preparation of sample solutions for method development

The drug substance being analysed should be stable in solution (diluent). During initial method development, preparations of the solutions in amber flasks should be performed until it is determined that the active component is stable at room temperature and does not degrade under normal laboratory conditions. The sample solution should be filtered; the use of a 0.22 or 0.45 μm pore-size filter is generally recommended for removal of particulates. Filtration is a preventive maintenance tool for HPLC analyses.17, 18, 19, 20 Sample preparation is a critical step of method development that the analyst must investigate. The effectiveness of the syringe filters is largely determined by their ability to remove contaminants/insoluble components without leaching undesirable artifacts (i.e., extractables) into the filtrate. If any additional peaks are observed in the filtered samples, then the diluent must be filtered to determine if a leachable component is coming from the syringe filter housing/filter.[23]

Method optimization: Identify the "weaknesses" of the method and optimize the method through experimental design. Understand the method performance with different conditions, different instrument set ups and different samples.[24]

6. Method validation

Validation is the confirmation by examination and the provision of objective evidence that the particular requirements for a specific intended use are fulfilled. A process of evaluating method performance and demonstrating that it meets a particular requirement. In essence, it knows what your method is capable of delivering, particularly at low concentrations.[25]

Components of method validation

The following are typical analytical performance characteristics which may be tested during methods validation:

1. System Suitability 2. Accuracy Precision 3. Repeatability 4. Intermediate precision 5. Linearity 6. Detection limit 7. Quantitation limit 8. Specificity 9. Range 10. Robustness 11. System suitability determination 12. Forced degradation studies 13. Solution stability studies

CONCLUSION

This review article aims to explain the key parameters of analytical method development using the chromatography techniques which are used for the identification, separation, purification, and quantitative estimation of complex mixtures of organic compounds

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A REVIEW ARTICLE ON GOLDEN SPICE: TURMERIC

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ABSTRACT

Turmeric, a spice that has long been recognized for its medicinal properties, has received interest from both the medical/scientific world and from culinary enthusiasts, as it is the major source of the polyphenol curcumin. It aids in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidemia. It may also help in the management of exercise-induced inflammation and muscle soreness, thus enhancing recovery and performance in active people. In addition, a relatively low dose of the complex can provide health benefits for people that do not have diagnosed health conditions. Most of these benefits can be attributed to its antioxidant and anti-inflammatory effects. Ingesting curcumin by itself does not lead to the associated health benefits due to its poor bioavailability, which appears to be primarily due to poor absorption, rapid metabolism, and rapid elimination. There are several components that can increase bioavailability. For example, piperine is the major active component of black pepper and, when combined in a complex with curcumin, has been shown to increase bioavailability by 2000%. Curcumin combined with enhancing agents provides multiple health benefits. The purpose of this review is to provide a brief overview of the plethora of research regarding the health benefits of curcumin.

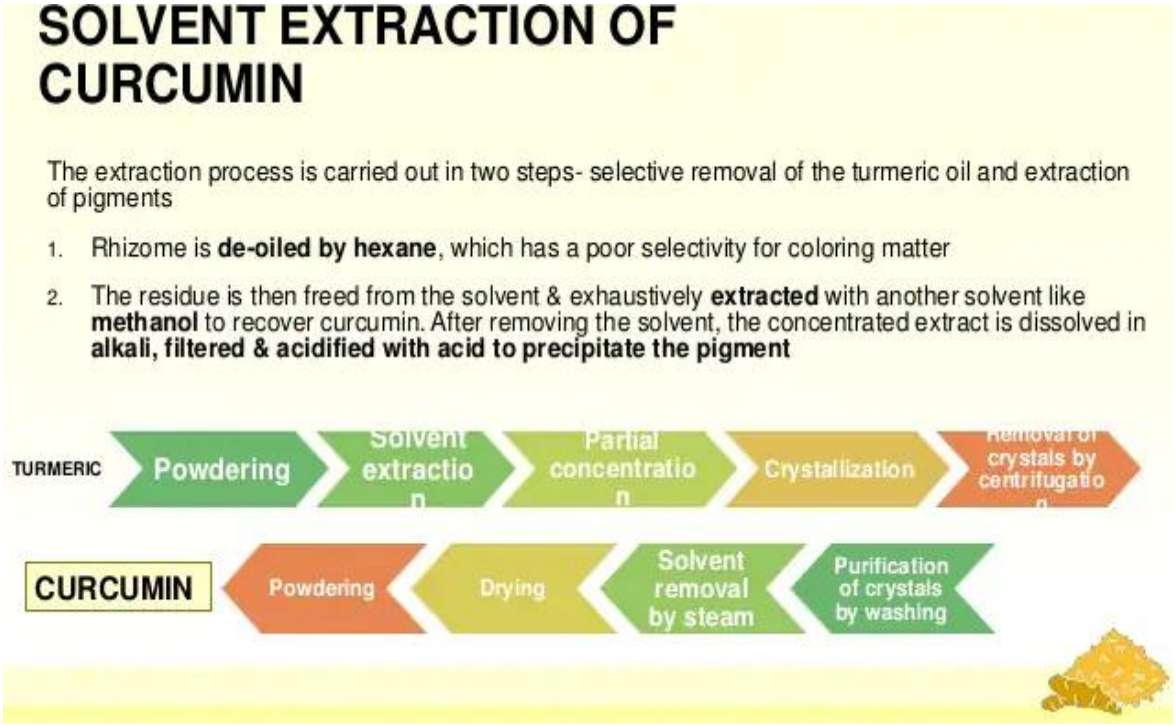
1. INTRODUCTION

Turmeric is a spice that has received much interest from both the medical/scientific worlds as well as from the culinary world. Turmeric is a rhizomatous herbaceous perennial plant

(*Curcuma longa*) of the ginger family.[1] Natural plant products have been used as the foundation of several medical treatments in humans.[1] Although modern aspects of Western medicine have become the forefront of clinical practice today, natural plant products continue to be used as remedies in alternative medicine throughout the world. It is estimated that 80% of individuals in developing countries depend primarily on natural products to meet their healthcare needs.[1] Even in the United States it has been found that approximately one in three Americans uses natural medicinal products daily.[2] The medicinal benefits of turmeric could be attributed to the presence of active principles called curcumin oids. One of the most interesting components of curcumin oid is curcumin, which is a small molecular weight polyphenolic compound and lipophillic in nature, hence insoluble in water and also in ether but soluble in ethanol, dimethyl sulfoxide, and other organic solvents.[3] Turmeric has been used in Asian cuisines for both its flavour and color and in the Chinese and Ayurvedic medicine particularly as an anti-inflammatory and for the treatment of jaundice, menstrual difficulties, hematuria, hemorrhage, and colic. It is official in the Pharmacopoeia of China as well as in other Asian countries such as Japan and Korea and its usage covers a wide range of health indications. In China it is ingested orally and applied topically for urticaria and skin allergy, viral hepatitis, inflammatory conditions of joints, sore throat and wounds.[4]

2. Isolation of curcumin

Curcumin is insoluble in water; an organic solvent has been used for its isolation.[26] developed a technique for isolating CUR from ground turmeric. They magnetically stirred the ground turmeric in dichloromethane and heated at reflux for 1 h. The mixture was suction-filtered, and the filtrate was concentrated in a hot-water bath maintaining at 50o C. The reddish-yellow oil residue was triturated with hexane and the resulting solid was collected by suction filtration. Further TLC analysis (3% methanol and 97% dichloromethane) showed the presence of all three components.[26] Extraction of CUR from turmeric powder with the use of a solvent consisting of a mixture of ethanol and acetone. Chemical analyses have shown that turmeric contains carbohydrates (69.4%), moisture (13.1%), protein (6.3%), fat (5.1%) and minerals (3.5%). The essential oil (5.8%) obtained by steam distillation of the rhizomes contains a-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpines (53%), curcumin (3-6%) is responsible for the yellow color.[5]



3. Pharmacokinetics and Pharmacodynamics

Prior studies have discussed the difficulty in achieving optimum therapeutic concentrations of the molecule due to low solubility and poor bioavailability of curcumin. Studies suggest that curcumin is first biotransformed to dihydrocurcumin and tetrahydrocurcumin, and subsequently converted to monoglucuronide conjugates.[6] Preliminarily animal studies demonstrate that curcumin is rapidly metabolized and conjugated in the liver, and then excreted in feces with limited systemic bioavailability. A 40 mg/kg intravenous dose of curcumin given to rats resulted in complete plasma clearance at one hour post-dose. An oral dose of 500 mg/kg given to rats resulted in a peak plasma concentration of only1.8 ng/Ml.[7] A common method that has been employed to increase the bioavailability of curcumin is to use agents that block the metabolic pathway of curcumin. One study exploring methods to increase the bioavailability of curcumin found that coadministration of oral curcumin with piperine, an alkaloid found in black pepper (Piper nigrum) and long pepper (Piper longa), increased serum concentrations of curcumin in rodents, as piperine is a known inhibitor of hepatic and intestinal glucoronidation. With high doses of oral curcumin (2000 mg/kg) and coadministration of piperine, systemic bioavailability was increased by as much as 154%.[8] Several phase I clinical trials report data on the pharmacokinetics, metabolites, and systemic bioavailability of curcumin in humans, mainly conducted on cancer patients. A trial conducted of 25 patients with various pre-cancerous lesions administered oral doses of 4, 6, and 8 g curcumin daily for three months yielded serum curcumin concentrations of only 0.51

± 0.11, 0.63 ± 0.06, and 1.77 ± 1.87 mM, respectively. However safety and patient tolerance was appreciated even at 8 g of curcumin. Serum levels peaked between one and two hours post-dose and declined rapidly; urinary excretion of curcumin was undetectable.[9] Another study of 15 patients with advanced colorectal cancer reported even lower serum curcumin concentrations. In this study curcumin doses between 0.45 and 3.6 g were given daily for four months. In three of six patients given the 3.6 g dose, mean plasma curcumin measured at all points during the first month of curcumin therapy was consistently 11.1 ± 0.6 nmol/L. Curcumin was not detected in the plasma of patients taking lower doses.[10] Due to the low bioavailability of curcumin, Theracurmin, a synthetically derived nano-particle form of curcumin was developed that has a higher bioavailability. Previous studies exploring the pharmacokinetics of Theracurmin in healthy patients achieved satisfactory plasma concentrations after one dose. Other studies to evaluate the safety of curcumin in cancer patients have yielded similar findings. In one study, Theracurmin was orally administered every day with standard gemcitabine-based chemotherapy. Peak plasma curcumin levels (median) after 200 mg of Theracurmin administration were 324ng/mL and at 400 mg of Theracurmin peak plasma level was 440 ng/ml with no unexpected adverse events during the 9 months of drug administration.[11] Another study of 24 patients aimed to quantify levels of curcumin and its metabolites in colorectal mucosa of patients rather than measuring serum concentration. Curcumin C3-complex (2.35 g) was administered daily for 14 days prior to endoscopic biopsy or colonic resection. Curcumin and its metabolites were detectable in 9/24 plasma samples, 24/24 urine samples and in the colonic mucosa of all 23 biopsied participants with mean tissue levels at 48.4 mg/g. The only adverse event reported was mild abdominal discomfort in six patients, and 67% expressed acceptability of the therapy longterm should it be of proven benefit.[12]

4. Medicinal uses

4.1. Gastrointestinal disorders

The fresh juice of Haridra is considered to be anthelmintic.[13] The Curcumin acts through nuclear factor (NF)-κB inhibition and it reduces the production of adhesion molecules and inflammatory cytokines, resulting in the amelioration of gastric injury in NSAIDs-induced gastropathy in rats. It also improves gastric mucosal damage and decreases in leukocyte adhesions, and intercellular adhesion molecule 1 and tumor necrosis factor (TNF)-α production after curcumin administration.[14] Curcuma longa extract tablet decreased IBS prevalence and abdominal pain/discomfort score significantly between baseline and after

treatment of eight-week. There were significant improvements in the IBS quality of life (QOL) scales.[15] In liver injury of Male mice Curcumin prevents APAPinduced hepatitis through the improvement of liver histopathology by decreased oxidative stress, reduced liver inflammation, and restoration of GSH.[16]

4.2 Respiratory disorders

The fresh juice of rhizome is given in bronchitis. In rhinitis and cough boil Haridra in milk and mixed with jiggery given internally. In catarrhal cough, sore throat, and throat infection the decoction of rhizome is used for gargle and also the piece of rhizome is slightly burnt and given for chewing.[17] The chemical constituents of Curcuma longa like Tumerones, curcuminoids, Curcumin and tetrahydrocurcumin has an anti-asthamatic action.[18] In asthma and congestion, fumes of Haridradi dhumvarti (fumes wick) is given.[19]

4.3 Inflammatory disorders

Curcumin has been shown to inhibit a number of different molecules involved in inflammation including phospholipase, lipooxygenase, COX-2, leukotrienes, thromboxane, prostaglandins, nitric oxide, collagenase, elastase, hyaluronidase, MCP-1, interferon-inducible protein, tumor necrosis factor, and interleukin-12.[20] Studies has proven bisdemethylcurcumin (BDC) is more potent as an anti-inflammatory agent as indicated by suppression of TNFinduced NF-κB activation, more potent as an anti-proliferative agent, and more potent in inducing reactive oxygen species(ROS). Hispolon analogues, which lacks one aromatic unit in relation to curcumin, also exhibited enhanced anti-inflammatory and anti-proliferative activities.[19] The beneficial effect of curcumin(antiinflammatory compound) in sepsis appears to be mediated by the upregulation of PPAR-γ, leading to the suppression of pro inflammatory cytokine, TNF-α expression and release.[21]

4.4 Diabetes mellitus

Turmeric rhizome powder is very useful with Amla juice and Honey in Madhumeha (diabetes mellitus).[22] The ingestion of 6 g Curcuma longa increased postprandial serum insulin levels, but did not seem to affect plasma glucose levels or GI, in healthy subjects. The results indicate that Curcuma longa may have an effect on insulin secretion.[23] The active principles in the rhizome of Turmeric plant viz; curcuminoids lower lipid peroxidation by maintaining the activities of antioxidant enzymes like superoxidedismutase, catalase and glutathione peroxidase at higher levels. Antioxidant properties of curcuma longa is due to curcumin and its three derivatives (demethoxy curcumin, bisdemethoxy curcumin and diacetyl

curcumin).[24] A scientific and systemic exploration reveals the antidiabetic, hypolipidemic and hepatoprotective effects of Curcuma longa freeze dried rhizome powder dissolved in milk which could be used as an effective and safe antidiabetic dietary supplement of high potential.[25] Curcuma longa is known to contain curcuminoids, glycosides, terpenoids, and flavonoids. Maximal inhibition of the enzyme Human Pancreatic Amylase (HPA) was obtained with Curcuma longa isopropanol extract and acetone extract. This inhibitory action on HPA causes reduction in starch hydrolysis leading to lowered glucose levels.[26]

4.5 Cardiovascular disorders

The antioxidants in turmeric also prevent damage to cholesterol, thereby helping to protect against atherosclerosis. In fact, the ability of the antioxidants in turmeric to decrease free radicals is similar to that in vitamins C and E. Since the antioxidant activities of turmeric are not degraded by heat (unlike most vitamins), even using the spice in cooking provides benefits. Animal studies show that curcumin lowers cholesterol and triglycerides, another fat that circulates in the blood stream and is a risk factor for cardiovascular disease.[27] In a recent study of atherosclerosis, mice were fed a standard American diet, rich in refined carbohydrates and saturated fat, but low in fiber. Some of the mice, however, received this diet plus turmeric mixed in with their food. After four months on these diets, the mice that consumed the turmeric with their food had 20 percent less blockage of the arteries than the mice fed the diet without the turmeric.[28] In another study, rabbits were fed turmeric plus a diet designed to cause atherosclerosis. Several risk factors for the disease were improved, including a decrease in cholesterol, triglycerides, and free-radical damage.[28]

4.6 Hepatoprotective

The powder of the rhizome mixed with amla juice is used in jaundice.[29] Corriliyum (Anjana) with Haridra, Red ochre (Gairika), and Amalaki (Emblica officinalis) cures jaundice.[30] Curcumin, the most common antioxidant constituent of Curcuma longa rhizome extract, was reported to enhance apoptosis of damaged hepatocytes which might be the protective mechanism whereby curcumin down-regulated inflammatory effects and fibrogenesis of the liver. The ethanolic extract of Curcuma Longa rhizomes showed a significant hepatoprotective effect when orally administrated in doses of 250 mg/kg and 500 mg/kg, and the protective effect was dosedependent. The main constituents of Curcuma longa rhizome ethanolic extract are the flavonoid curcumin and various volatile oils, including tumerone, atlantone, and zingiberene. The hepatoprotective effects of turmeric and curcumin might be

due to direct antioxidant and free radical scavenging mechanisms, as well as the ability to indirectly augment glutathione levels, thereby aiding in hepatic detoxification. The volatile oils and curcumin of Curcuma longa exhibit potent antiinflammatory effects.[31]

4.7 Neuroprotective activity

Curcuma oil significantly reduces the ill effect of ischemia by attenuating nitrosative and oxidative stress. Ischemia induces collapse of mitochondrial membrane potential, cytochrome c release, altering the Bax: Bcl-2 ratio and subsequently caspases activation led to induction of apoptosis in sequential fashion was reverse significantly by Curcuma oil. So there is an evidence for the high efficacy of Curcuma oil as a neuroprotective, with an excellent therapeutic window for the prevention of ischemic brain injury.[32]

4.8 Alzheimer's disease

Curcumin when fed to aged mice with advanced plaque deposits similar to those of Alzheimer's disease, curcumin reduced the amount of plaque deposition. It reduced oxidative damage and reversed the amyloid pathology in an Alzheimer's disease transgenic mouse. Alzheimer's disease symptoms characterized by inflammation and oxidation were also eased by curcumin's powerful antioxidant and anti-inflammatory properties.[33]

4.9 Chemoprotective activity

Curcumin activate the DDR (DNA damage response), providing an opportunity and rationale for the clinical application of these nutraceuticals in the chemoprevention of prostate cancer.[34] Chemoprotective effects in esophageal epithelial cells exposed to bile acids; Curcumin reverses bile acid suppression of gene expression of SOD-1 and also able to inhibit bile acid induction of COX-2 gene expression. Curcumin has demonstrated these chemopreventive properties in cell cultures, animal models and human investigations.

4.10 Anti cancer activity

Curcumin has been found to possess anticancer activities via its effect on a variety of biological pathways involved in mutagenesis, oncogene expression, cell cycle regulation, apoptosis, tumorigenesis and metastasis. Curcumin has shown anti-proliferative effect in multiple cancers, and is an inhibitor of the transcription factor NF-B and downstream gene products (including c-myc, Bcl-2, COX- 2, NOS, Cyclin D1, TNF-a, interleukins and MMP-9). In addition, curcumin affects a variety of growth factor receptors and cell adhesion molecules involved in tumor growth, angiogenesis and metastasis.[35] Curcumin asserts its

anti-tumor activity in cancer cells by altering the deregulated cell cycle via (a) cyclin-dependent (b) p53-dependent and (c) p53-independent pathways. Such influences of curcumin upon key signal transduction pathways of cell cycle and effectiveness in animal model systems have qualified it as a multiple edged sword in combating the deadly disease-cancer.[36] Curcumin as a natural phytochemicals could communicate with these novel targets and show synergism to chemotherapy. Additionally, curcumin is well tolerated in humans. Therefore, EGFR- miRNA- autophagy and cancer stem cell-based therapy in the presence of curcumin might be promising mechanisms and targets in the therapeutic strategy of lung cancer.[37]

4.11 Anti allergic activity

Curcumin suppressed compound 48/80-induced rat peritoneal mast cell (RPMC) degranulation and histamine release from RPMCs. Curcumin inhibited compound 48/80-induced systemic anaphylaxis in vitro and anti-DNP immunoglobulin E (IgE) mediated passive cutaneous anaphylactoid response in vivo. Curcumin has an ability to inhibit nonspecific and specific mast cell-dependent allergic reactions.[38]

4.12 Antidermatophytic activity

Fresh juice of rhizome of Haridra is used as antiparastic in many skin affections. Its rhizome powder mixed with cow's urine is taken internally in itching and dermatitis. Curcuma longa L. leaves have good promise as an antifungal agent that could be used as a therapeutic remedy against human pathogenic fungi on account of its various in vitro and in vivo antifungal properties, viz., strong fungicidal action, long shelf-life, its tolerability of heavy inoculum density, thermo stability, broad range of antidermatophytic activity and absence of any adverse effects. Curcumin obtained from the turmeric rhizome (Curcuma longa) have shown to possess the ability to protect the skin from harmful UV-induced effects by displaying antimutagen, antioxidant, free radical scavenging, anti-inflammatory and anti-carcinogenic properties.[39]

5. Safety, Efficacy and Contraindications

The use of turmeric as a spice and as a household remedy has been known to be safe for centuries. To date, no studies in either animals or humans have discovered any toxic effects associated with the use of turmeric, and it is clear that turmeric is not toxic even at very high doses. The U.S. Food and Drug Administration (FDA) has conducted its own clinical trials with turmeric and published a 300-page monograph. The FDA has declared turmeric and its

active component curcumin as GRAS (generally regarded as safe). Thus, in the United States, turmeric and its components are currently being used in mustard, cereals, chips, cheese, butter, and other products. In a phase I clinical study on the safety and tolerance of turmeric oil use, the oil was administered orally to healthy volunteers for 3 months. No side effects of turmeric oil intake were observed in 3 months on body weight, blood pressure, and hematological, renal, or hepatic toxicity.

CONCLUSIONS

Curcumin has received worldwide attention for its multiple health benefits, which appear to act primarily through its anti-oxidant and anti-inflammatory mechanisms. These benefits are best achieved when curcumin is combined with agents such as piperine, which increase its bioavailability significantly. Research suggests that curcumin can help in the management of oxidative and inflammatory conditions, metabolic syndrome, arthritis, anxiety, and hyperlipidemia. It may also help in the management of exercise-induced inflammation and muscle soreness, thus enhancing recovery and subsequent performance in active people. In addition, a relatively low dose can provide health benefits for people that do not have diagnosed health conditions.

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A SHORT REVIEW ON "LIPOSOMES"

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ABSTRACT
Liposomes, sphere – shaped vesicles consisting of one or more phospholipid bilayers, approved for clinical use in 1995. The term Liposome means lipid body. It has been derived on the basis of subcellular particles, Ribosomes. Their size ranges from 25 to 500nm. Liposomes present as an attractive delivery system due to their flexible physiochemical delivery considerations. In this review article, we discussed about Liposome, these are one among the various drug delivery system used to target the drug to particular tissue. The various other drug delivery includes noisome, microparticles, released erythrocytes, pharmacosomes etc. Research on liposome technology has progressed from conventional vesicles to "Second -generation liposomes", in which long circulating liposomes are obtained by modulating the lipid composition, size and charge of the vesicle. This paper summarizes exclusively components, methods of preparation, Drug delivery etc.

KEYWORDS: Drug delivery system using liposomes, advantages and disadvantages of liposomes, applications, Mechanism, Method of preparation of liposomes.

INTRODUCTION

In 1906 Paul Ehrlich introduced the era of development for targeted delivery mechanism that would target drug directly to diseased cell, what he called as a magic bullet.[1-4] Liposomes were first made synthetically in England in 1961 by Alec D. Bangham.[5] "Liposomes are colloidal, vesicular structures composed of one or more lipid bilayers surrounding an equal number of aqueous compartment."[6-7]

Drug is entrapped within the liposome and is released from the liposome for absorption at the intestinal membrane surface. The main component of liposomes are phospholipids which are amphiphilic molecules containing water soluble, hydrophilic head section and a lipid-soluble, hydrophobic tail section. This property of phospholipids give liposomes unique applications in different fields including food, cosmetic, agriculture and pharmaceutics.[8] A significant advantage of liposome is that it can incorporate and release two materials with different solubilities simultaneously. One example for which is the incorporation of two antioxidant agents namely alpha-tocopherol (a lipid – soluble molecule) and glutathione (a water – soluble molecule) in the same lipid vesicle.[8] The properties of liposomes are influenced by various factors, including lipid composition, surface charge, size, and the method of preparation.[9] Liposomes can be formed from naturally-derived phospholipids with mixed lipid chains (like egg phosphatidylethanolamine).[10]

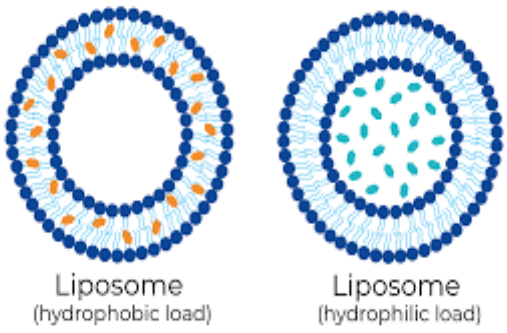

Fig:1

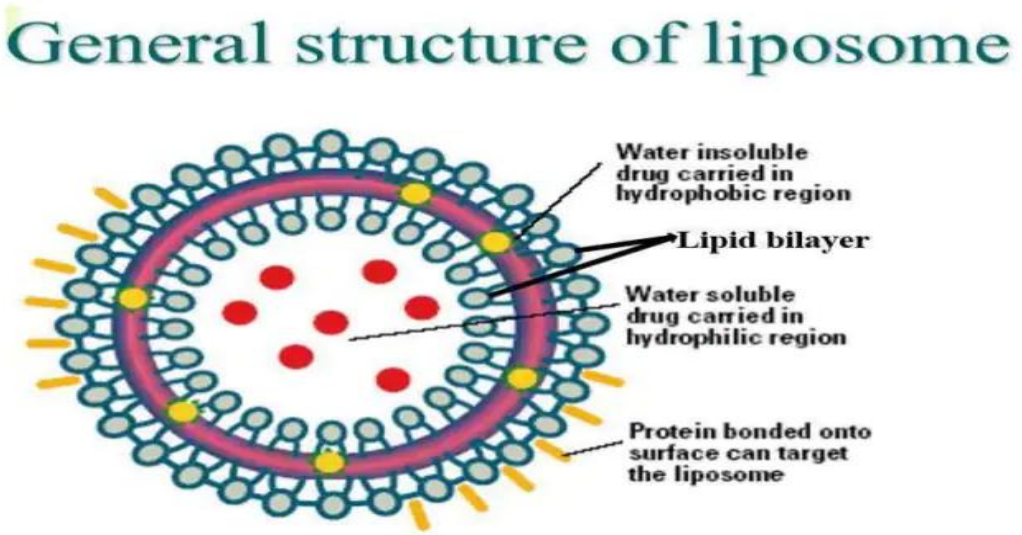

Fig:2

CLASSIFICATION OF LIPOSOME

- **Based on Structural parameters**

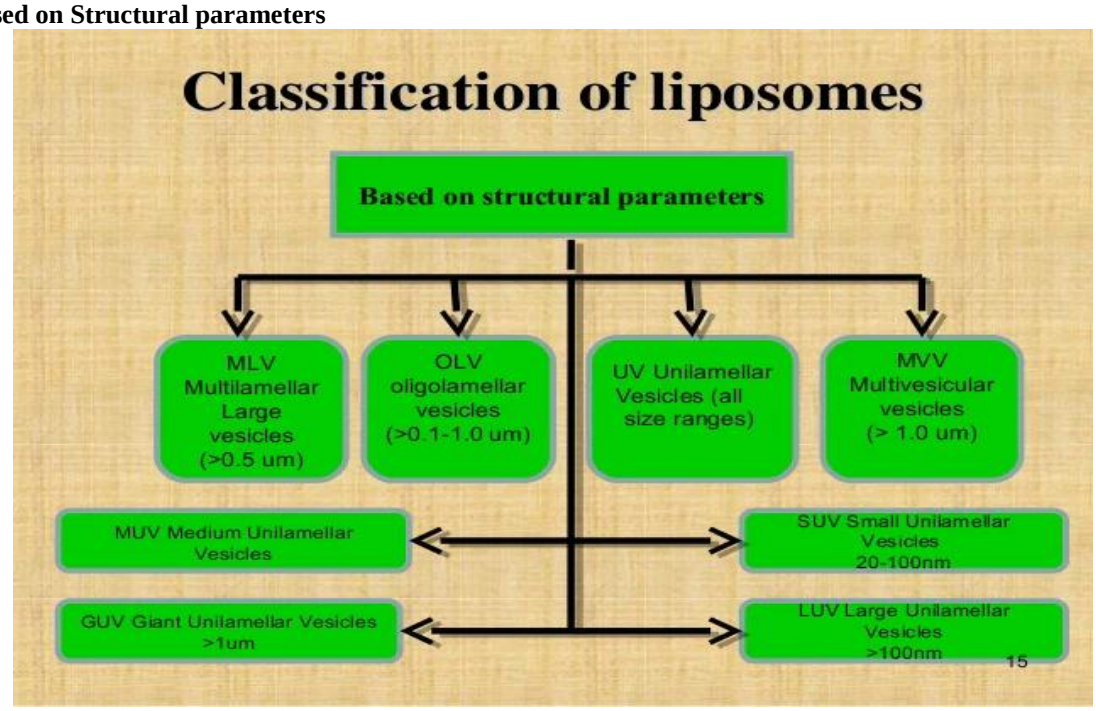

Fig:3

- **Based on method of preparation**

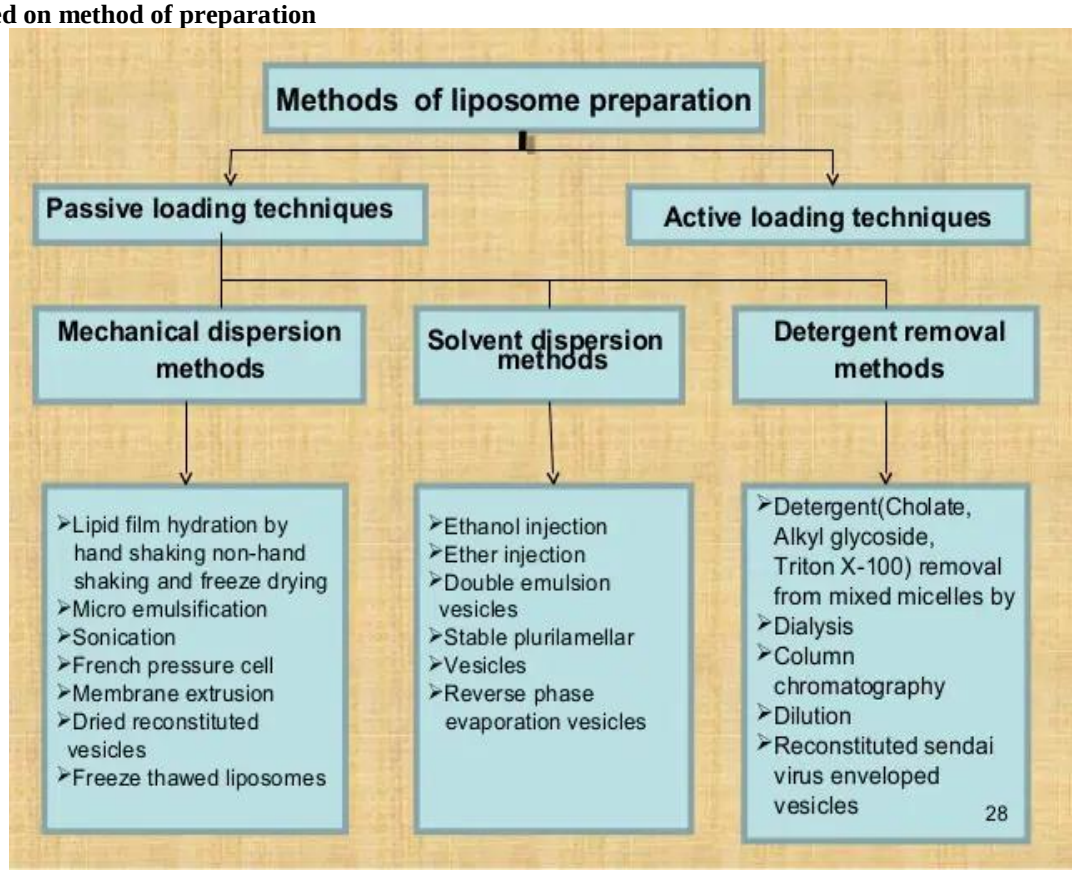

Fig:4

- **Based upon method of composition and application**

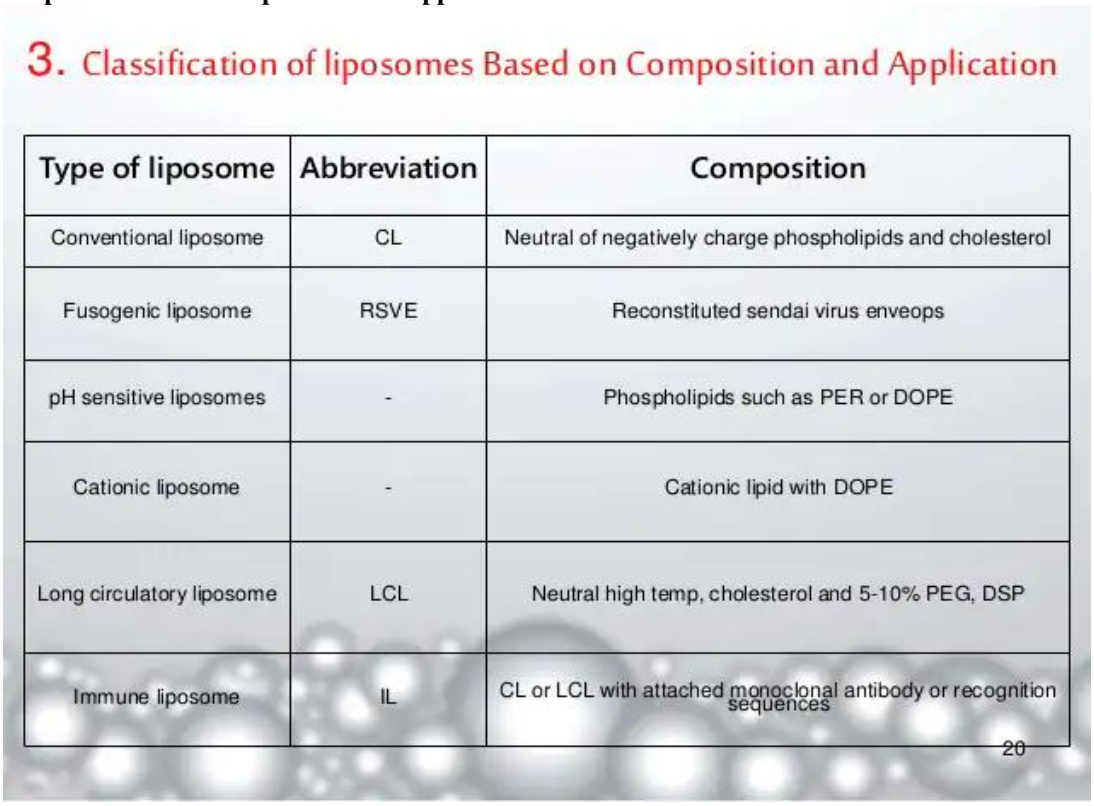

Fig:5

Advantages and disadvantages of liposomes

Table 1 Advantages and disadvantages of liposome [19]

Advantages of liposome	Disadvantages of liposome
Liposomes increased efficacy and therapeutic index of drug (actinomycin-D)	Low solubility
Liposome increased stability via encapsulation	Short half-life
Liposomes are non-toxic, flexible, biocompatible, completely biodegradable, and non-immunogenic for systemic and non-systemic administrations	Sometimes phospholipid undergoes oxidation and hydrolysis-like reaction
Liposomes reduce the toxicity of the encapsulated agent (amphotericin B, Taxol)	Leakage and fusion of encapsulated drug/ molecules
Liposomes help reduce the exposure of sensitive tissues to toxic drugs	Production cost is high
Site avoidance effect	Fewer stables
Flexibility to couple with site-specific ligands to achieve active targeting	

Applications of liposomes in medicine and Pharmacology

Applications of liposomes in medicine and pharmacology can be divided into diagnostic and therapeutic applications of liposomes containing various markers or drugs, and their use as a tool, a model, or reagent in the basic studies of cell interactions, recognition processes, and mode of action of certain substances.[25]

Unfortunately, many drugs have a very narrow therapeutic window, meaning that the therapeutic concentration is not much lower than the toxic one. In several cases, the toxicity can be reduced or the efficacy can be enhanced by the use of a suitable drug carrier which alters the temporal and spatial delivery of the drug, i.e., its biodistribution and pharmacokinetics. It is clear from many pre-clinical and clinical studies that drugs, for instance antitumor drugs, parceled in liposome demonstration reduced toxicities, while retentive enhanced efficacy.

