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RECENT APPROACHES AND PHARMACEUTICAL APPLICATIONS OF NATURAL POLYSACCHARIDES: A REVIEW

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ABSTRACT: Polysaccharides obtained from gums and mucilages are extensively used natural materials for conventional and novel dosage forms. Many natural gums are studied for use in novel drug delivery systems out of which polysaccharides, resins and tannins are most extensively studied and used. Because of advances in drug delivery technology, natural polysaccharides are included in novel drug delivery to fulfil multitask functions and in some cases directly or indirectly control the extent or rate of drug release. Regular research is going on in the field of use of naturally occurring biocompatible polymeric material in designing of dosage forms for oral controlled release administration. The natural polysaccharides improve the national economy by providing inexpensive formulations to people, by using locally available materials. The present review covers almost all the areas of interest of some very important naturally based polysaccharides, natural gums and mucilages with their sources, chemical constituents, chemical structures, isolation, purification, standardization and characterization along with their uses in various pharmaceutical formulations.

INTRODUCTION: Polysaccharides are a diverse class of polymeric materials of natural (animal, plant, algal) origin formed via glycosidic linkages of monosaccharides. Dependent upon the nature of the monosaccharide unit, polysaccharides can have a linear or branched architecture.

In addition to structural diversity, polysaccharides have a number of reactive groups, including hydroxyl, amino, and carboxylic acid groups, indicating the possibility for chemical modification. Moreover, polysaccharide molecular weight can vary between hundreds and thousands of Daltons, further increasing diversity [1].

Natural polysaccharides and their derivatives represent a group of polymers widely used in the pharmaceutical and biomedical fields for the controlled release of drugs. The advantages of controlled drug delivery systems are mainly the achievement of an optimum concentration, usually for prolonged times, the enhancement of the activity of labile drugs, due to their protection against hostile environments, and the diminishing of side effects due to the reduction of high initial blood concentrations. The polysaccharides have advantages over the synthetic polymers, generally because they are non-toxic, less expensive, biodegradable, and freely available, compared to their synthetic counterparts [2].

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Classification of natural polysaccharide:

1. According to the charge:

a. Anionic Polysaccharides:

i. Natural: Alginic acid, pectin, Xanthan gum, Hyaluronic acid, Chondroitin sulfate, Gum Arabic, Gum Karaya, Gum Tragacanth

ii. Semi-Natural: Carboxymethyl, Chitin, Cellulose gum

b. Cationic Polysaccharides:

i. Natural: Chitosan

ii. Semi-Natural: Cationic Guar gum

iii.Cationic: Hydroxyethylcellulose (HEC)

c. Nonionic Polysaccharides:

i. Natural: Starch, Dextrins, Guar gum

ii. Semi-Natural: Cellulose Ethers (e.g. hydroxyethyl cellulose, Methylcellulose, Nitrocellulose).

d. Amphoteric Polysaccharides:

i. Semi-Natural: Carboxymethylchitosan, N-hydroxyl-Dicarboxy- ethylchitosan, Modified Potato starch.

e. Hydrophobic Polysaccharides:

i. Semi-Natural: Cetylhydroxyethylcellulose, Polyquaternium.

2. According to the source:

a. Marine origin/algal (seaweed) gums: agar, carrageenans, alginic acid, laminarin.

b. Plant origin:

i. Shrubs/tree exudates: gum arabica, gum ghatti, gum karaya, gum, tragacanth.

ii. Seed gums: guar gum, locust bean gum, starch, amylose, cellulose

iii. Extracts: pectin, larch gum

iv. Tuber and roots: potato starch

c. Animal origin: chitin and chitosan, chondroitin sulfate, hyaluronic acid.

d. Microbial origin (bacterial and fungal): xanthan, dextran, curdian,pullulan, zanflo, emulsan, Baker'syeast glycan, schizophyllan, lentinan, krestin

e. Semi-synthetic Gums:

i. Starch derivatives: Heta starch, Starch acetate, Sarch phosphates.

ii. Cellulose derivatives: Carboxymethyl cellulose (CMC), Hydroxyethyl cellulose, Hydroxypropyl methylcellulose (HPMC), methylcellulose (MC) Microcrystalline cellulose (MC).

3. According to Manomeric units in chemical structure:

a. Homoglycans: Amylose, Arabinanas, Cellulose

b. Diheteroglycans: Algins, Carragennans, Galactomannans

c. Tri-heteroglycans: Arabinoxylans, Gellan, Xanthan

d. Tetra-heteroglycans: Gum Arabic, Psyllium seed gum

e. Penta-heteroglycans: Ghatti gum, Tragacanth [3, 4, 5].

Advantages of natural polysaccharides in pharmaceutical sciences are:

- **Biodegradable:** Naturally available biodegradable polymers are produced by all living organisms. They represent truly renewable source and they have no adverse impact on humans or environmental health.

- **Biocompatible and Non toxic:** Chemically, nearly all these plant materials are carbohydrates composed of repeating sugar (monosaccharide) units. Hence they are non-toxic.

- **Low cost:** It is always cheaper to use natural sources. The production cost is also much lower compared with the production of synthetic materials.

- **Environmental friendly processing:** Gums and mucilages from different sources are easily collected in different seasons in large quantities due to the simple production processes involved.

- **Local availability:** Especially in developing countries, government promote the production of plants like guar gum and

tragacanth because of the wide applications in a variety of industries.

- **Better patient tolerance as well as public acceptance:** There are less chances of side effects with natural materials compared with synthetic ones so they are well tolerated and accepted.

Disadvantages of natural polysaccharides:

- **Batch to batch variation:** Synthetic manufacturing is a controlled procedure with fixed quantities of ingredients, while the production of gums and mucilages is dependent on environmental and seasonal production.

- **Reduced viscosity on storage:** Normally, when gums and mucilages come into contact with water there is an increase in the viscosity of the formulations. Due to the complex nature of gums and mucilages (monosaccharides to polysaccharides and their derivatives), it has been found that after storage there is reduced in viscosity.

