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NATURAL GUM AND MUCILAGE FOR BIOPHARMACEUTICAL APPLICATIONS

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***Abstract*:**
Recent trend towards the use of plant based and natural products demands the replacement of synthetic additives with natural ones. All pharmaceutical dosage forms contain many additives in addition to the active ingredient to assist manufacturing and to obtain the desired therapeutic efficacy of the pharmaceutical active ingredients. There are number of synthetic polymers are available in market for pharmaceutical formulation, but these synthetic polymers have certain disadvantages such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, and poor patient compliance. Because of these disadvantages natural polymers such as natural gums and mucilage are preferred to semi synthetic and synthetic excipients because of the following advantages such as: low cost and natural origin, free from side effects, biocompatible and bio-acceptable, renewable source, environmental friendly processing, local availability etc. Natural gums and mucilages are available in nature freely. These natural gums and mucilages were successfully used in various dosage forms. The gums and mucilages obtained from natural sources are the complex polysaccharide which has many applications in the pharmaceutical industry and they also influence the rate and extent of drug release. This review discusses about the various natural sources of gums and mucilages, their advantages over synthetic polymers, applications in pharmaceutical industries.

***Keywords*:** Gums, Mucilage, Biocompatible, Biodegradable.

I. Introduction

In recent years, plant derived polymers have tremendous interest due to their diverse pharmaceutical applications such as diluent, binder, disintegrant in tablets, thickeners in oral liquids, protective colloids in suspensions, gelling agents in gels and bases in suppository. They are also used in cosmetics, textiles, paints and paper-making. Gums are abnormal products, resulting from pathological conditions brought about either by injury or by adverse conditions of growth and usually formed by changes in existing cell wall while, mucilage are generally normal product of metabolism, formed within the cell and are produced without injury to the plant. Natural gums can also be modified to meet the requirements of drug delivery systems and thus can compete with the synthetic excipients available in the market.

Polymers are used as excipients for the progress of polymer-based drug delivery systems with the purpose of targeted drug delivery. Synthetic polymers have high physical, chemical, and mechanical stability but can cause cytotoxicity and are bio-incompatible. Synthetic polymers have disadvantages, such as: poor adaptation to the patient's body, high cost, and can also cause acute and chronic side effects. The use of natural plant-derived polysaccharides as excipients has increased in the pharmaceutical industry and can solve formulation problems and reduce the side effects of synthetic polymers. Natural polysaccharides are formed by their O-glycosidic linkages by binding monosaccharide residues together and are known as biopolymers.

A. Gum and mucilage

Gums readily dissolve in water, whereas, mucilage form slimy masses. Gums are pathological products, whereas mucilages are physiological products. Acacia, tragacanth, and guar gum are examples of gums while mucilages are often found indifferent parts of plants. The plant based polymers have been studied for their application in different pharmaceutical dosage forms like matrix controlled system, film coating agents, buccal films, microspheres, nanoparticles, viscous liquid formulations like ophthalmic solutions, suspensions, implants and their applicability and efficacy has been proven. These have also been utilized as viscosity enhancers, stabilisers, disintegrants, solubilisers, emulsifiers, suspending agents, gelling agents, bioadhesives and binders.

Gums and mucilages are interesting polymer for the preparation of pharmaceutical formulations, because of their high water-swellability, non-toxicity, low cost and free availability. Gums and mucilages are polysaccharides or complex carbohydrate containing one or more monosaccharides or their derivatives linked in bewildering variety of linkages and structures. They are condensation polymers. The term gum refers to polysaccharide hydrocolloids, which do not form a part of cell wall, but are exudates or slims and are pathological products. Mucilages are part of cell and physiological products.

