



A Comprehensive Review on Natural Polymer: Application in Pharmaceutical Formulations

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Abstract: In recent years considerable development in pharmaceutical products for presented and newly discovered drug and core origin products. Natural polymers are broadly used for traditional and novel pharmaceutical dosage forms. Gums are the effective additives used in the number of pharmaceutical formulation. Gums are potential excipients for NDDS. It became useful additives in various pharmaceutical dosage forms. Because they having great availability, biodegradability, non-toxicity and low costing material. Natural gums are largely used in optimization and development in pharmaceuticals as a binder, disintegrant, suspending agents, and gelling agent. The use of gum from core origin as excipients in NDDS is a most interesting and remarkable area in pharmaceutical research. In this review article, we discuss various natural gum used in pharmaceutical formulation and that role in pharmaceuticals.

Keyword - Gums and Mucilages, Classification, Applications, Isolation and Characterization.

I. INTRODUCTION

Polymer is a complex having a long chain of repeating structural units called monomers. These monomers are linked by a covalent chemical bond[1]. Now a day's entire pharmaceutical industries are interested in the use of natural excipients in pharmaceutical formulation. In recent years, polymers obtained from plant origin are evoking great interest due to their different pharmaceutical applications. Such as binder, diluents, disintegrant in tablet, bases in a suppository, gel former in gels, thickening agents in oral liquids, and defensive colloids in suspension. Natural polymers are also used in cosmetics, paints industry, clothing factories, and paper-making. Polymers such as natural gum and mucilage are economically cheap, easily available and biocompatible. Natural gum and mucilage are referred against semi-synthetic and synthetic additives because of their minimum adverse reaction, easily available, soothing action, non-irritant and low cost[2]. The common application of plant origin polymers in the manufacturing of tablets, films, implants, beads, nanoparticles, as well as a viscous liquid formulation[3-5].

Excipients are sometimes used to bulk up formulation include an especially effective active pharmaceutical ingredient for accurate and easy handling dosage form. The use of natural excipients in pharmaceuticals is depending upon the type of medication and route of administration. To maintain the stability of active ingredient in formulation for a long period excipients and additives are added. Unpleasant taste or texture is masked by the addition of specific excipients in the product. The right amount of drug delivered at the right point of the body at the right time is possible due to the addition of excipients[6].

Natural excipients (polymers) and their applications in the development of the drug delivery system are discussed in this review. This review discusses the use of natural polymers as excipients in the formulation of drug delivery systems. The demand for these substances is increasing and new sources are being developed. India, because of its geographical and environmental position, has traditionally been a good source for such products among the Asian countries. Still, large quantities are imported from Europe to meet increasing demand[7].

GUMS AND MUCILAGE'S

Gums are pathological material obtain from the injury to the plant. Releases to unfavorable environment e.g. drought, by a breakdown of cell walls. Gums readily dissolve in water. E.g. Tamarind gum, Guar gum, and Xanthan gum. Mucilages are physiological material formed by intracellular formation without injury to the plant. Mucilage forms slimy masses in water. E.g. in the coating of seeds - linseed, psyllium, in roots- marshmallow, in the epidermal cells of leaves -senna, in the barks- slippery elm and middle lamella- aloe[8].

Similar properties of gum and mucilages:

1. Plant hydrocolloids
2. Semi-transparent
3. Amorphous substances
4. Monosaccharide or complex monosaccharide
 - Linear polysaccharides engage more volume and are more viscous than the highly branched compound of the same molecular weight.
 - Branched compound form gels more easily and is more stable.
5. Most of linked with uronic acids
6. Identical constituents
7. On hydrolysis
 - form a combination of uronic acids and sugars.
8. Include hydrophilic molecules
 - form viscous solutions or gels with water.