Advances in liposome are leading to new applications for the delivery of new biotechnology products, for example antisense oligonucleotides, cloned genes, and recombinant proteins. A vast literature define the viability of formulating wide range of conservative drugs in liposomes, frequently resultant in improved therapeutic activity and/or reduced toxicity compared with the free drug. As a whole, changed pharmacokinetics for liposomal drugs can lead to improve drug bioavailability to particular target cell that live in the circulation, or more prominently, to extravascular disease sites, for example, tumors. Recent improvements include liposomal formulations of all-trans-retinoic acid[26,27] and daunorubicin[28-31], which has received Food and Drug Administration consent as a first-line treatment of AIDS-related advanced Kaposi`s sarcoma. Distinguished examples are vincristine, doxorubicin, and amphotericin B.[32]

PREPARATION OF LIPOSOMES[11-23]

- GENRAL METHOD OF PREPARATION
- SPECIFIC METHODS OF PREPARATION

A) GENERAL METHOD OF PREPARATION

The lipid is dissolved in organic solvent. The solvent is evaporated leaving a small film of lipids on the wall of the container. An aqueous solution of drug is added. In first procedure the mixture is agitated to produce multi lamellar vesicle and then sonicated to get SUVs. In the second procedure the mixture is sonicated and the solvent is evaporated to get LUVs. After extrusion SUVs are formed. Drug can be incorporated into the aqueous solution or buffer if it is water soluble or included in organic solvent if it is hydrophobic. Free drug and liposomes can be separated by gel chromatography.

B) SPECIFIC METHODS

These are classified as 3 types based on the modes of dispersion. They are

1. Physical Dispersion methods
2. Solvent Dispersion methods
3. Detergent Solubilization methods

1) PHYSICAL DISPERSION METHODS: In these methods the aqueous volumes enclosed within lipid membranes is about 5- 10%, which is very small proportion of total volume used for preparation. So large amount of water- soluble drug is wasted during preparation. But lipid soluble drug can be encapsulated to high percentage. In these methods, MLVs are formed and further treatment is required for preparation of Unilamellar vesicles.

Hand Shaken Method: This is the simplest and widely used method. The lipid mixture and charged components are dissolved in chloroform and methanol mixture (2:1 ratio) and then this mixture is introduced in to a 250 ml round bottom flask. The flask is attached to rotary evaporator connected with vacuum pump and rotated at 60 rpm. The organic solvents are evaporated at about 30 degrees. A dry residue is formed at the walls of the flask and rotation is continued for 15 minutes after dry residue appeared. The evaporator is detached from vacuum pump and nitrogen is introduced into it. The flask is then removed from evaporator and fixed onto lypholizer to remove residual solvent. Then the flask is again flushed with nitrogen and 5 ml of phosphate buffer is added. The flask is attached to evaporator again and rotated at about

60 rpm speed for 30 minutes or until all lipid has been removed from the wall of the flask. A milky white suspension is formed finally. The suspension is allowed to stand for 2 hours in order to complete swelling process to give MLVs.

Non-Shaking Method: This is similar to shaking method except that care is taken in swelling procedure. The solution of lipid in chloroform and methanol mixture is spread over the flat bottom of the conical flask. The solution is evaporated at room temperature by flow of nitrogen through the flask without disturbing the solution. After drying water saturated nitrogen is passed through the flask until the opacity of the dried film disappears. After hydration, lipid is swelled by addition of bulk liquid. The flask is inclined to one side, 10 to 20 ml of 0.2M sucrose in distilled water is introduced down the side of the flask and then flask is slowly returned to upright position. The solution is allowed to run gently over the lipid layer on the bottom of the flask. The flask is flushed with nitrogen sealed and allowed to stand for 2 hours at 37 degrees for swelling. After that the vesicles are mixed to yield a milky suspension. The suspension is centrifuged at 1200 rpm for 10 minutes. The layer of MLVs floating on the surface is removed. From the remaining fluid, LUVs are produced.

Freeze Drying: Another method of dispersing the lipid in a finally divided form prior to addition of aqueous media is to freeze dry the lipid dissolved in a suitable organic solvent. The solvent usually used is tertiary butanol. All the above methods produce MLVs. These are too large or too heterogeneous. In order to modify the size, the prepared MLVs are further processed using the following procedures.

PROCESSING OF LIPIDS HYDRATED BY PHYSICAL MEANS

Micro-emulsification of liposomes: An equipment called micro fluidizer is used to prepare small vesicles from concentrated lipid suspension. The lipids can be introduced in to the fluidizer as a suspension of large MLVs. This equipment pumps the fluid at very high pressure through 5micrometer, screen. Then it is forced long micro channels, which direct two streams of fluids collide together at right angles at very high velocity. The fluid collected can be recycled through the pump and interaction chamber until vesicles of spherical dimensions are obtain Sonication: This method reduces the size of the vesicles and imparts energy to lipid suspension. This can be achieved by exposing the MLV to ultrasonic irradiation. There are two methods of sonication.

A) using bath sonicator

B) using probe sonicator.

The probe sonicator is used for suspensions which require high energy in small volume. (eg: high concentration of lipids or viscous aqueous phase) The bath sonicator is used for large volume of dilute lipids. The disadvantage of probe sonicator is contamination of preparation with metal from tip of probe. By this method small unilamellar vesicles are formed and they are purified by ultra-centrifugation.

Membrane Extrusion Liposome: In this method the size is reduced by passing them through a membrane filter of defined pore size. There are two types of membrane filter. The tortuous path type and the nucleation track type. The former is used for sterile filtration. In this random path arise between the criss cross fibers. The average diameter of these fibers is controlled by the density of fibers in the matrix. Liposomes that are larger than the channel diameter get struck when one tries to pass them through such membrane. The nucleation track type is composed of thin continuous sheet of polycarbonate. They will offer less resistance to passage of liposomes as these consist of straight sided pore holes of exact diameter bored from one side to another. This method can be used to process both LUVs and MLVs.

Freeze and Thaw Sonication: This is a method in which rupture and refusing of UVs are done during which the solute equilibrates between the inside and outside. This process increases the entrapment volume and entrapment efficiency. This method will result in the formation of vesicles with in vesicled and vesicle between lamellae. This method can increase the entrapment volume upto 30%.

2) SOLVENT DISPERSION METHODS: In these methods lipids are first dissolved in an organic solution and then brought into contact with aqueous phase containing materials to be entrapped within liposome. At the interface between the organic and the aqueous phases the phospholipids align themselves to form a monolayer, which is important step to form the bilayer of liposome.

Ethanol injection method: This is simple method. In this method an ethanol solution of the lipids is directly injected rapidly to an excess of saline or other aqueous medium through a fine needle. The ethanol is diluted in water and phospholipids molecules are dispersed evenly through the medium. This procedure yields a high proportion of SUVs (about 25nm diameter).

Ether injection: This method is similar to above one. It involves injecting the immiscible organic solution very slowly into an aqueous phase through a narrow needle at temperature of vaporizing of organic solvent. In this method the lipids are carefully treated and there is very less risk of oxidative degradation. The disadvantage is that long time is required for the process and careful control is needed for introduction of lipid solution.

3) DETERGNT SOLUBILIZATION TECHNIQUE: In this method the phospholipids are brought into close contact with the aqueous phase via detergents, which associate with phospholipids molecules. The structures

formed as a result of this association are known as micelles. They are composed of several hundereds of component molecules. The concentration of detergent in water at which micelles start to form is called CMC. Below CMC the detergent molecule exist in free solution. As the detergent molecule is dissolved in water at concentrations higher than the CMC, micelle form in large amounts. As the concentration of detergent added is increased more amount of detergent is incorporated into the bilayer, until a point is reached where conversion from lamellar form to spherical micellar form take place. As detergent concentration is further increased, the micelles are reduced in size.

MECHANISM OF FORMATION OF LIPOSOMES[12-14]

Lipids capable of forming liposomes exhibit a dual chemical nature. Their head groups are hydrophilic and their fatty acyl chains are hydrophobic. It has been estimated that each Zwitter ionic head group of Phosphatidyl choline has on the order of 15 molecules of water weakly bound to it, which explain it's over whelming preference for the water phase. The hydrocarbon fatty acid chains on the other hand vastly prefer each other company to that of H2O. This can be understood by taking the CMC of P.C into account. The CMC of Dipalmitoyl P. found to be 4.6 –10 M in water, which is a small number indicating the over whelming preference of this molecule for a hydrophobic environment such as that found in the core of micelle or bilayer. The free energy of transfer from water to micelle is 15.3 Kcal/mol for Dipalmitoyl PC and13.0Kcal/mol for Dimyristoyl P.C. These results clearly point out the thermodynamic basis for bilayer assembly that has been termed the hydrophobic effect. The large free energy change between a water and a hydrophobic environment explains the over whelming preference of typical lipids to assemble in bilayer structures, including water as much is possible from the hydrophobic core in order to achieve the lowest energy level, hence the highest stability for the aggregate structure.

List of marketed Product of liposomes

Brand name	Active constituent	Manufacturer
Intelectol®	Vinpocetine	Menory Secret Inc., USA
Efudex®	N3-o-toluyl-Fluorouracil	Valeant Pharma. Intl, USA
Amphocil®	Amphotericin B	Sequus Pharmaceuticals, Inc., C.A
Abelcet®	Amphotericin B	Liposome Company NJ,USA
MiKasome®	Amikacin	NeXstar Pharmceuticals, Inc., Co
Ambisome®	Amphotericin B	NeXstar Pharmceuticals, Inc., Co
DaunoXome®	Daunorubicin	NeXstar Pharmceuticals, Inc., Co
ELA-MAX®	Lidocaine	Biozone Labs, CA, USA
Epaxel®	Hepatitis A Vaccine	Swiss SerumInstitute, Switzerland
Lipofen®	Fenofibrate	Kowa Pharma Inc., USA
DC99®	Doxorubicin	Liposome Company NJ, USA
Doxil®	Doxorubicin	Sequus Pharmaceuticals, Inc., C.A
Ambisome®	Amphotericin B	Astellas Pharma Inc., USA

Source: Ravi et al. (2011) and Sharma et al. (2010).

CONCLUSION

Liposomes have been used in a broad range of pharmaceutical applications. Liposomes are showing particular promise as intracellular delivery systems for anti-sense molecules, ribosomes, proteins/peptides, and DNA. Liposomes with enhanced drug delivery to disease locations, by ability of long circulation residence times, are now achieving clinical acceptance. Also, liposomes promote targeting of particular diseased cells within the disease site. Finally, liposomal drugs exhibit reduced toxicities and retain enhanced efficacy compared with free complements. Only time will tell which of the above applications and speculations will prove to be successful. However, based on the pharmaceutical applications and available products, we can say that liposomes have definitely established their position in modern delivery system.

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Depression: Its Causes and Treatment –A Review

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Abstract - *Depression is the biggest sickness and can be the maximum focused factor of studies for researchers in India. India proving numerous elements of this common disorder. People may be sad and concerned of their life because of conditions going on of their life which includes checks, problems with own family or friends, monetary problems, fitness troubles. If the emotions of unhappiness move on for weeks or months and affect their lives each day, then someone may also have despair. Symptoms of melancholy in humans are feeling grumpy, problem sound asleep, feeling vain or responsible. Here, in this Research Paper, we can evaluate melancholy with various components. The search for extended know-how of the causes of depression, and the improvement of additional effective treatments is especially enormous. Clinical and pre-scientific research recommends strain as a key mediator inside the pathophysiology of depression.*

***Key Words*: Depression, Treatment, Antidepressant, Remedy.**

1. INTRODUCTION

Most people feel depressed now and again. Losing a friend or family member, finding terminated from a line of work, going through a separation, and other tough spots can lead an individual to feel miserable, forlorn, terrified, apprehensive, or restless. Depression is something other than pity. It meddles with day by day life and causes torment for you and each and every individual who thinks often about you. It's a typical ailment, however an intense one. The expression "sorrow" frequently describes sensations of being pitiful, debilitate, miserable, bad tempered, unmotivated, just as an overall absence of interest or delight throughout everyday life. At the point when these sentiments keep going for a brief timeframe, it could be known as a passing instance of "the blues." But it's probably going to be a burdensome problem when they keep going for over about fourteen days and meddle with standard every day exercises[1].

We depict depression in radical conduct terms, underlining the events on which the term is utilized and deemphasizing any basic unitary infection, physiological, or enthusiastic state to which the term alludes. Depression comes from the Late Latin word depressare and the old style Latin word deprimere. Depression in youth is a typical emotional wellness infection with predominance of 4–5% in mid to late pre-adulthood. It is a significant danger factor for self destruction and can likewise prompt social and instructive impedances. Therefore, recognizing and treating this issue is critical. General specialists and essential consideration suppliers are every now and again the first line of contact for teenagers in quite a while of pain and can be critical to distinguish emotional wellness issues among these patients. They can work with early distinguishing proof of discouragement, start treatment and allude the youths for emotional well-being experts [2]. Make an ideal and exact determination of melancholy in puberty and a right differential conclusion from other mental issues, because of the repetitive idea of this condition and its relationship with helpless scholastic execution, utilitarian weakness and risky associations with guardians, kin and companions[2].

According to WHO, depression shall become the second large disorder in terms of oppression in the future already one out of every twelve men, and five women have depression. Not only adults, but two percent of school children and five percent of teenagers are also affected by depression, and most of the cases are not identified. Depression has been the most common reason behind the rising demand for a psychiatrist, although the ordinary human approach is that all psychological problems are depression. The most common myth seen in the patient related to depression that it is because of some personality weakness or that one can cure it individually by medication or taking sedatives[3]. Depression is a typical mental problem that presents with discouraged disposition, loss of interest or joy, diminished energy, sensations of blame or low self-esteem, upset rest or craving, and helpless focus. Roughly, 350 million individuals are right now living with gloom. It is the fourth driving reason for incapacity around the world. Its lifetime predominance was one out of five ladies and one out of ten men[4]. Post pregnancy anxiety is the exceptional, supported, and periodically weakening melancholy that numerous ladies experience following labor. It is assessed that upwards of 10 to 15 percent of all ladies experience some type of post pregnancy anxiety, which onsets inside 90 days of conveyance. Breastfeeding ladies should know about taking just certain antidepressants[5]. Depression is one of the ultimate natural psychological disorders. Likewise, 15% of the population suffering at least one period of depression in advanced countries in their lifetime. The relationship between the mother and the child in childhood has been exposed to play an important role in neurodevelopment and nature feedback in adulthood. Parental care in early life is combining with advanced biological behavior and psychological advancement and subsequently raises social adjustment. Experience, unfortunately, events like maternal

separation in the initial stages of life have negativity on behavior and brain improvement and probably move as a risk factor for a psychological disorder like adulthood. Monoamine, serotonin or 5-hydroxytryptamine (5-HT) they are important neurotransmitters in the path physiology of depression disorder and are also associate in the mechanism of action which is used in antidepressant[6].

Examine in both animal and analytic models have presented that serotonin deficiency plays a role in depression in the CNS(central nervous system).5HT-3 receptors influence various biological and neurological processes such as aggression, anxiety, appetite, cognition, learning, memory, mood, and thermoregulation. Studies advise that the 5-HT3 receptor, as an ion channel ligand, is present in brain development and maturation. 5HT3 receptors are extensively located in the CNS and control different functions and various brain processes. The early studies fine represent that the 5-HT3 receptor antagonists were ondansetron and tropisetron, possessed antidepressant-like properties in an animal model of depression. Nonetheless, the specific components that are engaged with the stimulant like impact of tropisetron have not been completely resolved. Adenylyl cyclase (AC) is a catalyst that changes ATP over to cAMP [17, 18]. Various investigations have shown that AC is associated with the pathophysiology of discouragement [19, 20]. Platelet AC movement has been displayed to go about as a natural marker for the assessment of the burdensome state. This depends on the way that individuals with a background marked by melancholy have lower levels of platelet AC action. Forskolin is one of the AC agonists that increment the development of intracellular cAMP. Past investigations have showed that forskolin can be considered as a specialist with potential stimulant impact. Taking into account that tropisetron applied a stimulant like impact and furthermore inclusion of AC in the pathophysiology of misery, the current examination is intended to assess the conceivable association of AC in the energizer like impact of tropisetron on a mouse model of MS-instigated discouragement. Specialists were infused one hour before the conduct tests[6].

1.1 Types of depression

Burdensome sickness comes in various structures, similarly as numerous different diseases.

i. Major depression is showed by a mix of indications that meddle with the capacity to work, rest, eat and appreciate once pleasurable exercises. These impairing scenes of gloom can happen once, twice, or a few times in a lifetime[3]. Major depressive problem, or clinical discouragement, happens when an individual has at least one major depressive scenes. One occasion gets the finding—"Major Depressive Problem (single scene)"— while at least two scenes are renamed as "Major Depressive Issue (Intermittent)". Depressive problems are oftentimes undetected. A few subtypes of depressive issue included: Abnormal wretchedness, melancholic sadness, maniacal major gloom, mental despondency, occasional emotional issue, dysthymia, depressive behavioral condition, and post birth anxiety. Post pregnancy anxiety is the exceptional, supported, and periodically weakening melancholy that numerous ladies experience following labor. It is assessed that upwards of 10 to 15 percent of all ladies experience some type of post pregnancy anxiety, which onsets inside 90 days of conveyance. Breastfeeding ladies should know about taking just certain antidepressants[5].

ii. Dysthymia, a less severe type of depression, involves long-term, chronic symptoms that do not disable but keep you from functioning at "full steam" or from feeling good. Sometimes people with dysthymia also experience major depressive episodes

Persistent depressive disorder, or PDD, Is a type of depression that usually maintains for at least two years. Although it's miles much less severe than most important despair, it involves the same signs; sad temper blended with low electricity, bad appetite or overeating, and insomnia or oversleeping. It can display up as strain, irritability, and mild anhedonia that is the incapability to derive satisfaction from most activities[1].

iii. Manic-depressive or bipolar isn't nearly as normal as other sorts of depressive ailments. It includes cycles of depression and elation or mania. Sometimes the mood switches are dramatic and speedy; however, most often they're sluggish. When within the depressed cycle, one may have any or all different signs and symptoms of a depressive illness. When within the manic cycle, any or all signs and symptoms listed under mania can be skilled. Mania regularly impacts thinking, judgment, and social behavior in ways that could cause serious issues and embarrassment[3].

2. PREVALENCE OF DEPRESSION

WHO estimates that of the 322 million human beings affected with depression international, the following is the region-wise share?

Southeast Asia Region 27%
Western Pacific Region 21%
Eastern Mediterranean Region 16%
Region of the Americas 15%
European Region 12%
African area 9%

Depression is with the aid of some distance greater not unusual in girls everywhere in the international. However, if we see the occurrence of depressive disorders via a percent of the populace, girls in the African Region and Region of the Americas exceed the sector figure of 5.2% of girls tormented by depressive issues.

Globally, depression is most commonplace in the age organization of 60-sixty four years in ladies as well as men.

As in line with the Global Burden of Disease Study 2015, the prevalence of despair by way of a percentage of the population in the African Region and Region of the Americas some distance exceeds the sector average of 4 %[7].

3. INDIAN SCENARIO

Mental health has been recognized as a country of nicely-being in which the man or woman realizes his or her own abilities, can deal with the normal stresses of lifestyles, can work productively and fruitfully, and is capable of contributing to his or her community.

In India, joint family device aid keeps absorbing many ill effects of disorder and offers stable environments for shaping and developing lifestyles and character traits. This guide is gradually diminishing due to urbanization and industrialization and the migration of young humans to urban regions. Because of the strain and pressure of existence; unemployed teens; and disturbed intercourse ratio; mental problems are on the rise. ICMR has mentioned extreme mental morbidity starting from 4.6 to fourteen.1/one thousand. As in keeping with Ganglia (2000), the prevalence price of affective disorders in India is 34/1000 populace at danger. Prevalence prices are notably higher in city regions compared to rural regions, girls as compared to adult males, and nuclear households as compared to joint families.

Due to sizeable social stigma and social discrimination human beings do now not even expose the sickness to the close to and dear ones till they emerge as unmanageable. Existing mental health offerings are alas lacking in India- much less than one psychiatrist is to be had for each three lakh populace in India and 1 in keeping with million in rural regions. Even the to be had offerings for mental problems are being poorly utilized- almost two-thirds of persons with recognized intellectual problems never are searching for help from health experts and maximum customers make use of the services of different corporations and lodge to dangerous practices- maintain on touring religion healers and postpone the remedy until the condition deteriorates which compels them to are trying to find remedy from established government establishments. 'Mental Health Literacy' wishes to be constructed up strongly in the community to scale up the utilization of to be had mental health offerings and to lessen the remedy gap.

In India, a total of 56,675,969 cases of depression have been identified using WHO with an occurrence of 4, 5% of the populace. The fitness loss/ Disease Burden quantities to 10,050,411 Total Years Lived with Disability and 7.1% of total YLD[7].

4. SYMPTOMS OF DEPRESSION

Not everyone who is depressed or manic revel in every symptom. Some may also experience some signs and symptoms. Also, the severity of signs may vary with individuals.

A depression sign includes:

- Feelings of unhappiness or unhappiness
- Irritability or frustration
- Loss of interest or delight in normal sports
- Reduced sex drive
- Insomnia or excessive sound asleep
- Changes in appetite — melancholy often reasons reduced appetite and weight reduction, but in some human beings, it reasons elevated cravings for meals and weight advantage
- Agitation or restlessness — for example, pacing, hand-wringing, or an incapacity to take a seat still
- Irritability or indignant outbursts
- Slowed wondering, talking, or frame movements
- Indecisiveness, distractibility, and reduced awareness
- Fatigue, tiredness, and loss of electricity — even small tasks may additionally appear to require quite a few attempts
- Feelings of worthlessness or guilt, fixating on beyond failures or blaming yourself while matters are not going proper
- Trouble wondering, concentrating, making selections, and remembering matters
- Frequent thoughts of death, dying, or suicide
- Crying spells for no apparent purpose
- Unexplained physical troubles, along with returned ache or headaches Depression impacts absolutely everyone in one-of-a-kind methods, so signs and symptoms as a result of melancholy range from character to person. Inherited tendencies, age, gender, and cultural background all play a role in how despair can also affect you.

4.1 Depression symptoms in children and teens

Common signs of depression may be a bit distinctive in youngsters and teens than they may be in adults.

- In younger kids, signs and symptoms of despair may include sadness, irritability, hopelessness, and fear.
- Symptoms in teenagers and teens may additionally encompass anxiety, anger, and avoidance of social interplay.
- Changes in wondering and sleep are commonplace symptoms of melancholy in young people and adults but are not as commonplace in younger kids.
- In youngsters and teenagers, despair frequently occurs at the side of conduct problems and different mental health conditions, which include tension or attention-deficit/hyperactivity sickness (ADHD).
- Schoolwork can also suffer in kids who are depressed[8].

5. CAUSES OF DEPRESSION

5.1. Genetic Causes of Depression

In current years, the aggregate of advances in our understanding of human genomic variation and cost-powerful genotyping techniques haveled to amazing increase in molecular genetic studies of despair and other "complex" psychiatric phenotypes. These studies generally have a look at whether unique alleles or genotypes are associated with the phenotype of hobby. Until lately, genetic studies of melancholy targeted largely on candidate genes, or genes hypothesized to be implicated inside the neurobiology of depression. Some of the most typically studied candidate genes have been those regulating serotonin (5-HT) and dopamine (DA) neurotransmission, given the suspected involvement of those neurotransmitters within the pathophysiology of despair and the fact that these are objectives of antidepressant drugs. Unfortunately, maximum candidate gene studies were underpowered and replication of findings has been rare. More lately, the availability of DNA microarrays have enabled genomewide association studies (GWAS) that don't depend upon earlier hypotheses. The GWAS approach permits for the analysis of 1,000,000 or greater editions across the complete genome. The remaining goal of those genetic association studies is to improve diagnosis, prevention, and remedy via a nuanced knowledge of the genetic underpinnings of the ailment[9].

Much of what we understand approximately the genetic have an impact on scientific melancholy is based upon research that has been executed with equal twins. Identical twins are very beneficial to researchers given that they each have an exact equal genetic code. It has been located that after one same dual will become depressed the other can even increase medical depression about 76% of the time. When equal twins are raised aside from each other, they may each end up depressed about 67% of the time. Because both twins emerge as depressed at one of these excessive prices, the implication is that there may be a robust genetic impact. If it befell that once one twin turns into clinically depressed the other continually develops despair, then scientific despair could probable be totally genetic. However, due to the fact, the charge of each equal twin developing melancholy is not toward 100% this tells us that other matters impact someone's vulnerability to depression. These may additionally include environmental elements such as childhood stories, current stressors, worrying events, publicity to materials, medical ailments, and so forth[3].

5.2. Environmental Causes of Depression

Environmental reasons of melancholy consist of events consisting of stress, disturbing events, and formative year's problems. These are events that can manifest to all of us and they occur all through our everyday lives. They are considered elements that are outside people. Some researchers talk to those occasions as sociological or psychosocial elements because they may be a "meeting" or "mixture" of activities that occur in society and the function and workings of human thoughts. Researchers have recognized for some time that the studies (occasions) we've in our lives can and do affect our intellectual fitness. Thoughts, feelings, and behaviors of humans are motivated using the previous reviews in their lives. These stories can consist of beyond relationships, formative years improvement, and beyond crises. The key to the development of clinical depression in a few humans seems to be how they react to the various environmental causes or elements in their regular lives.

- Stress
- Traumatic Events
- Childhood Difficulties
- Noise Pollution
- Natural And Catastrophic Disasters[10]

6. TREATMENT

Regardless of the medication that can be used to deal with despair, practitioners have turned out to be greater aware that particular ethnic organizations may have one-of-a-type responses and characteristic unique dangers for thing results than others[11].

6.1 Types of remedy: - Support: This can range from discussing sensible answers and viable reasons to teaching own family participants.

Psychotherapy

Also called speakme therapy, a few alternatives consist of one-to-one counseling and cognitive behavioral therapy (CBT)[12].

Psychotherapy is often called "talk therapy." There are diverse strategies for psychotherapy. Many therapists specialize in a particular sort of therapy to deal with depression, however from time to time they pull from more than one procedure to create an extra individualized remedy this is based on your precise remedy needs.

Interpersonal Therapy

The interpersonal remedy is based totally on the concept that depression may be associated with our relationships. Therefore, the intention of this kind of therapy is that will help you improve your relationship skills, such as becoming a higher communicator.

Cognitive Behavioral Therapy

Cognitive-behavioral remedy (CBT) is a shape of talk remedy designed that will help you alternate any bad idea or conduct styles that may be contributing to or worsening your despair. This therapy is also typically short-term and makes a specialty of your present-day issues and learning new coping competencies.

Social Skills Training
Social abilities schooling teaches you a way to have interact with others extra effectively so that you could have healthy relationships. The intention is to enhance your communication skills and learn how to build a robust social network with others, which includes creating relationships primarily based on honesty and admire
Psychodynamic Therapy
The psychodynamic remedy is in the form of remedy regularly portrayed in films or popular culture. During those remedy classes, you learn how your depression can be related to stories, unresolved conflicts, or unhealed wounds. The therapist will assist you to cope with those troubles so you can flow forward in your lifestyle.
Supportive Counseling
Supportive counseling is much less structured than many alternative treatment plans and especially involves listening to you share whatever is for your thoughts. You are invited to talk approximately any issues you want and the therapist works with you to expose information and assist.
Behavioral Activation
Behavioral activation teaches you the way to set dreams and consist of extra satisfactory sports on your lifestyle. This remedy aims to keep away from.
Problem-Solving Therapy
Problem-solving therapy pursuits outline your maximum urgent issues, then publications you to give you a couple of approaches to triumph over them. The therapist compares all your alternatives and selects a great solution for you.
Family or Couples Therapy
Family or couples remedy may be taken into consideration when melancholy affects others in the household. This includes looking at each of your roles and expectations. This form of remedy additionally entails educating your cherished ones about melancholy and the way it impacts you.
Drug remedy: A medical doctor may also prescribe antidepressants[13].

6.2. Medication

Antidepressants can help deal with mild to severe despair. Several lessons of antidepressants are to be had:

- Selective serotonin reuptake inhibitors (SSRIs)
- Monoamine oxidase inhibitors (MAOIs)
- Tricycle antidepressants
- Peculiar antidepressants

Selective serotonin and norepinephrine reuptake inhibitors (SNRIs)
Each elegance acts on a distinctive neurotransmitter or combination of neurotransmitters.
Raise any issues about antidepressants with a doctor, including any purpose to prevent taking the medication. Here, learn greater about antidepressants and how they can help.

6.3 Mechanism of Action (Moa): - Antidepressant drugs Selective serotonin reuptake inhibitors (SSRIs) are the drug treatments that increase the amount of the neurochemical serotonin within the brain. As there, all implies the SSRIs paintings by using selectively inhibiting (blockading) serotonin reuptake inside the mind. This block happens at the synapse, the place in which thoughts cells (neurons) are related to each extraordinary. Serotonin is one of the chemical substances inside the mind that consists of messages in the course of those connections (synapses) from one neuron to each another. The SSRIs paintings through keeping serotonin discovered in immoderate concentrations inside the synapses. These tablets try this by using preventing the reuptake of serotonin once more into the sending nerve cellular. The reuptake of serotonin is accountable for turning off the manufacturing of recent serotonin. Therefore, the serotonin message keeps coming through. It is a notion that this, in turn, permits arousing cells that have been deactivated utilizing depression, thereby relieving the depressed character's signs. SSRIs have fewer factor effects than tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs), which can be mentioned underneath. SSRIs do no longer engage with the chemical tyramine in meals, as do the MAOIs, and consequently do not require the dietary regulations of the MAOIs. Also, SSRIs do not purpose orthostatic hypotension and coronary heart-rhythm disturbances, similar to the TCAs do. Therefore, SSRIs are often the number one-line treatment for melancholy. Examples of SSRIs include fluoxetine (Prozac), paroxetine (Paxil), sertraline (Zoloft), citalopram (Celexa), fluvoxamine.
Medication aspect effects
SSRIs and SNRIs may have aspect consequences. A character may also experience:

- Nausea
- Constipation
- Diarrhea
- Low Blood Sugar
- Weight Loss
- A Rash sexual dysfunction[14]

6.3 Side effects for Prolong Treatment

According to statistics, as much as 50% of all adults who be afflicted by essential depression don't are searching for any assistance.
Aside from that, a few of those who do get help may revel in a relapse of their circumstance, making depressive episodes a lifelong infection.
Depression conditions the frame and the mind insure ways, making some of its symptoms crippling based totally on the severity of the disorder.
But even then, when melancholy is going untreated, resurfaces regularly, or certainly lasts longer than expected, it can have devastating outcomes which can damage people for years to come[15].
The antidepressants are important for the remedy of depressive episodes in the extreme phase whilst untreated signs are at their worst. With long-time period use, however, the mind units to paintings compensating for the drug-

brought about changes with a system he calls oppositional tolerance. The mind tries to re-set up its typical stability of manufacturing, release, and reuptake of neurotransmitters – as each device of the body does while its regular functioning has been disturbed. The concept is that if the drugs artificially jack up the mind's level of serotonin or norepinephrine, the neurobiology of the machine reacts with the aid of lowering its own manufacturing of the neurotransmitter. In other phrases, if antidepressant use maintains long sufficient, the brain will create a gadget to cancel out its impact. There is a possibility that antidepressant use itself might be causing the problem. There are specific neurobiological reactions that would account for the emergence of higher ranges of resistance to treatment. In addition, there's proof that stopping antidepressants in folks who do not respond to them can cause a reversal of symptoms because the brain compensates another time, this time for the withdrawal of the drugs. For a few people, but, preventing the drugs has no impact. They maintain to have ordinary despair. If antidepressant treatment is restored as a reaction, those sufferers can develop completely ordinary contamination. This is tardive dysphoria[3] **(Depression – a Review Iyer K. and Khan Z.A.)** .Some of those outcomes might be irreversible.

Here are five of the lengthy-time period effects of melancholy on the mind and the body.

- Sleeping disorders
- Heart Disease
- Weight fluctuation and eating disorders
- Psychiatric disorders
- Social risks[15]

7. CONCLUSION

Nowadays, Depression is one of the most common disorders in primary care. The price of morbidity and mortality is higher because of Depression when it is left untreated. Most patients stricken by despair do not share that they're feeling depressed, but their unhappiness and anxiety explained all signs and symptoms. Although the development of depression is likely due to a combination of things, expertise the outcomes, possible triggers, and remedies of the disorder are essential for promoting the well-being of affected people. There is likewise a need to observe the route of depressive issues present within the world to determine the want and duration of continuation remedy. Prevention, early prognosis, and remedy of depression in youth should be considered worldwide goals, and the implementation of straightforward, powerful, and fee-conscious techniques for reaching such functions is essential. Amongst those targets, prevention is of utter significance and has to be a priority when defining political strategies and governmental programs associated with mental fitness. Studies should also evaluate the cost-effective models of treatment which can be easily used in the primary care setting to effectively treat depression.

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BIOGRAPHIES

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An Overview Of Diabetes:Review

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ABSTRACT
Diabetes mellitus is a fast-growing Global problem with huge health, social and economic consequences. Globally an estimated 463 million adults are living with diabetes, according to the latest 2019 data from the International Diabetes Federation. Diabetes prevalence is increasing rapidly; previous 2017 estimates put the number at 425 million people living with diabetes. The number is projected to almost double by 2030. This chapter introduces the types of diabetes, symptoms, treatment, causes, diagnosis and epidemiology of diabetes.