Properties of gum and mucilages

Gums and mucilages have certain similarities; both are plant hydrocolloids. They are also a mixture of clear amorphous polymers and monosaccharide polymers and are combined with uronic acid. Gums and mucilages contain hydrophilic molecules that can combine with water to form viscous or gel-like solutions.

a) Opportunities of natural gums and mucilage's in pharmaceutical sciences

1) Local availability: In developing countries, governments promote the production of plant like guar gum and tragacanth because of the wide applications in a variety of industries.
2) Biocompatible and non-toxic: Chemically, nearly all of these plant materials are carbohydrates composed of repeating sugar (mono saccharides) units. Hence, they are non- toxic.
3) Low cost: It is always cheaper to use natural sources. The production cost is also much lower compared with that for synthetic material. India and many developing countries are dependent on agriculture.
4) 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 (e.g.,skin and eye irritation).
5) Environmental friendly processing: Gums and mucilages from different sources are easily collected indifferent seasons in large quantities due to the simple production processes involved.
6) Economic: They are cheaper and their production cost is less than synthetic material.
7) Safe and devoid of side effects: They are from a natural source and hence, safe and without side effects.
8) Better patient tolerance as well as public acceptance: There is less chance of side and adverse effects with natural materials compared with synthetic one. For example PMMA, povidone.
9) Edible sources: Most gums and mucilages are obtained from edible sources

b) Obstacles of natural gums and mucilage's in pharmaceutical sciences

1) Microbial contamination:
   Ten percent or more equilibrium moisture content is present in the gums and mucilages and chemically gums are carbohydrates and, during production, they are exposed to the external environment and, so there is a chance of microbial contamination. However, this contamination can be prevented by proper handling and the use of preservatives.
2) Batch to batch variation:
   Synthetic manufacturing is controlled procedure with fixed quantities of ingredients while production of natural polymers is dependent on environment and various physical factors.
3) 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.
4) Slow Process:
   The production rate mainly depends upon the environment and many other factors, it can't be changed. So natural polymers have a slow rate of production.
5) Reduced viscosity on storage:
   The gums and mucilages when come in contact with water there is an increase in the viscosity of the formulations.Due to the complex nature of gums and mucilages [mono saccharides to poly saccharides and their derivatives], it has been found that the viscosity is reduced on storage.
6) Heavy metal contamination:
   There are chances of Heavy metal contamination often associated with herbal excipients.

c) Chemical nature of gums

Gums are polysaccharides in nature and they are also the translucent amorphous substances. Upon hydrolysis, gums produce an indefinite number of mono saccharides. They can be further classified into pentosans [e.g., xylan] and hexosans [e.g., starch and cellulose] depending on the type of hydrolysis products obtained. Gums contain 'polyuronides'. Polyuronides are the products that consist of complex substances of calcium, potassium and magnesium salts. Hemicelluloses produced by gums are galactose and arabinose. Gums are biodegradable and with few exceptions they are also biocompatible. There is possibility of chemical modifications. Natural gums are safe for oral consumption, hence can be used in the form of food additives or drug carriers. Gums are metabolised by the intestinal flora and are ultimately degraded into their individual component sugars. By the process of hydrolysis using dilute mineral acids, followed by the use of different chromatographic techniques for separation of liberated mono saccharides, constituent sugar units in a polysaccharide can be easily identified. By phenol-sulfuric acid method the total carbohydrate content of the polysaccharides and also the content of monosaccharide can be estimated. Methylation, periodate and lead tetra-acetate oxidation methods are used to determine the mode of linkage between the mono saccharides. For structural elucidation of gums is carried out using NMR and mass spectroscopy techniques.

d) Characterization of gums and mucilages:

The extraction and characterization of polysaccharide gums is an essential step in establishing their suitability as pharmaceutical excipients. The prospects of natural polymers are brighter but even here extensive testing will be required. A suitable strategy is required to save money and time. Over characterization is not desirable, because excessive use of time and resources could actually delay the launch of innovative excipients. The characterization of gums and mucilages is initially achieved by only a multiple-technique approach.

II. Classification of natural gums :

The natural gums are classified based on their chemical structure, shape, charge, gelation behaviour and origin.

a. Based on chemical structure:

Chemical Structure	Examples
Galactomannans	Fenugreek gum, guar gum, cassia gum, tara gum.
Glucomannans	Konjac glucomannan
Uronic acid conjugating systems	Xanthum gum
Tri-heteroglycans	Gellan gum, Arabino xylans
Tetra heteroglycans	Gum Arabic, Psyllium seed Gum
Penta-heteroglycans	Gum ghatti, tragacanth

b. Based on shape:

Shape	Examples
Linear	Algins, amylase, cellulose, pectins.
Branched a) Short branches b) Branch on branch	 Xanthan, Xylan Amylo pectin, gum arabic, tragacanth

c. Based on charge:

Category	Examples
Non-ionic seed gums	Guar gum, locust bean gum, tamarind seed gum, Xanthan gum, amylase, arabinans, cellulose, Galactomannans
Anionic gums	Arabic gum, karaya gum, tragacanth, gellan gum, agar, algin, Carrageenans
Cationic gums	Chitosan

d. Based on gelation behaviour:

Gels	Examples
Cold set gels [form gels on cooling the solution]	Gellan gun, flaxed gum, Gelatin
Heat set gels [forms gels on heating the solution]	Konjac glucomannan
Re-entrant gels [from which galactose residues are removed]	Xyloglucan

e. Based on origin:

Origin	Examples
Seed gums	Guar gum, tamarind gum, ipomea, locust bean gum, karaya gum
Plant exudates	Arabic gum, acacia gum, tragacanth, gum gatthi, chicle gum, Konjac glucomannan, karaya gum, locust bean gum.
Plant extracts	Pectin, larch gum.
Plant tuber and roots	Potato starch.
Microbial exudates	Gellan gum, tara gum, xanthan gum, dextran, spruce gum.
Sea weeds	Alginic acid, sodium alginate, agar-agar, carrageenans
Animal origin	Chitin, chitosan, chondroitin sulphate, hyaluronic acid

III. Characterization of gums and mucilage's

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.

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

2. Purity The purity of gum and mucilage's
- 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

i. 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.

ii. 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.

iii. Qualitative and Quantitative Analysis

- Elucidation of structure
- Determination of impurity and chemical constituents.
- Compatibility study
- By spectrophotometer, FTIR and differential scanning calorimetry

IV. Natural gums and their pharmaceutical applications

Guar gum	Sustained release Controlled drug delivery Suspending agent
Almond Gum	Emulsifying Thickening Suspending Adhesive Stabilizing ↑Drug release Uncoated tablet dosage form
Karaya gum	In vivo → gastric retentive dosage forms ↑Dissolution rate of drug solid dispersions Suspending agent Emulsifying agent Dental adhesive Sustaining agent Mucoadhesive Buccoadhesive
Tragacanth gum	Sustain release Suspending agent Emulsifying agent
Tamarind gum	Matrix tablets ↓Drug release Biodegradable carrier for colon specific release
Grewia gum	Controlled release dosage forms Suspending agent Binding property ↑Degree of packing ↑Fluidity granules In vitro drug release → control the release of cimetidine from tablets delaying the release of cimetidine from tablets Film forming property
Gum acacia	Binder Suspending agent Emulsifying agent Demulcent Emollient
Khaya gum	Binding agent Drug targeting Controlled release
Locust bean gum (carob gum)	Super disintegrant Controlled drug delivery Drug targeting to the colon Super disintegrants Mucoadhesive
Terminalia catappa gum	Oral sustained release tablets
Okra gum	Controlled release tablet Sustained-release tablets Suspending agent
Gum ghatti	Binder Emulsifier Suspending agent
Albizia gum	Tablet binder Emulsifier Coating materials in compression-coated tablets
Cashew gum	Suspending agent ↑Disintegration time ↑Polymer ratio → ↓drug release to a greater extent
Bhara gum	Sustained release Microcapsules employing bhara gum → ↓release of famotidine
Cordia gum	Oral sustained release matrix tablets
Honey Locust Gum	Matrix tablets at different concentrations (5% and 10%)
Tara Gum	Controlled release carrier
Neem Gum	Binding property Sustained release ↑Matrix tablet
Moringa oleifera Gum	Gelling property Binding property Release retardant property Disintegrating property Emulsifying property
Gum Damar	Sustained release
Hakea Gum	Sustained release Binding agent
Abelmoschus esculentus	Tablet binder
Acacia arabica	Suspending and emulsifying compound, tablets binder, demulcent and emollient in cosmetic, confectionary, beverages and baked products, sauces