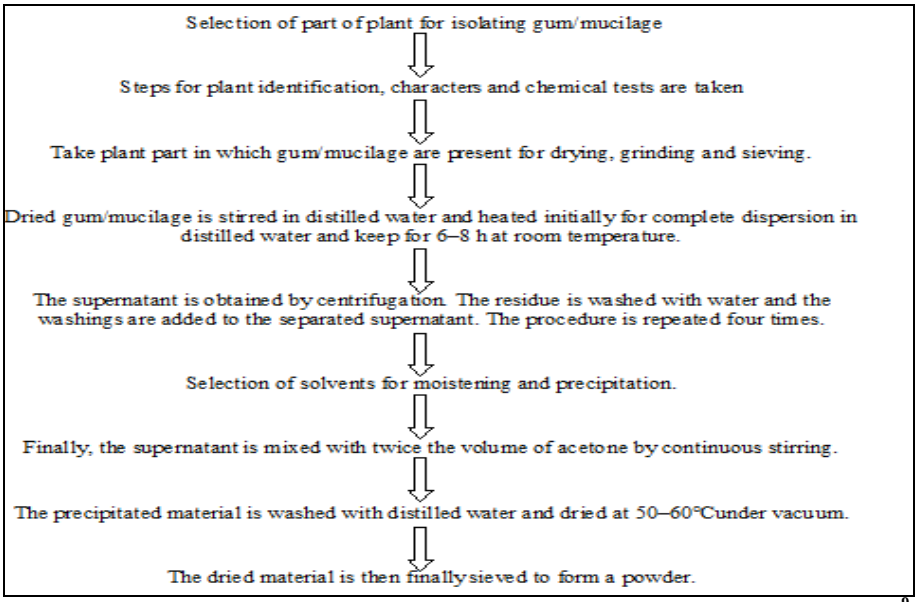
- **Microbial contamination:** The equilibrium moisture content present in the gums and mucilages is normally 10% or more and, structurally, they are carbohydrates and, during production, they are exposed to the external environment and, so there is a chance of microbial contamination. However, this can be prevented by proper handling and the use of preservatives.

- **Uncontrolled rate of hydration:** Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary. There is a need to develop suitable monographs on available gums and mucilages [6, 7].

Isolation and purification of gums/mucilages (Polysaccharides):

Plant material is dried in sunlight (preferably) to retain its properties unchanged. Generally, chlorophyll or pigments are present in the plant which should be removed before isolating the mucilage. Plant material must be treated with petroleum ether and chloroform (to remove pigments and chlorophyll) and then with distilled water. Care should be taken when drying the final isolated/extracted mucilage. It must be dried at a very low temperature (not more than 50˚C) or in a vacuum. The dried material is stored carefully in desiccators to prevent further moisture uptake or degradation [8].

The general isolation and purification processes for gums and mucilages are shown in the flowchart:



GENERAL ISOLATION/EXTRACTION PROCEDURE FOR POLYSACCHARIDES [9].

TABLE 1: PRELIMINARY CONFIRMATIVE TESTS FOR DRIED MUCILAGE POWDER [10, 11].

Test	Observations	Inferences
Molisch's test: (100 mg dried mucilage powder + Molisch's reagent + conc. H2SO4 on the side of a test tube)	Violet green colour observed at the junction of the two layers	Carbohydrate Present
Ruthenium test: Take a small quantity of dried mucilage powder, mount it on a slide with ruthenium red solution, and observe it under microscope.	Pink colour develops	Mucilage present
Iodine test: 10 0mg dried mucilage powder + 1 ml 0.2 N iodine solution**.**	No colour observed in the solution	Polysaccharides present (starch is absent)
Enzyme test: dissolve 100 mg dried mucilage powder in 20 ml-distilled water; add 0.5 ml of benzidine in alcohol (90%). Shake and allow to stand for few minutes	No blue colour is produced	Enzyme absent (Distinction between dried mucilage and acacia)

1. Okra gum:

The Botanical name of okra gum is *Abelmoschus esculentus Linn.* It is obtained from the fruits of *Hibiscus esculentus* belonging to the family Malvaceae [12]. The Chemical constituents include D-galactose, L-rhamnose and L-galacturonic acid with some proportions of glucose, mannose, arabinose and xylose [13].

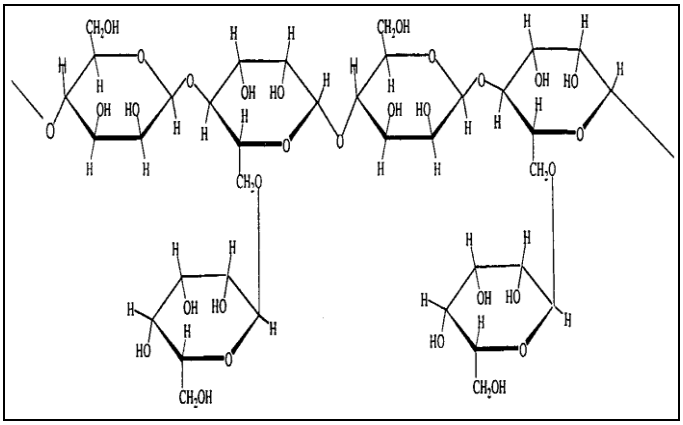


FIG.1: STRUCTURE OF OKRA GUM

It can be extracted from 1 kg of fresh immature fruits of Okra which were purchased from the market. The seeds were carefully removed from the fruits, and then the fresh immature fruits were cut into pieces, homogenized and then finally extracted with cold water containing 1% w/v of sodium meta-bisulphate. The crude mucilage was formed which was then centrifuged at 3000 rpm for 5 min. The gum formed was precipitated from the supernatant with acetone. The gum was washed several times with acetone to obtain a cream coloured product which was dried under vacuum in the desiccators. After complete removal of the moisture a light brown coloured product was obtained. The dried gum was then made into a powder form by pulverizing using an end runner mill and passed through 0.25 mm stainless steel sieve. The finally obtained powder was stored in a well closed amber coloured specimen bottle until ready for use [14, 15].