Keywords: - Diabetes, glucose, insulin, hyperglycemia

I. INTRODUCTION

Diabetes is a disease that occurs when the blood glucose, also called blood sugar, is too high. Blood glucose is the main source of energy and comes from the food we eat. Insulin, a hormone made by the pancreas, helps glucose from food get into our cells to be used for energy. Sometimes our body doesn't make enough—or any—insulin or doesn't use insulin well. Glucose then stays in the blood and doesn't reach the cells. When the amount of glucose in the blood increases, e.g., after a meal, it triggers the release of the hormone insulin from the pancreas. Insulin stimulates muscle and fat cells to remove glucose from the blood and stimulates the liver to metabolize glucose, causing the blood sugar level to decrease to normal levels.
In people with diabetes, blood sugar levels remain high. This may be because insulin is not being produced at all, is not made at sufficient levels, or is not as effective as it should be. The most common forms of diabetes are type 1 diabetes (5%), which is an autoimmune disorder, and type 2 diabetes (95%), which is associated with obesity. Gestational diabetes is a form of diabetes that occurs in pregnancy, and other forms of diabetes are very rare and are caused by a single gene mutation.

CLASSIFICATION

Diabetes is classified by underlying cause. The categories are:
I.Type 1 diabetes
II.type 2 diabetes
III. Gestational diabetes

I. Type 1 diabetes

WHAT IS TYPE 1 DIABETES?
Type 1 diabetes (T1D), previously known as juvenile diabetes, is an autoimmune disease that is a form of diabetes in which very little or no insulin is produced by the islets of Langerhans (containing beta cells) in the pancreas.Insulin is a hormone required for the cells to use blood sugar for energy and it helps regulate normal glucose levels in the bloodstream.
Type 1 diabetes is a condition in which our immune system destroys insulin-making cells in your pancreas. These are called beta cells. The condition is usually diagnosed in children and young people, so it used to be called juvenile diabetes.
Both of these are different from type 2 diabetes, in which the body doesn't respond to insulin the way it should.

SYMPTOMS

Signs are often subtle, but they can become severe. They include:
1. Extreme thirst
2. Increased hunger (especially after eating)
3. Dry mouth
4. Upset stomach and vomiting
5. Frequent urination
6. Unexplained weight loss, even though eating and feel hungry
7. Fatigue

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8. Blurry vision
9. Heavy, labored breathing
10. Frequent infections of the skin, urinary tract, or vagina
11. Crankiness or mood changes
12. Bedwetting in a child who's been dry at night
13. Signs of an emergency with type 1 diabetes include:
14. Shaking and confusion
15. Rapid breathing
16. Fruity smell of the breath
17. Belly pain
18. Loss of consciousness (rare)

Type 1 Diabetes Causes

Insulin is a hormone that helps move sugar, or glucose, into the body's tissues. The cells use it as fuel.

Damage to beta cells from type 1 diabetes throws the process off. Glucose doesn't move into the cells because insulin isn't there to do the job. Instead, it builds up in the blood, and cells starve. This causes high blood sugar, which can lead to:

Dehydration. When there's extra sugar in the blood, we pee more. That's our body's way of getting rid of it. A large amount of water goes out with that urine, causing our body to dry out.

Weight loss. The glucose that goes out when we pee takes calories with it. That's why many people with high blood sugar lose weight. Dehydration also plays a part.

Diabetic ketoacidosis (DKA). If the body can't get enough glucose for fuel, it breaks down fat cells instead. This creates chemicals called ketones. Our liver releases the sugar it stores to help out. But the body can't use it without insulin, so it builds up in our blood, along with the acidic ketones. This mix of extra glucose, dehydration, and acid buildup is known as ketoacidosis and can be life-threatening if not treated right away. Damage to our body. Over time, high glucose levels in our blood can harm the nerves and small blood vessels in our eyes, kidneys, and heart. They can also make us more likely to get hardened arteries, or atherosclerosis, which can lead to heart attacks and strokes.

We can get type 1 diabetes when something around us, like a virus, tells our immune system to go after our pancreas. Most people with type 1 diabetes have signs of this attack, called autoantibodies.

Type 1 Diabetes Risk Factors

Only about 5% of people with diabetes have type 1. It affects males and females equally. There is high risk of getting it if we:

1. Are younger than 20
2. Are white
3. Have a parent or sibling with type 1

Type 1 Diabetes Diagnosis

Diagnostic tests include:

Diagnosis of diabetes has historically included fasting blood glucose higher than 7 mmol/L (126 mg/dL), any blood glucose of 11·1 mmol/L (200 mg/dL) or higher with symptoms of hyperglycaemia, or an abnormal 2 horal glucose-tolerance test. In 2009, the American Diabetes Association modified their guidelines for diabetes diagnosis to include glycated haemoglobin (HbA_{1C}; a test that averages blood glucose concentrations over 3 months) of 6·5% or higher. Despite efforts to standardise diagnosis oftype 1 diagnosis, the causes and typology remain unclear. Particularly among adults, diagnosis of type 1 versus type 2 diabetes can be challenging. Around 5–15% of adults diagnosed with type 2 diabetes might actually have type 1 disease with islet autoantibodies present;if this is the case, perhaps as many as 50% of actual type 1 diabetes cases are misdiagnosed as type 2, meaning that the number of cases of type 1 disease is vastly underestimated. Accurate diagnosis of this disorder is crucial foroptimum care and avoiding complications, and correctly noting diabetic ketoacidosis at diagnosis of type 1 disease represents a key window for survival.

II. TYPE 2 DIABETES

Type 2 diabetes is a lifelong disease that keeps the body from using insulin the way it should. It is the most common type of diabetes.People with type 2 diabetes are said to have insulin resistance.

People who are middle-aged or older are most likely to get this kind of diabetes. It used to be called adult-onset diabetes. But type 2 diabetes also affects kids and teens, mainly because of childhood obesity.

Type 2 diabetes are so mild that we cannot notice them. Symptoms include:

1. Being very thirsty
2. Peeing a lot
3. Blurry vision
4. Being cranky

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5. Tingling or numbness in the hands or feet
6. Fatigue/feeling worn out
7. Wounds that don't heal
8. Yeast infections that keep coming back
9. Feeling hungry
10. Weight loss without trying
11. Getting more infections
12. Dark rashes around neck and armpits can sometimes be signs that body is becomingresistant to insulin.

Causes of Type 2 Diabetes

The pancreas makes a hormone called insulin. It helps our cells turn glucose, a type of sugar, from the food we eat into energy. People with type 2 diabetes make insulin, but their cells don't use it as well as they should. At first, the pancreas makes more insulin to try to get glucose into our cells. But eventually, it can't keep up, and the glucose builds up in our blood instead.

Usually, a combination of things causes type 2 diabetes. They might include: Genes. Scientists have found different bits of DNA that affect how our body makes insulin. Extra weight. Being overweight or obese can cause insulin resistance, especially if we carry our extra pounds around our middle.

Metabolic syndrome. People with insulin resistance often have a group of conditions including high blood sugar, extra fat around the waist, high blood pressure, and high cholesterol and triglycerides.

Too much glucose from our liver. When the blood sugar is low, our liver makes and sends out glucose. After we eat, our blood sugar goes up, and our liver will usually slow down and store its glucose for later. But some people's livers don't. They keep cranking out sugar.

Bad communication between cells. Sometimes, cells send the wrong signals or don't pick up messages correctly. When these problems affect how our cells make and use insulin or glucose, a chain reaction can lead to diabetes.

Type 2 Diabetes Risk Factors

Certain things make it more likely that we'll get type 2 diabetes. The more of these that apply to us, the higher our chances of getting it are. Some things are related to who we are:

Age. 45 or older

Family. A parent, sister, or brother with diabetes

Risk factors related to our health and medical history include:

1. Prediabetes
2. Heart and blood vessel disease

3. High blood pressure, even if it's treated and under control

4. Low HDL ("good") cholesterol

5. High triglycerides

6. Being overweight or obese

7. Having a baby who weighed more than 9 pounds

8. Gestational diabetes while you were pregnant

9. Polycystic ovary syndrome (PCOS)

10. Depression

Other things that raise risk of diabetes have to do with daily habits and lifestyle. These includes:

1. Getting little or no exercise

2. Smoking

3. Stress

4. Sleeping too little or too much

Type 2 Diabetes Diagnosis and Tests

Doctor can test blood for signs of type 2 diabetesTest on 2 days to confirm the diagnosis. But if blood glucose is very high or the patient have many symptoms, one test may be all they need.

A1c. It's like an average of blood glucose over the past 2 or 3 months.

Fasting plasma glucose.this is also known as a fasting blood sugar test. It measures blood sugar on an empty stomach. The patient won't be able to eat or drink anything except water for 8 hours before the test.

Oral glucose tolerance test (OGTT). This checks blood glucose before and 2 hours after drinking something sweet to see how your body handles the sugar.

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III.GESTATIONAL DIABETES

What Is Gestational Diabetes?

Gestational diabetes is a condition in which the blood sugar levels become high during pregnancy. It affects up to 10% of women who are pregnant in the U.S. each year. It affects pregnant women who haven't ever been diagnosed with diabetes.

There are two classes of gestational diabetes. Women with class A1 can manage it through diet and exercise. Those who have class A2 need to take insulin or other medications.

Gestational diabetes goes away after giving birth. But it can affect the baby's health, and it raises the risk of getting type 2 diabetes later in life.

Gestational diabetes GDM is a form of hyperglycemia. In general, hyperglycemia results from an insulin supply that is inadequate to meet tissue demands for normal blood glucose regulation. Studies conducted during late pregnancy, when, as discussed below, insulin requirements are high and differ only slightly between normal and gestational diabetic women, consistently reveal reduced insulin responses to nutrients in women with GDM (17–23). Studies conducted before or after pregnancy, when women with prior GDM are usually more insulin resistant than normal women (also discussed below), often reveal insulin responses that are similar in the 2 groups or reduced only slightly in women with prior GDM (18, 22–26). However, when insulin levels and responses are expressed relative to each individual's degree of insulin resistance, a large defect in pancreatic β cell function is a consistent finding in women with prior GDM (23, 25, 27).

Gestational Diabetes Symptoms

It include

Also symptoms include

•Thirstier than usual

•Hungrier and eat more than usual

•pee more than usual

Gestational Diabetes Causes

When we eat, our pancreas releases insulin, a hormone that helps move a sugar called glucose from your blood to our cells, which use it for energy.

During pregnancy, the placenta makes hormones that cause glucose to build up in our blood. Usually, our pancreas can send out enough insulin to handle it. But if your body can't make enough insulin or stops using insulin as it should, our blood sugar levels rise, and we get gestational diabetes.

Gestational Diabetes Risk Factors

Prone to gestational diabetes include overweight before pregnant.

Having blood sugar levels that are higher than they should be but not high enough to be diabetes (this is called prediabetes)

Have a family member with diabetes

Have had gestational diabetes before

Have polycystic ovary syndrome (PCOS) or another health condition linked to problems with insulin

Have high blood pressure, high cholesterol, heart disease, or other medical complications

Have given birth to a large baby (weighing more than 9 pounds)

Have had a miscarriage

Have given birth to a baby who was stillborn or had certain birth defects

Are older than 25

GestationalDiabetes Tests and Diagnosis

Gestational diabetes usually happens in the second half of pregnancy.Doctor will check for it between weeks 24 and 28, or sooner if we're at high risk.

Doctor will give a glucose tolerance test:

Giving the patient to drink 50 grams of glucose in a sweet drink, which will raise your blood sugar. An hour later, taking a blood glucose test to see how the body handled all that sugar. If the results show that blood sugar is higher than a certain level, a 3-hour oral glucose tolerance test is needed, doctor can also test the patient by making them fast for 12 hours, then giving a 75-gram glucose drink and a 2-hour blood glucose test.

The newly proposed criteria for diagnosing gestational diabetes will result in a gestational diabetes prevalence of 17.8%, doubling the numbers of pregnant women currently diagnosed. These new diagnostic criteria are based primarily on the levels of glucose associated with a 1.75-fold increased risk of giving birth to large-for-gestational age infants (LGA) in the Hyperglycemia Adverse Pregnancy Outcome (HAPO) study; they use a single OGTT. Thus, of 23,316 pregnancies, gestational diabetes would be diagnosed in 4,150 women rather than in 2,448 women if a twofold increased risk of LGA were used. It should be recognised that the majority of women with LGA have normal glucose levels during pregnancy by

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these proposed criteria and that maternal obesity is a stronger predictor of LGA. The expected benefit of a diagnosis of gestational diabetes in these 1,702 additional women would be the prevention of 140 cases of LGA, 21 cases of shoulder dystocia and 16 cases of birth injury. The reproducibility of an OGTT for diagnosing mild hyperglycaemia is poor. Given that (1) glucose is a weak predictor of LGA, (2) treating these extra numbers has a modest outcome benefit and (3) the diagnosis may be based on a single raised OGTT value, further debate should occur before resources are allocated to implementing this change.

GESTATIONAL DIABETES TREATMENT

Treatment should be done as soon as possible to keep the mother and the baby healthy during pregnancy and delivery. Doctor's will let the patient to

-Check blood sugar levels four or more times a day.

-check urine for ketones, chemicals

-eating a healthy diet

-making exercise a habit

Diet and Exercise for Gestational Diabetes

Eat a healthy, low-sugar diet. Talk to the doctor to be sure we're getting the nutrition we need. Follow a meal plan made for someone with diabetes:
Trade sugary snacks like cookies, candy, and ice cream for natural sugars like fruits, carrots, and raisins. Add vegetables and whole grains, and watch your portion sizes.

Have three small meals along with two or three snacks about the same times every day.

Get 40% of our daily calories from carbs and 20% from protein. Fifty percent of the carbs should be complex, high-fiber carbs, with fat being between 25% and 30%.

Aim for 20-35 grams of fiber a day. Foods such as whole-grain breads, cereals, and pasta; brown or wild rice; oatmeal; and vegetables and fruits will help get us there.

Limit your total fat to less than 40% of your daily calories. Saturated fat should be less than 10% of all the fat we eat.
Eat a variety of foods to make sure we get enough vitamins and minerals. we may need to take a supplement to cover our bases. Ask your doctor if they think we should take one.
Exercise throughout the pregnancy. Being active is a good way to help manage our blood sugar. Staying fit during pregnancy is also good for our posture and can curb some common problems, like backaches and fatigue.

Get active as soon as possible. Aim for 30 minutes of moderate activity most days of the week. Running, walking, swimming, and biking are good options.

Exercise can lower our blood sugar.Sowhen we work out, always have a form of quick sugar with us, such as glucose tablets or hard candy.

Get the right prenatal care: Not only can our doctor screen us for this condition; they can offer advice on food, activity, and weight loss. They can also point us to other health professionals, like nutritionists, that can help.

Ifyou have morning sickness, eat small snacks. Nibble on crackers, cereal, or pretzels before getting out of bed. As we go through our day, have small meals often and avoid fatty, fried, and greasy foods.

If we take insulin, make sure we got a plan to deal with low blood sugar. Throwing up can make our glucose level drop. Talk doctor if you are not sure what to do.

Safety and Mode of Action of Diabetes Medications in comparison with 5-Aminolev

Diabetes Management-Targeting Pathways

The targeted therapies for patients with type 2 diabetes are established based on various pathways through which glucose control can be achieved.
After food is consumed and digestion begins, glucose levels start to increase, as do other hormones such as glucagon-like peptide (GLP-1) which is released in the intestines. Glucagon-like peptide 1 (GLP-1) is an incretin, which works by triggering insulin production (as insulin acts to decrease glucose levels) and inhibiting glucagon

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production (glucagon acts to increase glucose levels). This occurs to counteract the increased glucose, and it induces the feeling of satiety and reduces apatite by sending signals to the brain that one is full . The consumption of food also triggers the release of pancreatic hormones like insulin, amylin, and glucagon. Insulin and amylin both work to decrease glucose levels and inhibit glucagon while glucagon acts on the liver to raise glucose levels.

Diabetes Medications

The American Diabetes Association's Standards of Medical Care in Diabetes Patients specifies the pharmacological management of type 2 diabetes, all of which are discussed below.

Metformin (Type: Biguanide)

Metformin is the most common initial drug prescribed for type 2 diabetes in the world. Metformin acts via an antihyperglycemic pathway through an increased glucose tolerance in patients with type 2 diabetes. Typically, this is measured via blood plasma glucose levels and postprandial plasma levels. As an antihyperglycemic agent, the mode of action entails decreasing hepatic glucose production and the intestinal absorption of glucose and increasing peripheral glucose uptake and utilization. It also helps break down free fatty acids by activating adenosine monophosphate- (AMP-) activated protein kinase in hepatocytes. Additionally, metformin does not affect insulin secretion levels; fasting insulin levels and 24-hour plasma response have been shown to actually decrease. Metformin is secreted without additional metabolization through tubular secretion in the kidney, and because of this, renal issues can prove fatal through lactic acidosis—a rare metabolic complication. This is caused by the inhibition of hepatic gluconeogenesis by inhibiting a mitochondrial isoform of glycerophosphate dehydrogenase (mGPD), preventing glycerol from participating in the gluconeogenic pathway.

SIDE EFFECTS ASSOCIATED WITH USING METFORMIN

Side effects of metformin include:

- physical weakness (asthenia)
- diarrhea
- gas (flatulence)
- symptoms of weakness, muscle pain (myalgia)
- upper respiratory tract infection
- low blood sugar (hypoglycemia)
- abdominal pain (GI complaints), lactic acidosis (rare)
- low blood levels of vitamin B-12
- nausea
- vomiting
- chest discomfort
- chills, dizziness
- bloating/abdominal distention
- constipation
- heartburn

Sulfonylurea (Glipizide, Gliclazide, and Glimepiride)

Sulfonylureas are only beneficial to patients who have retained some degree of residual pancreatic beta cell functionality, as they work by stimulating insulin secretion. This is often difficult due to the death/loss of function of the insulin-producing beta cells in the pancreas which accompanies diabetes. The necessity for beta cells' presence stems from the molecular mechanism of action: on the surface of these cells, sulfonylurea has specific neuronal receptors. When a sulfonylurea-type molecule binds, it causes the cellular membrane to depolarize, leading to the calcium channel opening and resultant calcium influx. Next, this change in the charge of the cell causes actomyosin filaments to contract and, in turn, release insulin from the cell. After a brief period, insulin granule transmission begins, and new insulin granules are formed. Sulfonylureas' target receptor is a complex of the sulfonylurea 1 receptor (SUR1), specifically the K-ATP channel, altering the resting potential. Adding 5-ALA has been shown to aid this process, especially with improved results in patients with consistent insulin resistance by increasing the availability of ATP, which aids with key metabolic processes (like the TCA cycle) within the mitochondria. Sulfonylureas are glucose-level independent, meaning that there is a higher sensitivity to amino acids and, in turn, higher insulin release. An increased sensitivity of beta cells to glucose and non-glucose secretagogues develops; thus, hypoglycemia and weight gain are resultant potential side effects. Finally, an increase in peripheral glucose utilization has been noted with this drug class by both stimulating hepatic gluconeogenesis and increasing the number/sensitivity of insulin receptors

Side Effects of Sulfonylureas Side effects of sulfonylureas may include:

- Signs of low blood sugar, such as sweating, dizziness, confusion, or nervousness

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- Hunger
- Weight gain
- Skin reactions
- Upset stomach
- Dark-colored urine

Meglitinides (Repaglinide and Nateglinide)

Meglitinides act on different beta cell receptors, but in a similar fashion to sulfonylureas. They work on the same K-ATP channels and increase insulin secretion. One potential downside is the lower binding affinity present at the surface level of the pancreatic beta cells; combined with the faster dissociation rates, the efficacy of this class of drugs is less than its parallel. Their adverse effects include hypoglycemia and weight gain. Lastly, they are more expensive than sulfonylureas and are commonly used in patients with allergies to the former

Side effects of Meglitinides

Meglitinides are well-tolerated by most people, including elderly people who need help lowering their mealtime blood sugars.

Common

Low blood sugar (hypoglycemia) is the most common side effect of meglitinides. Symptoms of hypoglycemia include sweating, shakiness, lightheadedness, and confusion.

These medications also can cause weight gain.

Severe

Meglitinides are relatively short-acting, which means they're unlikely to cause hypoglycemia. However, if taken without food, these drugs can cause a significant drop in blood sugar.

Someone experiencing hypoglycemia (blood sugar less than 70mg/dL) should consume some form of glucose, such as four ounces of juice. Anyone experiencing signs of diabetic coma, including confusion or loss of consciousness, should seek medical attention immediately.

Thiazolidinediones (Rosiglitazone and Pioglitazone)

Thiazolidinediones (TZDs) effectively attempt to mimic insulin by reducing hyperglycemia even with an impaired insulin tolerance. This leads to substantial reductions in hyperinsulinemia, which is caused by an increase of peripheral glucose consumption and decrease in hepatic glucose levels. There is no change in the secretion levels on insulin, but potential restoration of pancreatic beta cell insulin reserves has been observed. The exact mode of action has not been specified; however, there are two key effects to be discussed. First, the affinity of TZDs to the binding site known as peroxisome proliferator-activated receptor- (PPAR-) gamma on the adipocyte protein 2 (aP2) molecule, a key gene involved in weight loss efforts, has led to the connection between the TZD hypoglycemic action and the promoter region PPAR-gamma, especially with the PPAR-gamma agonist rosiglitazone. Ultimately, insulin sensitivity is not a direct by-product of this aspect, which raises the second point—TZDs are able to uniquely activate the phosphoinositide 3-kinase (PI3K) pathway with or without PPAR-gamma.

Side effects of Thiazolidinediones

Common side effects associated with TZDs include edema, weight gain, macular edema and heart failure. Moreover, they may cause hypoglycemia when combined with other antidiabetic drugs as well as decrease hematocrit and hemoglobin levels. Increased bone fracture risk is another TZD-related side effect. Thiazolidinediones tend to increase serum low density lipoprotein cholesterol levels, with rosiglitazone having a more pronounced effect compared with pioglitazone

GLP Agonists (Exenatide, Lixisenatide, Liraglutide, Albiglutide, and Dulaglutide)

Glucagon-like peptide (GLP-1), an incretin, is a gastrointestinal peptide involved in the regulation of glucose levels where the hormone is released upon consuming food. It stimulates insulin formation and release, and this occurs upon oral ingestion of food exclusively. GLP binds to receptors present in many tissues including beta cells, gastric mucosa, the kidney, the heart, etc. This hormone is targeted in diabetes because it causes insulin release from the beta cells, as well as slows down gastric emptying and inhibits excess glucagon release after meals. This, in turn, decreases appetite (causing weight loss). GLP agonists, however, are injectable medications that act by enhancing these effects in the body, thereby making it less appealing to some patients.

Side effects of GLP Agonist

Some of the more common side effects include:

- Nausea
- Vomiting
- Diarrhea

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DPP4 Inhibitors (Sitagliptin, Saxagliptin, Linagliptin, and Alogliptin)

DPP4 is an enzyme that deactivates the glucose-dependent insulinotropic polypeptide (GIP) and GLP-1. The inhibition of this enzyme causes an increased availability of GLP-1 levels in the body (as seen above). DPP4 inhibitors are a group of drugs that are an oral GLP-1-based therapy; however, they are not as effective at glucose or weight reduction. Their potential side effects are angioedema and pancreatitis, but they have a lower risk of hypoglycemia. This class may be considered in those who are intolerant of or have contraindications to metformin, sulfonylureas, or thiazolidinediones, such as patients with chronic kidney disease or who are at a high risk of hypoglycemia. They can also be considered an add-on medication; however, this is often cost prohibitive

Side effects of DPP4 Inhibitors Adverse effects of DPP-4 inhibitors include:

- gastrointestinal problems – including nausea, diarrhoea and stomach pain
- flu-like symptoms – headache, runny nose, sore throat
- skin reactions – painful skin followed by a red or purple rash

Sodium Glucose Co-Transporter-2 Inhibitors (Gliflozins)

Sodium glucose co-transporter-2 (SGLT2) works by inhibiting the SGLT2 receptors in the kidneys' proximal convoluted tubule, the site where most glucose is reabsorbed back into the body. These medications prevent the reabsorption of glucose and increase its urinary excretion and can cause polyuria which, in certain cases, can result in postural hypotension. They also contribute to weight loss and some side effects that include urinary and genital infections, as well as diabetic ketoacidosis.

Side effects of Sodium Glucose Co-Transporter-2 Inhibitors (Gliflozins)

Serious side effects of SGLT2 inhibitors include:

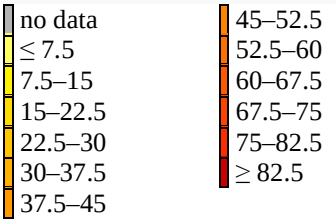
- Kidney failure.
- Hyperkalemia (high levels of potassium in the blood)
- Hypotension (low blood pressure)
- Ketoacidosis.
- Increased cholesterol levels.
- Serious urinary tract infections.
- Increased bladder cancer risk.
- Serious allergic reactions.

Epidemiology of diabetes

Globally, an estimated 463 million adults are living with diabetes, according to the latest 2019 data from the International Diabetes Federation. Diabetes prevalence is increasing rapidly; previous 2017 estimates put the number at 425 million people living with diabetes. The number is projected to almost double by 2030. Type 2 diabetes makes up about 85-90% of all cases. Increases in the overall diabetes prevalence rates largely reflect an increase in risk factors for type 2, notably greater longevity and being overweight or obese.

Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, occurring in low- and middle-income countries including in Asia and Africa, where most patients will probably be found by 2030. The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, including increasingly sedentary lifestyles, less physically demanding work and the global nutrition transition, marked by increased intake of foods that are high energy-dense but nutrient-poor (often high in sugar and saturated fats, sometimes referred to as the Western pattern diet).

Prevalence (per 1,000 inhabitants) of diabetes worldwide in 2000 - world average was 2.8%.



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Disability-adjusted life year for diabetes mellitus per 100,000 inhabitants in 2004

No data	600–700
<100	700–800
100–200	800–900
200–300	900–1,000
300–400	1,000–1,500
400–500	>1,5
500–600	

CONCLUSION:

From the above studies, it briefly explains the diabetes and its types. It emphasizes on diagnostic, treatment and medication. Taking medicine has its treatment properties as well as there is side effects.

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A Review on: HIV Therapy – The Influence of New Drugs

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ABSTRACT: The discovery of the human immunodeficiency virus (HIV) as the causative organism of acquired immunodeficiency syndrome (AIDS) and the inability of modern medicine to find a cure for it have placed HIV as the one of the most dreaded pathogens of the 21st century. With millions of people infected with HIV, it was once thought to result in "medical apocalypse". However, with the advent of antiretroviral therapy (ART), it was now possible to control HIV. Adherence to ART helps to keep the viral load under control and prolong the time of progression to AIDS, resulting in near normal life expectancy. Even with the introduction of ART, a substantial number of patients fail to adhere due to a variety of reasons, including adverse effects, drug abuse, mental disorders, socioeconomic status, literacy, and social stigma. With the availability of so many options for HIV treatment at each stage of the disease progression, physicians can switch between the treatment regimens to avoid and minimize the adverse effects of drugs. Close monitoring, major social reforms, and adequate counselling should also be implemented to circumvent other challenges.
Categories: Infectious disease, Allergy/Immunology, HIV/AIDS

KEYWORDS: HIV, AIDS, drug adverse effects, HIV/AIDS, highly active antiretroviral therapy (HAART), antiretroviral therapy.

I. INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a medical condition caused by the human immunodeficiency virus (HIV). HIV infection is a very current threat and can easily be termed as a course upon the human race. The scientific community first noticed and recognized the presence of AIDS as an actual disease following an increase in the incidence of very rare opportunistic infections and cancers among otherwise healthy homosexual men (Accessed: December 28, 2015). HIV -1 was identified as the causative organism soon after the first official recognition of HIV patients in the USA. HIV-2 was reported first in Africa in 1985 and is markedly different from HIV-1. It closely resembles a simian virus that infects macaques in capacity. Simian viruses that naturally infect Africa primates are suspected to reach humans via multiple cross-species transmissions resulting in the spread of HIV-1 and HIV-2. The global prevalence of HIV has expanded since its discovery and has now spread across the globe despite advances in antiretroviral treatment (ART). The mortality and morbidity rates related to HIV infections remain high in developing countries largely due to food insecurity and malnutrition. Long term concomitant sexual relationships and high infectivity during the early phase of HIV infections are other factors behind the extensive spread of HIV in the general population (Tadesse WT: BMC Pharmacol Toxicol. 2014, 15:32.).

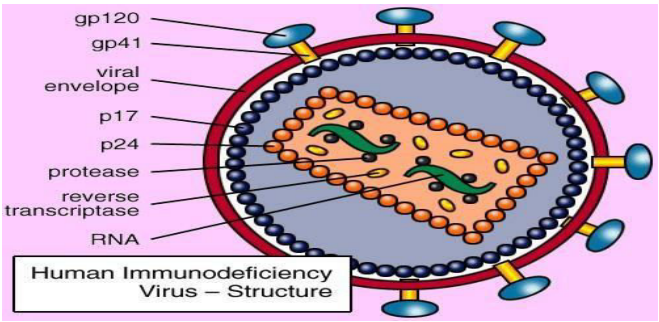

Fig.1:Structure of HIV Virus

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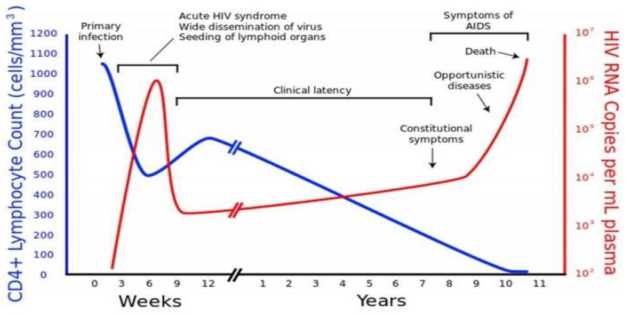
II. THE INFECTION

The main site of the attack is the immune system, especially the CD4 T-lymphocytes (CD4 cells). Once infected, the virus gradually and silently overpowers the host's defence mechanism, resulting in opportunistic infections and cancers that are otherwise rare. Activated and differentiated CD4 cells have a pivotal role in the activation of cell-mediated and humeral immune systems (AIDS behave.2011, 15;687-92). HIV infection results in the depletion continue over a course of several years until the patient succumbs to AIDS. It is the last stage of the HIV infection, and it presents itself anywhere between two and 15 years post infection. The following figure represents the timeline of HIV infection from initial infection to the expression of AIDS defining symptoms (figure2:).(Garnett GP: Concurrent sexual partnership and primary HIV infection A critical interaction).



HIV SUBGROUP

HIV-1

HIV-1 is well-known for its extensive genetic diversity. There are four different lineages coming under HIV-1: M, N, O, and P. The most commonly reported HIV virus across the globe is group M. Group N less prevalent, reported only from Cameroon. Group P is the rarest of all and has been identified in Cameroon pregnant women in France. It has a prevalence of 0.06% of total HIV infections (AIDS behave.2011, 15;698).

Current status of HIV infection and mortality rate

Western, Central Europe, and North America

Approximately 2.4 million individuals are HIV-positive in this region. An estimated 102,000 new HIV infections were reported in 2019, and more than 50% of infections were from the USA. About 36,000 AIDS related deaths were also reported in the same period.(Eaton JW: Concurrent sexual partnership and primary HIV infection A critical interaction).

Asia and Pacific

As of 2019, approximately six million individuals were previously infected in Asia and the Pacific, with as many as 430,400 new HIV infections arising that year. China, Indonesia, and India contribute to about 78% of the total new disease burden in Asia and the Pacific with about 340,000 deaths. Patients receiving ART are approximately 36%, with 4.2 million active HIV patients having no access to ART (Tadesse YT: Self-reported adverse drug reactions and their influence on highly active antiretroviral therapy).

Nationally, there were an estimated 20.52 thousand pregnant women who would require ART to prevent mother-to-child transmission of HIV.(HIV/AIDS Accessed: December 6, 2015).

1. **India**
2. As per recently released, India HIV estimation 2019 report, overall, the estimated adult (15-49 years) HIV prevalence trend has been declining in India since the epidemic peak in the year 2000 and has been stabilizing in recent years. The estimate for this indicator was 0.22% (0.17-0.29%) in 2019. In the same year, HIV prevalence among adult males was estimated at 0.24% and among adult female at 0.20%.
3. Nationally, there were 69.22 thousand estimated new HIV infections in 2019. This translates into 190 new infections every day and eight new infections every hour.
4. Nationally, 58.96 thousand AIDS related deaths were estimated in the year 2019.

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How is HIV Spread

5. Sexual intercourse

HIV can be found in the semen and vaginal fluids of a person who is HIV infected. He or she can pass HIV onto another person through unprotected sex (not using a condom) vaginal, oral and anal sex.

6. Pregnancy

HIV may be passed onto a baby from an HIV positive mother. Not all HIV positive mothers give birth to babies on HIV to the babies' increases if the mother is sick with an AIDS illness or if the mother gets infected with HIV during pregnancy.

HIV can pass to the baby during:

- The pregnancy
- At the time of delivery
- In breast milk

Many women only find out they have HIV when fall pregnant. By this time the unborn child is at risk of getting HIV. The chances of HIV passing from mother to child are between 20% and 40% during pregnancy and at the time of delivery. The risk of infection increases if the mother breast feeds. There are now medicines available to help reduce the spread of HIV to the baby.

7. Blood

HIV can pass from one person to another through his or her blood. Sometimes sick people are given extra blood through a blood transfusion. In India are safe because blood is tested before it is given to sick people.

HIV can be passed on in very small amounts of blood, for example when people share razor blades which are not cleaned properly.

HIV can also be passed on by injection drugs and sharing needles.

People most at risk of this happening are:

- Injecting drug users
- Doctors and nurses treating with HIV.

HIV can also be pass on when handling blood without gloves, e.g. after an accident, as this blood may contain the HIV germ that could enter cuts and open wounds (Plantier: A new immunodeficiency virus derived from gorillas. Nat. Med.2009).

Agree that you cannot get HIV from:

- Eating food prepared by someone by with HIV
- Sharing cups, mugs, plates, food, spoons, forks etc.
- Door handles or rails
- Sneezing or coughing
- Tears or saliva
- Toilet seats
- Holding or shaking hands
- Mosquitoes
- Swimming pools or baths
- Working or attending school with someone who is HIV positive
- Donating blood
- Living with someone who has HIV
- Being next to or close to someone who has HIV
- Kissing, hugging or touching.

(M, Rowland-Jones SL: HIV-2: The forgotten AIDS virus .Trends microbial.2008).

Symptoms of HIV infection

What are the symptoms of HIV infection?

Within a month or two of getting infected with HIV, many people (but not all) can develop flu-like symptoms, swollen glands or a rash. These symptoms usually go away within a couple of weeks, and a person can look and feel well for many years before thesymptoms come back.

This period when you look and feel well canlast five to seven years or longer in adultsand two to five years or longer in childrenborn with HIV. As HIV continues to attack theimmune system, the illnesses start to showagain (Ishikawa K, west Africa. 2001).

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What will happen when someone with HIV gets sick?
It can take many years for HIV to make you sick. When you start to feel sick because of serious infections, it means that you may have AIDS. Some early signs include: painful skin rashes (shingles), sores on the lips which do not heal, thrush (a white rash inside the mouth or on the private parts), and swelling in the neck, behind the ear, under the arm and in the groin. Signs and symptoms of TB include coughs, sweating and weight loss, fevers and sweating at night, as well as enlarged glands (Simbayi LC, Soc.Sci.Med.2007,64:1823-31).

Later signs of AIDS

You can also develop any of the following problems when you get very sick with AIDS: TB, bad cough and fever (pneumonia), 'pins and needles' and pains in the hands and feet, diarrhoea that does not stop, weakness and tiredness, tumours on the skin, losing weight, headaches, seizure, black-outs, loss of memory, difficulty in concentrating and difficulty in swallowing (UNAIDS: Fact sheet 2015).