Disadvantages of synthetic polymers in pharmaceutical sciences:[8]

- 1) Toxicity
- 2) High price
- 3) Ecological toxic waste during production,
- 4) Non-renewable source,
- 5) Side effects,
- 6) Poor patient compliance
- 7) Skin and eye irritation- methyl methacrylate and poly- (methyl methacrylate)
- 8) Povidone- subcutaneous granulomas
- 9) Acute oral toxicity-carbomer-934P
- 10) Carbomer dust is irritating to mucous membranes, eyes and respiratory tract
- 11) 5% polyvinyl alcohol (aq) inject subcutaneously- anemia
- 12) Poor biocompatibility- poly glycolides, polylactides show satisfactory biocompatibility but show systemic or local reactions due to acidic degradation

Advantages of natural gums and mucilage's in pharmaceutical sciences

- 1) Naturally available and Formed by living organisms
- 2) Easily collected in different seasons and stand for renewable source
- 3) No adverse effect on humans
- 4) No environmental pollution during produced
- 5) Biodegradable and Edible sources
- 6) Biocompatible and non-toxic
- 7) Low cost
- 8) Environmental-friendly processing and simple production processes
- 9) Local availability especially in developing countries
- 10) Better patient tolerance and public acceptance.

Disadvantages of Natural Gums in pharmaceutical science[8]

- 1) Microbial contamination
- 2) Exposed to the external environment- prevented by accurate treatment and the use of preservatives.
- 3) Synthetic production is a restricted procedure with unchanging quantities of ingredients
- 4) Production dependent on ecological and regular factors
- 5) Unrestrained rate of hydration
- 6) The percentage of chemical constituents present depends on the area, species, and environmental conditions.
- 7) Contact with water increase in the viscosity of the formulations

II. CLASSIFICATION OF GUMS [6]

The different available Gums can be classified as follows:

A) ACCORDING TO THE CHARGE

- 1) Anionic Polysaccharides
 - a) Natural:

E.g. Xanthan gum, Arabic Gum, Karaya Gum, Tragacanth Gum, Alginic acid
 - b) Semi-Natural:

E.g. Chitin, Cellulose gum, Carboxymethyl
- 2) Cationic Polysaccharides
 - a) Natural:

E.g. Chitosan
 - b) Semi-Natural:

E.g. Guar gum.
 - c) Cationic-

E.g. Hydroxyethylcellulose
- 3) Nonionic Polysaccharides
 - a) Natural:

e.g. Starch, Dextrin, Guar gum.
 - b) Semi-Natural:

E.g. Cellulose Ethers (e.g. hydroxyethylcellulose, Methylcellulose, Nitrocellulose).
- 4) Amphoteric Polysaccharides

Semi-Natural:

E.g. Carboxymethylchitosan, N-hydroxyl-Dicarboxyethylchitosan, Modified Potato starch.
- 5) Hydrophobic Polysaccharides

Semi-Natural:

E.g. Cetylhydroxyethylcellulose, Polyquaternium.

B) ACCORDING TO THE SOURCE

- 1) Marine origin/algal (seaweed) gums:

E.g. Agar, Carrageenans, Alginic acid, Laminarin.
- 2) Plant origin
 - a) shrubs/tree exudates

E.g. Gum Arabica, Gum Ghatti, Gum Karaya, Gum Tragacanth, Khaya and Albizia gums;
 - b) Seed gums

E.g. Guar Gum, Locust bean Gum, Starch, Amylose, Cellulose
 - c) Extracts –

E.g. Pectin, Larch gum;

d) Tuber and roots

E.g. Potato starch.

3) Animal origin

E.g. Chitin and chitosan, Chondroitin sulfate, Hyaluronic acid.

4) Microbial origin (bacterial and fungal):

E.g. Xanthan, Dextrin, Curdian, Pullulan, Zanflo,

Emulsion, Baker's yeast glycan, schizophyllan, lentinan, krestin, scleroglucan.

5) Prepared gums

– Biosynthetic gums Xanthan, scleroglucan, dextrans.

– Starch and its derivatives, dextrin.

– Cellulose derivatives.

6) Semi-synthetic

– Starch derivatives

E.g. Heat starch, Starch acetate, Search phosphates.

– Cellulose derivatives

E.g. Carboxymethyl cellulose, Hydroxyethylcellulose, Hydroxypropyl methylcellulose, methylcellulose, microcrystalline cellulose.

C) ACCORDING TO SHAPE

1) Linear: E.g. Algins, Amylose, Cellulose, pectins.