Pharmaceutical applications:

- **Emulsifier in emulsions:** Okra extracts showed potential as emulsifier in acidic environments producing fine emulsions with good stability against coarsening in case of oil in water emulsions with n-hexadecane as dispersed phase [16].
- **Controlled drug releaser:** Polymer swelling studies were carried out with both poorly soluble drug (flurbiprofen) and soluble drug (theophylline). The stydy revealed that the release rate of flurbiprofen was slower than theophylline [16].
- **Retarding agent:** Ookra gum is an effective retarding polymer to develop sustained release tablets. It is able to formulate propranolol hydrochloride tablets showing a release up to 24 hours as compared to HPMC and sodium alginate as retarding agents [17].
- **Sustained release candidate**: Ibuprofen and Calcium acetate tablets containing Okra gum showed sufficient hardness, desirable disintegration time and low friability. The percent of drug released after 45 minutes was 15 %, 44 % and 96 % for Acetaminophen, Ibuprofen and Calcium acetate tablets, respectively. Okra gum produces some tablet formulations with good hardness and friability. However, this binder prolongs the dissolution rate of some

slightly soluble drugs and hence may be a good candidate for sustained release formulations[18].

- **Release modifier:** Okra gum was successfully employed for formulating the sustained release matrix tablets of diclofenac sodium and 10-15% concentration of okra gum was capable of prolonging the release of drug for 10 hours. Drug release was found to follow near zero order kinetics and mechanism of drug release was observed to be following the korsmeyer-peppas model [19].

- **Mucoadhesive Gel for Nasal Delivery:** The permeation of rizatriptan benzoate through the nasal epithelia was clearly influenced by the types of gelling agents and permeation enhancers used. It was found that okra nasal gel was influenced more by permeation enhancer (sodium taurocholate and sodium thioglychollate) than the synthetic gels tested. The reason considered may be that okra gel leads to easy availability of the enhancers for action on epithelial membrane by facilitating rapid release from the gel matrix, whereas in case of synthetic polymers they affect sustained release of enhancers in the same manner as they do to drugs. Overall, okra mucilage seems a better alternative to the synthetic polymers for safe delivery of drug via nasal route [20].

- **Colon-targeted drug delivery systems:** The formulated and prepared Ibuprofen matrix tablets using okra as a polymer were evaluated for their integrity in the physiological pH of stomach, the small intestine and colon [21].

- **As a binder:** Okra gum as a binder produces some tablet formulations (paracetamol and ibuprofen) with good hardness, friability, and disintegration time and dissolution rate. However, this binder prolongs the dissolution rate of slightly soluble drugs [22].

2. Tamarind gum: The botanical name of tamarind gum is *Tamarindus indica* which is obtained from the endosperm of seeds of the tamarind tree *Tamarindus indica*, belonging to the family Leguminosae. Tamarind Gum is also known as Tamarind Kernel Powder (TKP) which is extracted from the seeds [23].

The Chemical constituents includes 15.4 - 12.7 % Protein, 3 - 7.5 % Oil, 7 - 8.2 % Crude fibre, 61 - 72.2 % Non fibre carbohydrates, 2.45 - 3.3 % Ash. Chemically tamarind kernel powder is highly branched carbohydrate polymer. Its backbone consists of D-glucose units joined with (1-4) b-linkages similar to that of cellulose. It consists of a main chain of b-D- (1-4)- galactopyranosyl unit with a side chain of single xylopyranosyl unit attached to every second, third and fourth of D-glucopyranosyl unit through a-D- (1-6) linkage. One galactopyranosyl unit is attached to one of the xylopyranosyl units through b-D- (1-2) linkage. The exact sequential distribution of branches along the main chain is uncertain [24, 25].

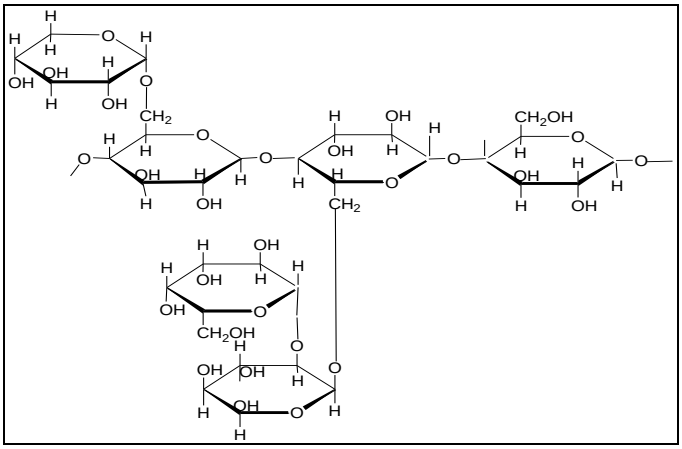


FIG.2: STRUCTURE OF TAMARIND GUM

Tamarind gum is extracted from the tamarind kernel powder which was collected from seeds of plant. To 20g of tamarind kernel powder 200ml of cold distilled water was added and slurry was prepared. The slurry was poured into 800ml of boiling distilled water. The solution was boiled for 20 minutes under stirring conditions on a water bath. The resulting thin clear solution was kept overnight so that most of the proteins and fibres settle down. The solution was then centrifuged at 500 rpm for 20 minutes. The supernatant was separated and poured into twice the volume of absolute ethanol by continuous stirring. The

product was filtered through muslin cloth and was washed with absolute ethanol, isopropanol, methanol and then dried at -50-60˚C under freeze dryer. The dried material was ground and sieved to obtain granules of different particle size range and stored in a desiccator until further use [26, 27].

Pharmaceutical applications:

- **Suspending and Emulsifying Agent in Liquid Orals:** It is used in the formulation of paracetamol suspension.

- **Binders in Solid Dosage Forms:** The binding character of tamarind powder was investigated in tablets using ibuprofen as the model drug tamarind powder, in spite of being used as a binder, it was also found to be used as a functional excipient for obtaining delayed release formulations, as the formulation containing 30% of tamarind powder maintained a zero-order release up to 24 h by swelling, diffusion and erosion, which were better than the commercial brand product (UREGENDOL SR).