How will I know that I have HIV?
You can look and feel healthy for years when you first have HIV in your body. There is only one way to find out whether you are living with HIV - by having an HIV test.

Should I have an HIV test?
Find out as early as possible after being infected with HIV is important. This way you can get help and avoid spreading HIV without knowing it.

Why must I have an HIV test?

- Knowing the result can reduce the stress and uncertainty of not knowing. Your doctor or clinic will be able to tell you if worrying signs and symptoms are HIV/AIDS-related.
- You cannot lose your job just because you are HIV positive – there are laws to protect you.
- You can change your lifestyle to protect sexual partners from future infections, so that you do not infect your sexual partner with the virus without knowing.
- Decisions about having children or entering into new relationships can be considered.
- A lot can be done to help you lead a healthy, normal life and slow down the time to developing AIDS if HIV is found early (before getting sick) in your blood.
- If you are HIV positive and register with Aid for AIDS, approval can be provided for multivitamins and preventative vaccinations to help you remain healthy.

How do I have an HIV test?

- You should go to a clinic if you are thinking about having an HIV test. The health worker should sit down and talk to you about the test. You can decide whether or not to have the test. No one can force you to have an HIV test – it is your choice. If you decide to test, the health worker will take a blood or saliva (spit) sample. This will be checked for HIV antibodies, which are made by the immune system soon after you are infected. Some of the tests will give the results within a few minutes, but other tests need to be sent away to get the results. If your test has been sent away you will need to visit the health worker about one week later to get the result. If antibodies are found you have a 'positive test' and are infected with HIV. This is why people living with HIV are often called 'HIV positive (WHO: Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV,2015).

TREATMENT OF AIDS

What are my rights?
You have to decide whether to go for the test. Nobody, not even a doctor or your employer, has the right to force you to have the test without your permission. The test result is confidential. It is against the law for the health worker to tell someone else the result without your permission. It is important that the health worker explains the meaning of the test to you so you can decide if you want it.

"Aid for AIDS can help you lead a healthy, normal life"

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Should I have counselling when going for an HIV test?
Taking an HIV test is very personal and the test result can be difficult to handle. It is important to get counselling to prepare yourself for the test result. Try a local counselling centre or your local ATICC (AIDS Training, Information and Counselling Centre), if you do not know where to find one.

What if my HIV test is positive?
• You are infected with HIV.
• You can spread it to your sexual partners if you have unsafe sex.
• You must always use a condom if you have sex.
• It is important to tell sexual partners that you are HIV positive. Discuss this with a counsellor or health worker.
• You must not donate blood. Pregnant women who are HIV positive may infect their babies. Not all babies will be infected with HIV. HIV can also be passed on during breast-feeding. The test cannot tell when you got the infection or when you will get sick (MMWRMorb Mortal Wkly Rep. 1981, 30:305–308).

What if the HIV test is negative?
• No HIV has been detected in your blood.
• You may not have HIV if the test is negative. However, it may be necessary to test again. You could be in the 'window period', which is the time between when you are infected with HIV and the tests used by doctors and clinics become positive. This is usually two to four weeks (Sharp PM, Hahn B H: Origins of HIV and the AIDS pandemic).

"If you are HIV negative, keep yourself safe from HIV in the future. The key is to stay negative!"

Preventing the spread of HIV
How do I stop myself from being infected with HIV?
"There is no cure for HIV. Once a person has HIV, they will remain
infected for the rest of their life. Therefore preventing the spread is the most important way of controlling HIV"

The following actions will prevent the spread of HIV:
Protected sex – with a condom, used correctly.
• Sex without penetration – this is when a man's penis does not enter the woman's vagina or anus. This is also safe sex. Sex can be a way of showing love but not the only way. You can also show love by kissing, touching and holding each other.
• You can have sexual climax without penetration by rubbing the person's private parts with hands or fingers.
• It is important to reduce the number of different sexual partners.
• New relationships – you should use a condom. Both of you should go for an HIV test before you stop using condoms. It is safe to have sex without protection if both HIV tests are negative. This means you are both free of HIV.
• Remember that both partners must stay in a sexually faithful relationship with only each other; otherwise the sex will no longer be safe. This is a faithful relationship(Sharp PM: Serological evidence for virus related to simian T-lymphotropic retrovirus in residents of West Africa Lancet.1985,2:1387-8).

Sexually transmitted infections
How do I get my partner to agree to have protected sex?
One of the reasons why HIV is spreading so fast is that many people do not want to talk about sex. The key here is communication. You should have open discussions about having an HIV test, using condoms, being faithful and the dangers of unsafe sex. Discussion about sex and relationships with your partner needs to happen if you are going to protect yourself from HIV. If you are unsure of how to deal with this, contact the National AIDS Helpline, your local ATICC (AIDS, Training, Information and Counselling Centre) or Aid for AIDS (Eaton JW: A critical interaction. AIDS Behav. 2011, 15:687–92).

"Have open talks with your partner"
Sexually Transmitted Infections can increase the chance of HIV infection
Any sickness passed on from one person to another during sex. Gonorrhoea, the drop, syphilis and herpes are STIs. A person with an STI may have a discharge or sores on his or her private parts. This makes it easier for the HIV to get into blood and the body during sex. STIs can be very dangerous and can cause bad infections and HIV can get into your body and blood more easily through broken skin if you already have an STI. This means that HIV can be spread from one person to another more easily.

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How do I know if I have a sexually Transmitted Infection

• Sores on your genitals or anus
• White, yellow or green discharge from your penis or vagina
• Pain in the lower stomach
• Burning or pain when going to the toilet
• Itching or redness around the private parts
• Painful sex
• Pain in the testicles
• Swelling in the groin

It is important that you have an STI treated. Clinics and doctors can treat STIs with tablets or with an injection. Treatment of STIs usually works quickly (Watson R:Wageningen, Netherlands; 2015. 10:537–562).

"STIs are passed on during unprotected sex"

Living with HIV/AIDS
I have heard that you cannot treat people who have HIV or AIDS? What should I do to stay healthy if I am HIV positive?
Although there is no cure for HIV, there is a lot that can be done to lead a healthy and 'normal' life. Good medical care and hygiene can do a lot to keep people well for a long time and lengthen the time before you get sick and develop AIDS.
• Register on the Aid for AIDS programme if you are a member of a contracted medical scheme or company (they are there to assist you). Contact the programme on 0860 100 646.

• Stay working and active for as long as possible.
• Have protected or safe sex (correctly using a condom).
• Visit the doctor or hospital for regular checkups.
• Eat good food and stay strong for as long as possible.

Improve your lifestyle by keeping healthy, including:
• Exercise regularly.
• Eat a healthy balanced diet (vegetables, beans, eggs and fruit).
• Stop smoking and avoid alcohol. (These things make your body weak so it is easier for HIV to get strong and you to get AIDS earlier.)
• Medication can help slow down HIV, the disease and to prevent illnesses.
• Get enough rest and reduce stress levels.
• Take multivitamins.
• Drink lots of water.
(Dellar R, Karim QA: HIV/AIDS food insecurity, and undernourishment).

"Stay healthy!"
Treatments options for HIV
HIV infection has a very complex pathogenesis and varies substantially in different patients. Therefore, it can easily be considered as a very host-specific infection. The specificity of pathogenesis often complicates treatment options that are currently available for HIV infection. Effective management of HIV infection is possible using different combinations of available drugs. This method of treatment is collectively known as antiretroviral therapy (ART). Standard ART is comprised of a concoction of at least three medicines (termed as "highly active antiretroviral therapy" or HAART). Effective ART often helps control the multiplication of HIV in infected patients and increases the count of CD4 cells, thus, prolonging the asymptomatic phase of infection, slowing the progression of the disease, and also helps in reducing the risk of transmission (Luckheeram RV, Xia B: CD4+T cells:2015).

FDA-approved HIV drug classes
Reverse Transcriptase Inhibitors
Reverse transcriptase inhibitors are a group of drugs, which can bind and inhibit the reverse transcriptase enzyme to intercept the multiplication of HIV. There are two types of inhibitors: non-nucleoside reverse transcriptase inhibitors

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(NNRTIs) and nucleoside reverse transcriptase inhibitors (NRTI). Examples of this group of drugs include zidovudine, didanosine, abacavir, tenofovir, and Combivir.

Protease Inhibitor
Regulation of HIV protease is of high importance for the correct assembly and production ofHIV. Protease inhibitors effectively block the functioning of protease enzymes in acutely andchronically HIV-infected CD4 cells. Inhibition of HIV protease enzymes results in the liberationof immature and non-infectious viral particles. Examples of this group of drugs includelopinavir/ritonavir, indinavir, ritonavir, nelfinavir, and amprenavir.

Fusion Inhibitors
This class of drugs acts by blocking HIV from entering the CD4 cells of infected patients. They inhibit the fusion of HIV particles with the CD4 cells. Enfuvirtide is an example of a fusion inhibitor used in HIV treatment.

Chemokine Receptor 5 Antagonist
This group of drugs prevents the infection by blocking the chemokine receptor 5 (CCR5) antagonist receptor present on CD4 cells. In the absence of vacant CCR5 receptors, HIV fails to gain entry and infect the cell. Maraviroc is an example of a CCR5 antagonist used in HIV treatment.

Integrase Strand Transfer Inhibitors
Strand transfer inhibitors prevent the integration of viral DNA into the host genome of CD4 cells by an integrase enzyme. Blocking integrase prevents HIV from replicating. Raltegravir, elvitegravir, and dolutegravir are some medications in this category.

Treatment regimen for HIV
Present HIV treatment guidelines recommend ART treatment for all patients, irrespective of the CD4 cell count, to improve and prolong the progression of disease to AIDS. Adherence to treatment is of paramount importance in order to achieve the full efficacy of treatment and also to prevent the incidence of drug resistance (Brenchley JM, Douek DC: CD4-2013).

Latest WHO recommendations for ART
A concise form of 1st, 2nd, and third line treatment options recommended by the World Health Organization (WHO) is given below.

First-line ART
Adults: First-line ART treatment for adults consists of two NRTIs and one NNRTI. Tenofovir disoproxil fumarate (TDF) + lamivudine (3TC) or emtricitabine (FTC) + efavirenz (EFV) as a fixed dose is the favoured choice for this type of ART. When this drug combination is contraindicated or is unavailable, 1) zidovudine (AZT) + 3TC + EFV, 2) AZT + 3TC + nevirapine (NVP), or 3) TDF + 3TC (or FTC) + NVP is used (Moss AR, Bacchetti P: Seropositivity for HIV and the development of AIDS or AIDS related condition: three year follow up of the San Francisco General Hospital cohort. Br Med J. 1988).

Contraindications:
1. Creatinine clearance is less than 50 ml per minute: Tenofovir.
2. Patients on psychoactive drug treatment: Efavirenz.
3. Patients who are pregnant or who are trying to conceive: Efavirenz.
4. ALT elevation: Nevirapine.

Pregnant and breastfeeding patients:
First-line ART in this subpopulation is comprised of a single daily dose of TDF + 3TC (or FTC) + NVP. Breastfeeding infants of mothers who are receiving ART must receive six weeks of infant prophylaxis with a daily dose of NVP. The preventive medication should commence immediately post-delivery or when HIV exposure is identified.

Pediatric patients:
Patients below three years of age should be given Lopinavir/Ritonavir (LPV/r)-based treatment, even under NNRTI exposure. When LPV/r is not a viable option, NVP based treatment should be used. For infected children who are over age three, EFV is the ideal NNRTI while NVP has been identified as the second option. For infected children younger

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than three years of age, who develop TB while on the Lopinavir/Ritonavir (LPV/r)-based treatment, the NRTI regimen should be switched to abacavir (ABC) + 3TC or AZT + 3TC until the TB infection is cleared. NRTI regimens similar to that of adults (TDF + 3TC (or FTC)) or (AZT + 3TC) or (ABC + 3TC) are preferred for patients between 10 and 19 years of age who weigh 35 kg or more (Vallari A: Prevalence continues to be low. AIDS Res Hum Retroviruses. 2010).

Second-line ART

Adults, including pregnant and breastfeeding patients: When a first-line treatment of ART fails,a second-line ART should be utilized. The second-line ART is comprised primarily of twoNRTIs and a Ritonavir-boosted PI. The recommended option for second-line ART includes AZTand 3TC as the NRTI. After the failure of AZT or stavudine (d4T) + 3TC based first-line regimen,TDF + 3TC (or FTC) as the NRTI should be considered. When first-line NNRTI-based treatmentfails, two NRTIs + a boosted PI are suggested

Pediatric patients:

For children below three years of age, first-line ART is continued even when it fails. No change in treatment is recommended; instead, adequate steps should be taken to improve adherence to the ART regimen. If first-line ART fails in children ages three and up, a second-line treatment consisting of one NNRTI and two NRTIs should be given. If ABC or TDF + 3TC (or FTC) fails, the recommended option is AZT + 3TC. After a failure of AZT or d4T + 3TC (or FTC) in first-line treatment, the preferred NRTI option is ABC or TDF + 3TC (or FTC).

Third-line ART

If first- and second-line ART fails, the WHO recommends inclusion of new medicines with the least amount of risk for development of cross-resistance towards previously used drugs (e.g. integrase inhibitors and second-generation NNRTIs and PIs).

Factors to consider when selecting ART

The major factors that deserve thorough consideration while choosing an ART for a patient include the viral load and CD4 cell count before the treatment, the result of HIV genotypic drug resistance test, HLA-B*5701 status, patient preferences, and anticipated adherence. Comorbid conditions to screen prior to ART include cardiovascular disease, hyperlipidemia, renal disease, osteoporosis, psychiatric illness, neurologic disease, drug abuse or dependency requiring narcotic replacement therapy, pregnancy, infections with hepatitis C (HCV), hepatitis B (HBV), and tuberculosis (Peeters M: Geographical distribution of HIV-1 group O viruses in Africa. AIDS. 1997).

CD4 count monitoring for therapeutic response

Monitoring patients' viral load is critical to identify ART response (WHO 2015). When the viral load analysis is not practical via polymerase chain reaction (PCR), branched chained DNA (bDNA), and nucleic acid sequence-based amplification (NASBA), the CD4 count is used as an indicator of HIV treatment response. During the first year of treatment, increases in CD4 count from 50 - 150 cells/mm3 with an increased response in the first trimester are considered as a positive response. CD4 count rises steadily ranging from 50 to 100cells/mm3 per year until equilibrium is reached in the subsequent years (normal range: 500 cells/mm 3 to 1200 cells/mm3). Periodic monitoring of CD4 count is required during and even after the patient achieves normal CD4 count under ART. A number of treatment independent factors like age, viral load, genetic make-up, lifestyle, quality of health care etc., negatively influence the CD4 counts and HIV disease progression. Under such circumstances, a change in ART medication might be required (UNAIDS: Fact sheet 2015).

III. ADVERSE EFFECTS

Major factors for ART non-adherence

Adverse Effects of ART

One of the major challenges that patients and physicians face with ART is the incidence of adverse drug reactions (ADR). ADR is defined as "a response to a drug that is noxious and unintended and occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for modification of physiological function". ADR often persuades patients from continuing treatment, thus resulting in suboptimal efficacy. A serious consequence of treatment discontinuation is the emergence of drug resistance, making future therapeutic interventions ineffective.

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The major adverse effects of ART can be grouped into the following categories:

1. Gastrointestinal: Nausea, diarrhoea, vomiting, taste perversion, constipation, dyspepsia, abdominal pain, hepatotoxicity, and pancreatitis.
2. Central nervous system: Headache, vision problems, dizziness, tinnitus, insomnia, paresthesia, pain/numbness/tingling in extremities, peripheral neuropathy, somnolence, excessive sleep at night, memory problems, loss of olfactory function, and hearing impairment.
3. Haematological: Anaemia, bilirubinemia, increased urate, and blood in the urine.
4. Psychological: Anxiety, confusion, depression, nightmares, elation, and delusions.
5. Metabolic: Abnormal fat distribution (lipodystrophy), anorexia, dyspnoea, fatigue, lethargy, and weight gain.
6. Dermatological: Skin rash, facial discoloration, and pruritus.
7. Musculoskeletal*:* Body aches and vague chest pain.
8. Miscellaneous: Hypersensitive reactions, oral ulcerations, fever, and irregular menstrual cycles (Khanani RM. AIDS Res Hum retrovirus).

Drug Abuse

Continuous drug abuse is an important risk factor in HIV/AIDS patients ART, no adherence, and mortality. In a study conducted on HIV-positive drug addicts in Canada, heroin and cocaine injections were reported to adversely affect adherence to ART. In a separate six-month long longitudinal study, which examined the effect of drug use and abuse on ART among 150 HIV positive patients, it was discovered that acute effects of intoxication negatively influence ART adherence. The major mechanisms by which drug abuse results in ART

Non adherence include drug abuse induced neurocognitive/psychosocial impairment and psychiatric dysfunctions (Brass AL: Identification of host proteins required for HIV infection through a functional genomic screen. Science. 2008).

Mental Disorders

The prevalence of psychiatric disorders is reported to be very high among HIV-infected individuals. In a longitudinal study investigating the mental health, substance abuse, and psychosocial predictors among HIV-positive mothers, the presence of psychiatric disorders, stressful lifestyles, suboptimal living conditions, and parenting stress were associated significantly with ART non adherence. Childhood sexual violence-induced anxiety and depression may also result in ART non adherence. Hazardous drinking is another significant precipitator of anxiety and depression among HIV patients that results in ART non adherence.

Socioeconomic Status

Socioeconomic status is strongly associated with HIV-related mortality in the contemporary universal healthcare system because opportunities for patients of lower socioeconomic status to receive ART are meagre. In a study conducted among HIV-positive Cambodian women, 80% of those who discontinued ART were of low socioeconomic status. The estimated risk for low adherence in this population was reported to be five times higher for women than those in a medium or high social position. Poverty-induced stress is an important aspect that has to be addressed in issues regarding ART non adherence. The quality of housing and access to food are the two most important factors that prevent the poverty-ridden population from ART adherence.

Poor Literacy

Literacy is another major factor closely associated with ART non adherence with people of lower health literacy experiencing higher illness severity than people with better health literacy. Health literacy has been defined by the WHO as “the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand, and use information in ways which promote and maintain good health”. Many reports suggested that the inability to comprehend medication instructions by illiterate HIV-positive patients is an important factor resulting in failure to follow accurate daily medication therapy.

Social Stigma

The stigma of HIV and AIDS is assumed to have a negative influence on ART adherence. Stigma can be defined as an “attribute that is deeply discrediting” imposed by society that reduces someone “from a whole and usual person to a tainted, discounted one”. In a cohort study conducted in five African countries (Lesotho, Malawi, South Africa, Swaziland, and Tanzania) among 1,457 HIV-positive patients over a period of 12 months, individuals perceiving a high HIV stigma reported greater non adherence to ART. Symptom intensity is also high when compared to those who did not experience such a stigma. One study conducted in South Africa reported that internalized stigma is responsible for

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4.8% of the variance in cognitive-affective depression leading to ART non adherence. Furthermore, the researchers urge the medical community to introduce social reform efforts to reduce stigma and assist people living with HIV/AIDS in adjusting and adapting.
(WHO: Antiretroviral therapy2015)

IV. REVIEW OF LITERATURE

The discovery of the human immunodeficiency virus (HIV) as the causative organism of acquired immunodeficiency syndrome (AIDS) and the inability of modern medicine to find a cure for it have placed HIV as the one of the most dreaded pathogens of the 21st century. With millions of people infected with HIV, it was once thought to result in "medical apocalypse". However, with the advent of antiretroviral therapy (ART), it was now possible to control HIV. Adherence to ART helps to keep the viral load under control and prolong the time of progression to AIDS, resulting in near normal life expectancy. Even with the introduction of ART, a substantial number of patients fail to adhere due to a variety of reasons, including adverse effects, drug abuse, mental disorders, socioeconomic status, literacy, and social stigma. With the availability of so many options for HIV treatment at each stage of the disease progression, physicians can switch between the treatment regimens to avoid and minimize the adverse effects of drugs. Close monitoring, major social reforms, and adequate counselling should also be implemented to circumvent other challenges (de Bethune MP: Antiviral Res. 2010, 85:75–90).

Objectives
The primary objectives of the review were to systematically collect and review studies on HIV, AIDS, STIs and STDs conducted in India between 2007 and 2019; to assess the quality and reliability of these studies; and to synthesize the research findings under common thematic areas. The secondary objective of the review was to identify relevant recommendations for researchers, policy makers, practitioners, and stakeholders.

Search strategy
Electronic databases were systematically searched using pre-determined search terms. Internet searches were conducted, and key informants were contacted, in an effort to identify potential studies. The overall search for studies took place between January and May 2021.

Selection criteria
The inclusion criteria allowed for the following study designs: Randomized Controlled Trials, Cohort Studies, Systematic Reviews, Meta-analyses, Intervention Studies and Evaluations, Case Control Studies, Cross-sectional Studies, Descriptive/Qualitative Studies and Ethnographic Studies. Expert Opinion Studies and Secondary Research Studies were excluded from the review. Studies with participants who were male or female of any age living in India at the time of the study were included in the review. Studies were considered for inclusion if the purpose of the study was to evaluate interventions specific to HIV, AIDS, STIs, or STDs; or if the purpose of the study was to measure outcomes specific to HIV, AIDS, STI or STDs. In addition, studies with the purpose of describing or investigating issues directly related to HIV, AIDS, STIs or STDs in India were also considered for inclusion (Whitcomb JM: Broad nucleoside reverse-transcriptase inhibitor cross-resistance in human immunodeficiency virus type 1 clinical isolates. J Infect Dis. 2003).

Data collection and analysis
The two authors independently screened the results of the search. The full text of all potentially relevant studies was obtained and studies were independently assessed using pre-determined criteria. The quality of studies included in the review was assessed using validated quality appraisal tools. Common themes were identified via a subgroup analysis (Hughes PJ: A comparative overview.

Main Results
From the search strategy a total of 2735 citations were identified; 2572 citations were excluded as clearly irrelevant and the full text of 163 studies was reviewed. A total of 23 studies met the inclusion criteria and were assessed for research quality and then analysed for common themes. The majority of studies (n=33) were conducted in National Capital and no studies were conducted in Delhi. Most of the studies were unpublished literature (56%; n=35), and the large majority of studies were cross-sectional in design (92%; n=57). The quality of the studies varied although the majority were rated 'moderate.'

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Discussion

Limitations of the review were related to publication date, types of study designs, study quality, lack of information, and lack of access to a few electronic databases. The proposed course of action based on this literature review is for a new approach to the HIV national response in India, calling for a 'change to the face of HIV and AIDS.' Under this new approach recommendations include: engagement with the Church as a primary partner in all aspects of strategic planning and implementation; guidance from tradition and culture; more options for women; targeted interventions for married couples; creation of a new national strategy for HIV messages and awareness; prioritization of provincially and community led and driven response; strategies for condom use; positive engagement with PLHIV, and support towards public sector strengthening. Other recommendations are specific to research study type and design as well as suggested indicators for population-based surveys.

Outline of common themes and key findings

Tradition, culture, customs, and norms

• Progression from traditional to modern culture
• Socio-cultural norms and practices *(marriage, family and childbearing; violence as a social norm)*
• Interpretations of HIV *(Culture and tradition; conflict between biomedical, Hinduism and traditional beliefs; terminology and language; communication on reproductive and sexual health)*

Gender

• Gender identities and norms *(men and masculinity; women and femininity)*
• Gender-based violence *(physical violence; sexual violence; counselling and support)*

Sexuality

• Sexual norms *(traditional and modern meanings of sexuality; sexual identity)*
• Sexual practices *(pre-marital sex and sexual debut; changes in traditional sexual practices; sexual desire; sexual networks, transactional sex; sexual violence and negotiation; types of sex)*

Sexually Transmitted Infections

• Burden of disease
• Cultural interpretations
• Biomedical treatment and knowledge
• Barriers to STI testing
• STI treatment resistance

HIV Knowledge

• Modes of transmission
• HIV knowledge in rural settings
• HIV risk perceptions
• Knowledge verses behaviour change

HIV Vulnerability

• Women
• Men
• Children and young people
• Vulnerability related to poverty and socio-economic decline
• High risk settings and periods of time
• High risk practices

HIV Prevention

• HIV awareness campaigns *(exposure and sources of information; community led initiatives; responses to the NACO mass media campaign; ABC model)*
• Male condom *(knowledge and use; access and availability; beliefs and experiences)*
• Female condom
• Male circumcision

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HIV Testing
• National and group testing
• Knowledge and attitudes
• Provider initiated counselling and testing
• Barriers to testing (fear of stigma and discrimination; lack of privacy and confidentiality; lack of information and risk perceptions; availability and access of testing sites; testing and treatment)

Living with HIV and AIDS
• Community responses *(Christian response and socio cultural response; stigma and discrimination)*
• People living with HIV within communities *(knowledge of someone living with HIV; biomedical treatment; traditional medicine and Christian healing; care and support; AIDS related deaths)*

Leadership
Fear as a Responses to HIV

Public services and government sectors
• Health sector
• Education sector
• Law and justice sector
• Agriculture

Epidemiology
• National surveillance
• HIV prevalence in a hospital setting
• Projection of HIV prevalence
• Genetics and transmission patterns
(Greenberg ML: Resistance to enfuvirtide, 2004).

Analysis
Descriptive and analytical studies that met the literature review inclusion criteria were analysed using grounded theory. A subgroup analysis was performed with the aim of identifying common themes specific to geographical context (study locations and regions), age, gender and areas of interest related to the HIV epidemic in India, including HIV risk, HIV vulnerability, the affects of HIV on particular groups (including people living with HIV), as well as culture, tradition, and religion(RaoPKS;Indian J Sex Transm Dis. 2009).

V. RESULTS

Outcome of study
Based on the search strategy, a total of 2735 citations were identified. After reviewing the title and/or abstract of all the citations and removing duplicates, 2572 citations were excluded as clearly irrelevant. The full text was retrieved for the remaining 163 studies. These were reviewed independently by the two investigators. A final number of 23 articles met the inclusion criteria (Arrivillaga M: social determinants of health approach. Rev PanamSalud Publica. 2009, 26:502–10).

VI. CONCLUSION

Recent advances in HIV treatments have dramatically altered the nature and progression of HIV/AIDS. It can be safely considered as a “chronic” disease, provided the infected patients receive proper ART. Unfortunately, current statistics of the worldwide HIV burden tells another story: one with a steady rate of HIV-related deaths. More people die of complications and the progression of HIV to AIDS than should be when ART is used properly. The major hurdle a physician faces with ART is the incidence of adverse side effects of the treatment, which persuade patients to discontinue the treatment. Poverty, lack of awareness, and the social stigma associated with the infection complicate an already complicated situation. Appropriate changes in treatment regimens and medications can help patients overcome such adverse effects and potential complications inherent to the disease. Additionally, it is highly advisable to provide patients and their immediate family members with appropriate counselling for treatment compliance and psychological support (Willie TC, Hansen NB: Barriers to HIV medication adherence: Behav Med. 2016).

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A Review: Mucoadhesive Drug Delivery System

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ABSTRACT

Drug moves may be progressed with the aid of using new drug transport machine, consisting of mucoadhesive machine. This machine stays in near touch with the absorption tissue, the mucous membrane, liberating the drug on the motion webweb page main to development in each nearby and systemic effects. There are many routes of mucoadhesive drug transport machine, oral course is the maximum historical in addition to favored with the aid of using affected person being handy to take. However, peroral course has shortcomings consisting of hepatic first by skip metabolism and enzymatic degradation in GIT that's a dilemma to the absorption of maximum proteins and peptides agencies of drugs. The mucosa of the oral hollow space provides a powerful barrier to drug penetration, and one technique of optimizing drug transport is with the aid of using the usage of adhesive dosage bureaucracy and the mucosa has a wealthy blood deliver and it's far rather permeable. The buccal mucosa could be very appropriate for a bioadhesion machine due to a easy and rather motionless floor and accessibility. Mucoadhesion may be completed with the aid of using the use of mucoadhesive polymers. There are unique varieties of mucoadhesive polymers are available. Laminated gadgets were advanced to attain sustained drug release.

Introduction

MUCOADHESIVE DRUG DELIVERY SYSTEM Mucoadhesive drug transport structures are transport structures which make use of the assets of bioadhesion of sure polymers which emerge as adhesive on hydration and consequently may be used for focused on a drug to a specific area of the frame for prolonged intervals of time. Bioadhesion is an interfacial phenomenon wherein materials, at the least certainly considered one among that is biological, are held collectively by using interfacial forces. The Attachment might be among an synthetic fabric and organic substrate, which includes adhesion among a polymer and a organic membrane. In the case of polymer connected to the mucin layer of a mucosal tissue, the term "mucoadhesion" is used. [1] Mucoadhesive drug transport structures may be introduced through numerous routes:-

- Buccal delivery system
- Oral delivery system
- Vaginal delivery system
- Rectal delivery system
- Nasal delivery system
- Ocular delivery system

Mucoadhesive Oral Drug Delivery Systems

Oral course is the maximum desired course for the transport of any drug. Drug transport thru the membranes of the oral hollow space may be subdivided as:-

- Sublingual transport: This is systemic transport of capsules via the mucosal membranes lining the ground of the mouth.
- Buccal transport: This is drug management via the mucosal membranes lining the cheeks (buccal mucosa).
- Local transport: This is drug transport into the oral hollow space. Within the oral mucosal hollow space, the buccal area gives an appealing course of management for managed systemic drug transport. Buccal transport is the management of medication via the mucosal membrane lining the cheeks. Although the sublingual mucosa is thought to be extra permeable than the buccal mucosa, the latter is the desired course for systemic transmucosal drug transport. This is due to the fact the buccal mucosa has an expanse of easy muscle and comparatively motionless mucosa, which makes it a extra applicable area for retentive systems. Thus, the buccal mucosa is extra suitable for sustained route of drug transport. [2]

Advantages of Oral Mucoadhesive Drug Delivery Systems:

- Prolongs the house time of the dosage shape on the web website online of absorption, for this reason will increase the bioavailability.
- Excellent accessibility, fast onset of action.

- Rapid absorption due to sizable blood deliver and suitable blood waft rates.
- Drug is blanketed from degradation withinside the acidic surroundings withinside the git.
- Improved affected person compliance. [3]

Disadvantages of Mucoadhesive Drug Delivery Systems:

- Occurrence of nearby ulcerous outcomes because of extended touch of the drug owning ulcerogenic property.
- One of the principal boundaries withinside the improvement of oral mucosal shipping is the dearth of an amazing version for in vitro screening to pick out tablets appropriate for such administration.
- Patient acceptability in phrases to flavor and irritancy.
- Eating and Drinking is prohibited. [3]

Components / Structural Features of Oral Cavity

Oral hollow space is that vicinity of mouth delineated with the aid of using the lips, cheeks, difficult palate, tender palate and ground of mouth. The oral hollow space includes regions.

- Outer oral vestibule, that's bounded with the aid of using cheeks, lips, tooth and gingival (gums).
- Oral hollow space proper, which extends from tooth and gums returned to the fauces (passage which lead to pharynx) with the roof comprising the difficult and tender palate. The tongue initiatives from the ground of the hollow space.

Anatomy and Nature of Oral Cavity:

The oral hollow space can be divided into regions, the outer oral vestibule, bounded with the aid of using the lips and cheeks And the oral hollow space itself the borders being, and shaped with the aid of using the hardened tender palates, the ground of the mouth and tonsils .Physical Description of Oral Cavity: The mucosa that strains the oral hollow space can be divided into 3 types, categorized in step with their feature as:-

1. Masticatory mucosa: Which consists of the mucosa across the enamel and at the difficult palate and those areas have keratinized epithelium.
2. Lining mucosa: Which covers the lips, cheeks, base of the oral hollow space, decrease a part of tongue, buccal mucosa and the tender palate and those areas have non keratinized epithelium.
3. Specialized mucosa: Covering the dorsum of the tongue with especially keratinization. [1]

Overview of The Oral Mucosa Structure

The oral mucosa is made from squamous stratified (layered) epithelium, basement membrane, the lamina propria and submucosa. It additionally consists of many sensory receptors inclusive of the flavor receptors of the tongue. The epithelium of the buccal mucosa is approximately 40-50 mobileular layers thick, at the same time as that of the sublingual epithelium consists of rather fewer. Permeability The oral mucosa in wellknown is rather leakyepithelia intermediate among that of the epidermisand intestinal mucosa. It is anticipated that thepermeability of the buccal mucosa is 4-4000 timesextra than that of the skin. In wellknown, the permeabilities of the oral mucosae lower withinside the order of sublingual extra than buccal and buccal extra than palatal. This rank order is primarily based totally at therelative thickness and diploma of keratinization of those tissues, with the sublingual mucosa being fantastically skinny and non-keratinized, the buccal thicker and non-keratinized, and the palatal intermediate in thickness however keratinized. Environment The cells of the oral epithelia are surrounded through an intercellular floor substance, mucus, the precept additives of that are complexes made of proteins and carbohydrates. These complexes can be freed from affiliation or a few perhaps connected to sure areas at the mobileular surfaces. This matrix can also additionally simply play a function in mobileular-mobileular adhesion, in addition to appearing as a lubricant, permitting cells to transport relative to at least one another. Along the equal lines, the mucus is likewise believed to play a function in bioadhesion of mucoadhesive drug transport systems. Composition of Mucus Layer: Mucus is a translucent and viscid secretion which paperwork a thin, contentious gel, suggest thickness of thislayer varies from approximately 50-450 μm in human beings secreted through the globet cells lining the epithelia. It has the subsequent wellknown composition.

- Water -95%
- Glycoprotein and lipids – 0.5-3.00%
- Mineral salts – 1%
- Free proteins – 0.5-1.0% [1]

Functions of Mucus Layer:

1. Protective: ensuing mainly from its hydrophobicity.
2. Barrier: The function of the mucus layer as a barrier in tissue absorption of the medicine and affect the bioavailability.
3. Adhesion: Mucus has robust adhesion properties.
4. Lubrication: It is to preserve the mucus from the goblet mobileular is essential to atone for the elimination of the mucus layer because of digestion, bacterial degradation and solubilisation of mucin molecules. [1]

Role of Saliva:

Saliva consists of 99% water and is complicated fluid containing natural and inorganic material. Secretion of saliva is maximum throughout operating hours.

1. Protective fluid for all tissues of the oral cavity.
2. Continuous mineralization / demineralization of the enamel enamel.

3. Moisten the oral cavity. [4]

Theories of Mucoadhesion

There are six trendy theories of adhesion, which were tailored for the research of mucoadhesion:- **The electronic concept** shows that electron switch takes place upon touch of adhering surfaces due to variations of their digital structure. This is proposed to bring about the formation of an electrical double layer on the interface, with next adhesion because of appealing forces.

The wetting concept is mostly carried out to liquid structures and considers floor and interfacial energies. It includes the capacity of a liquid to unfold spontaneously onto a floor as a prerequisite for the improvement of adhesion. The affinity of a liquid for a floor may be observed the usage of strategies along with touch attitude goniometry to degree the touch attitude of the liquid at the floor, with the overall rule being that the decrease the touch attitude, the extra the affinity of the liquid to the solid.

The adsorption concept describes the attachment of adhesives on the premise of hydrogen bonding and van der Waals` forces. It has been proposed that those forces are the principle individuals to the adhesive interplay. A subsection of this, the chemisorptions concept, assumes an interplay throughout the interface takes place due to sturdy covalent bonding.