Albizia zygia	Tablet binder
Aloe species	Gelling compound
Anacardium occidentale	Suspending compound
Anogeissus latifolia	Binder, emulsifier, and suspending compound
Asparagus racemosus	Binding and sustaining compound in tablets
Orange peel pectin	Binding, suspending and sustained release dosage form
Astragalus gummifer	Emulsifying and suspending compound, demulcent, emollient in cosmetic, confectionary, beverages and baked products, sauces
Cassia tora	Binding agent
Chondrus cryspus	Gelling compound, stabilizer in emulsions and suspensions, in toothpaste, demulcent and laxative, stabilizers for ice-cream, meat products and instant pudding
Citrus aurantium	Thickening, suspending and protective compound, confectionary, beverages and baked products, sauces
Banana peel mucilage	Binding and suspending agent
Hibiscus mucilage	Emulsifying agent, sustained release agent and suspending agent.
Cyamompsis tetraganolobus	Binder, disintegrant, thickening agent, emulsifier, laxative, water retention and stabilization agents in food industry
Gelidium amansii	Emulsifying and suspending compound, gelling agents in suppositories, surgical lubricants, laxative, tablet disintegrant, medium for bacterial cultures, dairy, meat, and confectionary products
Hibiscus esculentus	Emulsifier and suspending compound
Hibiscus rosasinensis	Suspending compound
Ispagol mucilage	Cathartic, lubricant, demulcent, laxative, sustaining agent, binder, emulsifying and suspending agent
Satavari mucilage	Binding agent and sustaining agent in tablets
Ocimum seed mucilage	Suspending agent and binding agent.
Leucaena seed gum	Emulsifying agent, suspending agent, binder in tablets and disintegrating agent in tablets
Khaya gum	Binding agent
Karaya gum	Suspending agent. Emulsifying agent, sustaining agent in tablets and bulk laxative
Fenugreek mucilage	Gelling agent
Cassia tora	Binding agent
Cashew gum	Suspending agent, jelling agent in canned food
Abelmoschus mucilage	Binder in tablets and sustained release
Lepidum sativum	Suspending and emulsifying compound
Leucaena sps.	Emulsifier, suspending compound, tablets binder, disintegrating agent in tablets
Macrocytis pyrifera	Suspending compound, gelation for dental films, stabilizer, sustained-release compound, tablet coating
Plantago psyllium	Cathartic, lubricant, demulcent, laxative, sustaining compound, binder, emulsifying and suspending compound
Ocimum canum	Suspending and emulsifying compound
Albizia gum	Tablet binder

Tamarind seed polysaccharide	Binding agent, emulsifier, suspending agent and sustaining agent
Bhara gum	Microencapsulation
Cordia gum	Novel oral sustained release matrix forming agent in tablets
Hakea	Sustained release and peptide mucoadhesive for buccal delivery
Mucuna gum	Microspheres.
Gellan gum	Ophthalmic drug delivery, sustaining agent, beads, hydrogels, floating in-situ gelling and controlled release
Leucaena seed gum	Emulsifying agent, suspending agent, binder in tablets and disintegrating agent in tablets
Badam gum	Binding, sustaining and transdermal film forming agent
Grewia gum	Suspending agent and binder
Sesbania gum	Gelling agent
Hupu gum (gum kondagogu)	Gastric floating drug delivery
Katira gum	Colon drug delivery.
Malva nut gum	Stabilizer and thickening agent
Welan gum	Thickening agent
Almond gum	hair and skin
Agar gum	preparation of jellies, confectionery
Katira gum	gelling agent
Lemon-scented gum	treat bladder inflammation
Odina gum	Anti-inflammatory, respiratory irritation
Red gum (eucalyptus Kino)	Astringent