- **Novel Controlled Release Modifiers:** The polysaccharide that was isolated from the seeds of tamarind was found to have hydrogel property, and hence can be used as a release modifier in various formulations. Diclofenac sodium spheroids were prepared with tamarind seed powder using extrusion spheronisation technique. The results were found to be significant and gave evidence for its use as a release modifier.

- **Matrix Oral Drug Release Modifiers:** Diclofenac sodium matrix tablets were formulated by wet granulation technique using tamarind seed powder as a release modifying excipient, i.e. as the release retardant, where the drug release was prolonged up to a period of 12 hours. The release profile was zero-order controlled release and it was observed that an increase in polymer content resulted in decreased drug release from the tablets.

- **Buccal Drug Release Modifiers:** Mucoadhesive buccal tablets of nitrendipine were prepared using two different natural polymers (*Ziziphus mauritiana* and Tamarind seed powder) and synthetic polymers, Na CMC and HPMC K15M. Various parameters like mucoadhesive strength, swelling index and other physico-chemical parameters showed more potential results for the series of formulations containing natural polymers as compared to the synthetic ones; also, 100% drug release was achieved in tablets containing tamarind seed powder. Tamarind seed powder was also used in combination with carbopol, HPMC K4M and CMC for the fabrication of buccal mucoadhesive tablets of the drug nifedipine for avoiding first-pass metabolism and prolonging the duration of action.

- **Ophthalmic Drug Release Modifiers:** The property of tamarind seed powder as a mucoadhesive was successfully employed for ocular administration of hydrophilic and hydrophobic antibiotics like gentamicin, ofloxacin, etc. The tamarind seed powder viscosified solutions of the drug instilled into rabbit showed that the aqueous humour and corneal concentration of the dose was remarkably higher than the drug alone. The absorption and elimination of drug was prolonged by tamarind seed powder. The mucoadhesive polymer extracted from tamarind seeds proved as an effective candidate for ocular delivery of antibiotics, rufloxacin and ofloxacin, for the treatment of bacterial keratitis.

- **Carrier for Colon Targeted Delivery:** The studies carried to evaluate the use of tamarind seed powder as a carrier for colon drug delivery using ibuprofen as the model drug gave significant results during *in vitro* studies carried out on rat caecal contents. The matrix tablets of ibuprofen which was made using tamarind seed powder prevented the release of drug in upper gastrointestinal into the colon region.

- **Substitute for Petroleum-based Polymer:** Recently, XG polysaccharide from tamarind

seed waste (natural resources) was identified as a high-performance biopolymer having great application in replacement for petroleum-based polymers.

3. Guar gum:

The botanical name of guar gum is *Cyamompsis tetraganolobus*, it is a galactomannan, obtained from the ground endosperm of the guar plant, Cyamompsis tetraganolobus belonging to family Leguminosae.

Guar gum is a polysaccharide composed of the sugars galactose and mannose. The backbone is a linear chain of β 1,4- linked mannose residues to which galactose residues α-1,6 are linked at every second mannose, forming short side branches.

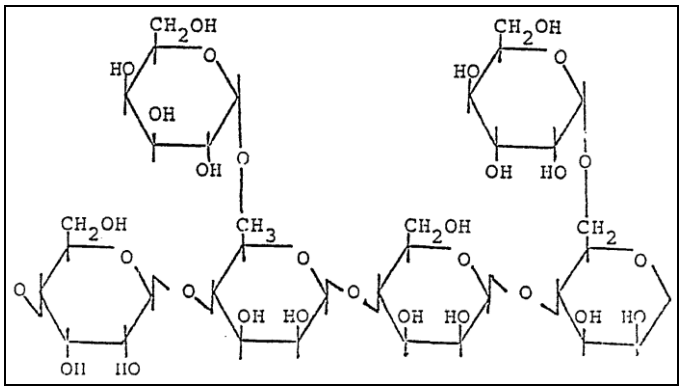


FIG.3: STRUCTURE OF GUAR GUM

Guar gum is extracted and prepared by first drying the pods in sunlight, then manually separating from the seeds. The gum is commercially extracted from the seeds essentially by a mechanical process of roasting, differential attrition, sieving and polishing. The seeds are broken and germ is separated from the endosperm. Two halves of the endosperm are obtained from each seed and are known as undehusked guar splits. Refined guar splits are obtained when the fine layer of fibrous material, which forms the husk, is removed and separated from the endosperm halves by polishing. The refined guar splits are then treated and finished into powders by a variety of routes and processing techniques depending upon the desired end product[28].

Pharmaceutical applications:

- **As rate controlling polymer:** Use of natural hydrophilic polymer like guar gum was successful in the formation of matrix tablet and at the same time it is effective in retarding the drug release of zidovudine over a period of 12 hours [29].

- **Carrier for colon specific delivery:** The study was aimed at finding the influence of metronidazole and tinidazole on the usefulness of guar gum as a carrier for colon specific drug delivery using guar gum matrix tablets of albendazole as model formulation. Hence the matrix tablets of albendazole containing 20% guar gum were chosen as model formulation to access the influence of metronidazole/tinidazole treatment on the usefulness of guar gum as a carrier.

- Guar gum has also been investigated as a carrier for indomethacin for colon-specific drug delivery using in vitro methods Studies in pH 6.8 phosphate buffered saline (PBS) containing rat caecal contents have demonstrated the susceptibility of guar gum to the colonic bacterial enzyme action with consequent drug release. The pre-treatment of rats orally with 1 ml of 2% w/v aqueous dispersion of guar gum for 3 days induced enzymes specifically acting on guar gum thereby increasing drug release. A further increase in drug release was observed with rat caecal contents obtained after 7 days of pre-treatment. The presence of 4% w/v of caecal contents obtained after 3 days and 7 days of enzyme induction showed biphasic drug release curves. The results illustrate the usefulness of guar gum as a potential carrier for colon-specific drug delivery [30].