The diffusion concept describes interdiffusion of polymers chains throughout an adhesive interface. This manner is pushed with the aid of using awareness gradients and is laid low with the to be had molecular chain lengths and their mobilities. The intensity of interpenetration relies upon at the diffusion coefficient and the time of touch. Sufficient intensity of penetration creates a semi-everlasting adhesive bond.

The mechanical concept assumes that adhesion arises from an interlocking of a liquid adhesive (onsetting) into irregularities on a hard floor. However, hard surfaces additionally offer an extended floor location to be had for interplay along side an superior viscoelastic and plastic dissipation of power throughout joint failure, that are notion to be greater critical withinside the adhesion procedure than a mechanical effect.

The fracture concept differs a touch from the opposite 5 in that it relates the adhesive power to the forces required for the detachment of the 2 worried surfaces after adhesion.[5]

Mechanisms f Mucoadhesion

The mechanism of mucoadhesion is commonly divided in steps,

1. Contact level
2. Consolidation level

The first level is characterised via way of means of the touch among the mucoadhesive and the mucous membrane, with spreading and swelling of the formulation, starting up its deep touch with the mucus layer. In a few cases, consisting of for ocular or vaginal formulations, the shipping machine is routinely connected over in different cases, the deposition is promoted via way of means of the aerodynamics of the organ to the membrane, the machine is administered, consisting of for the nasal route.

In the consolidation step, the mucoadhesive substances are activated via way of means of the presence of moisture. Moisture plasticizes the machine, permitting the mucoadhesive molecules to interrupt loose and to hyperlink up via way of means of vulnerable van der Waals and hydrogen bonds. Essentially, there are theories explaining the consolidation step:

1. The diffusion concept
2. The dehydration concept. [6]

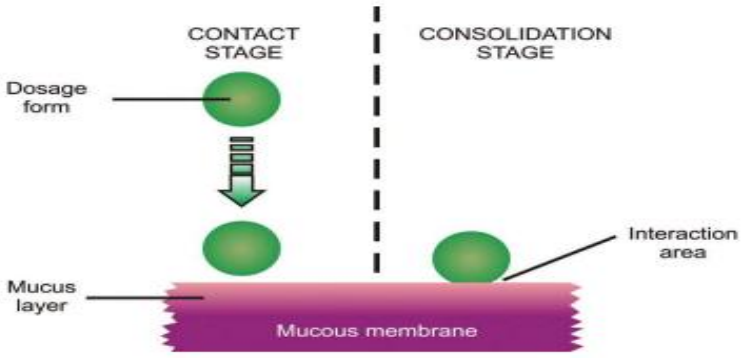

Fig. Two steps of mucoadhesion (6)

According to diffusion theory, the mucoadhesive molecules and the glycoproteins of the mucus together engage by using interpenetration of their chains and the constructing of secondary bonds. For this to take area the mucoadhesive tool has functions favouring each chemical and mechanical interactions. According to dehydration theory, substances which can be capable of with ease gelify in an aqueous environment, whilst located in touch with the mucus can reason its dehydration because of the distinction of osmotic pressure.

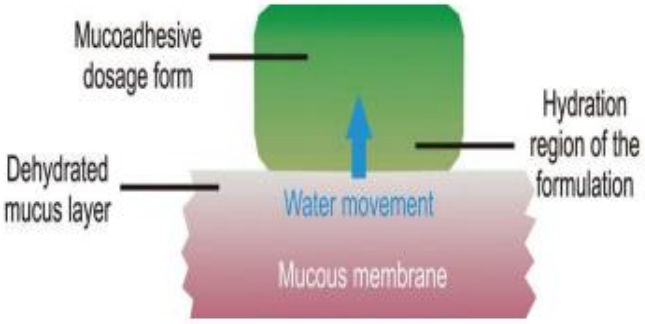

Fig. Dehydration theory of mucoadhesion

Factors Affecting Mucoadhesion :

FACTORS	PROPERTIES	COMMENTS
a. Polymer related factors	1. Molecular weight	The mucoadhesive force increases with molecular weight of polymer, up to 1, 0000 and beyond this level there is no much effect.
	2. Concentration of active polymers	For solid dosage forms such as tablets showed that the higher the polymer concentration the stronger the mucoadhesion. There is an optimum concentration of polymer corresponding to the best mucoadhesion.
	3. Flexibility of polymer chain	Flexibility is an important factor for interpenetration and enlargement.
b. Environment related factors	1.pH	pH influences the charge on the surface of both mucus and the polymers.
	2.Applied strength	To place a solid mucoadhesive system, it is necessary to apply a defined strength.
	3. Initial contact time	The mucoadhesive strength increases as the initial contact time increases.
	4. Swelling	Swelling depends on both polymers concentration and on presence of water.
c. Physiological Variables	1.Mucin turn over	a. The mucin turnover is expected to limit the residence time of the mucoadhesive on the mucus layers.
	2.Diseased state	b. Mucin turnover results in substantial amounts of soluble mucin molecules. Physicochemical properties of mucus are known to change during diseased states, such as common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, bacterial and fungal infections of the female reproductive tract and inflammatory conditions of the eye.

Table 1: Commercial Mucoadhesive Drug Delivery System [7]

DRUG	MUCOADHESIVE POLYMERS	APPLICATION SITE	NAME & FORM
1) Triamcinolone acetonide	Hydroxypropyl cellulose, cabopol 934	Oral cavity	Attach tablet
2) Nitroglycerin	Synchron (modified HPMC)	Buccal	Susadrintablet
3) Prochlorperazine Maleate	Ceronia, Xanthum Gum	Buccal	Buccastem tablet
4) Beclomethasone dipropionate	Hydroxypropyl cellulose	Oral cavity	Salcoat powder spray
	Sodium CMC, pectin, and gelatin inpoly-ethylene mineral ail base	Oral cavity	Oral base gel
	Sodium CMC ,pectin, and gelatin in polyisobutylene spread ontopolyethylene film	Oral cavity	Orahesive bandage
5) Beclomethasone dipropionate	Hydroxypropyl cellulose	Oral cavity	Rhinocort powder
	Polyacrylic acid	Vaginal	Raplens gel
6) Aluminium hydroxide	Sucrose octasulfate	GIT ulcers	Sucralfate
7) Fantanyl citrate	HPMC, Chitosan	Oral cavity	Fentora tablets
8) Nitroglycerine	Carbopol, HPMC K15M, K4M	Oral cavity	Nitrostat tablet
9) Miconazole	Na CMC, HEC	Oral cavity	Loramyc
10) Testosterone	HPMC,PVA,Chitosan PC and EudragitR S-100 (Polymethacrylic acid-co-methyl methacrylate)	Oral cavity	Striant SR
12) Buprenorphine	Gelatin and CP 934P CP 934P, Polyisobutylene, and Polyisoprene	Oral route	Subutex tablets

Mucoadhesive Polymers

Mucoadhesive drug shipping structures are primarily based totally at the adhesion of a drug/ provider to the mucous membrane. To sell this adherence a appropriate provider is required.

Ideal Characteristics of Mucoadhesive Polymers:

A mucoadhesion promoting agent or the polymer is brought to the components which allows to sell the adhering of the lively pharmaceutical component to the oral mucosa. The agent may have such extra houses like swelling with a view to sell the disintegration while in touch with the saliva.

1. Polymer have to have a excessive molecular weight as much as 100.00 or extra. This is important to sell the adhesiveness among the polymer and mucus.
2. Long chain polymers-chain period have to be lengthy sufficient to sell the interpenetration and it ought to now no longer be too lengthy that diffusion turns into a problem.
3. High viscosity.
4. Degree of cross linking- it impacts chain mobility and resistance to dissolution. Highly pass related polymers swell in presence of water and hold their shape. Swelling favours managed launch of the drug and will increase the polymer/mucus interpenetration
5. Spatial conformation.
6. Flexibility of polymer chain- this promotes the interpenetration of the polymer in the mucus network.
7. Concentration of the polymer- an most useful awareness is needed to sell the mucoadhesive electricity. It relies upon however, at the dosage shape.
8. Charge and diploma of ionization- the impact of polymer rate on mucoadhesion changed into without a doubt proven through Bernkop-Schnurch and Freudl. Cationic chitosan HCl confirmed marked adhesiveness while in comparison to the control. The attachment of EDTA an anionic institution improved the mucoadhesive electricity significantly. DTPA/chitosan gadget exhibited decrease mucoadhesive electricity than cationic chitosan and anionic EDTA chitosan complexes due to low rate. Hence the mucoadhesive electricity may be attributed as anion>cation>non-ionic.
9. Optimum hydration- immoderate hydration results in reduced mucoadhesive electricity because of formation of a slippery mucilage.
10. Optimum pH – mucoadhesion is most useful at low pH situations however at better pH values a alternate withinside the conformation takes place right into a rod like shape making the ones extra to be had for inter diffusion and interpenetration. At very improved pH values, definitely charged polymers like chitosan shape polyelectrolyte complexes with mucus and show off sturdy mucoadhesive forces.

11. It ought to non toxic, economic, biocompatible ideally biodegradable. [8] Various mucoadhesive polymers can extensively be labeled as follow: Synthetic polymers:
    1. Cellulose derivatives (Methylcellulose, Ethyl cellulose, Hydroxyl ethyl cellulose, Hydroxyl propyl cellulose, Hydroxy propyl methylcellulose, Sodium carboxy methylcellulose).
    2. Poly (Acrylic acid) polymers (Carbomers, Polycarbophil).
    3. Poly hydroxyl ethyl methylacrylate.
    4. Poly ethylene oxide.
    5. Poly vinyl pyrrolidone.
    6. Poly vinyl alcohol.

Natural polymers: Tragacanth, Sodium alginate, Guar gum, Xanthum gum, soluble starch, Gelatin, Chitosan . Mucoadhesive polymers also can classify into following categories:

Traditional non-particular first-era mucoadhesive polymers First-era mucoadhesive polymers can be divided into 3 most important subsets, namely:

1) Anionic polymers,

2) Cationic polymers,

3) Non-ionic polymers.

Of these, anionic and cationic polymers had been proven to show off the best mucoadhesive electricity. Consequently, such charged polymeric structures will now be tested in extra depth.

Anionic polymers are the maximum extensively hired mucoadhesive polymers inside pharmaceutical method because of their excessive mucoadhesive capability and occasional toxicity. Typical examples encompass poly (acrylic acid) (PAA) and its weakly cross-connected derivatives and sodium carboxymethylcellulose (NaCMC). PAA and NaCMC own terrific mucoadhesive traits due to the formation of robust hydrogen bonding interactions with mucin.Polycarbophil (Noveon) and Carbomers (Carbopol), PAA derivatives had been studied substantially as mucoadhesive systems for drug transport to the GI tract.

Cationic Polymers

Of the cationic polymer structures, certainly chitosan is the maximum substantially investigated inside the modern medical literature. Chitosan is a cationic polysaccharide, produced through the deacetylation of chitin, the maximum considerable polysaccharide withinside the world, subsequent to cellulose. The interesting houses of chitosan had been acknowledged for decades with many examples of its use in agriculture, enterprise and medicine. [9]

Novel second-technology mucoadhesive

The main downside in the use of conventional nonspecific mucoadhesive structures (first technology) is that adhesion may also arise at webweb sites aside from the ones intended. Unlike first-technology non-unique systems, sure second-technology polymer systems are much less at risk of mucus turnover rates, with a few species binding without delay to mucosal surfaces; greater correctly termed ``Cytoadhesives".

Lectins

The maximum extensively investigated of such structures in this recognize are lectins. Lectins belong to a set of structurally various proteins and glycoproteins that can bind reversibly to unique carbohydrate residues. After preliminary mucosal mobileular-binding, lectins can both continue to be at the mobileular floor or withinside the case of receptor mediated adhesion in all likelihood come to be internalised via a procedure of endocytosis.

Thiolated polymers:

The presence of unfastened thiol organizations withinside the polymeric skeleton allows withinside the formation of disulphide bonds with that of the cysteine-wealthy sub-domain names gift in mucin that can extensively enhance the mucoadhesive houses of the polymers (e.g. poly (acrylic acid) and chitosan).Various thiolated polymers encompass chitosan–iminothiolane, poly(acrylic acid)– cysteine, poly (acrylic acid)–homocysteine, chitosan–thioglycolic acid, chitosan–thioethylamidine, alginate–cysteine, poly (methacrylic acid)– cysteine and sodium carboxymethylcellulose–cysteine.

Polyox WSR

A elegance of excessive molecular weight polyethylene molecular weight polyethylene oxide homopolymers having the subsequent houses,

- Water soluble hydrophilic nature
- Functional organization for hydrogen bonding
- Biocompatible and non poisonous
- High molecular weight

Novel polymers

- Tomato lectin confirmed that it has binding selectivity to the small gut epithelium.
- A new elegance of hydrophilic strain touchy adhesives (PSA) had been evolved with the aid of using corium technologies. Complex had been organized with the aid of using non covalent hydrogen bonding crosslinking of a movie forming hydrophilic polymer with a brief chain plasticizer having reactive OH organizations at chain ends. [8]

Recent Advances in Mucoadhesive Drug Delivery System

Mucoadhesive Polymers

Diverse training of polymers were investigated for capacity use as mucoadhesive. PAA has been taken into consideration as an awesome mucoadhesive. PAA is copolymerised with polyethylene glycol (PEG) or poly(vinyl pyrrolidone) (PVP) to enhance those properties.

Devices

Several laminated gadgets were advanced to gain sustained drug launch. It may be categorized as:-

- Monolithic (or matrix) structures wherein the drug is dissolved or dispersed withinside the polymer device – diffusion of drug from the drug/polymer matrix controls the general fee of its launch from the device.
- Reservoir (or membrane) structures wherein diffusional resistance throughout a polymeric membrane controls the general drug launch fee.[11]

Conclusion

The phenomenon of mucoadhesion may be used as a version for the managed drug shipping strategies for some of drug candidates. There isn't any doubt that the oral path is the maximum favoured and likely maximum complicated path of drug shipping. The buccal mucosa gives numerous benefits for managed drug shipping for prolonged durations of time. The mucosa is properly provided with each vascular and lymphatic drainage and first-by pass metabolism withinside the liver and pre-systemic removal withinside the gastrointestinal tract are avoided.

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NOVEL DRUG THERAPY IN PARKINSON'S DISEASE

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ABSTRACT

Parkinson`s ailment is the maximum not unusual place Neuro-degenerative disorder. Several new medicinal drugs are discovered, maximum of which might be versions of formerly current merchandise, such new dosage varieties of already-authorized merchandise, or cost-saving usual formulations were proposed. These new merchandise make contributions to the general public health, protection of the people, extra get right of entry to to medication, greater client choice, and a aggressive market that complements affordability and first-rate and care. However, those new approvals that we seek advice from as novel capsules are most of the greater honestly modern merchandise that regularly assist earlier scientific care to some other level. This article consists of observe of current capsules and novel capsules withinside the Parkinson`s ailment remedy and additionally describes their medicinal chemistry i.e knowledge its structure, synthesis, structural pastime relationships, mechanism of action, healing uses, negative consequences etc. These capsules are capable in diverse regions to satiate, cause them to appropriate for its healing use and for drug formulations and discoveries

Keywords: *Neuro-degenerative disorder, new approvals, medicinal chemistry, novel capsules, synthesis, structural pastime relationship, medication.*

1. INTRODUCTION

A lack of dopamine-producing cells withinside the mind that outcomes in a complicated array of signs and symptoms is referred to as as Parkinson`s ailment (PD) however it's far in most cases related with modern lack of motor control. Major reason of incapacity some of the elder is Parkinson`s ailment. After Alzheimer`s.

Common diagnostic standards usually require the initiation of antiparkinson`s medicinal drug earlier than the prognosis may be confirmed. This ambiguity may be perplexing for number one care physicians, ailment, presently the second one maximum not unusual place neurological degenerative ailment affecting global is Parkinson`s ailment. Young-onset Parkinson`s ailment is a circumstance in which an person beneath neath forty years of age may also increase PD. It is hard to diagnose PD.

Fig: 1

Fig. 1: Parkinson`s ailment. Especially whilst the ailment provides with out the feature tremor. Some- instances PD circumstance wherein no tremors arise can be unsuitable for a Parkinson ailment is frequently viable in number one care.[1]

Objective:

This article offers a dialogue concerning latest improvement of drug medicinal drugs to deal with Parkinson's ailment. The predominant goal is to go looking the latest novel tablets used and to make out the Parkinson ailment circumstance whose predominant functions are:

- Slowed movement
- Balance
- Gait & stability problems.

Drugs utilized in PARKISON DISEASE THERAPY, and to supply a element facts specifying the medication and NOVEL DRUGS accredited so far, for the remedy of this Neuro- degenerative ailment and describe approximately the chemistry.

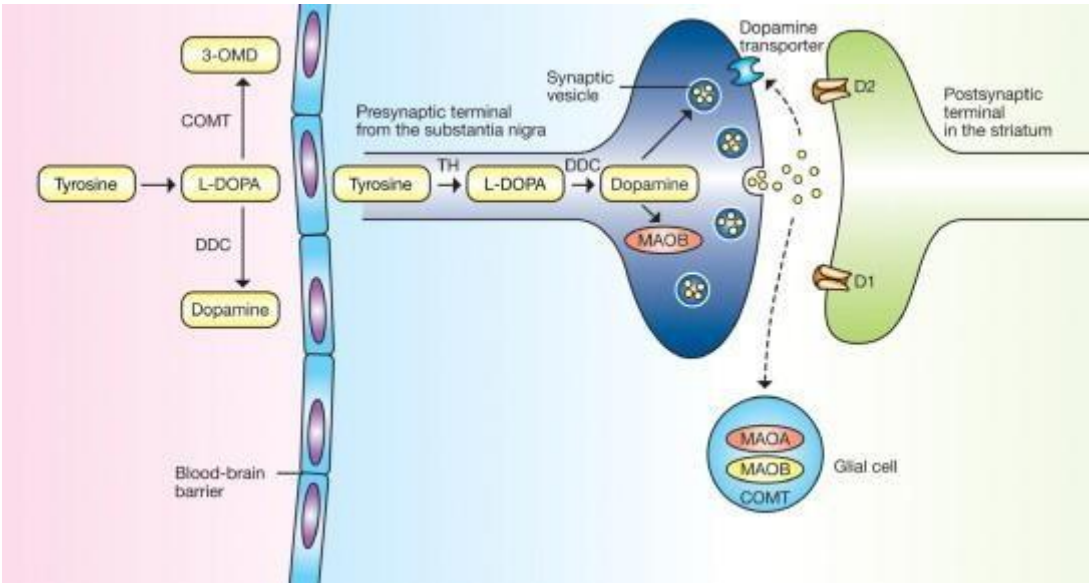
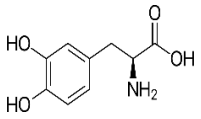
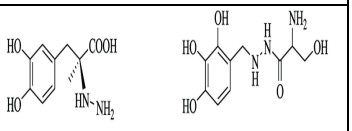


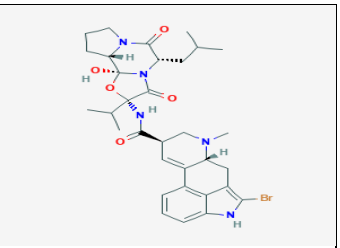
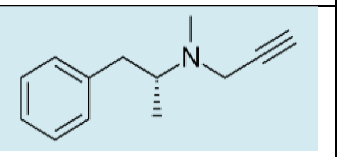
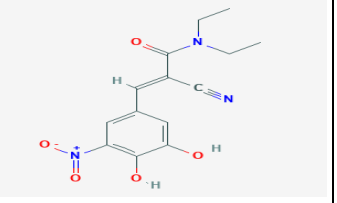
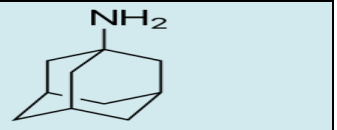
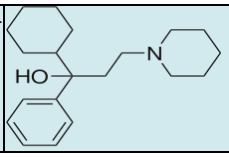
Fig-3: Mechanism of Action of Dopamine

General Mechanism of Action Parkinson's :

Disease is a progressive neurodegenerative disorder with motor defects due to the imbalance between the dopaminergic (inhibitory-D2, excitatory-D1 receptors). These are amplified by K+ channels, respectively. Parkinson's disease is characterized by dopamine deficiency. Levodopa is considered to act through D1 and D2 receptors present in the straitum and it regulates the activity of the two pathways having opposite effects on the thalamic input to the motor cortex.

Classification of Anti Parkinson's Drugs:

Drugs affecting Brain Dopaminergic system			
Class	Example	IUPAC	Structure
Dopamine precursor	Levodopa	(2S)-2-amino-3-(3,4-dihydroxyphenyl)propanoic acid	
Peripheral decarboxylase inhibitors	Carbidopa Benserazide	(2S)-3-(3,4-dihydroxyphenyl)- 2-hydrazino-2- methylpropanoic acid	

Dopaminergic agonists	**Bromocriptine** Ropinrole Pramipexole	(6aR,9R)-5-bromo-N- [(1S,2S,4R,7S)-2-hydroxy-7- (2-methylpropyl)-5,8-dioxo-4- propan-2-yl-3-oxa-6,9-diazatricyclo[7.3.0.02,6]dodec an-4- yl]-7-methyl-6,6a,8,9- tetrahydro- 4H-indolo[4,3- fg]quinoline-9- carboxamide	
MAO-B ***inhibitors***	**Selegeline** Rasageline	(R)-N-methyl-N-(1-pheny lpropan- 2-yl)prop-3-yn-1- amine	
COMT inhibitors	**Entacopone** Tolcopone	(E)-2-cyano-3-(3,4- dihydroxy-5-nitrophenyl)- N,N-diethylprop-2-enamide	
Glutamate (NMDA)receptor agonist(Dopamin e facilitator)	**Amantadine**	Adamantan-1-amine	
Drugs Affecting Brain Cholinergic System			
Central anticholinergics	**Trihexylphenidyl** Procyclidin Biperiden	(RS)-1-Cyclohexyl-1-phenyl- 3-(1-piperidyl)propan-1-ol	
Antihistaminics			
	Orphenadrine Promethazine	N,N-dimethyl-2-[(2- methylphenyl)- phenylmethoxy]ethanamine	
Miscallaneous Drugs			
Antidepressents	Amitryptillin e Trazadol	3-(10,11-dihydro-5H- dibenzo[a,d]cycloheptene- 5-ylidene)-N,N-dimethylpropan-1-amine	
Vitamin-E	Tocopherol	2,7,8-trimethyl-2-(4,8,12- trimethyltridecyl)-3,4- dihydrochromen-6-ol	
Glutamate release inhibitor	Lamotrigine	6-(2,3-dichlorophenyl)- 1,2,4-triazine-3,5-diamine	
Glutamate release antagonist	Remacimide	2-amino-N- (1,2diphenylpropan-2- yl)acetamide	
Glialderived neurotrophic factor	GDNF		

A novel drug or novel molecular entity (NME) is a drug complex molecule previously not approved by the FDA / EMA. This i s different from the drug previously approved , which is different but approved in the new state. It also distinguishes from generics. Generic drug is the same NME generic

(usually) patent-free formulation, but manufactured by an alternative company. To minimize these clinical complications, a new compound has been developed. New drugs and bioproducts for the treatment of of PD need to address dopaminergic neuroprotection, reduce early neurodegeneration and improve dopaminergic neurotransmission. [Four]

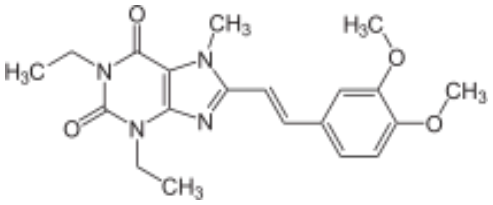
Many of the new drugs have been introduced for the treatment of in Parkinson's disease, some of which are briefly described here.

1. Istradeyfylline
2. Nilotinib
3. 3.Safinamide
4. Isradipine
5. Ionosine
6. Stalevo
7. Idazoxan
8. Mirtazapine
9. Apomorphine Infusions
10. Rotigotine Skin patches
11. Pimavanserin

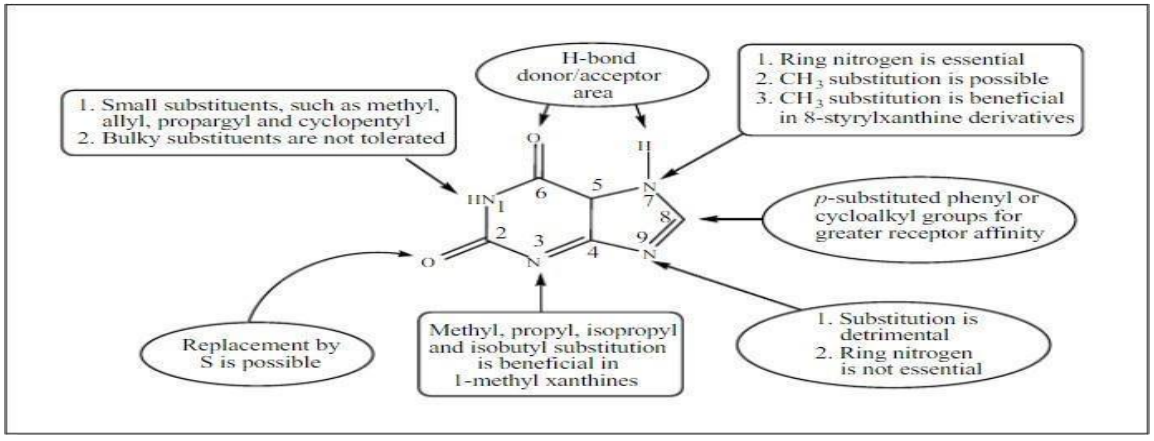
Istradefylline :

Istradefylline or KW6002 was developed by Japanese Kyowa Hakko Kirin for the treatment of Parkinson's disease as an adjunct to standard of care. Unlike preferred dopaminergic treatment plans for Parkinson`s. Istradefylline objectives adenosine A2A receptors withinside the basal ganglia. This vicinity of the mind is fantastically concerned in motor control. Istradefylline is indicated as an accessory remedy to [levodopa] and[carbidopa] for Parkinson's disease. This drug changed into first permitted in Japan on 25 March 2013. Istradefylline changed into granted FDA approval on 27 August 2019[5] Istradefylline, bought below the logo call Nourianz.

Structure



Structural Activity Relationship Synthesis



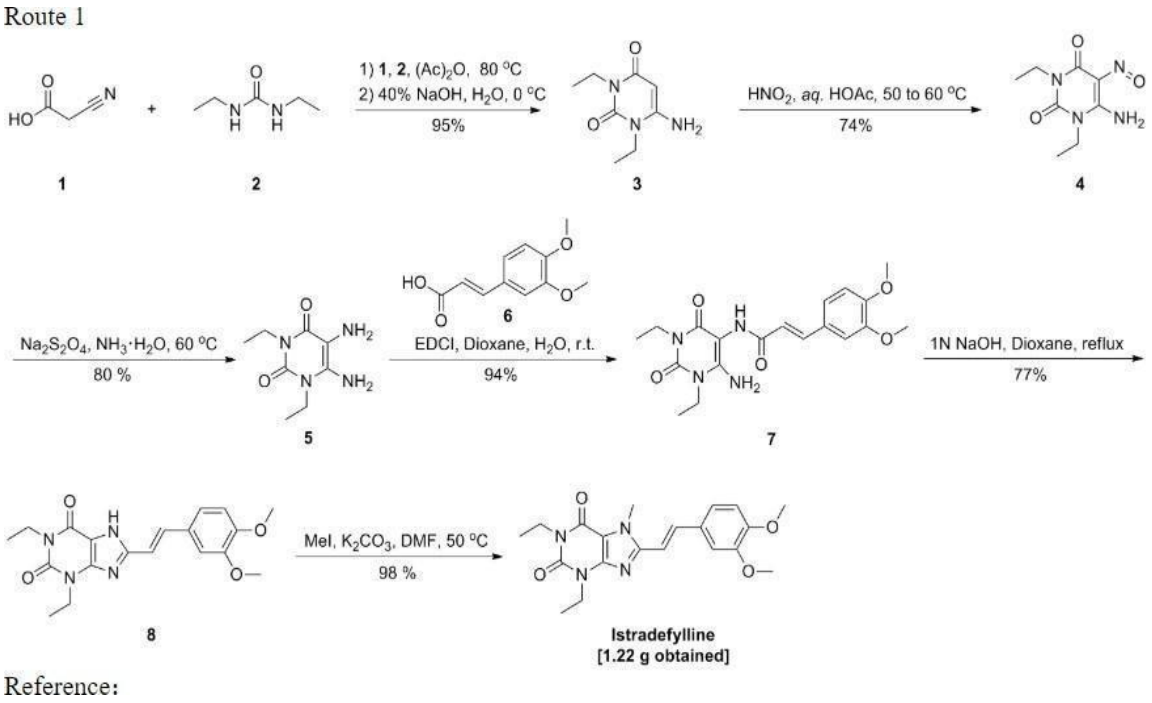


Fig. 5: SAR of Istradeyfylline.

Antagonist used similarly to carbidopa and levodopa for the remedy of "off" episodes. The unique mechanism of motion of the drug is unknown however it's far presumed to lessen the over pastime of the striatal pathway, restoring the stability of basal ganglia.

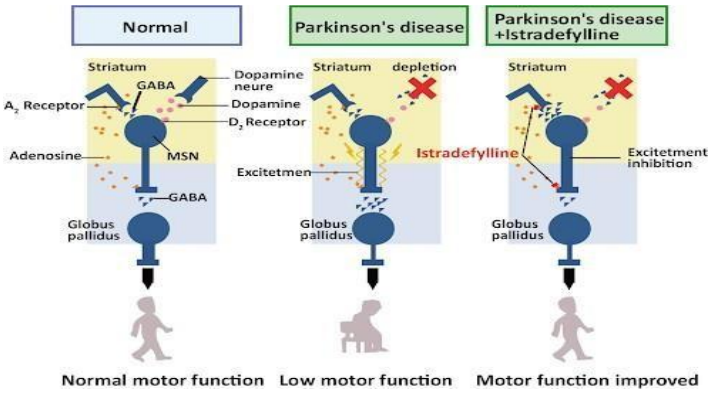


Fig-4: Motor function in PD.

Therapeutic uses Istradefylline is utilized by human beings with Parkinson`s sickness taking carbidopa/levodopa to lessen the quantity of "off" time (durations of gradual motion or stiffness.

Adverse effects

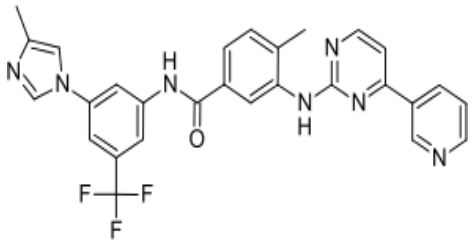
- Involuntary muscle movements,
- dizziness,
- constipation,
- nausea,
- hallucinations, and
- Insomnia

Nilotinib:

Nilotinib via way of means of Novartis is a ability new remedy for Parkinson`s sickness (PD).

A medical trial investigating the repurposed most cancers drug Nilotinib in human beings with Parkinson's sickness unearths that it within reason secure and properly tolerated. Researchers additionally document locating an growth in dopamine, the chemical misplaced becau se of neuronal destruction, and a lower in neurotoxic proteins withinside the mind amongst examine participants. Finally, they are saying Nilotinib, a tyrosine kinase inhibitor, doubtlessly halts motor and non-motor decline.

Structure:



IUPAC name: 4-methyl-N-[3-(4-methyl- 1H-imidazol1-yl)- 5- (trifluoromethyl) phenyl]-3- [(4-pyridin-3- ylpyrimidin2-yl) amino]benzamide.

Molecular formula: C28H22F3N7O

Molecular weight: 529.52 g/mol

Mechanism of Action:

Nilotinib blocks the non-receptor Abelson (Abl) tyrosine kinase, however its precise mechanism of movement in Parkinson`s disorder remains beneath neath investigation. The desire is this technique should sluggish down or prevent Parkinson`s progression. The consequences of the first protection observe have to be to be had soon.

Synthesis:

The5-bromo-3-(tri fluoro methyl) phenyl amine became reacted with four-methyl-1H- imidazole withinside the presence of cesium carbonate and cuprous iodide to gain 3-trifluoromethyl-5-(four-methyl-1H-imidazol- 1- yl) phenyl amine(four). Ethyl 3-amino-four- methyl benzoate became reacted with cyanamide to gain the guanidine, which cyclized with 3-dimethylamino 1-(3- pyridinyl) -2- propylene-1-one to offer ethyl4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl] amino] benzoate(eight). Compound eight became subjected to Boc protection, hydrolysis, amidation and then condensation with compound four to offer 4methyl-N-[3-(4-methyl-1H-imidazol-1- yl)-5- (trifluoromethyl)phenyl]-3-[N-tert butoxycarbonyl-[4-(3-pyridinyl)-2-pyrimidinyl] amino] benzamide(10). After deprotection, nilotinib became obtained.

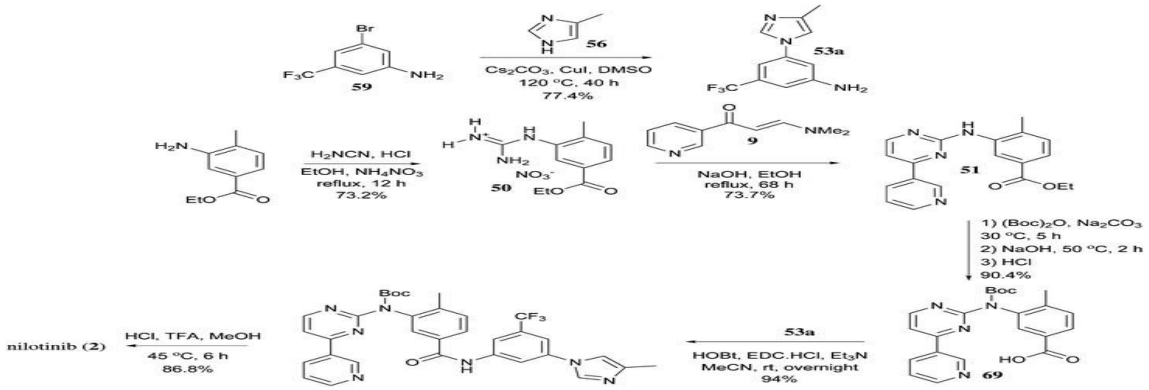


Fig-6: Synthesis of Nilotinib.

Therapeutic uses:

Parkinson`s sickness and experimental Parkinsonism.[69] Idazoxan, as an accessory Nilotinib is used withinside the remedy of Parkinson sickness. Nilotinib is used to deal with a positive kind of blood most cancers (continual myelogenous leukemia-CML). It works via way of means of slowing or preventing the increase of cancer cells.

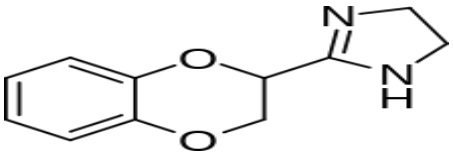
Adverse effects

- Itching,
- Headache,
- Nausea,
- Fatigue,
- Tiredness,
- Joint or muscle aches or pain,
- Back Pain,
- Diarrhoea,
- Constipation.