2) Branched

-Short branches— E.g. Xanthan, Xylan, Galactomannans;

-Branch-on-branch— E.g. Amylopectin, Gum Arabic, Tragacanth

D) ACCORDING TO MANOMERIC UNITS IN CHEMICAL STRUCTURE

1) Homoglycans

E.g. Amylose, Arabinanas, Cellulose;

2) Diheteroglycans

E.g. Algins, Carrageenans, Galactomannans;

3) Tri-heteroglycans

E.g. Arabinoxylans, Gellan, Xanthan;

4) Tetra-heteroglycans

E.g. Gum Arabic, Psyllium seed gum;

5) Penta-heteroglycans

E.g. Ghatti gum, Tragacanth.

III. PHARMACEUTICAL APPLICATION

In pharmaceutical formulation gum and mucilage's are frequently used excipients, because they give specified adhesive and cohesive property to dosage forms. In sustained and controlled release formulations mucilages are used as release modifiers. Gum and mucilages are functional candidates as a disintegrating agent, binders, suspending agents, emulsifiers, thickening agents, gel former, stabilizer in suspension and release modifying agents in tablets. They used as an adjuvant in several pharmaceutical formulations[6,9].

1. Application in tablets formulation

In the development of tablet formulation gums and mucilage's are largely used excipients as a binder because it has adhesive properties. They convert the powder mass into granules form and give cohesiveness to the material.

They can also be used as disintegrates in tablets. The disintegrating behavior of gums due to soak up water and swell. They can enlarge up to 5 time their initial volume this swelling lead to crack of tablets into a small particle which responsible to improve dissolution rate.

Example

- Buteamonospermalam gum act as a binder in ibuprofen tablets[10].
- *Mangifera indica* gum and *Cassia roxbughii* gum used as the binder in paracetamol tablets[11,12].
- Cashew tree gums as a binder in the metronidazole tablet[13].
- Ziprasidone tablets based on dissolutions and dissolution efficiency value of the performance of gums are as follows gum karaya> acacia>olibanum>tragacanth>guar gum[14].

2. as an emulsifying and suspending agent.

Gums and mucilage act as suspending agent and emulsifier in emulsion; they successfully maintain the stability of an emulsion. In an emulsion, gums impart interfacially. They enhance the stability of o/w emulsion by forming strong multi molecular film round each oil globule thus retards the coalescence by the hydrophilic barrier between the oil and water phase.

Natural gums enhance the hydration of suspended particles through molecular interaction and hydrogen bonding. Because this agent does not decrease the surface and interfacial tension, they work better in the presence of the wetting agent. Both are hydrophilic which produces dispersion in the presence of water and enhance the stickiness of the continuous phase. Since the solid particle suspended in emulsion are sufficient for a long time to measure the uniform dose. e.g. *Cordia gharaf* Gum[15].

3. as sustaining materials in the dosage form.

Gums and mucilages are used as a rate-controlling agent in sustain release formulation. They control the release of drug from the tablet. In case some, drug exits dose dumping; this error is reduced by using natural gum and mucilages as rate controlling polymers. This polymer gets hydrate and form gel; when contact with water. And release the drug from this gel by diffusion mechanism. Hence drug release will be sustained for a long time. e.g., xanthenes gums, karaya gums, and guar gums[16].

4. as a coating agent.

Most of gums and mucilage's act as a coating agent. They can sustain or control the release of drug from the dosage form. Also, keep the drug from degradation in GIT. The number of coating increase the release of drug is reduced from the tablet. E.g. *Grewia* Gum[17].

5. Application in microencapsulation.

The gums have significant coating ability. Because of these properties, they used in microencapsulation of drug particles for sustaining the release of the drug. *Acacia Senegal*, *Acacia nilotica* delile and amizo gum have been considered for their microencapsulating properties using the spray drying technique. Among these three *A. nilotica* is recommended to be a better microencapsulating agent. E.g. Xanthan gum, guar gum, and kondagogu gum[18].

6. as a gelling agent.

Gums produce a gel with or without combination. Gelling is an outcome of many inter and intramolecular unions to make a 3D network. In this reaction, a water molecule is entrapped with the proportion of gum by a change in pH, temperature, the addition of a chemical reagent. The mechanism of gelatin in acidic polysaccharides such as pectin is different. In this case, the macromolecular chain is commonly hydrogen-bonded and as a result junction zone are formed between hydrogen-bonded segments of chain. In the case of Alginic acid, gel formation occurs as product interaction with calcium ions. Galactomannan interacts synergistically with xanthan gums and carrageenan to form an elastic gel e.g. locust bean gum.