- **Sustaining agent:** Sustained release tablets of furosemide were fabricated using pectin, guar gum and xanthan gum. The tablets were evaluated for physical characteristic like hardness, weight variation, friability and drug content. In-vitro release of drug was performed in PBS pH 7.2 for fifteen hours. All the physical characters of the fabricated tablet were within acceptable limits. The tablet with guar gum exhibited greater swelling index than those with

pectin and xanthan gum. A better controlled drug release (80.74%) was obtained with the matrix tablet made-up of the guar gum than with the pectin and xanthan gum. It is cleared through the dissolution profile of furosemide from matrix tablets prepared using different natural polymers were retarded approx 15 hrs [31].

4. Locust bean gum: Biological name of locust bean gum is *Ceratonia siliqua.* Carob or locust bean gum is obtained from the endosperm of the seeds of tree known as *Ceratonia siliqua* belonging to family Fabaceae [32].

Chemically Locust Bean Gum, like Guar Gum, is a polysaccharide consisting of a straight chain of D-mannopyranose unites joined by β-1α-4 linkages with a side-branching unit of a single D-galactopyranose unit joined to every fourth mannose unit by a-(1α-6) linkages. The molecular weight of Locust Bean Gum is 330,000 +10%. An average quality Locust Bean Gum contains about 78% galactomannan, 12% water, 6% protein, 3% acid insoluble residue or crude fibre, 0.8% ash, 1% fat, a trace of heavy metals, zero arsenic, and zero lead.

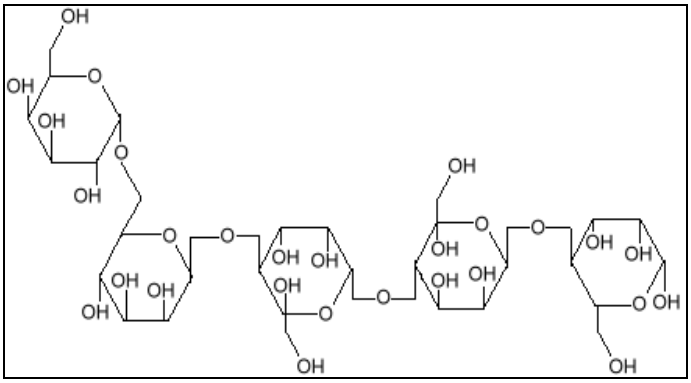


FIG.4: STRUCTURE OF LOCUST BEAN GUM

The seeds are dehusked by treating the kernels with thermal mechanical treatments, followed by milling and screening of the peeled seeds to obtain the endosperm (native carob bean gum). The pre-treated dry powder of crude carob bean gum CBG was extracted with distilled water (ratio of water to endosperm of seeds (197:1), temperature of the water bath 97°C, for a given time (extraction time 36 min). The solution and the solid-phase were separated by centrifugation at (21875rpm, 1h). The Carob Bean Gum is precipitated with one volume excess of isopropanol. The white fibrous precipitate formed was collected by filtration with screen 45µm, and washed twice with isopropanol and with acetone. After drying under vacuum overnight at 30°C, the precipitate was ground to a fine powder [33].

Pharmaceutical applications:

- **Mucoadhesive in buccal tablets:** Locust bean gum has find a wide place in the preparation of mucoadhesive buccal tablets in combination with Chitosan in different combinations where the locust bean gum to chitosan ratios are 2:3, 3:2, 4:1. Mucoadhesive buccal tablets of Propranolol HCl containing various weight ratios of Locust bean gum and Chitosan were prepared and coated with 5% w/v Ethyl Cellulose. The mucoadhesive property of the formulation containing 2:3 was highest compared with other ones. Even its drug release profile was 98% in 60 minutes [34].

- **Bioadhesive in tablets:** Tablets of anhydrous theophylline were prepared by direct compression method and were subjected to in vitro drug dissolution for 12 hours using the USP dissolution apparatus basket type at a speed 100rpm.The bioadhesive strength of the tablets were measured as the force of detachment against the porcine gastric mucosa. The *in vitro* release study as well as the retention time of the bioadhesive tablets on the mucous based controlled release delivery system and to evaluate the performance of such a delivery device. The formulation containing locust bean gum showed a good bioadhesive property. It was also found that an increase in the gum combination increases the drug release profile beyond 12 hours whereas there is no significant effect of gum concentration on the bioadhesive strength of the tablets [35].

- **Colon targeted drug delivery systems**: Locust bean Gum is also used for the preparation of Colon targeted drug delivery system along with Chitosan. If Locust bean

gum and Chitosan is taken in the ratio of 2:3, then a good colonic activity is obtained. From in vitro and in vivo studies revealed that locust bean gum and chitosan was capable of protecting the drug from being release in the stomach and small intestine and was susceptible to colonic bacterial enzymatic action with resulting drug release in colon [36].

- **Emulsifying agent:** Carragenan- Locust bean Gum mixture was taken in multiphase emulsification technique for sustained drug release of gentamicin. In the preparation of w/o/w emulsion various proportions of iota-carragenan and locust bean gum were investigated [37].

- **Solubility enhancer for poorly soluble drugs:** Locust Bean gum has a property to increase the solubility of some lipophilic drugs. This has been proved by the that when lovastatin, a poorly soluble drug was taken to prepare solid dispersion by using modified locust bean gum as a carrier there was an increase in the solubility of lovastatin [38].

- **Ophthalmic preparations:** Locust bean gum is incorporated in ophthalmic preparations of cholinergic agents like Echothiophate iodide to enhance drug's therapeutic activity therapy allowing a reduction in dosage. Locust Bean Gum potentiates the action of the drug therapy reducing the side effects of the drug. Generally the concentration of gum is 0.02% to about 1%w/v [39].

5. Ispaghula husk (psyllium):

The biological name of ispaghula is *Plantago ovata* which is derived from the dried ripe seeds of *Plantago psyllium* and *Plantago indica*, the ispaghula husk is derived from the ripe seeds of *Plantago ovate* belonging to the family Plantaginaceae [40]. Chemically the seed contains pentosan and aldobionic acid, 5-10% lipids with unsaturated fatty acids, sterols, proteins (15-18%), traces of cyclopentano pyridine-type of alkaloids, aucubin and carbohydrates-planteose, also a trisaccharide, and 10-12% mucilage of the heteroxylan type [41].