IDAZOXAN:

It has been proposed that Idazoxan in aggregate with L-dopa can also additionally offer a unique technique to the remedy of Parkinson`s sickness with a view to now no longer most effective lessen the dyskinetic aspect effects, however enlarge the anti-parkinsonian movements of L- dopa. The a2-adrenoceptor antagonist idazoxan can also additionally enhance motor signs in to dopamine replacement, can also additionally show beneficial withinside the remedy of parkinsonian sufferers in any respect ranges of sickness progression.

Structure:



IUPAC Name: (±)-2-(2,3-dihydro-1,4- benzodioxin-2- yl)-4,5-dihydro-1H- imidazole.

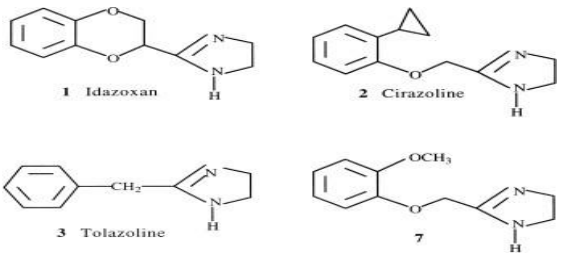
Molecular formula: C11H12N2O2 Molecular weight: 204.225g.

Mechanism of action:

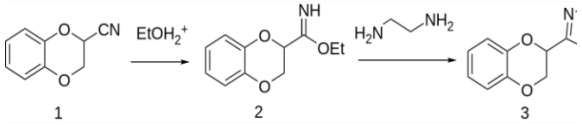
Idazoxan complements the antiparkinsonian moves of levodopa and decreases dyskinesia in MPTP dealt with primates. It has been proven time and again that stimulation of the noradrenergic device will beautify reminiscence retrieval idazoxan, will increase firing of noradrenergic neurons of the locus coeruleus twofold at a dose that has no detectable impact on overt conduct which includes locomotor pastime.

Structure Relation Activity:

Although on the α1-adrenoreceptor all of the compounds displayed a widespread agonist pastime, on the α2 -adrenoreceptor they confirmed both agonist or antagonist pastime relying on the character of the phenyl substituent. The qualitative structure–pastime courting led us to the realization that the oxygen atom withinside the side-chain is vital for α1-agonist pastime, at the same time as the cyclopropyl ring is not, and can be changed through numerous corporations. Of the corporations studied, isopropoxy seems to be the best. Instead, the identical substitution (i.e., isopropoxy for the cyclopropyl ring) at α2-adrenoreceptors reasons a reversal of pastime. On the different hand, the cyclopropyl ring appears to be important for α1-selectivity.



Synthesis:



Therapeutic uses:

- It has antidepressant impact however has now no longer been reached the market
- Antipsychotic
- In pathogenesis of schizophrenia.

Adverse reactions:

Dyskinesia is a common and disabling facet impact in sufferers with Parkinson`s, Idazoxan without a doubt extends LDOPA's anti parkinsonian benefits.[17]

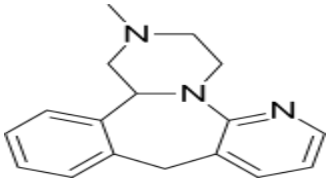
Isradipine:

Isradipine Fails to Slow Early Parkinson Disease Progression in Phase three Study.[19] Isradipine is a medicine presently used to deal with excessive blood strain and is going via way of means of the emblem call of DynaCirc®. It is classed as a calcium channel blocker. Isradipine stuck the eye of researchers for Parkinson`s disease (PD) whilst facts from huge medical research confirmed that human beings taking isradipine had a decrease threat of growing PD. It is concept that during dopamine neurons withinside the brain, neurons which die in Parkinson`s disease, the access of calcium in those neurons over time ends in damage. Isradipine blocks the interest of unique channels withinside the neuron that permit the calcium to enter, as a result stopping the dying of the neurons (nerve cells) that produce dopamine and might sluggish the development of PD. It isn't but recognized if Isradipine has useful results on PD. Data from the trial will offer greater statistics on its effectiveness in human beings with PD. In addition, low blood strain is a not unusual place symptom of PD, so this medicine can also additionally get worse the condition.

MIRTAZAPINE:

Pramipexole (Mirapex®) is a drug this is powerful at assuaging motion deficits related to Parkinson`s disorder. However, pramipexole can set off compulsive behaviours and behavioral addictions, such as trouble gambling, in a few patients. Mirtazapine, an strange antidepressant reduces the consequences of drug dependancy in pre-scientific fashions and in humans. This examine targets to decide if mirtazapine can lessen pramipexole-brought on gambling-like conduct in a version of PD, even as leaving the motor blessings intact.[20] Psychotic signs regularly arise as a worry in Parkinson`s disorder patients, and a fixed of standards for Parkinson's disorder with psychosis (PDPsy) has been established. Mirtazapine progressed the patient's refractory psychotic signs, specially her visible hallucinations, with out worsening her motor signs.

Structure:



IUPAC name:(±)-2-Methyl- 1,2,3,4,10,14b hexahydropyrazino [2,1- a]pyrido[2,3-c],[2]benzazepine

Molecular formula: C17H19N3 Molecular weight: 263.35 g/mol.

Mechanism of action:

- Blockade of pre-synaptic alpha 2 receptors, which reasons the growth withinside the launch of nor- epinephrine from the nor- adrenergic nerve endings and of serotonin from serotonergic nerve endings.
- Blockade of 5HT-2A Presynaptic receptors.
- Blockade of H1 receptors. (It isn't recognized which of this movements greater essential for the antidepressant effect.)

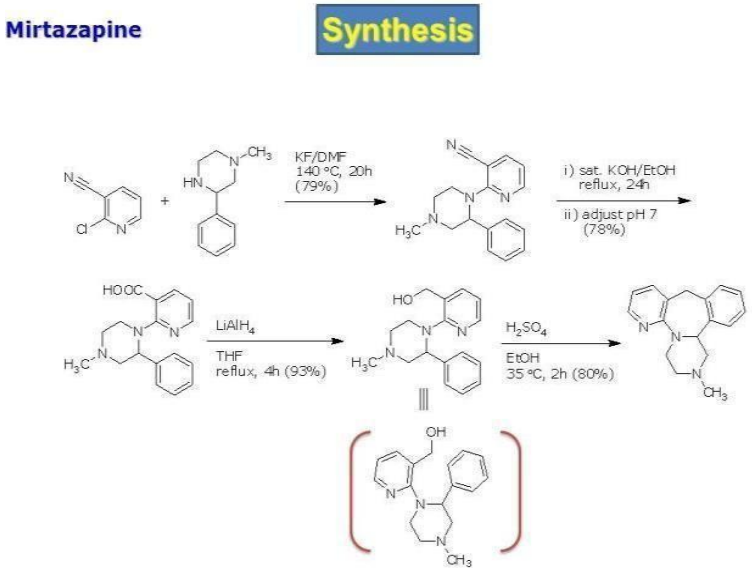


Fig. 7: Synthesis of Mirtazapine Therapeutic uses.

Synthesis:

- Psychosis associated Parkinson therapy
- Antidepressant

Adverse reactions:

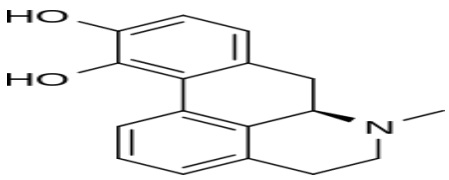
- Sedation and drowsiness.
- Constipation, urge for food stimulation, Weight gain.

Contraindications:

- REMERON (mirtazapine) Tablets are contraindicated in sufferers with a acknowledged allergic reaction to mirtazapine.
- Starting REMERON in a affected person who's being dealt with with MAOIs consisting of linezolid or intravenous methylene blue is likewise contraindicated due to an improved hazard of serotonin syndrome.

Apomorphine INFUSION:

Apokyn (apomorphine) is utilized by injection to deal with loss of frame motion manipulate in sufferers with superior Parkinson`s ailment among doses of levodopa treatment. It has the equal impact as dopamine, a certainly going on chemical messenger observed withinside the brain.



IUPAC Name: (6aR)-6-methyl-5,6,6a,7- tetrahydro-4Hdibenzo[de,g]quinoline- 10,11-diol

Molecular formula: C17H17NO2 Molecular weight: 267.332g/mol.

Mechanism of action:

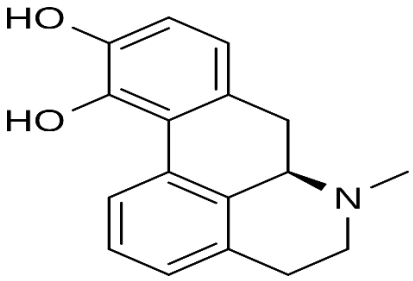
Apomorphine`s R-enantiomer is an agonist of each D1 and D2 dopamine receptors, with better pastime at D2. Apomorphine improves motor feature with the aid of using activating dopamine receptors withinside the nigrostriatal pathway, the limbic system, the hypothalamus, and the pituitary gland It additionally will increase blood go with the drift to the supplementary motor region and to the dorsolateral prefrontal cortex (stimulation of which has been located to lessen the tardive dyskinesia effects of L-DOPA). Parkinson's has additionally been located to have extra iron on the web sites of neurodegeneration; each the R- and S-enantiomers of apomorphine are potentiron chelators and radical scavengers. Apomorphine additionally reduces

the breakdown of dopamine withinside the brain (aleven though it inhibits its synthesis as well).[19][20] It is a effective up regulator of sure neural increase factors,[21] specifically NGF and BDNF, epigenetic down law of which has been related to addictive behaviour in rats.

Apomorphine reasons vomiting with the aid of using appearing on dopamine receptors withinside the chemoreceptor cause region of the medulla; this turns on the close by vomiting center.

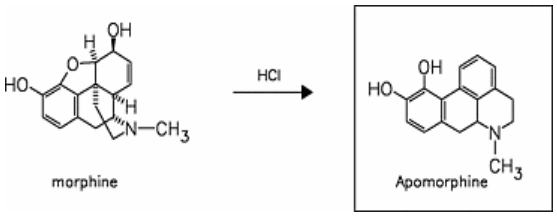
Structure Activity relationship

- The facet chain of dopamine (DA) is bendy (rotation round β- carbon phenyl bond).
- Compounds with catechol ring & amino-ethyl moiety of DA are held in inflexible conformation are synthesized. Ex: Apomorphine.
- It has shape similarities in trans- α- rotamer conformation.



STRUCTURE

Synthesis:



Therapeutic uses:

Apokyn can be used as much as 5 instances an afternoon as a small injection beneath neath the skin, the use of a tool just like the only used for insulin injection in human beings with diabetes. Apokyn begins off evolved operating as early as 10 mins after the injection, with maximum human beings feeling comfort from the "off" episode inside 20 mins. It typically lasts for as much as ninety mins, so it`s critical sufferers now no longer forestall taking their different Parkinson`s medications.

Adverse reactions:

Apokyn have to now no longer be occupied with drugs for nausea, vomiting, or irritable bowel syndrome, as critical facet results might also additionally occur, including seriously low blood stress and lack of consciousness.

Contraindications:

- The main and absolute contraindication to the use of apomorphine is the concurrent use of adrenergic receptor antagonists; combined, they reason a excessive drop in blood stress and fainting.
- IV management of apomorphine is extraordinarily discouraged, as it could crystallize withinside the veins and create a blood clot (thrombus) and block a pulmonary artery (pulmonary embolism).

2. DISCUSSION

Parkinson`s disorder changed into observed in historic era. It changed into defined in historic writing. There isn't anyt any precise remedy for PD however exceptional medicines are to be had that are used to deal with PD. The remedy consists of plant primarily based totally remedy, medicinal capsules inclusive of dopamine which replaces with dopamine substitute therapy, surgical remedy inclusive of deep mind stimulation (DBS). These signs are examined with the aid of using medicinal drug with levodopa. According to researchers there's desire for improvement for technique which now no longer handiest treatment plans PD however additionally assist to manage improvement of PD. The remedy is turning into greater state-of-the-art as there are new techniques are evolved as NOVEL DRUGS FOR PARKINSON which lead a course to deal with this neurodegenerative disorder, many capsules were observed and this play an crucial function in stopping the disorder. This novel capsules along side their medicinal chemistry

primarily based totally on its structure, synthesis, SAR`S, mechanism of action, healing uses, Adverse outcomes and contraindications etc. are mentioned above withinside the concept that's useful in drug layout and modulation.

3. SUMMARY

Parkinson`s sickness is the maximum not unusual place Neuro-degenerative ailment. Several new medicines are observed, maximum of which can be versions of formerly present products, such new dosage kinds of already approved products, or cost-saving time- honored formulations the NOVEL DRUGS for its remedy were proposed. This thesis describes concerning the PARKINSON DISEASE and its hi story, genetics, the generally used tablets for its remedy and their medicinal chemistry and additionally it describes approximately the newly observed tablets for the remedy of this ailment alongside with their medicinal chemistry. This technique turned into mentioned to make out a quick concept concerning the medicine used these days maximum generally to deal with the sickness and the primary aim turned into to have a look at concerning tablets to get a clean concept approximately its chemistry which used for its method and in numerous different aspects.

4. CONCLUSION

In conclusion, the technique has been implemented to apprehend the aetiology of PD and to discover its genetic reasons in addition to remedy strategies. Based at the strong and green technique implemented on this study, which turned into executed with out dimensionality reduction, greater biologically treasured consequences were obtained.

In this study, a few pills were proposed as novel remedies for PD. Parkinson`s ailment is maximum not unusual place form of motion ailment visible in medical practice. Early prognosis may be made with excessive index of suspicion. Most of the sufferers reply to dopa agonists or L- dopa preparations.

Parkinson`s ailment is an incurable ailment that has proved tough to manipulate and deal with with current therapies.

Disease change is the remaining aim for drug improvement however has, so far, remained elusive.

Several NOVEL DRUGS has been evolved and are determined beneficial for the remedy and prevention of Parkinson`s ailment as mentioned above i.e Istradeyfylline, Nilotinib, Safinamide, Stalevo, Idaoxazon, Ionosine, Mirtazapine, and it additionally offers a quick rationalization concerning their medicinal chemistry.

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A Review: Evaluation & Modernization of Pharmaceutical Industry (4.0)"

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Overview

Industry 4.0 is a new industrial revolution that uses cyber-physical technology to improve system intelligence. The use of autonomous devices and systems is crucial in the manufacture of pharmaceuticals and has the potential to bring products to market with high levels of quality, low cost and time. The R & D phase of developing a new drug or drug can be very long and costly compared to traditional products, so applying Industry 4.0-related technology to the drug development process could bring significant benefits to the biomedicine and pharmaceutical industry. there is. It also could open new windows for regulators to track and track all stages of the drug development process with less effort. This chapter describes the first various phases of the drug development process, then details the use of computers and digital technologies in each phase, and finally introduces the Pharma 4.0 ecosystem.

Industry 4.0 is the latest move towards intelligent automation technology. In this new era, the integration of modern manufacturing and new information technologies will play an important role in economic competitiveness . This review examines future technological trends in the pharmaceutical industry. In the pharmaceutical industry, Industry 4.0 can support extended manufacturing personalized medicine, layered modeling, localized 3D printing of treatments, and even a future in which humans are no longer closely involved in production. This future will be possible when industry and educational institutions work together to promote advanced research and implementation of Industry 4.0. With the advent of the new cyber-physical system design paradigm, the variety of systems that future enterprises will need to collaborate with has increased significantly. Industry 4.0 is an industrial approach that addresses all aspects of the industrial management model, including culture, management accountability, and regulatory interaction. Manufacturing is moving from mass production to mass customization , with industry 4.0-related trends such as data integrity by design, overall control strategy, personalized processing, and industry-wide end-to-end supply chain integration. Is spurring on. Industry 4.0 will enable cyber and physical systems to work together to build smart factories by redefining the role of humans in manufacturing. Industry 4.0's new technology enables the creation of sustainable value, leading to a more agile and intelligent personalized pharmaceutical industry, enabling pharmaceutical companies to achieve a competitive advantage. A more sustainable drug supply chain needs to be implemented to coordinate future operations and management throughout the drug lifecycle. The 4.0 technology emerging industry is now aiming for flexible and localized production close to its customers. Manufacture "on demand" and try to avoid large inventories. Innovative, adaptable technology helps pharmaceutical companies establish a more robust and agile manufacturing process that features reduced interruptions, reduced errors, and improved quality control .

Keywords: Industry 4.0 · Pharma 4.0 · Intelligent manufacturing · Drug development process

Introduction

Three major revolutions in the manufacturing industries have already occurred: Industry 1.0 was introduced when mechanization and steam power were employed to perform over human power processes, Industry 2.0 was introduced when mass production and electric energy provided a huge improvement in the productibility level of manufacturing systems, and Industry 3.0 introduced the power of automation, computer, and IT to the manufacturing industries. The fourth industrial revolution has been called Industry 4.0 .Consider a production system with robots, CNC machines, automatic storage, and handling systems and operators that communicate with one another using a computerized network system, and each of them autonomously rearranges their operation through a cloud-based central decision-maker. Imagine a city where transportation systems, traffic control systems, grid, ports, healthcare systems, parking, waste management systems, and air pollution control systems negotiate with each other, and a cloud-based intelligence system arranges all operations on an optimal level to promote safety and cost issues of the people. Imagine a health center that can communicate with many different sections, aiming to provide the finest quality of services. These are a few examples of the future of Industry 4.0 that could be enabled by cyber-physical systems (CPS) technology.. CPS is defined as the calculation, interconnection, and integration of physical processes for the purpose of controlling the process. CPS is a combination of nodes with different roles and properties. These nodes adapt to new states based on the knowledge available in the system and the actual feedback from other nodes.

This technology, which is changing the way people interact with industrial systems, is very similar to the Internet, which has changed the way people interact with IT and information. Industry 4.0 uses CPS technology to bring intelligence to the system. CPS consists of many different and heterogeneous elements that require research to properly define each subelement and its specifications. The main technologies are the Internet of **Things (IoT)**, **artificial intelligence (AI)**, **cloud computing (CC)**, smart embedded devices, and the Internet . These technologies are at the core of CPS, but several other technologies such as digital twins, cloud manufacturing, virtualization, and green waste management can play a supporting role.

The role of CPS in pharmaceutical manufacturing has the potential to transform the control and management systems of biotechnology and pharmaceutical companies into what can be called the Pharma 4.0 revolution. These changes include reliable medical devices and systems, drug design and development, on-demand drug manufacturing, 3D printed drugs, Logistics 4.0 for drug distribution management, and green waste management. In pharmaceutical production where timing accuracy and quality issues are not noticeable, it is easy to consider and adopt new models such as "collaborative network organization" and "collaborative design & development". Autonomous and connected facilities can significantly increase the productivity of the pharmaceutical industry, leading to more effective detection and recovery of defective products.

Cyber-Physical Embedded PAT can significantly improve system intelligence and product quality and reduce reliance on human decision making. In monitoring, regulatory oversight benefits from a distributed consensus on the available bandwidth and technology of distributed control technology. Consumer networks can change dramatically at the right time. A distributed real-time quality controller that integrates sensors and actuators can change the nature of the Internetquelle1 **real-time release test (RTRT)** system. The economic impact of any of these applications is enormous. However, today's pharmaceutical industry can unnecessarily impede progress towards these applications. This chapter first briefly discusses Industry 4.0 technology, then the computing applications of the pharmaceutical and biotechnology industries, and finally the Pharma 4.0 ecosystem, and several (potential) exit applications.

Emerging 4.0 Technologies.

The industry today aims for flexible and localized production close to its customers. Manufacture "on demand" and try to avoid large inventories.

Adaptive and innovative technology helps pharmaceutical companies establish a more robust and agile manufacturing process featuring reduced interruptions, reduced errors and improved quality control . .. Vertical integration of Industry 4.0 will upgrade pharmaceutical manufacturing plants to "reconfigurable factories", allowing flexible, agile and intelligent production lines to support mass customization of personalized medicines to meet different needs. Will be . Efficient cross-company communication and big data analytics can improve process monitoring performance and detect and reduce material waste, overproduction, and energy consumption .

Topics covered in this article include Augmented Reality (AR) and Virtual Reality (VR). 3D printing and personalized medicine; digital twins and simulations. Cyber physical system, cloud.

Industry 4.0

Industry 4.0 is a new chapter in the Industrial Revolution related to the use of cyber-physical system technology in manufacturing, aimed at increasing system intelligence through networking, automation, machine learning and real-time monitoring. Figure 1 shows a schematic diagram of the CPS. As shown in the figure, the system contains several physical objects such as CNC machines, robots, automations, etc.0 Designer mobile and data capabilities. Imagine a computer. This entire physical object is an embedded device connected to the Internet. In addition, these devices include processors for decision making. Devices on the network are to exchange data with cloud services for monitoring and control using IoT technology and the Internet. To identify devices on the network, IoT technology provides nodes in the network with unique identities. The status of the device is captured by the sensor and monitored by the cloud service. The device is controlled by a cloud service using comments generated by AI tools and shared with the device via the IoT. The main goal of using CPS is to improve the intelligence of resources (devices, humans, etc.) and the level of integration between resources.

Drug Development Life Cycle:

Drug development is a step-by-step process that involves a series of stages, including drug discovery, preclinical trials, clinical trials, approval processes, and post-marketing surveillance. The following subsections briefly describe each of these steps.

Drug discovery: which is the first step of drug development process, brings thousands of potential candidate compounds as a medical treatment. However, only a few numbers of compounds have been forwarded to the next steps after early testing. Commonly, drug design and discovery are performed through the following steps:

Focusing on a disease process and etiologies to discover and identify a proper target

- Finding or designing a compound that interacts with the specified target to change disease situations
- Finding possible beneficial effects for lead identification by performing numerous molecular compound tests
- Searching among the unforeseen effects of current treatment protocols, aiming to find a possible new effect on the target
- Synthesizing a novel compound from existing materials that will be effective in manipulating the target

Ecosystem Pharma 4.0:

Ecosystem pharma 4.0 is a manifestation of Industry 4.0 in the pharmaceutical industry and can be defined as employing the medical cyber-physical system (MCPS) in any stage of the drug development life cycle (Ding 2018). MCPS refers to life-critical,context-aware, networked systems of medical tools and devices that are collectively involved in the treatment protocols of a patient. The main missions of using this paradigm in the drug development process are to reduce the developmental costs and cycle time and also to improve the quality of the drug products by(a) improving the smartness of the contributors (i.e., humans, tools, and devices),(b) connecting and integrating the smart contributors, and (c) providing real-time status and awareness information to the stakeholders and the regulatory authorities. MCPSs employ the technology of cyber-physical systems (CPSs) to provide high-quality continuous care for patients in complex medical scenarios such as clinical trials. CPSs are integrations of computation, networking, and physical processes. Embedded computers and networks monitor and control the physical processes with feedback loops, where physical processes affect computations and vice versa. Figure 1demonstrates the Pharma 4.0 ecosystem. It shows the process of collecting big data from several sources into a data pool and then performing the necessary analytics using AI, ML, or cognitive process to predict stream line drug life cycle processes. The ecosystem connects two separate worlds of embedded tools and devices (ETDs) and cybernetics in the life cycle of medicines. As shown in the figure, the drug life cycle includes three major steps: joint drug development, intelligent drug manufacturing, and post-marketing recognition systems. Other stakeholders, including regulatory agencies and customers, are also connected to the system via cybernetics. Cybernetics uses a variety of AI techniques and tools for decision making, communication, and automated control of healthcare systems. The ecosystem supports the Green Drug Lifecycle System. medical systems use less natural resources, reduce pollution and waste, recycle and reuse materials, and reduce emissions in the process. On the way to Pharma 4.0, we outlined current data science applications in various phases of the bioprocess life cycle. Recently, a Pharma 4.0 application in smart drug manufacturing was reported, and the author proposed a cyber physical-based PAT (CPbPAT) framework for implementing smart manufacturing systems in the pharmaceutical industry .The impact of data analysis techniques, digitization, Industry 4.0, artificial intelligence, digital twins, and continuous manufacturing on Pharma 4.0 has recently been reported in another paper.

The Need for Artificial Intelligence in Pharma 4.0:

Artificial intelligence in medicine and healthcare is growing rapidly. It uses a variety of software and complex algorithms to simulate human intelligence and cognition to analyze and interpret comprehensive complex healthcare and Medical data. AI has used different computational approaches and techniques in different medical disciplines, especially in diagnostic and therapeutic protocols

Medical AI has been able to recognize significant correlations in the data provided in many clinical conditions to help diagnose, treat, or predict non-clinical conditions such as medical conditions and laboratory tests. In medicine, this technology is rapidly evolving as a reliable solution to complex situations. With the development of new smart devices, such as wearables, smartphones, and biosensors, some techniques of AI, like deep learning, can deal with the provided big data of such smart devices meaningfully AI in pharmaceutical sciences and drug development process is associated with the use of different automated approaches and techniques to replace the traditional methods that rely on the human brain with these new technologies. It is not surprising that almost all aspects of the pharmaceutical industry, from drug discovery and laboratory studies to clinical researches of drug development, epidemic predictions, remote monitoring, and regulatory supervision, manufacturing processes, and marketing, can apply AI, which leads to increased operational efficiency and cost-effectiveness. AI can help to design and identify new molecules based on target validation very effectively. Complicated pharmaceutical and pharmacological networks with large databases always need to solve different complex issues and challenges, and AI is one of the best approaches to identify obscurant patterns between diseases, drug composition, and developmental qualities. Machine learning is currently merging quickly evolving methods in computer-aided drug discovery. To develop drugs with significant biological and chemical properties, ML is an applicable tool that mines chemical and biological information from large databases. To predict the physical, biological, and chemical properties of new compounds, the ML method uses pattern recognition algorithms to empirically differ significantly from physical models that rely on physical equations such as quantum chemistry. Build a generalized mathematical model under the results. Converting a composite structure into the chemical information used in the ML technique requires multi-layered computation (that is, chemical graph acquisition, descriptor generation, fingerprinting, similarity analysis). Each layer has a significant impact on the quality of the chemical data and is built on the previous layer. Machine learning methods can be divided into supervised learning and unsupervised learning. Supervised machine learning models include regression analysis, k-nearest neighbors (kNN), Basilian probability learning, SVMs, random forests, and neural networks. Unsupervised techniques include dimensionality reduction techniques such as: B. Principal Component Analysis (PCA), Independent Component Analysis (ICA), and several supervised methods that can support unsupervised learning (eg B. SVM, probabilistic graphical models and neural networks. Another of the unsupervised algorithms. One family is clustering algorithms. Discovering abuse relationships between chemical structures and their SAR or biological activity is one of the major areas of application of ML in drug discovery. Achine learning techniques can be used to model QSARs or quantitative structure-activity relationships (QSPRs) to develop artificial intelligence programs that accurately predict in silico how chemical modifications affect biological behavior. Many physicochemical properties of drugs, such as toxicity, metabolism, drug-drug interactions, and carcinogenesis, are effectively modeled by quantitative structure-activity relationship (QSAR) techniques. QSAR is a very important strategy in chemistry and pharmacies, based on the idea that changing the structure of a molecule changes the activity and properties of a substance . The general protocol for building QSAR models for drug discovery is systematic and consists of several modular steps, including chemo informatics and machine learning techniques. The first step is "molecular coding". This coding searches for experimental results to see if chemical features and properties are derived from the chemical structure. It then uses unsupervised learning techniques to perform feature selection steps to identify the most relevant features and reduce the dimensions of the feature vector. Finally, in the learning phase, a supervised machine learning model is applied to detect empirical functions (explicit or implicit) that can achieve the optimal association between the input feature vector and the biological response (Hunter). Computational drug discovery provides researchers with pharmacodynamic and pharmacodynamic information such as absorption, distribution, metabolism, excretion, mechanism of action, route of administration, side effects and toxicity, demographic changes, and drug-drug interactions. Helps identify promising compounds for development to improve. In the pharmaceutical R & D process, the combination of cloud

computing power and AI makes the process faster, more cost-effective, and more accurate. These benefits allow large companies to evaluate different new approaches to developing traditional drugs in the old and new categories at the cellular and molecular levels using AI with the high computing power of the cloud. It becomes more important when effectively validating targets. The combination of AI and cloud computing is the perfect combination for many innovative purposes. With quick access to large amounts of data and big data, and cloud technology undoubtedly providing this, the success rate of various approaches such as AI's cognitive capabilities and machine learning will increase. Cloud adoption leads enterprises to AI as vendors offer more and more tools and services without large upfront investment. Clouds and AI are perfectly compatible in many ways, and experts say AI is just the technology that will revolutionize cloud computing solutions. AI is a type of know-how that has the potential to evolve today's cloud infrastructure and enhance the latest cloud computing technologies. Advances in AI and cloud technologies are helping healthcare and pharmaceutical companies improve their services

Conclusion:

Industry 4.0 indicates the new stage of the modernized industrial revolution with a high concentration on interconnectivity, flexible automation, artificial intelligence, and real-time data exchange and sharing using advanced technologies, such as cyber-physical systems, IoT, cloud computing, big data, and advanced robotics and virtual reality. Pharma 4.0 is a manifestation of Industry 4.0 in the pharmaceutical industry. Pharma 4.0 can be defined as the digitalization of pharmaceutical industries from the supply, production (with planning), and delivery operations` points of view by networked firms and uses intensively digital models and ontologies. The main missions of using this paradigm are to reduce the development costs and cycle time and to also improve the quality of the drug products by (a) improving the smartness of the contributing resources (i.e., humans, devices), (b) connecting and integrating all the contributing resources at any stage of the cycle, and (c) providing real-time status and awareness information to the regulatory organization. Pharma4.0 is powered by the cyber-physical platform, which enhances the processing of bigdata, maximizes the interconnectivity and collaborative robotics, and optimizes the artificial intelligence and distributed cloud architectures. This modern digitalization allows pharmaceutical and biotechnological organizations to change their network policies with higher efficiency and performance in different aspects. Networked embedded computers control and monitor the drug design, development, and production processes, usually with feedback circles from cloud-based computation unit. The economic and societal potential of the paradigm is vastly greater than what has been realized, and major investments should be made worldwide to develop the technology. The challenges are still considerable because pharmaceutical development and production systems should follow the tough instructions of the regulatory organizations to grasp safety and reliability requirements. Moreover, the tools used (i.e., PAT, QbD, RTRT) for the design, monitoring, and control of the drug production system are qualitatively different from other production industries. For example, the lack of temporal semantics and adequate concurrency models in computing and today`s “best-effort” networking technologies make predictable and reliable real-time performance difficult. Software component technologies such as object-oriented design and service-oriented architecture are based on software-like abstractions rather than physical systems. Many applications can only be achieved with significant changes to the core abstraction. The current drug development life cycle has the following problems:

- The drug development life cycle requires input from many contributors (devices, organizations, people, etc.). Participants employed in the drug development life cycle are not smart enough and unconnected.
- All decisions must be made by humans.
- This cycle is not integrated with the regulatory body. – This cycle is very long, costly and time consuming (12 years, B $ 2) The future drug development life cycle has the following benefits:
- All contributors are connected to cloud computing entities that have AI tools available and are ready for decision making. Contributors will be very smart.
- Contributors will cooperate. This will ignore duplicate processes.
- Regulatory tracking and tracking of medicines is much easier.

This chapter describes a series of phases of drug development, highlights the role of computers in drug development, and introduces the Pharma 4.0 ecosystem. Pharma 4.0 concludes that by increasing the level of intelligence, it may be possible to improve current drug design and development processes and validate manufacturing facilities. To realize Pharma 4.0 more effectively, we will rebuild new paradigms such as PAT (Process Analytical Technology), RTRT (Real-Time Release Testing), and QbD (Quality by Design) to reconstruct physical equipment and computing equipment. Must be covered in an integrated manner.

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THE EFFECT OF OPIUM ON THE CARDIOVASCULAR SYSTEM

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ABSTRACT

Opioids have the best price of illicit drug intake after hashish worldwide. Opium, after tobacco, continues to be the maximum generally abused substance withinside the Middle East. In addition to the convenience of availability, one cause for the excessive intake of opium in Asian international locations is probably a conventional notion amongst Eastern human beings or even scientific team of workers that opium may also have ameliorating consequences on cardiovascular diseases (CVDs) in addition to diabetes mellitus, hypertension, and dyslipidemia. Over the final decade, many studies were achieved on human beings and animals to assess the interaction among opium intake and solid coronary artery disease, acute coronary syndromes, and atherosclerosis. In this review, we finish that opium intake must be taken into consideration a chance thing for CVDs. Healthy individuals, as nicely as cardiac and diabetic patients, must be knowledgeable and knowledgeable approximately the dangerous consequences of opium intake on cardiovascular and different persistent diseases.

1. Introduction

Papaversomniferum L. is among the oldest medicinal plants, and the dried latex of its poppy, opium, has been used for medicinal or leisure functions conventionally.1 Opioids have the highest fee of illicit drug intake after hashish worldwide. In 2017, the United Nations Office on Drugs and Crime suggested that 29 million persons, 50% better than estimates, had used opiates withinside the previous yr globally.2 Notably, opium, after tobacco, continues to be the maximum usually abused substance withinside the Middle East.three One of the motives for the excessive use of opium on this location is probably the convenience of get entry to and additionally the area withinside the predominant pathway of the opium transit as the principle opium-generating nations which includes Afghanistan, and to a lesser extent, Myanmar, and Laos are positioned on this region. In addition to the benefit of availability, any other motive is probably a conventional perception amongst Eastern humans or even scientific team of workers that opium may also have ameliorating outcomes on cardiovascular diseases (CVDs) in addition to diabetes mellitus, hypertension, and dyslipidemia.4e9 Over the remaining decade, many research were executed on people and animals to assess the impact of opium consumption on blood lipid and glucose profiles, and additionally on CVDs. In 2013, we posted the primary assessment article at the cardio-metabolic outcomes of opium consumption.1 In this assessment, we aimed to acquire and combine the latest proof with our preceding expertise to make clear the outcomes of opium on CVDs and its underlying mechanisms.

2. Pharmacotoxicology

The phrase opium (lachrymapapaveris, Teriak) is derived from the Greek call for juice; a milky juice extracted with the aid of using incising the unripe capsules (poppy) of Papaversomniferum L. 10 After being uncovered to air, it turns into a brown, sticky, or crumbly substance. It is a complex Cocktail of materials that, similarly to water, includes extra than forty alkaloids11 and over 70 components.12 Only 5 of those alkaloids account for certainly all the quantitative alkaloid content material of opium (Fig. 1), inclusive of morphine (8e17% through weight), noscapine (1e10%), papaverine (0.5e1.5%), codeine (0.7e5%), and thebaine (approximately 0.2%). eleven Morphine and codeine are powerful ache relievers thru the activation of the m (mu) opioid receptor. However, they also are abused for leisure functions due to the fact the activation of the m receptor reasons euphoria and drowsiness. thirteen Noscapine (previously referred to as narcotine) is an antitussive agent.14 Papaverine has no morphine-like actions, however because it relaxes clean muscles, it is usually used for the prevention and remedy of vasospastic illnesses along with the spasm of coronary artery skip grafts.eleven,14 Opium is used thru special routes.