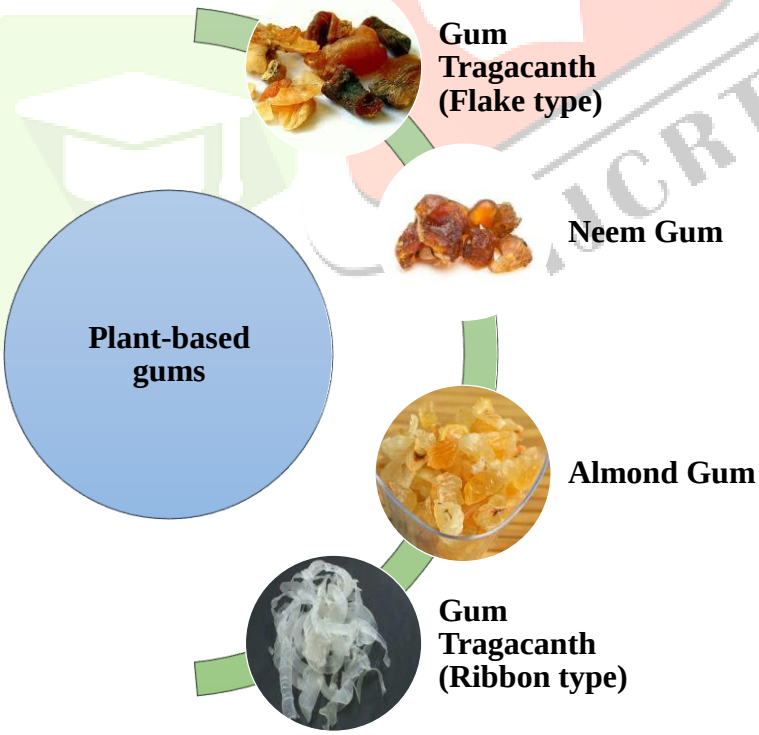

Figure 1. Some of the most important gums used in the world

V. Application of gums in novel drug delivery system

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

VI. Applications of gums:

Gums of different sources and their derivatives represent a group of polymers widely used in pharmaceutical dosage forms. Various kinds of Gums are used in the food industry and are regarded as safe for human consumption. However, there is growing concern about the safety index of pharmaceutical excipients derived from natural sources. Plant gums and exudates are now screened for their use as pharmaceutical excipients. Newer uses of different gums in cosmetics and textiles have increased the demand and screening of gums has become an important pharmaceutical area. However, different gums and mucilages used as pharmaceutical adjuvants have stringent specifications, which few natural agents can fulfil.

Gums are the complex, branched polymeric structures because of which they exhibit high cohesive and adhesive properties. These properties are highly useful in pharmaceutical preparations.Hence, gums find diverse applications in pharmacy. They are used in medicine for their demulcent properties for cough suppression. They are ingredients of dental and other adhesives and can be used as bulk laxatives.These hydrophilic polymers are useful as tablet binders, disintegrants, emulsifiers, suspending agents, gelling agents, stabilizing agents, thickening agents, protective colloids in suspensions and sustaining agents in tablets and coating agents in microcapsules including those used for protein delivery.

Pharmaceutical applications of Gums and Mucilages

Gums and mucilages possess a complex, branched polymeric structure because of which they exhibit high cohesive and adhesive properties. Such properties are highly useful in pharmaceutical preparations. Hence, gums and mucilages find diverse applications in pharmacy. They are ingredients in dental and other adhesives and as bulk laxatives. These hydrophilic polymers are useful as tablet binders, disintegrants, emulsifiers, suspending agents, gelling agents, stabilizing agents, thickening agents, protective colloids in suspension and sustaining agents in tablets.

VII. Applications in the food industry

Gums have a variety of applications in the food industry. Different gums have different uses like water retention and stabilization [guar and locust bean gum], stabilizers for ice-cream, meat products and instant pudding [carrageenanas], dairy, confectionary and meat products [agar], confectionary, beverages, backed product, and sauces [gum arabic, tragacanth, pectins, alginates and xanthan gum]. Industrial uses Gums used in cosmetics [acacia, tragacanth and karaya gum], textiles [starch, dextrin, cellulose, pectins,

and tamarind gum], adhesives [acacia gum, and tragacanth], lithography [gum arabic, tragacanth, and locust bean gum], paints [pectins, hemicellulose, and resins] and paper manufacturer [tamarind, and cellulose].