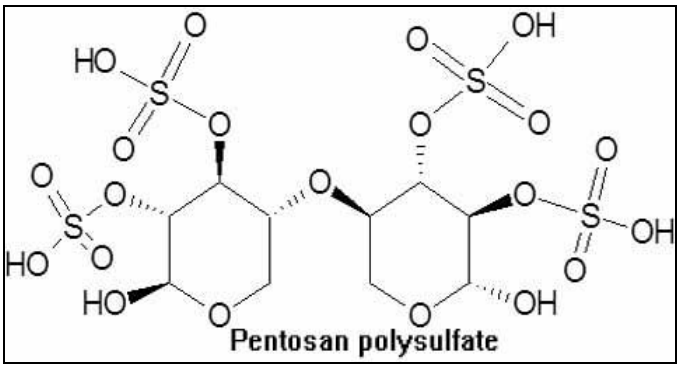


FIG.5: STRUCTURE OF PENTOSAN POLYSULFATE

Ispaghula husk mucilage can be extracted by dispersing 2.5 g of ispaghula husk in about 500 ml of phosphate buffer of pH 7.4 at 80 ºC under constant magnetic stirring for 2 h. Then the resulting ispaghula husk mucilage was allowed to cool which was then filtered through a nylon filter followed by a muslin cloth to get a viscous solution [42].

Pharmaceutical applications:

- **Release retardant:** Aspirin was taken as a model drug to prepare microspheres by spray drying using ispaghula husk mucilage and arabinoxylan as carriers. Aspirin is known for its property of ester hydrolysis and the degradation rate depends on the pH. An attempt was made for encapsulating aspirin using ispaghula husk mucilage and arabinoxylan at pH of 3 and 7.4. The pH selected was based on the lowest rate of degradation reported. However, encapsulation of aspirin using arabinoxylan and ispaghula mucilage by spray drying was unsuccessful as neither the carrier nor the spray drying method were able to prevent the hydrolytic degradation of the aspirin [42].

- **Extended release candidate:** diclofenac sodium with varying proportions was selected as a model drug to formulate tablets in combination with ispaghula husk by wet granulation technique at a fixed compression force of 10 kN. The formulated tablets were further evaluated for physicochemical parameters by Fourier

transform infrared spectroscopy (FTIR), as well as differential scanning calorimetry (DSC) and x-ray diffraction (XRD). The study revealed that the tablets formulated with 1:0.25 and 1:0.5 drug: husk ratio failed to extend the drug release whereas tablets prepared with 1:0.75 and 1:1 ratio were successful in extending release up to 5 and 6 h, respectively [43].

- **Suspending agent:** An effective alternative to commercially used excipients for the preparation of pharmaceutical suspensions use of arabinoxylan as a potential suspending agent was evaluated. Alkali extraction of arabinoxylan was done to separate it from ispaghula (*Plantago ovata*) seed husk, alkali extraction was used for its physicochemical characterization and the suspending properties of the isolated arabinoxylan were evaluated in comparison with those of bentonite at various concentration ranges of 0.125, 0.25, 0.5 and 1% in Zinc oxide suspension. As a result arabinoxylan produced stable and highly flocculated suspension, which fulfilled parameters like microbiological and particle size specifications. Therefore it was concluded that arabinoxylan could be used as an effective suspending agent at low concentrations in Zinc oxide suspension [44].

- **Disintegrating agent:** Ibuprofen was selected as a model drug for the formulation of dispersible tablets using *plantago ovata* mucilage powder, *ocimum basilicum* mucilage powder, *plantago ovata* husk powder, *ocimum basilicum* seed powder were prepared as disintegrants and there disintegrating property was studied. The study revealed that plantago ovate seed powder and mucilage powder both were effective in low concentrations (5%) for their disintegrating property as compared to others. The study further also revealed poor relation between the swelling index and disintegrating efficiency [45].

6. Gellan gum: Biological name of gellan gum is *Sphingomonas elodea.* Gellan gum is a polysaccharide manufactured by microbial fermentation of the *Sphingomonas paucimobilis* microorganism.

Chemically it consists of repeating tetrasaccharide units of glucose, glucuronic acid and rhamnose residues in a ratio of 2:1:1. [→3)–β–D–glucose–(1→4)–β–D–glucuronic acid–(1→4)–β–D–glucose–(1→4)–α–L–rhamnose–(1→]. In the native polymer two acyl substituents, L-glyceryl at O(2) and acetyl at O(6), are present on the 3-linked glucose. On average, there is one glyceryl per repeating unit and one acetyl for every two repeating units [46].

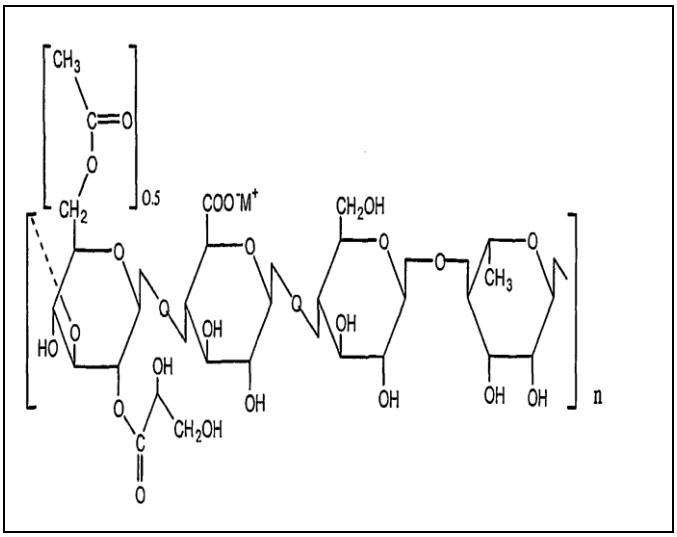


FIG.6: STRUCTURE OF GELLAN GUM

Pharmaceutical applications:

- **Disintegrating agent:** Matrix tablets of metronidazole using gellan gum were prepared in different concentrations and its release profile was studied. It was concluded from the study that optimum concentration of gum (0.2% w/w) showed most effective as a disintegrating agent.