It may be ingested orally or smoked after direct heating with burning charcoal in specialized gadgets along with an opium pipe (Vafour). In every other route (SikhSang), a stick is heated and the opium is placed on the heated stick with a hairpin, after which the smoke is inhaled.15 When opium is ingested, the onset of motion is delayed.1 This is while, withinside the case of opium smoking, morphine reaches the mind inside seconds due to the fast absorption of its vapor throughout the pulmonary capillaries into the bloodstream. Therefore, the onset of motion is an awful lot extra fast and extreme after smoking, however the period of motion is longer after oral consumption due to the fact the absorption from the intestine, despite the fact that slower, keeps over a extended period.

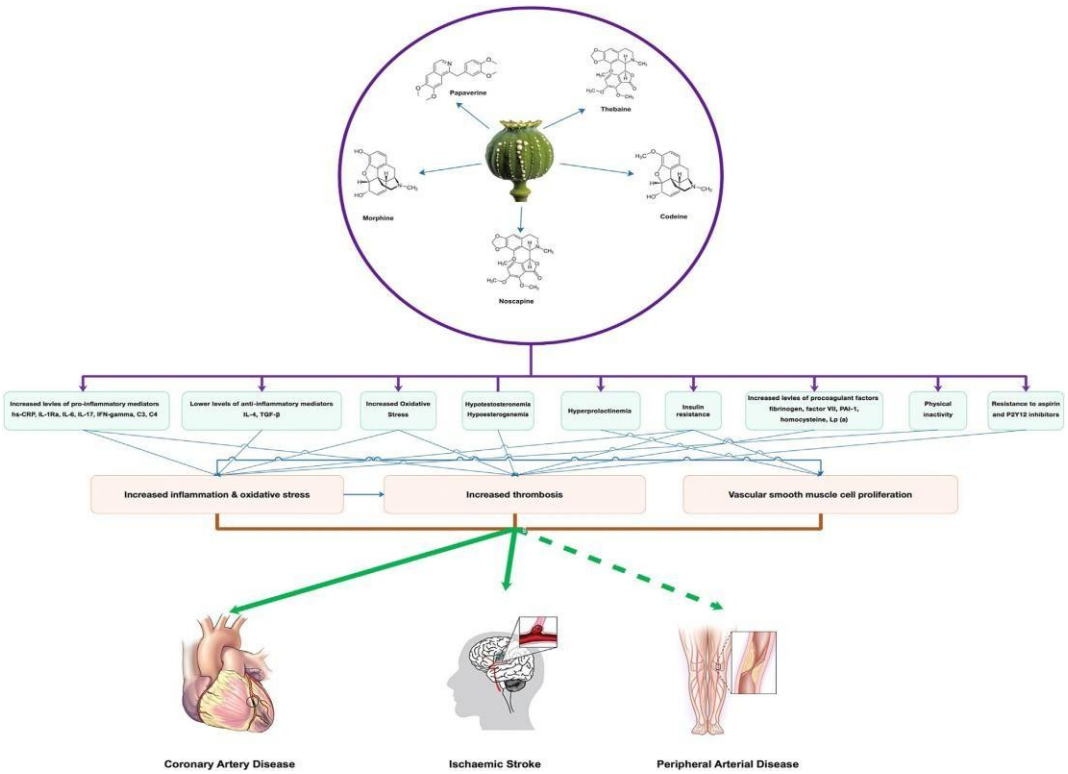

Fig. Central illustration: Chemical structure of five main alkaloids of opium (*Papaversomniferum L.*) and the potential mechanisms of the harmful effects of opium consumption on coronary artery disease, ischemic stroke, and peripheral arterial disease. hs-CRP, high sensitivity C-reactive protein; IL, interleukin; IL-1Ra, interleukin-1 receptor antagonist; IFN- g, interferon-g; Lp (a), lipoprotein (a); PAI-1, plasminogen activator inhibitor-1; TGF-b, transforming growth factor-b.

3. Stable coronary artery disease

Clinical research

In the first actual look at at the affiliation among opiates and coronary artery disease (CAD), investigators as compared ninety eight decedents with methadone or opiate (M/O) of their blood on the time of post-mortem and ninety seven decedents with out M/O, and located a decreased severity of CAD many of the former sixteen Although they concluded that long-time period opiate publicity would possibly mitigate CAD severity and its fatal consequences, they referred to as for warning at the same time as decoding their outcomes primarily based totally on numerous limitations, which includes a loss of information at the decedents` smoking histories, lipid profiles, and lifestyles. sixteen Subsequently, majority of research besides few located that opium intake is related to greater excessive and extensive involvements of coronary arteries, even after modifications for viable confounders (Table 1).10,17e22 A cross-sectional take a look at determined no affiliation among opium intake with the aid of using any route and ischemic coronary heart diseases.23 However, the authors referred to as for warning at the same time as decoding their outcomes because the opium dosage, the suggest period of opium intake, and the purity of opium had been now no longer assessed of their take a look at (Table 1).23 A latest meta-analysis confirmed that opium intake turned into related to a extensively more threat of CAD (odds ratio [OR]: 2.77, 95% confidence interval [CI]: 2.04 to 3.75).24 Besides research comparing the affiliation among opium intake and the presence, severity, and extension of stable CAD, opium abuse has been validated to be associated to coronary microvascular dysfunction.

Opium abuse turned into an unbiased predictor of coronary microvascular dysfunction (OR: 3.575, 95% CI: 1.418 to 9.016; p ¼ 0.0069) in a cross-sectional take a look at on sufferers with documented microvascular dysfunction.25 Further, every other latest take a look at found out that opium intake turned into an unbiased threat thing for CAD and coronary artery ectasia.

Animal studies

It has been verified that opium dependancy has aggravating results at the development of atherosclerosis withinside the aorta of hypercholesterolemic rabbits.four However, this atherogenic impact was confined to hypercholesterolemic as opposed to normocholesterolemic conditions.four Concordantly, 4 weeks of opium smoking increased the atherogenic index in hypercholesterolemic rabbits and now no longer in normocholesterolemic ones.27 Another look at confirmed that despite the attenuation of myocardial necrosis in rabbits with myocardial ischemia, opium publicity annoyed ischemia susceptibility, myocardial congestion, and hemorrhage.28 In summary, there's steady proof helping the affiliation among opium intake and solid CAD.

4. Acute coronary syndromes

Although there's an settlement amongst contemporary research that opium intake is undoubtedly related to the presence and severity of CAD, there's controversy approximately the affiliation between opium intake and acute myocardial infarction (MI).29 Some investigations have suggested unfavorable effects,30,31 whilst others have proven impartial effects (Table 2).32 Despite the talk concerning the affiliation between opium intake and the occurrence of acute MI, there's an settlement concerning the effect of opium intake at the inhospital and mid-time period effects of acute MI. Research has proven that opium use isn't correlated with multiplied rates of posteMI mortality, morbidity, and readmission.6,31,33e35 Nevertheless, some investigators have suggested remarkably longer health facility lengths of stay,35 better readmission rates,36 and borderline extensively better in-health facility mortality rates (11.5% vs. 5.9%;p ¼ 0.072)36 in opium-established sufferers with acute MI in preference to non-opium users (Table 2). Altogether, now no longer handiest is there no proof for assisting a reduced hazard of acute MI or a good posteMI final results in opium-established sufferers however additionally it can be related to more posteMI complications. Summary of studies evaluating the association of opium consumption with acute coronary syndrome and its outcomes.

Study	Method	Sample	Incidence	Results
Klodkgetther *et al.* (1997)	Case report Gluteal compartment syndrome	30-year-old male IV heroin user	Symptoms: painful swelling of right leg, complete sciatic nerve palsy following IV injection of heroin Elevated serum CK, rhabdomyolysis	Neurological recovery after 4 weeks; rhabdomyolysis suspected as cause
Melandri *et al.* (1996)	Case report	Opioid user with hypoxic coma	Myocardial biopsy showed damage: focal lesions formed by small mononuclear inflammatory cells with a few neutrophils, associated with degenerated and necrotic myocardial fibers, interstitial edema and congestion of intrinsic blood vessels	Suggested that hypoxic coma following opioid overdose led to rhabdomyolysis and myocardial damage
Yang *et al.* (1996)	Case report	29-year-old male 1 day after heroin overdose	Symptoms: paralysis of lower extremities, swelling and tenderness of the four extremities, absent lower extremity deep tendon reflexes and positional sense Elevated plasma CK; transient acute renal failure	Resolution of most neurological signs and symptoms in 4 weeks

Study	Method	Sample	Incidence	Results
Binder & Vavrinkova (2008)	Prospective randomized comparative study Opioid replacement therapy in pregnancy and infant outcomes	117 women, randomized to 3 groups: 47 no replacement (on heroin), 32 methadone substitution, 38 buprenorphine substitution Infants: no premature delivery prior to 34 weeks	Heroin-exposed infants: highest incidence of LBW, IUGR, placental changes ($p < 0.05$); NAS most severe in methadone-exposed infants ($p < 0.001$)	Confounding variables may account for some findings; buprenorphine substitution therapy recommended rather than methadone
Kuczkowski (2007)	Literature review Risks associated with drugs of abuse and pregnancy	All drugs of abuse and management of patients in perinatal period	Maternal medical complications opioid use: cellulitis, skin abscesses, thrombophlebitis, hepatitis, AIDS, endocarditis, malnutrition Infant outcomes: IUGR, fetal distress	Methadone recommended for replacement therapy; anesthesia can precipitate hypotension, and larger doses of pain medication are needed because of cross-tolerance
Jansson *et al.* (2007)	Descriptive study Severity of NAS in infants ECG	50 methadone-maintained pregnant women	Vagal tone response to methadone during times of trough or peak (effect on respiratory sinus rhythm, autonomic control): maternal vagal responders more likely to have infants with NAS ($p < 0.05$); NAS: unrelated to substance abuse history, methadone maintenance, exposure to psychotropic drugs; male infants more likely to develop NAS, require medication ($p < 0.05$)	Maternal vagal tone's response to methadone may be a predictor of NAS severity
Fajemirokun-Odudeyi *et al.* (2006)	Retrospective study NAS symptoms in infants born to women who used heroin or methadone during late pregnancy	110 newborns from 108 mothers using heroin or on methadone maintenance during late pregnancy	Comparing infants of heroin-using group with methadone group, morphine therapy needed by 40% vs. 19%; length of stay 17.2 vs. 11.8 days	Heroin use in late pregnancy is associated with increased need for morphine therapy for the newborn, higher NAS scores, and longer hospital stays when compared with infants born to mothers on methadone maintenance

CI, Confidence interval; MI, Myocardial infarction; OR, Odds ratio. a An opium dependent and a non-dependent group (age- and smoking-matched) of alive poste MI patients were followed up for 12 months.

four.1. Clinical research on sufferers present process revascularization

Some research on coronary artery pass grafting surgical treatment (CABG) applicants have confirmed that opium intake is now no longer correlated with multiplied in-sanatorium mortality rates, postoperative hardship rates, or sanatorium lengths of stay.37e40 However, others have proven that opium use is immediately correlated with intra- and post-operative bleeding ,forty one readmission,38 and longer sanatorium lengths of stay. forty Recently, we studied 28,691 sufferers who underwent CABG for a mean of fifty six months to assess the results of opium intake and cessation at the long-time period results of those sufferers. forty two In this cohort, 3636 sufferers endured opium intake after surgical treatment, even as 1436 sufferers stopped opium use. After modifications for viable confounders, we discovered that in assessment with the in no way customers of opium, chronic opium intake after CABG changed into related to multiplied 5-12 months all cause mortality (danger ratio [HR]:1.28, 95% CI:1.06 to 1.54; p ¼ 0.009) and 5-12 months important damaging cardiac events (MACE) (HR: 1.25, 95% CI: 1.thirteen to 1.forty; P<0.0001). Still, individuals who quitted opium use after surgical treatment have been now no longer at an multiplied chance of mortality (HR: 1.09, 95% CI: 0.eighty three to 1.forty three; p ¼ 0.514) or MACE (HR: 1.03, 95% CI: 0.88 to 1.21; p ¼ 0.645) at 5 years in comparison with the in no way customers of opium. forty two In a retrospective cohort study, opium intake changed into now no longer related to 12-month MACE amongst male sufferers after optional percutaneous coronary interventions, and not one of the additives of MACE, inclusive of goal vessel revascularization, goal lesion revascularization, CABG, and non-deadly MI, changed into unique among opium customers and non-customers. forty three Nonetheless, it have to be stated that even as age is an vital predictor of MACE, specially mortality, the authors did now no longer make modifications for the confounding impact of age on MACE notwithstanding the extensively lower age of the opium customers via way of means of assessment with the non-customers (55.7 as opposed to 58.four years, respectively; p < 0.001). This bias may probably underestimate MACE withinside the opium consumer group. forty three Altogether, it seems that opium intake now no longer best has no ameliorating impact on sufferers present process coronary revascularization however additionally can also additionally have dangerous results on mid-time period and longer moutcomes

5. Stroke

There are scarce reviews approximately the correlation among opium and stroke (Table 3). In a case control look at, opium abuse was independently related to ischemic stroke.forty four Other studies have established that opium dependancy is related to expanded intima-media thickness, greater atherosclerotic plaques, and a extra pulsatility index and imply go with the drift pace of the middle cerebral artery, which might be the markers of cerebral atherosclerosis.45e47 In a look at on male CABG candidates, there has been no distinction in the superiority of enormous carotid artery stenosis among opium-addicted and non-addicted sufferers. forty eight Nevertheless, there's a enormous bias on this look at because the authors said a better incidence of diabetes (17% as opposed to 11.4%) and hypertension (88.6% as opposed to 11.4%) in addition to a decrease incidence of smoking (27.1% as opposed to 65.5%) withinside the non-addicted sufferers than withinside the opium addicted ones, respectively. Indeed, no end may be drawn approximately the affiliation among opium intake and carotid stenosis with out adjusting for such essential confounding factors (Table 3) .

forty eight In summary, the presently constrained proof shows the destructive outcomes of opium on cerebral atherosclerosis and hemodynamic abnormalities, and its affiliation with ischemic stroke Nonetheless, in addition research are had to elucidate the association among opium intake and stroke.

6. Peripheral arterial disorder

Despite numerous research assessing the connection among opium intake and CAD, there may be confined facts concerning the affiliation among opium intake and peripheral arterial disorder. In a take a look at on sufferers with peripheral arterial disorder who underwent decrease extremity vascular reconstruction surgery, investigators determined that the patency price changed into extensively decrease in opium customers than non-customers (32% as opposed to 67%, respectively).forty nine However, the authors did not modify this locating for potential confounders. forty nine Future well-designed research have to elucidate the actual position of opium intake in peripheral arterial disorder.

7. Heart failure

The affiliation among opium intake and left ventricular systolic disorder has been evaluated in lots of latest research. The contemporary proof means that opium intake is now no longer related to a reduced practical elegance.23,33,34,37e39,50e52 Nevertheless, there are conflicting consequences concerning the affiliation among opium intake and the left ventricular ejection fraction (LVEF). Some research have proven that opium customers, with or with out CAD, are much more likely to have decreased LVEF than nonusers,50,51,fifty three, fifty four whilst others have observed a impartial impact on this regard.10,20,23,31,33e35,37-39,43,52,fifty five A latest meta-evaluation confirmed that opium use changed into related to extensively decrease LVEF in opium customers who have been applicants for CABG (mean variations ¼ 2.15, 95% CI: 3.31 to 1).24 However, this statistically good sized distinction of 2%, perhaps of no or minimum medical importance. Moreover, this correlation did now no longer attain statistical importance in different subgroups of sufferers with CAD (mean variations ¼ 0.29, CI: 0.fifty seven to 1.14).24 Taken these types of strains of proof together, we might also additionally finish that opium intake has impartial outcomes at the LVEF and practical elegance of people with coronary heart failure.

8. Cardiac arrhythmias

Studies have verified that opium use is related to a better occurrence of ventricular arrhythmias withinside the poste MI course, even after changes for confounders,52,fifty six whilst every other take a look at confirmed a impartial impact on this regard.34 Whereas a take a look at confirmed that opium dependancy changed into related with better post-CABG arrhythmias, fifty three every other take a look at observed defensive outcomes for opium use

in phrases of post-CABG atrial traumatic inflammation. fifty seven Despite those controversies in medical research, animal studies27,fifty eight have always indicated a proarrhythmic impact for opium.29 Future well-designed potential medical research have to elucidate the precise position of opium intake in inducing or stopping cardiac arrhythmias.

9. Interactions with cardiovascular tablets

The contemporary proof suggests that opiates can intrude with cardiovascular medicinal drugs via changes of their pharmacokinetics or pharmacodynamics. fifty nine In a massive take a look at, an evaluation of prescriptions for sufferers with non-valvular atrial traumatic inflammation who have been below remedy with warfarin and had a solid international normalized ratio (INR) indicated that the intake of opiates, consisting of herbal opium, buprenorphine, and tramadol, changed into related to an extended INR in those sufferers, which would possibly suggest a clinically crucial interplay.60 Furthermore, it's been proven that the concomitant use of opium and digoxin might also additionally boom the danger of digoxin toxicity. sixty one Another clinically applicable interplay of opium is with antiplatelets. Research has proven that the management of opiois inclusive of opium, methadone, and morphine attenuates the antiplatelet moves of aspirin, sixty two ticagrelor,63e65 prasugrel,64,sixty six and clopidogrel.67,sixty eight This listing of doubtlessly lethal interactions among opium and cardiovascular tablets shows that cardiologists and cardiac surgeons act carefully while prescribing antiplatelets, digoxin, and warfarin for an opium-abusing patient.

10. Temporal dating among opium intake and cardiovascular diseases

Although the medical research at the affiliation among opium intake, and CAD and stroke have set up a systematic base withinside the proof pyramid, there are not unusual place obstacles of their methodologies that name for warning in decoding their consequences. First, all of those research have case control or cross-sectional designs. Some sufferers with CAD or stroke possibly begin the use of opium due to their signs or their ideals approximately the useful outcomes of opium use on CVDs following the improvement of their diseases. Hence, whilst we have a look at a better incidence of opium intake amongst sufferers with CVDs than healthful people, we can not make a causal interpretation due to the fact the tempora courting among opium intake and CVDs can't be decided in those research. Another problem is the possible occurrence-prevalence bias, which ought to be taken into consideration in cross sectional and case control research. If opium intake affects the survival of sufferers with ischemic coronary heart diseases, then the outcomes of cross-sectional research with popular instead of incident instances might be biased. Community-primarily based totally cohort research can conquer those boundaries and assist us to make causal interpretations of the connection among opium and CVDs. With the growing use of opioids for persistent non-most cancers pain, a huge nested case control examine established that using opioids become related to an expanded danger of MI (OR: 1.28, ninety five% CI: 1.19 to 1.37).69

In our opinion, the maximum supportive proof for a possible dangerous function of opium intake in CVDs got here from the Golestan Cohort Study.70 The Golestan Cohort Study recruited 50,half human beings elderly 40e75 years from January 2004 to June 2008 from Golestan Province, placed in North Iran. As distinctive exposure data, a scientific follow-up approach, and the ascertainment of the purpose of demise have been available, the investigators evaluated the affiliation among opium intake and all-purpose mortality and predominant categories, consisting of circulatory reasons for mortality after a mean follow-up of 4.7 years. The adjusted HR for all-purpose mortality related to ever use of opium become 1.86 (ninety five% CI: 1.sixty eight to 2.06).

They additionally determined that opium customers have been at an expanded danger of demise from ischemic coronary heart diseases (adjusted HR: 1.90; ninety five% CI: 1.fifty seven to 2.29). Moreover, after apart from the men and women who started opium use after receiving a analysis of predominant illnesses, namely ischemic coronary heart diseases, cerebrovascular occasions, diabetes mellitus, and hypertension, they observed a doseeresponse affiliation among the period of opium use and cardiovascular in addition to all cause mortality. Unlike preceding cross-sectional and case control research, the Golestan Cohort Study become now no longer problem to the aforementioned predominant boundaries and, therefore, it's far affordable to finish causality primarily based totally on its findings.

11. Association among opium intake and cardiovascular diseases: impartial or confounded through smoking?

Cigarette smoking is one of the predominant danger elements for CVDs. It has been proven in all preceding research that opium abusers smoke cigarettes greater frequently.10,36,forty eight Thus, it isn't always clean whether or not the affiliation among opium intake and CVDs is a dependent affiliation confounded through smoking or opium intake is an impartial danger thing for CVDs. Numerous research have attempted to solution this question. In a propensity rating matched analysis, the examine found out that diabetic opium customers had greater intense CAD than matched diabetic non-customers.10A huge cross-sectional examine indicated a better occurrence of CAD in opium customers than non-customers, even after the exclusion of cigarette smokers (Table 1).17 In a nested case control examine, opium dependancy become an impartial danger thing for CAD amongst non-smokers, whilst this affiliation become now no longer great in cigarette smokers.20 Hence, we are able to finish that the courting among opium intake and CVDs is impartial.

12. Why ought to opium intake be related to cardiovascular diseases?

Current understanding is scarce approximately the results of opium on blood glucose, dyslipidemia, and hypertension. seventy one Although animal research show the dangerous results of opium at the aforementioned danger elements, there are a few discrepancies in medical research. seventy one Thus, it requires destiny well-designed medical research to cope with this gap of understanding. Here, we are able to attention on different danger elements and novel mechanisms of opium results on CVD.

Studies have established that opium exerts its dangerous results on CVDs thru expanded infection and oxidative pressure, expanded thrombosis, and vascular clean mobileular hyperplasia (Fig. 1). Although there's a complicated courting, we in brief speak those interwoven elements here. Recent research have more and more more said that opium addicts have multiplied stages of pro-inflammatory mediators15,72e76 and decrease stages of anti inflammatory cytokines.74,seventy five On the opposite hand, it's been proven in numerous research that morphine and heroin set off systemic oxidative pressure and decrease the full antioxidant potential impartial of cigarette smoking.

Hypotestosteronemia and hypoestrogenemia in opium addicts78 can also additionally bring about CVDs thru all the aforementioned mechanisms. These hormonal imbalances are related to expanded stages of procoagulant elements and insulin resistance.79e86 Studies have additionally established that opium-addicted individuals have remarkably better stages of procoagulant elements than nonaddicted individuals.15,87e90 Additionally, studies has validated a country of insulin resistance, much like sufferers with kind 2 diabetes mellitus, ninety one which reasons CVDs.79e86,89,92,ninety three Opium abusers have hyperprolactinemia,78,ninety four which ends up withinside the proliferation of vascular clean muscle cells and CVDs.ninety five Another mechanism is the discount of bodily pastime because of the depressant results of opium at the significant anxious system, ninety six that's related to an expanded danger of CVDs.97e100

Last however now no longer least, is the resistance to aspirin and P2Y12 inhibitors in opium customers. We formerly mentioned that opium intake blunts the pharmacological results of aspirin,62 ticagrelor,63e65 prasugrel,64,sixty six and clopidogrel.67,sixty eight These findings can also additionally render opium customers with preceding CVDs greater prone to acute thrombotic occasions and is probably a singular justification for better dangers of MI and stroke in those sufferers.

13. Strategies for the remedy of opioid dependence

For the a success remedy of opioid dependence, we ought to rent pharmacological interventions except psychosocial supportive measures. There are techniques towards pharmacological remedy: 1) opioid agonist preservation remedy with long-performing opioids together with methadone or buprenorphine, which is the best and the favored method, and 2) detoxification, observed through remedy with long-performing opioid antagonists together with naltrexone, to save you relapses. Other than those medications, alpha-2 adrenergic agonists together with clonidine for the remedy of opioid withdrawal and naloxone for the remedy of opioid overdose ought to be available.101

14. CONCLUSION

People have used opium for decades now no longer handiest as a habit, however primarily based totally on their conventional ideals approximately its useful results on diabetes mellitus, dyslipidemia, hypertension, and CVDs. Considering the modern-day proof, opium now no longer handiest has no ameliorating impact on CVDs, however the medical, animal, and potential cohort research continuously suggest that opium intake is associated with CVDs and cardiovascular mortality. Moreover, the rapidly developing organic motives for a causal courting among opium intake and CVDs underscore the caution that opium intake ought to be taken into consideration a danger thing for CVDs. Unfortunately, fake ideals concerning the useful results of opium are common, and it's far the duty of fitness professionals102 and fitness government to warfare in opposition to those fake beliefs. Healthy people, in addition to cardiac and diabetic patients, need to be informed and knowledgeable approximately the dangerous results of opium consumption on cardiovascular and different continual diseases

Highlight

- There is regular proof helping the affiliation among opium intake and strong coronary artery disease.
- Persistent opium intake after coronary artery pass grafting surgical treatment is related to increased long-time period dangers of mortality and primary destructive cardiac events.
- The presently confined proof indicates the detrimental outcomes of opium on cerebral atherosclerosis, and hemodynamic abnormalities and its affiliation with ischemic stroke.
- A dose response affiliation exists among the duration of opium use and all-motive and cardiovascular mortality.
- Opium intake must be taken into consideration a chance factor for cardiovascular diseases.
- Physicians must war towards fake ideals approximately the useful outcomes of opium.

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A Short Assessment on "Needle Free Injection"

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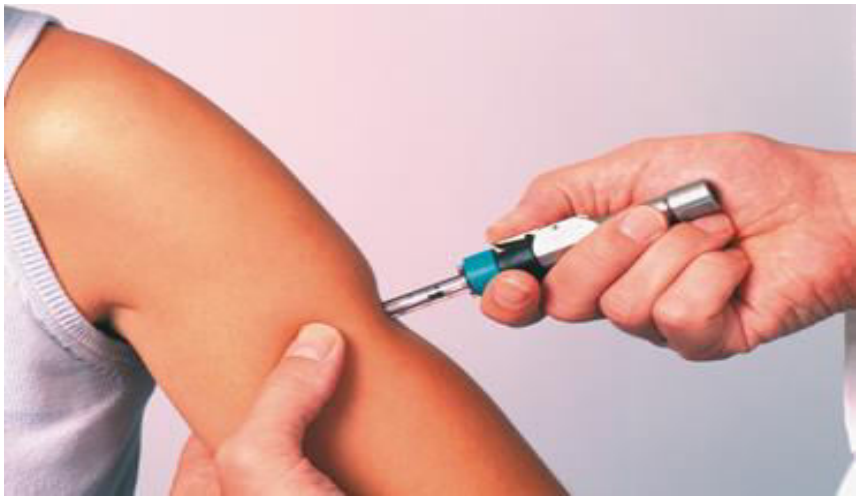
ABSTRACT: Needle free injection gadget are to introduce the more than a few drug treatments into sufferers without piercing the skin with a traditional needle. Needle-free science presents the many benefits of decreasing patient concern about the use of needle. Needle free injection is the very effective injections a large vary of pills and bioequivalent to springe and needle. It consequences in much less pain, and is strongly preferred with the aid of patients. Additional advantages consist of very fast injection comparedwith traditional needles and no needle disposal issues. Not solely benefit of the pharmaceutical enterprise to the increasing product sales, it has the introduced practicable to amplify compliance with dosage regimens and expanded outcomes. Today, they are a gradually developing technological know-how that guarantees to make the administration of medicine more efficient and less painful.

KEYWORDS:-
Needle free injection, Needle free devices, Needle free technology, Drug administration and drug shipping system.



I. INTRODUCTION

Needle-free injection machine are novel approaches to introduce a variety of medicines into sufferers besides piercing the pores and skin with a traditional needle. Needle-free injection strategies can be used to administer vaccines and medications in the pork industry. They are promoted as a possible option for patients with needle phobia. The needle free is used to describe the an sizeable range of drug delivery technologies, which consists of science that do now not have a needle however make use of electrophoresis to force pills thru the skin, applied sciences that use one or more very small needled, however needles nevertheless. Needle free units are taken to the shape ofpower sprays, fit to be eaten products, inhalers, and pores and skin patches.

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Devices are on hand in reusable and disposable forms, for home or physician's workplace use, and also in variations for a couple of patients and institutional uses.

HISTORY :-

The first syringes had been the first developed through a French surgeon, Charles Gabriel Pervez, in 1853, hypodermic there is a minor development in syringes is the science has been remained unchanged for closing one hundred fifty year. Needle free structures were the first described through marshalllockhart in 1936 in his patent jet injection. Then in the early 1940's higson and others developed high pressure "guns" the use of a fantastic jet of liquid to pierce the pores and skin and deposit the drug in underlying tissue.

Classification of Needle Free Injection Technology:-

1.On the groundwork of working.

a) Spring Systems.
b) Laser powered.
c) Energy propelled systems.
i) Lorentz force.
ii) Gas propelled/air forced.
iii)Shock waves.

2. On the basis of type of load.

a) Liquid.
b) Powder.
c) Projectile.

3. On the basis of mechanism of drug delivery.

a) Nano-patches.
i) Sandpaper assisted delivery.
ii) Iontophoresis enabled.
iii)Micro-Needles.

4. On the groundwork of site of delivery.

a) Intra dermal injectors.
b) Intramuscular injectors.
c) Subcutaneous Injectors.

Types of Needle Free Injection:-

Needle-free injection drug shipping systems are categorized as follows

1. Powder injections
2. Liquid injections
3. Depot or Projectile Injection

Type 1 – Powder Injection
Design of powder injection systems

These injections consist of a chamber crammed with stable drug content and a nozzle for firing drug particles into the pores and skin via making use of the power source which commonly is compressed gas. The injection has a diaphragm (a few microns thick) on either side of the chamber to cover the drug chamber.

Mechanism of powder injection :-

* Particles exist from the nozzle along with a gas stream.

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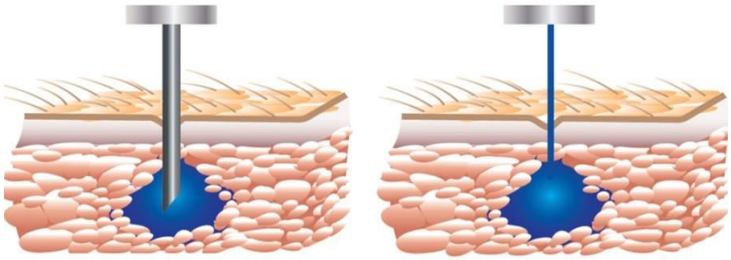
* Particles impinge the pores and skin surface leading to the formation of a gap into the skin with the progression of the injection.
* Drug particles get deposited in a spherical sample at the give up of the hole and penetrate throughout the stratum corneum.
* After their penetration into the skin, drug particles get distributed completely into the stratum corneum and the viable epidermis.Powder injection is accomplished by a light gas gun. It provides the required particle velocity by use of an accelerating piston which accelerates and carries particle with it. Particle leave piston surface by means of a deceleration mechanism which slow down the piston. This leads to ejection of particle that act on the target tissue area

Mechanism of Working: -

Needle-free injection technology is used force generated by a compressed gas (typically air, CO2 or nitrogen) to propel the



vaccine Start Paraphrasing at excessive speed through a tiny orifice. When administered thru the skin, an ultrafine move of fluid penetrates the skin, handing over the vaccine in a fraction of a 2d to the skin, subcutaneous tissue, and intramuscular tissue. Injection event requires less than 0.5 seconds.

Stage of Delivery

There are three stages in the needle free drug delivery:

* The top pressure phase-is choicest stress used to penetrate the skin is 0.025 sec
* Delivery or dispersion segment is up to 0.2 sec
* Drop off segment is

The whole quantity of time required to deliver the vaccine is upto 0.5 seconds.

Components of the Needle Free Injection Systems

*** Nozzle**

The nozzle has the two huge functions it acts as the passage for the drug and as the surface which contacts the skin. The nozzle contains a flat surface and an office. The nozzle gives the surface which comes in contact in the skin and the orifice which has the drug passes thru when injected. The orifice controls the drug stream diameter and speed. A flow diameter of approximately 100 micrometer and touring at 100 m/s can achieve the desired injection depth of two mm.

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*** Drug reservoir**

The drug volume is holds the injection fluid interior the device.

*** Pressure source**

The power source is furnished to the essential using energy to the injection. Then many gadgets in the market use both mechanical or stored strain as power storage elements. The mechanical method stores energy in a spring which is released by way of pushing a plunger to provide to the crucial pressure. The pressure storage method is used to compressed gas in vessel which is launched at the time of injection.

II. CONCLUSION

Needle free science presents the very apparent advantage of minimizing patients worry concerning the use of a needle. Other benefits contain very quick injection as compared to usual needles and injection disposal troubles are not often seen. Not only it can help the pharmaceutical enterprise in rising product sales, however also it has the more workable to amplify conformity with dosage regimens and enhanced outcomes. In the creating world, there are predominant task of disease transmission due to reuse of needle which can overcome by using the use of needle free injection technology.

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FAST DISSOLVING DRUG DELIVERY SYSTEM

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INTRODUCTION

Recent developments in technology have presented viable dosage alternatives for patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients. However, some patients, particularly pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms.[1] Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking.[2] For example, a very elderly patient may not be able to swallow a daily dose of antidepressant.

An Eight-year-old with allergies could use a more convenient dosage form than an antihistamine syrup. A schizophrenic patient in the institutional setting can hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic. A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker.

Fast-Dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients.[3] Fast-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There are multiple fast-dissolving OTC and Rx products on the market worldwide, most of which have been launched in the past 3 to 4 years. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology.

Definition

Fddts disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are

truefast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets.

When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.[4,5]

The advantage of Fast Dissolving Dosage Forms are increasingly being recognized in both industry and academia6 Their growing importance was underlined recently when European Pharmacopoeia adopted the term "Orodispersible Tablet" as a tablet that to be placed in oral cavity where it disperses rapidly before swallowing.[7]

Field of the invention

The present invention relates to a fast dissolving tablet comprising a pharmacologically active ingredient, such as a vitamin, antipyretic-analgesicantiinflammatory agent, antihypertensive drug, psychotropic drug, antidiabetic drug or the like, and a carbohydrate, having an adequate strength and capable of dissolving and disintegrating at a high rate in the oral cavity and to a method of producing the tablet.

Background of the invention

Recently much research has been undertaken in the geriatric field ranging from the physiology of aging to the design of drugs and pharmaceutical preparations to daily care and assistance. According to, inter alia, the silver science research conducted by the Japanese Ministry of Health and Welfare, there is an interesting research report entitled `Studies for the construction of new pharmaceutical preparations and new packaging containers optimal for administration to elderly subjects` (Masayasu Sugihara, Tokyo Women's Medical College, and others) (Aug. 22, 1989 issue of the YakujiNippo). By way of illustration, as such new preparations, a) buccal dissolution type preparations, b) paste-like preparationsand c) jelly-like preparations are described. Particularly, buccal dissolution type and paste-like preparations are claimed to be easy for elderly persons to ingest and excellent in stability.

the buccal dissolution type preparations, in particular, contain polyethylene glycol 1000 as the base which dissolves in the oral cavity and an oleaginous base as the base which melts at the temperature prevailing in the oral cavity and, in consideration of sensory factors such as

taste and texture as well as moldability, further contain sucrose and mannitol. These are molded by filling the pocket of a vinyl chloride molding sheet for pressthrough package (PTP) use with a heatmelted medicated base and allowing it to cool and take form. In this manner, a buccal dissolution type solid preparation for elderly persons is manufactured.

Advantages of FDT

1. Improved patient compliance
2. Rapid onset of action and may offer an improved bioavailability.
3. Patient having difficulty in swallowing tablet can easily administer this type of dosage form
4. Useful fropediatric, geriatric and psychiatric patients
5. Suitable during traveling where water is may not be available
6. Gives accurate dosing as compared to liquids
7. Good chemical stability.
8. Free of need of measuring, an essential drawback in liquids.