IV. APPLICATION OF GUMS IN NOVEL DRUG DELIVERY SYSTEM[6]

Application of gums in NDDS is described in Table No 1

Common name	Novel drug delivery system	Drug
Acacia	Osmotic drug delivery.	Water-insoluble naproxen.
Bhara gum	Microencapsulation	Famotidine.
Cordia gum	Novel oral SR matrix-forming agent in tablets. Suspension.	Diclofenac sodium. Paracetamol.
Guar gum	Colon targeted drug delivery, Cross-linked microspheres.	Albendazole Metronidazole methotrexate
Gellan gums	Ophthalmic drug delivery, Beads, Floating in-situ gelling.	Timolol propranolol Amoxicillin
Karaya gums	Mucoadhesive and mucoadhesive.	Nicotine
Locust bean gum	Controlled release agent.	Nimodipine, Glipizide,
Sodium alginate	Bioadhesive microspheres,	Gatifloxacin. MetforminHCL
Tamarind gum	Mucoadhesive drug delivery. SR	Diclofenac. Verapamil.HCL
Xanthan gum	Pellets. Controlled drug delivery system.	Diclofenac sodium. theophylline

Table No.1 Application of gums in NDDS

V. EXTRACTION:

The completely dried part of the plant is extracted with hot distilled water. Proportions of dried powder of specific part of plant- 1:10. Extraction is proceeding for 24 hr with continuous stirring. The thick extract obtain is clean throughout muslin, while the remaining matter is the return to the container for double extractions. Remaining extracts are then filtered through a bed of glass wool and muslin to separate unidentified particle and the filtrate poured into alcohol, which precipitates a fibrous gelatinous product. Filtration, re-resolution, and reprecipitation of the mucilage are carried out many times, the product then being precipitated in successive increasing concentrations of alcohol. The precipitated mucilage is dried at 45-50°C and stored in desiccators[19].

VI. CHARACTERIZATION AND STANDARDIZATION OF GUMS AND MUCILAGE'S[7]

A suitable approach is necessary to save money and time. For excipients analysis; analytical techniques can be classified according to the type of information generated.

a) Structural

Gums and mucilages both are polysaccharides and it consists of sugars.

- Identification of the sugars- chromatography
- Structure arrangement- NMR and mass spectroscopy.

b) Purity

The purity of gum and mucilage's is determined by following tests,

- Tests for alkaloids and glycosides
- Tests for carbohydrates
- Tests for flavonoids, steroids
- Tests for amino acids
- Tests for terpenes
- Tests for saponins
- Tests for oils and fats
- Tests for tannins and phenols

c) Impurity profile

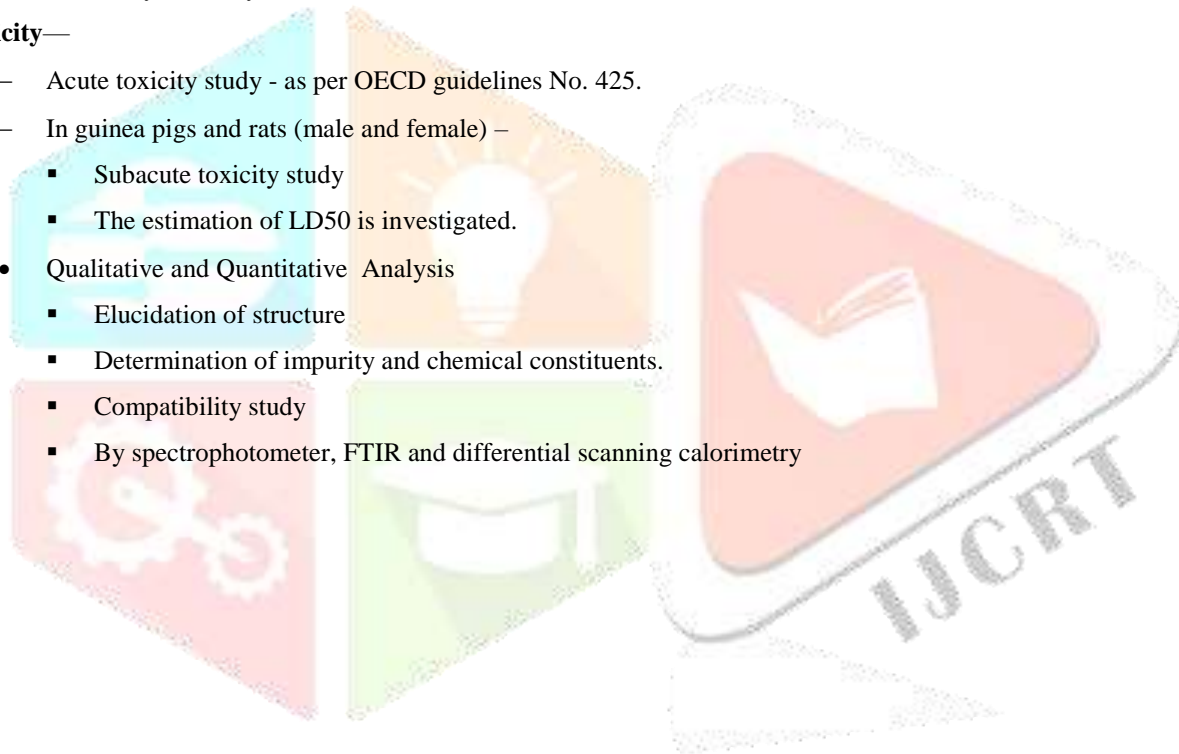
The determination of impurities is processed using appropriate analytical methods.