- Bi layer tablet of Metoclopramide Hydrochloride and Ibuprofen were prepared for the effective treatment of migraine. Metoclopramide hydrochloride was formulated as an immediate release layer using gellan gum as disintegrants.

- **Carrier for colon specific drug delivery:** Gellan beads were prepared to deliver azathioprine as a potential colonic delivery

system by ionotropic gelation and were coated with Eudragit S-100. Gum releases drug in controlled manner. Thus, it was suggested the use of gellan gum as a carrier for controlled colonic specific drug delivery systems [47].

- **Mucoadhesive agent:** gellan gum was used in the preparation of stomach-specific controlled release mucoadhesive drug delivery system. They employed amoxicillin trihydrate as model drug. The in vitro dissolution study showed that drug release up to 7 h in a controlled manner and following the Peppas model. From the results of both *in vitro* and *in vivo* mucoadhesivity study, it was revealed that gellan gum beads possess good mucoadhesivity even after 7 h [48].

- **As a hydrogel:** hydrogels containing different amounts of Gellan gum and NaCMC were prepared by the chemical cross linking using two different crosslinkers. The composition of the gel and nature of the cross linking agents influence the surface morphology, thermal behaviour, swelling characteristics and drug release behaviour. Both type of gels exhibit a good pH responsive behaviour with 3 times higher swelling in pH 7.4 compared to pH1.2. The extent of drug release significantly increased when pH of the medium was changed from acidic to alkaline. The results indicated that this system may find useful as a matrix for slow release tablet formulations of the drug 'ketoprofen'[49].

- **Protein delivery systems:** a procedure was developed for the preparation of gellan films. The effects of the concentration of each ingredient in the prepared gellan films were studied. *In-vitro* release behaviour of fluorescein isothiocyanate dextran from these films was examined. This film device was implanted in diabetic rats for observing the insulin delivery. Both in vitro and in vivo studies indicated that the gellan film could be an ideal candidate in the development of protein delivery systems.

- **In-situ gel formulations:** sustained delivery of paracetamol by the preparation of gellan gum in-situ gel formulations was studied and reported that the bioavailability of paracetamol from the gels formed in situ in the stomach of rabbits following oral administration of the liquid formulations was similar to that of a commercially available suspension containing an identical dose of paracetamol.

- In situ gellan gum based gel with ciprofloxacin hydrochloride was formulated and studied for diffusion characteristics. The gel formulation containing ciprofloxacin hydrochloride showed a prolonged drug release pattern.

- A gellan gum based in situ gel system of clindamycin for vaginal application was developed and optimized. The developed formulations were characterized for various in-vitro parameters. Performed studies and obtained results prove the efficacy of gellan gum based clindamycin in situ gel system[50].

7. Fenugreek gum:

Biological name of fenugreek is *Trigonella Foenum-graceum.* It is obtained from the endosperm of the seeds belonging to family Leguminosae. Chemically fenugreek seeds contain oils, alkaloids, amino acids like (lysine, argenine, tryptophan, threonin, valyn and methionin) and musilages that is most famous in this plant is galactomannan, it also contains vitamins A, C, D, B1 and , minerals calcium, iron and zinc. Fenugreek seeds also contain 50% fibre out of which 20% is insoluble fibre and 30%is soluble fibre [51].

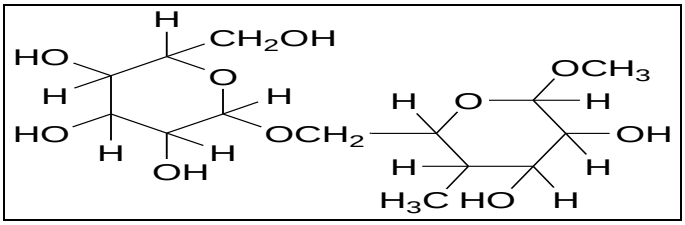


FIG.7: STRUCTURE OF FENUGREEK GUM

Fenugreek polysaccharide is extracted by dissolving 20gm of fenugreek seeds in 200ml double distilled water and boiled with stirring up till the slurry is formed, further it was kept to cool for 3 to 4 hours so as to separate the supernatant liquid. The clear solution at the top was decanted and the rest was centrifuged at 500rpm for 20 minutes. The supernatant was separated and heated at 60ºC on water bath to concentrate the supernatant. The solution after heating was cooled to the room temperature and was then poured into thrice the volume of acetone with continuous stirring. The precipitates were formed and then the precipitated material was washed with distilled water and again dried at 50-60º under vacuum. The powder so obtained was stored in a desiccator until use [52].

Pharmaceutical applications:

- **Controlled release polymer:** Highly purified fenugreek gum was investigated as an emulsifier and hydrophilic solid carrier in drug delivery systems of a hyperlipidemic drug simvastatin which was selected as a model drug because of its poor solubility in water and low biocompatibility. The study revealed improved dissolution rate and solubility due to improved wetting [53].

- **As a binder in tablets:** Three model drugs calcium acetate, theophylline and ibuprofen were taken as model drugs of freely soluble, slightly soluble and practically insoluble in water to formulate and prepare tablets using fenugreek gum as a tablet binder. The study revealed that fenugreek gum which is used as a binder sustains the dissolution rate of the water soluble drugs [54].

- **Gelling agent:** five batches of Diclofenac gel were prepared with different concentration of mucilage (viz; 4.0%, 5.0%, 6.5%, 8.0%, 10%w/w), Diclofenac sodium 1%w/w, Glycerin 10%w/v, Methyl paraben 0.02%. The gels prepared with 8.0% of mucilage were found to be ideal and comparable with commercial preparation. The gels were evaluated for drug content, viscosity determination, *in-vitro* permeation, skin irritation etc. The prepared gels did not produce any dermatological reactions and were well tolerated by the albino mice. The gels were found to be stable with respect to viscosity, drug content and physical appearance at all temperature conditions for 3 weeks. Studies indicate that the extracted mucilage may be a good substitute as a pharmaceutical excipient specifically as a gelling agent [55].