Salient features of fast dissolving drug delivery system[8- 12]

- Ease of administration for patients who are mentally ill, disabled and uncooperative.
- Requires no water
- Quick disintegration and dissolution of the dosage form.
- Overcomes unacceptable taste of the drugs.
- Can be designed to leave minimal or no residue in the mouth after administration and also to provide a pleasant mouth feel.
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and ameanable to existing processing and packaging Machinery Cost- effective

1. Ease of administration:

- Fast dissolving delivery systems are easy to administer and handle hence, leads to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and dysphasia. Fast Dissolving Delivery Systems may offer a solution for these problems.

Characteristics of fast dissolving delivery systems[13]

2. Taste of the medicament: As most drugs are unpalatable, mouth dissolving delivery systems usually contain the medicament in taste masked form. Delivery systems dissolve or disintegrate in patient's mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

3. Hygroscopicity: Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal condition from humidity which calls for specialized product packaging.[14]

4. Friability: In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous and soft- moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle which are difficult to handle, often requiring specialized peel-off blister packaging. To overcome this problem, some companies introduced more robust forms of fast dissolving tablets.

5. Mouth feel[15,16]: Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the "dryness" of a product.

Approaches for fast dissolving tablets

The fast-dissolving property of the tablet is attributable to a quick ingress of water into the tablet matrix resulting in its rapid disintegration. Hence, the basic approaches to developing fast dissolving tablets include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent, and using highly water-soluble excipients in the formulation.

Conventional techniques used in the preparation of fast dissolving drug delivery systems

Various technologies used in the manufacture of Fast dissolving tablets include

1. Freeze –drying or lyophilization
2. Tablet Molding
3. Direct compression
4. Spray drying
5. Sublimation
6. Taste masking
7. Mass extrusion

Excipients of FDDTs

Addition of disintegrants

Addition of disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution. The introduction so-called superdisintegrants and a better understanding of their properties have increased the popularity of this technology.[36] Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration, tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases.[37]

Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorb water and swell due to capillary action and are considered as effective disintegrants in the preparation of first dissolving tablets. Bi et al.38 and Watanbe et al.,[39]

Used microcrystalline cellulose (MCC) and low substituted hydroxypropyl cellulose (HPC) to manufacture rapidly disintegrating tablets. The ratios of MCC to HPC varied from 8:2 to 9:1. Ito and Sugihan investigated applying agar powder as a disintegrants because the powder absorbs water and swells considerably without forming a gel at physiological temperatures.[40]

Fast disintegration of tablets can also be achieved by incorporating effervescent disintegrating agents, which generates carbon dioxide. This phenomenon also resulted in partial taste masking of unacceptable taste of the drug.[41] The major drawback of effervescent excipients is their hygroscopicity (i.e., the ability to absorb atmospheric moisture). Hence, their manufacture requires control of humidity conditions and protection of the final product. This is reflected by the overall cost of the product.

Sugar-based Excipients

Another approach to fast dissolving tablets by direct compression is the use of sugar-based excipients (e.g., dextrose, fructose, isomalt, maltitok, maltose, mannitol, sorbitol, starch hydrolyse, polydextrose, and xylitol), which display high aqueous solubility and sweetness, and hence, impart taste masking and a pleasing mouthfeel. T

Aste masking

Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredients can be achieved by various techniques. Drugs with unacceptable bitter taste can be microencapsulated into pH sensitive acrylic polymers.[42] Cefuroxime axetil is microencapsulated in various types of acrylic polymers (e.g., Eudragit E, Eudragit L-55 and Eudragit RL) by solvent evaporation and solvent extraction techniques. These polymer microspheres showed efficient taste masking and complete dissolution in a short period. Fine granules of drug and disintegrant (e.g. low substituted hydroxypropyl cellulose) when coated with a water insoluble polymer (e.g. ethylcellulose) masked the bitter taste of sparfloxacin.[43] The addition of low substituted hydroxypropyl cellulose as disintegrant to the drug in cores, resulted in increased dissolution rate and bioavailability of sparfloxacin compared to its conventional tablets.[44]

Ozer and Hincal[45] reported a simple coacervation method using gelatin, and anhydrous sodium sulphate as coacervating agent for taste making of beclamide. Beclamide is an anti-epileptic drug with unpleasant taste. It is microencapsulated into gelatin, with sodium sulphate as coacervating agent, and glutaraldehyde as hardening agent. The microcapsules after formation are dehydrated using alcohol. The core: wall substance ratio was 1:1, and the taste could be successfully masked.

A novel technique for taste masking of macrolides (e.g. erythromycin and clarithromycin) is reported by Yajima et al, 46. Monoglycerides having a low melting point which can form

good elaborate film, and easily soluble in intestine, and polymers which are insoluble in the mouth (pH 5-8), but are freely soluble in stomach (pH 1-4), are selected for taste masking of drugs with unpleasant taste. The polymer is dissolved or dispersed in monoglyceride, and the drug is granulated with above mixture and the resultant granules are cooled.

Mass extrusion[47]

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

MATERIALS AND METHODS

Materials

Valdecoxib (VALD) was a gift sample from Ajanta Pharma (Mumbai, India). Polyvinyl pyrrolidone (PVP-K30) was kindly provided by BASF India (Mumbai). All reagents and solvents used were of analytical grade.

Methods

Preparation of PVP-VALD Solid Dispersion

A mixture of PVP and VALD (1:1 and 1:2 by weight) was wetted with water and kneaded thoroughly for 30 minutes in a glass mortar. The paste formed was dried under vacuum for 24 hours. Dried powder was passed through sieve no. 60 and stored in a dessicator until further evaluation.

Physical mixtures (PM) were obtained by pulverizing in a glass mortar and carefully mixing accurately weighed (1:1 and 1:2 by weight) amounts of VALD and PVP.

For convenience, all binary systems were given a code name, which issummarized in Table 1.

Table 1: Percentage Dissolution and Dissolution efficiency of valdecoxib from different binary systems in comparison with original drug.

System	DP5 †	DE15 †	DE60 †
VALD	10.18 ± 0.25	8.51 ± 0.74	11.89 ± 0.42
PM1	23.22 ± 1.06	23.43 ± 0.53	39.04 ± 2.42
PM2	38.48 ± 5.97	39.41 ± 3.16	62.74 ± 2.93
SD1	69.89 ± 3.42	67.46 ± 0.57	90.8 ± 0.14

SD2	86.80 ± 0.42	80.03 ± 1.39	98.53 ± 2.99

Advantages of mouth dissolving tablets

1. Improved patient compliance
2. Rapid onset of action and may offer an improved bioavailability.
3. Patient having difficulty in swallowing tablet can easily administer this type of dosage form
4. Useful fropediatric, geriatric and psychiatric patients
5. Suitable during traveling where water is may not be available
6. Gives accurate dosing as compared to liquids
7. Good chemical stability.
8. Free of need of measuring, an essential drawback in liquids

Formulation Design and Optimization of mouth dissolving tablets

Description

The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance.

To overcome this weakness, scientists have developed innovative drug delivery systems known as "melt in mouth" or "mouth dissolve (MD)" tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bed-ridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market.[1,2]

The basic approach used in the development of the fast-dissolving tablet is the use of superdisintegrants. Croscarmellose sodium, sodium starch glycolate, and crospovidone were screened in the present study, and the best one was used for further studies. Another approach used in developing MD tablets is maximizing pore structure of the tablets. Freeze-drying[3,4] and vacuum-drying[5-7] techniques have been tried by researchers to maximize the pore structure of tablet matrix. Freeze drying is cumbersome and it yields a fragile and

hygroscopic product. Therefore, it was decided to adopt the vacuum-drying technique in the present investigation. Vacuum drying was adopted after addition of a subliming agent to increase porosity of the tablets. It is likely that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly.

Patented technologies for fast dissolving tablets

Some patented technologies are described here. Each technology has a different mechanism, and each fast-dissolving/disintegrating dosage form varies regarding the following48:

- Mechanical strength of final product;
- Drug and dosage form stability;
- Mouth feel;
- Rate of dissolution of drug formulation in saliva;
- Swallowability;
- Rate of absorption from the saliva solution; and
- Overall bioavailability.

Various technologies

1. ZydisTechnology
2. Durasolv Technology
3. Orasolv Technology
4. Flash Dose Technology
5. Wowtab Technology
6. Flashtab Technology
7. Oraquick Technology
8. Quick –Dis Technology
9. Nanocrystal Technology

Evaluation of fast mouth dissolving tablets of terbutaline sulphate

(A) General Appearance and Physical parameters

a) Thickness of tablets

The thickness of six tablets was measured using Vernier calipers. The extent to which the thickness of each tablet deviated from ± 5% of the standard value was determined.

b) Taste, Colour, Odour of tablets

Organoleptic properties such as taste, colour, odour were evaluated. Ten tablets from each batch were randomly selected and taste tested, colour visually compared and odour checked.

c) Hardness and Friability of tablets

Hardness

The tablet was determined by Monsanto Hardness Tester. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger is placed in contact with the tablet, and a zero reading is taken. The upper plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. As the spring is compressed, a pointer rides along a gauge in the barrel to indicate the force. zero reading is deducted from it. Six tablets from each batch were selected and evaluated, and the average value with standard deviation was recorded.

Friability

Tablets was performed in a Roche Friabilator. It consists of a plastic chamber thatrevolves at 25 rpm. About ten tablets were weighed together and then placed in the chamber. The friabilator was operated for 100 revolutions and the tablets were subjected to the combined effects of abrasion and shock because the plastic chamber carrying the tablets drops them at a distance of six inches with every revolution. The tablets are then dusted and re-weighed

d) Wetting time of tablets

A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of simulated saliva pH (Phosphate buffer pH 6.8). A tablet was put on the paper, and the time required for complete wetting was measured. Six trials for each batch were performed; average time for wetting with standard deviation was recorded.

e) Moisture uptake by the tablets

Ten tablets from each formulation were kept in a desiccator, over calcium chloride at 37ºC for 24 hours. The tablets were then weighed and exposed to 75% RH, at room temperature for two weeks in the dessicator. Required humidity was achieved by keeping saturated Sodium chloride solution at the bottom desiccator for three days. Tablets were re-weighed and the percentage increase in the weight was recorded in each days.

(B) Drug Content and Release studies

1. Assay of pooled sample of tablets

As in IP, twenty tablets were weighed and powdered. A quantity of powder equivalent to 5mg of Terbutaline sulphate was accurately weighed and transferred into a 50 ml volumetric flask, added 30 ml of distilled water. After shaking for 10 minutes, the volume was made upto 50 ml. The solution was filtered, first 5 ml of the filtrate was rejected, and after suitable dilution (here10 times), the sample was analyzed spectrophotometrically at 276.0 nm and the percentage of Terbutaline Sulphate in the solution was determined.

2. Weight Variation and Uniformity of drug content

Weight variation test:

Uniformity of weight test as described in the IP was followed. Twenty tablets were selected at random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with the average weight. The percentage deviation was calculated and checked for weight variation. Using this procedure weight variation range of all batches of formulations were determined and recorded. Uniformity of drug content: Uniformity of drug content test as described in the IP was followed. One tablet was powdered and transferred to a 25 ml volumetric flask. 15 ml of distilled water was added and the mixture shaken for 10 minutes. The volume was made up and filtered. The first 5 ml of the filtrate was rejected, and after suitable dilution (here 10 times) the sample was analyzed spectrophotometrically at 276.0 nm, and the drug was determined. This test was carried out individually for five tablets from each batch of formulations and the drug content range of five from minimum to maximum was recorded.

f) In-vitro Dissolution studies

In-vitro dissolution study was performed by using USP Type II Apparatus (Paddle type) [Electrolab (TDT-06T) Tablet Dissolution Tester] at 100 rpm. Distilled water 900 ml was used as dissolution medium, and the temperature of which maintained at 37 ± 0.5ºC. Aliquots of dissolution medium (10 ml) was withdrawn at specific time intervals (3 minutes) and was filtered and the first 5 ml of the filtrate was rejected. The amount of drug dissolved was determined by UV spectrophotometer by measuring the absorbance of the sample at 276.0 nm. Three trials for each batch were performed and average percentage drug release with standard deviation was calculated and recorded.

Counseling points for fddts

Pharmacists are in the ideal position to become familiar with the different technologies, and educate their patients on what to expect upon taking their first dose. The majority of patients receiving FDDT preparations have little understanding of this new dosage form. Patients may be surprised when tablets begin to dissolve in the mouth. They might expect a faster onset of therapeutic action. Clarification from the pharmacist can avoid any confusion or misunderstanding. As with all dosage form technologies, some patient populations are better served by their use than others. Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs. Similarly, patients with Sjögren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.

Although no water is needed to allow the drug to disperse quickly and efficiently, most technologies utilize the body's own salivation. Decreased volume of saliva may slow the rate of dissolution/disintegration and decrease the bioavailability of the product. Although chewable tablets have been on the market for some time, they are not the same as the new FDDTs. Patients for whom chewing is difficult or painful can use these new tablets easily. FDDTs can be used easily in children who have lost their primary teeth, but do not have full use of their permanent teeth.

Patients may mistake fast-dissolving/disintegrating for effervescent tablets. Pharmacists may wish to stress the difference between the use of quickdissolving and effervescent tablets. The Cima technologies, OraSolv and DuraSolv, use slight effervescence. Patients may experience a pleasant tingling on the tongue with OraSolv and DuraSolv.

Pharmacists have been alerted to exercise additional care when dispensing new prescriptions for FDDT formulations. Most such products are available in the same strengths as traditional dosage forms. Prescribing physicians must make an additional notation for the dispensing of a FDDT. A physician may also mistakenly believe the drug brand name is Zydis, for example, without identifying a specific drug.[12] Verification with the prescribing practitioner may be necessary in some cases and can clear up any confusion.

There are not commercially available fast-dissolving/disintegrating products for all of our patients' needs. Pharmacists may wish to consider compounding as a unique way to treat the unmet needs of individual patients. When a manufactured FDDT is not available,

compounding pharmacists can consider tablet triturates. These largely forgotten dosage forms have fast-disintegrating properties similar to many manufactured products. All of the patients described earlier will benefit greatly from FDDT formulations. The elderly patient, for example, could be prescribed Remeron SolTab for depression.With a pharmacist's

CONCLUSION

Besides delivering drug to the body, a drug delivery system aim to improve patient compliance and convenience, and fast dissolving tablets are no exception. The introduction of fast dissolving dosage forms has solved some of the problems encountered in administration of drugs to the pediatric and elderly patient, which constitutes a large proportion of the world's population. Hence, patient demand and the availability of various technologies have increased the market share of Fast dissolving tablets, which in turn prolongs the patent life of a drug. Keeping in view of the advantages of the delivery system, rapidly disintegrating dosage forms have been successfully commercialized, and because of increased patient demand, these dosage forms are expected to become more popular.

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The Divine Tulsi :- A Herb For All Reasons (Ocimum Sanctum)

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ABSTRACT

The predominant cause of global morbidity and mortality is lifestyle-related chronic diseases, many of which can be addressed through Ayurveda with its focus on healthy lifestyle practices and regular consumption of adaptogenic herbs. Of all the herbs used within Ayurveda, tulsi (*Ocimum sanctum* Linn) is preeminent, and scientific research is now confirming its beneficial effects. There is mounting evidence that tulsi can address physical, chemical, metabolic and psychological stress through a unique combination of pharmacological actions. Tulsi has been found to protect organs and tissues against chemical stress from industrial pollutants and heavy metals, and physical stress from prolonged physical exertion, ischemia, physical restraint and exposure to cold and excessive noise. Tulsi has also been shown to counter metabolic stress through normalization of blood glucose, blood pressure and lipid levels, and psychological stress through positive effects on memory and cognitive function and through its anxiolytic and anti-depressant properties. Tulsi's broad-spectrum antimicrobial activity, which includes activity against a range of human and animal pathogens, suggests it can be used as a hand sanitizer, mouthwash and water purifier as well as in animal rearing, wound healing, the preservation of food stuffs and herbal raw materials and traveler's health. Cultivation of tulsi plants has both spiritual and practical significance that connects the grower to the creative powers of nature, and organic cultivation offers solutions for food security, rural poverty, hunger, environmental degradation and climate change. The use of tulsi in daily rituals is a testament to Ayurvedic wisdom and provides an example of ancient knowledge offering solutions to modern problems.

Introduction

Diseases of Modern Life

Despite the many wonders of science and industry, modern life is fraught with stress. Mobile devices and the web have vastly increased the pace of life so that many people feel that they are now drowning in an ever-expanding ocean of data, while industrial agriculture has burdened us with increasing exposure to unhealthy processed and packaged food and a plethora of pesticides, food packaging materials and other toxic industrial chemicals. Urban dwellers are also faced with increasing wealth inequality, social isolation, excessive noise, air, water and soil pollution and disconnection from nature. Thus, while industrialization has led to longer lifespans and vast increases in human populations, it is now recognized that the greatest causes of death and disease on the planet are preventable lifestyle related chronic diseases.

We are in the midst of a global pandemic of obesity, diabetes, cancer, dementia, depression and other chronic diseases caused by modern lifestyles and their associated lack of physical activity, high intake of sugar, fat, salt, alcohol and tobacco and exposure to a toxic cocktail of industrial chemicals. The solutions to this current health crisis are therefore more likely to be found in the homes and behaviors of individuals than in medical clinics, hospital or pharmacies.

Ayurveda and Lifestyle Medicine

As a science of life and the world's oldest medical system, Ayurveda has a holistic approach to health and disease that focuses on preserving and promoting good health and preventing disease through healthy lifestyle practices. These practices include consumption of fresh, minimally processed foods, the use of Rasayanas (formulas) that eradicate ageing and disease, sophisticated detoxification practices and regular consumption of adaptogenic herbs that enhance the body's capacity to maintain balance in the midst of a variety of stressors.

Ayurveda's use of medicinal and culinary herbs draws upon India's incredible biodiversity with a variety that is unsurpassed by any medical system; yet, of all the herbs used, none has a status comparable to tulsi or holy basil (*Ocimum sanctum*).

Tulsi: A Potent Adaptogen

Tulsi is an aromatic shrub in the basil family Lamiaceae (tribe ocimeae) that is thought to have originated in north central India and now grows native throughout the eastern world tropics. Within Ayurveda, tulsi is known as "The Incomparable One," "Mother Medicine of Nature" and "The Queen of Herbs," and is revered as an "elixir of life" that is without equal for both its medicinal and spiritual properties.[3] Within India, tulsi has been adopted into spiritual rituals and lifestyle practices that provide a vast array of health benefits that are just beginning to be confirmed by modern science. This

emerging science on tulsi, which reinforces ancient Ayurvedic wisdom, suggests that tulsi is a tonic for the body, mind and spirit that offers solutions to many modern day health problems. Tulsi is perhaps one of the best examples of Ayurveda's holistic lifestyle approach to health. Tulsi tastes hot and bitter and is said to penetrate the deep tissues, dry tissue secretions and normalize kapha and vata. Daily consumption of tulsi is said to prevent disease, promote general health, wellbeing and longevity and assist in dealing with the stresses of daily life. Tulsi is also credited with giving luster to the complexion, sweetness to the voice and fostering beauty, intelligence, stamina and a calm emotional disposition.[3-6] In addition to these health-promoting properties, tulsi is recommended as a treatment for a range of conditions including anxiety, cough, asthma, diarrhea, fever, dysentery, arthritis, eye diseases, otalgia, indigestion, hiccups, vomiting, gastric, cardiac and genitourinary disorders, back pain, skin diseases, ringworm, insect, snake and scorpion bites and malaria.

Considered as a potent adaptogen, tulsi has a unique combination of pharmacological actions that promote wellbeing and resilience. While the concept of an "adaptogen," or herb that helps with the adaptation to stress and the promotion of homeostasis, is not widely used in Western medicine, Western science has revealed that tulsi does indeed possess many pharmacological actions that fulfill this purpose.

The medicinal properties of tulsi have been studied in hundreds of scientific studies including *in vitro*, animal and human experiments. These studies reveal that tulsi has a unique combination of actions that include: Antimicrobial (including antibacterial, antiviral, antifungal, antiprotozoal, antimalarial, anthelmintic), mosquito repellent, anti diarrheal, anti oxidant, anti cataract, anti inflammatory, chemopreventive, radioprotective, hepato protective, neuro protective, cardio protective, anti diabetic, anti hypercholesterolemia, anti hypertensive, anti carcinogenic, analgesic, anti pyretic, anti-allergic, immunomodulatory, central nervous system depressant, memory enhancement, anti asthmatic, anti-tussive, diaphoretic, anti thyroid, ant fertility, anti ulcer, anti emetic, anti spasmodic, antiarthritic, adaptogenic, anti stress, anti cataract, anti leukodermal and anti-coagulant activities. These pharmacological actions help the body and mind cope with a wide range of chemical, physical, infectious and emotional stresses and restore physiological and psychological function.

Protection and Detoxification

Many of the physiological benefits of tulsi can be attributed to its ability to assist with the body's internal housekeeping and protection of the body from toxin-induced damage. These functions are often attributed to tulsi's high content of phenolic compounds and anti oxidant properties, with Krishna tulsi (black/purple variety) having a higher phenolic content and anti-oxidant capacity than white Vana (wild) tulsi.

Laboratory studies have shown that tulsi protects against toxic chemical-induced injury by increasing the body's levels of anti-oxidant molecules such as glutathione and enhancing the activity of anti-oxidant enzymes such as superoxide dismutase and catalase, which protect cellular organelles and membranes by mopping up damaging free radicals caused by lack of oxygen[9] and other toxic agents.

Tulsi also helps to prevent cancers caused by toxic compounds by reducing DNA damage[12] and inducing apoptosis in precancerous and cancerous cells, thereby reducing the growth of experimental tumors and enhancing survival. Furthermore, tulsi not only protects against the damage caused by toxic compounds, but also enables the body to more effectively transform and eliminate them by enhancing the activity of liver detoxification enzymes such as the cytochrome P450 enzymes, which deactivates toxic chemicals and enables them to be safely excreted.

While these actions are vitally important for protecting against natural toxins produced within the body or by animals or plants, they are perhaps even more important in the modern age to protect against the vast range of pollutants, pesticides, pharmaceuticals, heavy metals, radiation and other industrial toxicants created from human activity.

Toxicant Stress: Chemicals, Heavy Metals and Radiation

The ability of tulsi to protect against the damaging effects of various toxicants has been documented in numerous experimental studies. These studies attest to the ability of tulsi to prevent liver, kidney and brain injury by protecting against the genetic, immune and cellular damage caused by pesticides, pharmaceuticals and industrial chemicals. Thus, tulsi has been shown to protect against the toxic effects of industrial chemicals such as butylparaben, carbon tetrachloride, copper sulfate and ethanol and common pesticides such as rogor, chlorpyrifos endosulfan and lindane. Tulsi has also been shown to protect against the toxic effects of many pharmaceuticals drugs including acetaminophen] meloxicam, paracetamol haloperidol and antitubercular drugs.

In addition to protecting against toxic chemicals, tulsi has also been shown to protect against the toxic effects of heavy metals such as lead, arsenic, cadmium, chromium and mercury and the toxic effects of radiation. Tulsi exerts its radio protective effects by scavenging free radicals and reducing the oxidative cellular and chromosomal damage induced by radiation, thereby reducing organ damage and enhancing postradiation survival in experimental animals.

Physical Stress

The actions that protect against the toxic effects of chemicals and radiation also help to address the toxic effects of many physical stressors. Prolonged physical exertion, physical restraint, exposure to cold and excessive noise disturb homeostasis by inducing physiological and metabolic stress. When the capacity to adapt to these stressors is exceeded, maladaptation occurs resulting in damage to biochemical pathways, organ function and health. Through enhancing various cellular and physiological adaptive functions, adaptogenic herbs such as tulsi are able to protect against this damage.
Studies using forced swimming, restraint and cold exposure stress in laboratory animals have shown that tulsi enhances aerobic metabolism, improves swimming time, reduces oxidative tissue damage and normalizes many physiological and biochemical parameters caused by physical stressors. Similarly,

experimental studies have shown that tulsi helps reduce the effects of acute and chronic noise induced stress in experimental animals, with enhancement of neurotransmitter and oxidative stress levels in discrete brain regions along with improved immune, ECG and corticosteroid responses.

Metabolic Stress

Metabolic stress due to poor diet, low physical activity and psychological stress is a prominent feature of modern lifestyles and "metabolic syndrome" is estimated to affect as much as one third of modern populations. Metabolic syndrome, also known as "prediabetes" or "Syndrome X," includes the "deadly quartet" of centripetal obesity, hypertension, high cholesterol and poor glucose regulation and is associated with chronic inflammation and a greater risk of diabetes, heart disease and stroke. While the exact causes of metabolic syndrome are still being debated, there is evidence to suggest that tulsi can assist in dealing with many features of metabolic syndrome and their consequences.

Numerous test tube and animal experiments as well as human clinical trials have shown that tulsi has anti diabetic activity. Studies using diabetic laboratory animals have shown that tulsi can reduce blood glucose, correct abnormal lipid profiles and protect the liver and kidneys from the metabolic damage caused by high glucose levels. Tulsi has also been shown to improve lipid profiles, prevent weight gain, hyperglycemia, hyperinsulinemia, hypertriglyceridemia and insulin resistance, and protect the organs and blood vessels from atherosclerosis in laboratory animals fed high fat diets. Similarly, in human clinical trials, tulsi has shown to decrease glucose levels, improve blood pressure and lipid profiles and reduce many diabetic symptoms in patients with type 2 diabetes.

The beneficial metabolic effects of tulsi are multiple and include protecting the liver, kidneys and pancreatic islet cells from free radical damage] enhancing liver bile acid synthesis and reducing liver lipid synthesis; enhancing insulin secretion and action; lowering cortisol levels; and reducing inflammation. The anti inflammatory action of tulsi, which has been observed in both acute and chronic inflammatory models in animals is attributed to tulsi's eugenol and linoleic acid content and the inhibition of both the cyclooxygenase and the lipoxygenase pathways of arachidonic acid metabolism This enables tulsi to exert anti inflammatory effects comparable to nonsteroidal anti inflammatory drugs such as phenylbutazone, ibuprofen, naproxen, aspirin and indomethacin..

Infection Protection

Modern research has revealed that tulsi has antibacterial, antiviral and anti fungal activity that includes activity against many pathogens responsible for human infections. Tulsi has also been shown to boost defenses against infective threats by enhancing immune responses in nonstressed and stressed animals and healthy humans. While no human trials have been published, there is experimental evidence that tulsi may help in the treatment of various human bacterial infections including urinary tract infections, skin and wound infections, typhoid fever, cholera, tuberculosis, gonorrhea, acne, herpes simplex, leishmaniasis, various pneumonias and fungal infections, as well as mosquito borne diseases such as dengue, malaria and filariasis.

Tulsi has also been shown to be active against many animal pathogens, and this has led to tulsi being used in animal rearing to reduce infections in cows, poultry, goats, fish and silkworms. Tulsi's activity against water borne and food borne pathogens further suggests that it can be used in the preservation of food stuffs and herbal raw materials as well as for water purification and as a hand sanitizer.

Tulsi's broad spectrum activity, which includes activity against *Streptococcus mutans*, the organism responsible for tooth decay, further suggests that it can be used as a herbal mouth wash for treating bad breath, gum disease and mouth ulcers. This has been confirmed in clinical trials that have demonstrated that rinsing with tulsi is as effective as 0.2% Chlorhexidine and Listerine in reducing the levels of *Streptococcus mutans* and that a herbal mouthwash that includes tulsi is preferred for its taste and convenience.

Tulsi's unique combination of antibacterial antioxidant, anti inflammatory and analgesic activities also makes it useful in wound healing. This is supported by experimental evidence that has shown that tulsi can increase wound breaking strength and accelerate wound healing in laboratory animals. Tulsi has also been shown to have anti ulcer and ulcer healing activity that has been observed in many different animal models including aspirin, indomethacin, alcohol, histamine, reserpine, serotonin, acetic acid, meloxicam, cold restraint, pyloric ligation and stress induced ulceration models. This anti ulcer activity is attributed to multiple actions including the reduction of offensive factors such as acid pepsin secretion and lipid peroxidation and the enhancement of gastric defensive factors such as mucin secretion, cellular mucus and longevity of mucosal cells.

Mental Stress

In addition to physical, toxic and infective stress, modern living is associated with heightened levels of psychological stress caused by the many demands and fast pace of modern life. This stress compounds the toxic effects of chemical pollutants and the constant fear of pervasive toxic chemicals can itself lead to even further stress and anxiety that may be just as toxic as the chemicals causing it. While the reality of daily chemical exposure cannot be denied, regular consumption of tulsi not only helps protect and detoxify the body's cells and organs, it can also help reduce toxic stress by relaxing and calming the mind and offering many psychological benefits including anti depressant activity and positive effects on memory and cognitive function. The psychotherapeutic properties of tulsi have been explored in various animal experiments that reveal that tulsi has anti anxiety and anti depressant properties, with effects comparable to diazepam and antidepressants drugs. Animal studies further reveal that tulsi enhances memory and cognitive function and protects against aging induced memory deficits Similarly, in human studies, tulsi has been observed to reduce stress, anxiety and depression, with a 6 week, randomized, double blind, placebo controlled study reporting that tulsi significantly improves general stress scores, sexual and sleep problems and symptoms such as forgetfulness and exhaustion.

While modern scientific studies suggest that tulsi is effective in treating a range of stressful conditions, within Ayurveda, tulsi is more commonly recommended as a preventive measure to enhance the ability to adapt to both psychological and physical stress and therefore prevent the development of stress-related diseases. To this end, many Ayurvedic practitioners recommend the regular consumption of tulsi tea as an essential lifestyle practice.

Liquid Yoga

Regular consumption of tulsi tea may be compared with the regular practice of yoga, which can be considered "adaptogenic" through nurturing and nourishing the body mind spirit while fostering a sense of relaxation and wellbeing. In contrast, regular consumption of caffeinated beverages such a black and green tea (*Camellia sinensis L.*) and coffee (*Coffea arabica L.*) may be compared with more aerobic exercise, which confers health benefits through stimulation and activation.

Like yoga, tulsi has a calming effect that leads to clarity of thought, along with a more relaxed and calm disposition. The cognitive and memory enhancing properties of tulsi therefore differ from those of caffeine containing beverages such as coffee and tea, which heightens arousal and may cause physical and mental agitation. Furthermore, tulsi does not produce the same physical dependence as caffeine and can be safely consumed on a regular basis without the fear of withdrawal effects.

The drinking of tea and coffee has become an integral part of modern life and has been ritualized in many cultures to guide social interactions, set social agendas and invoke spiritual awareness. For example, sophisticated Asian tea ceremonies involve a whole set of rituals, tools and gestures that serve to transcend normal consciousness, while in the west the ritual of "afternoon tea" or "high tea" emphasizes the surroundings, equipment, manners and social circle. In lessformal situations, many people ritualize their morning cup of coffee and use the "meetup for coffee" to arrange their social agendas, while the "tea break" is often built into the modern day work routine. Yet, while tea and coffee have infiltrated their way into modern living, they have not yet attained the status that tulsi has within traditional Indian life.

Divine Tulsi

In Hinduism, tulsi is worshipped as a goddess and every part of the tulsi plant is revered and considered sacred, including the leaves, stem, flower, root, seeds and oil. Even the surrounding soil, which has recently been found to harbor beneficial endophytic fungi, is considered an aspect of the divine. As such, Hindi households are considered incomplete without a tulsi plant, typically in an ornate earthen pot situated in a courtyard where tulsi serves both practical and ceremonial purposes. For example, tulsi's distinct clove-like aroma arising from its high eugenol content serves to link the householder to the divine while also repelling mosquitoes, flies and other harmful insects. Tulsi is further integrated into daily life through evening and morning rituals and other spiritual and purification practices that can involve ingesting its leaves or consuming tulsi tea.

In addition to sanctifying the home, tulsi is used ceremonially in Hinduism and some Greek Orthodox Churches to create "holy water." Tulsi wood or seeds are also used to make tulsi malas, which are strings of beads used to help the mind focus during meditation, chanting and devotional practices and therefore ceremonially connect mind, body and spirit. Tulsi has also been used in cities to combat air pollution and hundreds of thousands of tulsi plants have been planted around the Taj Mahal in Agra to help protect the iconic marble building from environmental pollution damage.[127]

Nature Nurture

The cultivation and reverence for the tulsi plant in the home not only serves specific religious purposes it also directly connects the devotee with the creative power of nature. Connection with nature is profoundly healing and life affirming; yet, the potential health, emotional, social and cognitive benefits of connection with nature are only just being realized in the west where disconnection from nature and "nature deficit" are common. A review of the scientific literature on the health benefits of connection to nature suggest that "access to nature plays a vital role in human health, wellbeing and development that has not been fully recognized,'' and there is now a global movement to reconnect people with nature that has arisen out of concerns over nature deficit, sedentary lifestyles, obesity, mental health issues, excessive use of electronic media, environmental degradation, wildlife conservation, sustainability and climate change The placing of a living tulsi plant at the center of the household, therefore, has applicability beyond the realms of Hinduism and may play a useful role in addressing modern day issues through embodying the healing power of the natural world and serving as a constant connection to living nature.

Quality Assurance and Identification

Like any medicinal plant, optimal cultivation, harvesting, preservation and storage methods are required to preserve tulsi's medicinal value. For example, it is suggested that tulsi should be grown employing organic methods in rural areas free from environmental pollution. This is supported by the finding of toxic elements at almost twice the concentration in tulsi leaves grown in polluted compared with unpolluted areas.

It is also important to ensure the correct herb is used and that manufacturers adopt stringent quality assurance standards and processes. Concerns about product quality in European "tulsi" products have been raised by reports of a high frequency of substitution with surrogate herbs such as *Ocimum basilicum L.* This may be addressed using high performance liquid chromatography fingerprints and microscopic assays to ensure batch to batch quality and the safety and botanical integrity of standardised extracts of standardized extracts.

Tulsi as a Vehicle of Consciousness

Perhaps one of the greatest of tulsi's benefits in the modern world comes from its global distribution based on its cultivation using ethical, fair trade, organic and ecological farming practices. There is a growing realization that in order to tackle issues of food security, rural poverty, hunger, environmental degradation and climate change a shift in agriculture is needed from a "green revolution" to an "ecological intensification revolution. This has been highlighted in a recent United Nations document titled "Wake Up Before It's Too Late," which calls for the global community to endorse and advocate for local solutions to toxicity, food insecurity and poverty, such as the use of organic and small scale farming over the use of genetically modified organisms and monocultures.

While ecological farming methods are not specific to tulsi, they have been effectively applied to tulsi cultivation by Organic India Pvt. Ltd. This company, which was established as a "vehicle of consciousness," works with thousands of organic tulsi farmers in India to produce a business ecology whereby rural Indian farmers gain their dignity and a healthy and sustainable livelihood while serving to nurture the land they live on and produce a range of teas that enable consumers around the world to access the benefits of tulsi.

Conclusion

Modern day scientific research into tulsi demonstrates the many psychological and physiological benefits from consuming tulsi and provides a testament to the wisdom inherent in Hinduism and Ayurveda, which celebrates tulsi as a plant that can be worshipped, ingested, made into tea and used for medicinal and spiritual purposes within daily life. In providing a focus for ethical, sustainable and ecological farming practices that provides a livelihood for thousands of farmers, the cultivation of tulsi goes beyond providing benefits for individuals and households and begins to address broader social, economic and environmental issues.

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