d) Physical-chemical properties

- Color, shape, odor
- Taste, touch, texture,
- Solubility and pH
- Swelling index and loss on drying
- Hygroscopic nature
- The angle of repose and flow properties
- Bulk and true densities
- Porosity
- Surface tension and rheological properties
- Estimation of ash value
- Determinations of the presence of microbial load and pathogen
- *In vitro* cytotoxicity.

e) Toxicity—

- Acute toxicity study - as per OECD guidelines No. 425.
- In guinea pigs and rats (male and female) –
 - Subacute toxicity study
 - The estimation of LD50 is investigated.
- Qualitative and Quantitative Analysis
 - Elucidation of structure
 - Determination of impurity and chemical constituents.
 - Compatibility study
 - By spectrophotometer, FTIR and differential scanning calorimetry



VII. SOME REPORTED NATURAL GUMS AND THEIR USES[20]

1. Pharmaceutical uses

No.	Gum	Botanical Name	Family	Uses
1	Almond gum	<i>Prunus amygdalus</i>	Rosaceae	hair and skin
2	Agar gum	<i>Gelidium mansion</i>	Gelidaceae	preparation of jellies, confectionery
3	Abelmoschus	<i>Abelmoschus esculentus</i>	Malvaceae	polymer for the gastric floating dosage form
4	Cashew gum	<i>Anacardium occidentale</i>	Anacardiaceae	jelling agent in canned food
5	Guar gum	<i>Cyamopsis tetraganolobus</i>	Leguminosae	appetite suppressant & Medicine for constipation.
6	Ghatti gum	<i>Anogeissus latifolia</i>	Combretaceae	non-petroleum waxes
7	Guggal gum	<i>Commiphora weightii</i>	Burseraceae	anti-inflammatory, essence sticks
8	Honey locust gum	<i>Gleditsia tricanthus</i>	Leguminosae	Used as insecticides
9	Katira gum	<i>C. religiosa</i>	Bixaceae	gelling agent
10	Lemon-scented gum	<i>Eucalyptus citriodora</i>	Myrtaceae	treat bladder inflammation
11	Mango gum	<i>Mangifera indica</i>	Anacardiaceae	treat laxative and antioxidant
12	Odina gum	<i>Odina wodier</i>	Anacardiaceae	Anti-inflammatory, respiratory irritation.
13	Red gum (eucalyptus Kino)	<i>Eucalyptus rostrata</i>	Myrtaceae	Astringent
14	Tragacanth gum	<i>A. gummifer labill</i>	Leguminosae	Confectionery
15	Xantham gum	<i>Xanthomonas lepestris</i>	-	food industry
16	Tamarind gum	<i>Tamarindus indica</i>	Fabaceae	textile, paper, pet food, mining industry