- **Disintegrating agent:** fast disintegrating tablets consisting of fenugreek seeds powders were prepared by wet granulation method. Crosspovidone and *Platego ovata* powder were used as super disintegrants by making use of self-disintegration property of fenugreek seeds. Pre-formulation studies showed that the powder blend was not having a free flowing nature because of which wet granulation technique was used and appropriate tablet formulations were prepared. Formulations were aimed to develop tablets having minimum possible disintegration time. Tablets were evaluated for various parameters like hardness, weight variation, and friability, wetting time, disintegration time and stability. Results revealed that fast dissolving tablets made up of fenugreek seed powder could be prepared at any level of superdisintegrants. The results from the study concluded that fast dissolving tablets of fenugreek seed powder will lead to improved effectiveness and better patient compliance in future [56].

- Fenugreek mucilage derived from the seeds of fenugreek, was investigated as an disintegrant for its application in mouth dissolving tablet formulations containing metformin hydrochloride as a model drug. Therefore, the study revealed that fenugreek mucilage a natural disintegrant showed better disintegrating property than the most widely and most commonly used synthetic super disintegrants like Ac-di-sol in the formulations of fast dissolving tablet formulations.

8. *Moringa oleifera* Gum: *Moringa oleifera* is the most widely cultivated species of a monogeneric family, the Moringaceae that is native to the Sub-Himalayan tracks of India, Pakistan, Bangladesh and Afghanistan**.**

Stem exudes a gum which is initially white in colour but changes to reddish brown or brownish 3 black on exposure. It has the capability to protect the active drug from stomach and small intestine and so it can be used in colon targeted drug delivery. It has been reported to have binding property, release retardant property and gelling effect [57, 58].

Chemically it consists of 92.3% of the total oil, and hydrocarbons represented the 91.1% of the oil. Hexacosane (13.9%), pentacosane (13.3%) and heptacosane (11.4%) were the most abundant compounds. Such a composition is similar to that of the oil obtained from leaves of M. oleifera grown in Taiwan, in which pentacosane (17.4%), hexacosane (11.2%) and (E)-phytol (7.7%) were the major component. Phytol (21.6%) and thymol (9.6%) have been reported as the most abundant compounds in the leaves oil of M. oleifera from Ceará (Brazil).

Nonacosane (18.6%), 1,2,4-trimethyl-benzene (16.9%) and heptacosane (7.4%) are the major components in the essential oil of M. oleifera obtained by Soxhlet extraction, while nonacosane (13.4%–60.1%), heptacosane (5.0%–22.6%) and pentacosane (1.0%–6.3%) were among the most abundant components in the essential oil obtained.
Moringa Oleifera gum can be extracted after collecting it from the trees (Injured site). It was dried, ground and passed through sieve no 80. Dried gum (10g) was stirred in distilled water (250ml) for 6- 8 hours at room temperature. The supernatant was obtained by centrifugation. The residue was washed with water and the washings were added to supernatant.

The procedure was repeated four times. Finally the supernatant was made up to 500 ml and the treated with twice the volume of acetone by continuous stirring. The precipitated material was washed with distilled water and dried at 50-60ºC under vacuum [59].

Pharmaceutical Applications:

- **Gelling agent:** A study was carried out to find the gelling potential of gum exudates from the stem of *Moringa oleifera*. Diclofenac sodium gels were formulated with concentration of mucilage ranging from 5.5 to 8.5%w/w. Better gel characteristics were observed at the concentration of 8%w/w. As the pH of the gum is below 5.77 and the viscosity of the formulation (8.5%w/w) is 4.6x106cps, it is ideal for topical application [60].

- **Suspending agent:** A comparative study of gums of *Moringa oleifera* and tracaganth was reported. Zinc oxide suspensions were prepared with gum of *Moringa oleifera* and tracaganth. Their sedimentation profile, redispersibility, degree of flocculation and rheological behaviour were compared. The results revealed that the suspending properties of *Moringa oleifera* gum are comparable with that of gum tragacanth [61].

- **Surfactant behavior:** A study on interfacial properties and fluorescence of a coagulating protein extracted from *Moringa* seeds and its interaction with sodium dodecyl sulphate (SDS) was carried out. The study reported that; a) the protein extracted from *Moringa* seeds has significant surfactant behavior; b) the coagulant protein interacts strongly with SDS and the protein might have specific binding sites for SDS; c) there is formation of protein-SDS complex [62].

- **As stabilizer:** Plant phenolics have gained considerable interest in recent years for their potential effects against food related microorganisms. Phenolic extract obtained from the leaves of *M. oleifera* & *M. orusindica* showed stabilizing activity. In the present study effect of addition of phenolic extract from leaves of *M. oleifera* and *M. indica* on the shelf life of pineapple juice stored at 4 0 C was investigated by monitoring the changes in titrable acidity and sensory parameters for 8 weeks. Results observed that the extracts of natural

phenolics can be used to improve the quality and safety of foods [63].

- **Film forming property:** Studies reported that gum of *M. oleifera* has enormous potential for use in the preparation of polymeric films as drug delivery systems. The films prepared using gum of *Moringa oleifera* (5 parts of 10% w/w of mucilage of gum of *Moringa oleifera* with different proportion of plasticizers) were evaluated for parameters like water uptake, tensile strength, folding endurance and water vapour transmission rate. The films were found to be comparable with films made from other polymers and in terms of above parameters therefore the gum can be used for preparing polymeric drug delivery systems and as a film coating agent in tablets as it has low vapour transmission rate and satisfactory tensile strength [64].

CONCLUSION: Polymers play a essential role in the drug delivery. So, the selection of polymer plays an important role in pharmaceutical formulation. Care has to be taken while selecting polymers, regarding its toxicity, drug compatibility and degradation pattern. Natural gums are promising biodegradable polymeric materials. The use of natural gums for pharmaceutical applications is attractive because they are economical, readily available, non-toxic, and capable of chemical modifications, potentially biodegradable. However, there is a need to develop other natural sources as well as with modifying existing natural materials for the formulation of novel drug delivery systems, biotechnological applications and other delivery systems. Therefore, natural polymer and their modifications have gained continue interest for the development of better materials for drug delivery system.

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