VIII. Pharmaceutical Formulations based on grafted gum

Gum	Grafting Component	Drug	Formulation
Xanthan gum	Amylose	-	Hydrogels
Xanthan gum	Acrylamide	Carvedilol	Tablets
Okra gum			
Kondagogu gum	Poly(acrylamide)	Diclofenac Sodium	Tablets
Kondagogu gum	Poly(acrylamide)	Diclofenac sodium	Tablets
Kondagogu gum	Chitosan	Ofloxacin	Nanoparticles
Kondagogu gum	Poly (*N*-vinyl-2-pyrrolidone	Metronidazole	Buccal discs
Ghatti gum	Acrylic acid	-	Hydrogel
Ghatti gum	Polymethacrylic acid-polyanilline	-	Hydrogel
Ghatti gum	Poly (acrylamide-*co*-methacrylic acid)	-	Hydrogel
Ghatti gum	Polyacrylamide	-	Flocculant powder
Karaya gum	2-hydroxy methyl methacrylate	Ornidazole	Hydrogels
Karaya gum	Polyacrylamide	Ranitidine HCl	Hydrogels
Locust bean gum	Poly (vinyl alcohol)	Buflomedil HCl	Microspheres
Locust bean gum	Acrylamide	Buflomedil HCl	Tablets
Guar gum	Polyacrylamide	Triamcinolone	Tablets
Guar gum	Polyacrylamide	5-amino salicylic acid	Tablets
Guar gum	Sodium acrylate	Cloisite	Superabsorbent nanocomposites
Guar gum	Multiwall carbon nanotube	Iron oxide	Nanoparticles
Cashew gum	Acrylic acid	-	Nanoparticles
Cashew gum	Chitosan	*Lippia sidoides* oil	Nanogel
Tara gum	Acrylamide	-	Hydrogels
Gellan gum	Pectin	Ketoprofen	Beads
Gellan gum	Polymethacrylamide	Diclofenac Sodium	Tablets
Tamarind seed gum	Glutaraldehyde cross-linked chitosan	Aceclofenac	Microparticles
Tamarind seed gum	Methyl methacrylate	Metoprolol succinate	Buccal patches

IX. Natural gums used for polymer grafting

Natural Gum	Biological Name	Family	Use
Albizia Gum	Albizia Zygia	*Leguminosae*	Emulsifier, Coating materials
Cashew Gum	Anacardium Accidentale	*Anacardiaceae*	Gelling gent, binding agent
Neem gum	Azadirachta indica	*meliaceae*	Binding agent, sustained release property
Gum Gopal	Bursera bipinnata	*burseraceae*	Film forming agent, coating material
Mango gum	Mangifera indica	*anacardiaceae*	Binding, disintegrating agent, sustained release agent
Locust bean gum	Ceratania siliqua	*legumimosae*	Carrier for colonic drug delivery, controlled drug delivery system
Tara gum	Caesalphinia spinosa	*leguminosae*	Controlled release carrier
Honey locust gum	Gleditsia triacanthos	*leguminosae*	For matrix tablet
Almond gum	Prunus amygdalus	*rosaceae*	Thickening, emulsifying, suspending, stabilizing as well as adhesive agent
Moringa gum	Moringa oleifera	*moringaceae*	Binding, releasee retardant and disintegrant property
Gum damar	Shorea wiesneri	*Dipterocarpaceae*	Water resistance coating agent, sustained release property, microencapsulating agent
Moi gum	Lannea coromandelica	*anacardiaceae*	Microencapsulating agent
Kandagogu gum	Cochlospermum religiosum	*bixaceae*	Microadhesive property

X. Conclusion

The natural gums are more economical, abundantly available, biodegradable, biocompatible and non toxic. There is also possibility of modification of gums. These all reasons made the natural gums more superior over the synthetic ones. As the natural gums have wide spread applications in pharmaceutical industries the researchers are attracted towards the role of natural polymers in the development of novel drug delivery systems. They have a major role to play in pharmaceutical industry. Therefore, in the years to come, there is going to be continued interest in the natural excipients to have better materials for drug delivery systems.

Conventional pharmaceutical excipients as bulking agents, substance used for masking taste/texture or as a substance use to aid during manufacturing process, Novel excipients offer broad range of additional properties suitable to preserve the integrity of active constituents of the formulation and enhances it's self life. The synthetic polymers can be designed or modified as per requirement of the formulation; by altering polymer characteristics and on the other hand herbal pharmaceutical excipients are biocompatible, non toxic, environment friendly and economical.

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