Table no 2: some reported natural gums and their pharmaceutical uses

2. Medicinal uses

No.	Gum	Botanical Name	Family	Uses
1	Asafoetida	<i>Ferula foetida Regel</i>	Umbelliferae	powerful nervine stimulant
2	Aegle gum	<i>Aegle marmelos</i>	Rutaceae	printing and used Medicinally
3	Bhara gum	<i>Terminalia Billerica</i>	Combretaceae	medicinal purpose
4	Bengal Kino (butea gum)	<i>Butea monosperma</i>	Leguminosae	diarrhea and dysentery
5	Baheda gum	Bibhitaki (<i>Terminalia Billerica</i>)	Combretaceae	herb of Triphala
6	Cordio gum	<i>Cordio oblique</i>	Boraginaceae	anti-fungal
7	Copal gum	<i>Bursera bipinnata</i>	Burseraceae	printing ink, paints, and films
8	Combi gum	<i>Gardenia gummier</i>	Rubiaceae	Insecticide
9	Ferula gum	<i>Ferula gummosa</i>	Apiaceae (or) Umbelliferae	the treatment of chronic bronchitis asthma
10	Guggal gum	<i>Commiphora weightii</i>	Burseraceae	anti-inflammatory, essence sticks
11	Gamboge	<i>Garcinia henburii</i>	Guttiferae	hydragogue cathartic
12	Kino gum	<i>Pterocarpus marsupium</i>	Fabaceae	treat boils and other skin diseases
13	Leucaena seed gum	<i>Leucaena leucocephata</i>	Leucocephata	control stomach ache and contraception
14	Mastic gum	<i>Pistacia lentiscus</i>	Anacardiaceae	intestinal ulcers and muscle aches
15	Myrrh gum	<i>Commiphora mol mol</i>	Burseraceae	Uterine stimulant.

Table no 3: some reported natural gums and their medicinal uses

3. Industrial uses

No.	Gum	Botanical Name	Family	Uses
1	Albizia odoratissima	<i>Mimosa odoratissima</i>	Leguminosae	indoor construction
2	Acacia gum	<i>Acacia Senegal</i>	Leguminosae	pigment binder and adhesive in painting
3	Chicle gum	<i>Manilkara Zapata</i>	Apocynaceae	chewing gum
4	Carob gum	<i>Ceratonia siliqua</i> Linn.	Leguminosae	food industry for calico printing
5	Carrageenan	<i>Chondrus Crispus</i>	Gigarginaceae	The food industry, medicinal and industrial
6	Dammar gum	<i>Shorea wiener</i>	Dipterocarpaceae	foods and glazy agent
7	Honey locust gum	<i>Gleditsia tricanthus</i>	Leguminosae	Used as insecticides
8	Kondagogu gum	<i>Cochlospermum religiosum</i>	Bixaceae	the paper, textile, paint and ink products
9	Locust bean gum	<i>Ceratonia siliqua</i> Linn.	Leguminosae	food industry
10	Mimosa scabrella gum	<i>mimosa scabrella</i>	Mimosaceae	paper industry
11	Moringa oleifera gum	<i>Moringa oleifera</i>	Moringaceae	herbal medicine
12	Mucuna gum	<i>Mucuna flagellates</i>	Papillionaceae	herbalism and food crop
13	Malva nut gum	<i>Scaphium scaphigerum</i>	Sterculiaceae	Chinese medicine as a coolant
14	Neem gum	<i>Azadirachta indica</i>	Anacardiaceae	Insects repellent,
15	Olibanum gum	<i>Boswellia serrate</i>	Burseraceae	plasters and fumigating pastilles
16	Rosin gum	<i>Pine pix styvestris</i>	-	photocopying and laser printing paper
18	Tara gum	<i>Caesalpinia spinosa</i>	Leguminosae (or) Fabaceae	food industry

Table no 5: some reported natural gums and their industrial uses

VIII. CONCLUSION

Polymers play a vital role in the drug delivery. So, the selection of polymer plays an important role in drug manufacturing. But, while selecting polymers care has to be taken regarding its toxicity, drug compatibility and degradation pattern. By this review, we can say that natural polymers can be good substitute for the synthetic polymers and many of the side effects of the synthetic polymers can be overcome by using natural polymers.

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