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Natural gums and its pharmaceutical application

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Abstract

Gums are widely used natural excipients for conventional and novel dosage forms. With the increasing interest in polymers of natural origin, the pharmaceutical world has compliance to use most of them in the formulations. In recent years, there has been a tremendous development in natural products, which are needed to be used for a variety of purposes. Nature has provided us a wide variety of materials to help improves and sustains the health of all living things either directly or indirectly. These natural materials have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, biodegradable and widely available. They can also be modified in different ways to obtain tailor made materials for drug-delivery systems and thus can compete with the available synthetic excipients. Moreover, the tremendous orientation of Pharma world towards these naturally derived polymers has become a subject of increasing interest to discover, extract and purify such compounds from the natural origin. Gums are the potent candidates to be used in various pharmaceutical formulations as a potential candidate for novel drug delivery system (NDDS). In this review, we describe the developments in natural gums for use in the pharmaceutical sciences.

Keywords: Natural gum, Natural polymer, Pharmaceutical excipients, Natural polysaccharide, NDDS.

Introduction

Excipients are additives used to convert the active pharmaceutical ingredients into dosage forms suitable for administration to patients.1 Synthetic polymers offer a broad range of properties that can be reasonably well "built- in" by design and modified by altering polymer characteristics. Plant products are therefore, attractive alternatives to synthetic products because of biocompatibility, low toxicity, environmental "friendliness" and low price compared to synthetic products. Natural gums obtained from plants have diverse applications in drug delivery as a disintegrant, emulsifying agent, suspending agents and as binders. They have also been found useful in formulating immediate and sustained-release preparation.[1, 2]

Definition of Gums

The most common theories says that gums are formed as a natural phenomenon of the plant in which internal plant tissues disintegrate through a process called gummosis. This in turn form cavities, which exudes transformed carbohydrates called gums. Secondly it is caused as a result of injury to the bark or stem. Thirdly, some others attribute to fungi and bacteria attack to the plant. Majority of the gums are exuded from the stem. Only a few gums are obtained from roots, leaves and other parts of the plant. These gums on heating decompose completely without melting. Gums are found in large number of families. Notable among them are Leguminosae and Sterculiaceae. Other important gum yielding families are Anacardiaceae, Combretaceae, Meliaceae, Rosaceae and Rutaceae.[3]

Classification of Gums

Gums are present in high quantities in a varieties of plants, animals, seaweeds, fungi and other microbial sources, where they perform a number of structural and metabolic functions; plant sources provide the largest amounts. The different available Gums can be classified as follows.[4]

- ***According to the charge***
  - **Anionic Polysaccharides**
    - **Natural**: Alginic acid, pectin, Xanthan gum, Hyaluronic acid, Chondroitin sulfate, Gum Arabic, Gum Karaya, Gum Tragacanth
    - **Semi-Natural**: Carboxymethyl, Chitin, Cellulose gum
  - **Cationic Polysaccharides**
    - **Natural**: Chitosan
    - **Semi-Natural**: Cationic Guar gum.
    - **Cationic**- Hydroxyethylcellulose (HEC).
  - **Nonionic Polysaccharides**
    - **Natura**l: Starch, Dextrins, Guar gum.
    - **Semi-Natural**: Cellulose Ethers (e.g. hydroxyethyl cellulose, Methylcellulose, Nitrocellulose).
  - **Amphoteric Polysaccharides**
    - **Semi-Natural**: Carboxymethylchitosan, N-hydroxyl-Dicarboxyethylchitosan, Modified Potato starch.
  - **Hydrophobic Polysaccharides**
    - **Semi-Natural**: Cetylhydroxyethylcellulose, Polyquaternium.
- ***According to the source***
  - **Marine origin/algal (seaweed) gums:** Agar, Carrageenans, Alginic acid, Laminarin.
  - **Plant origin**
    - **shrubs/tree exudates**—Gum Arabica, Ggum Ghatti, Gum Karaya, Gum Tragacanth, Khaya and Albizia gums;
    - **Seed gums**—Guar Gum, Locust bean Gum, Starch, Amylose, Cellulose
    - **Extracts -**Pectin, Larch gum;
    - **Tuber and roots**—Potato starch.
  - **Animal origin:** Chitin and chitosan, Chondroitin sulfate, Hyaluronic acid.
  - **Microbial origin (bacterial and fungal):** Xanthan, Dextrin, Curdian, Pullulan, Zanflo, emulsan, Baker's yeast glycan, schizophyllan, lentinan, krestin, scleroglucan.
  - **Prepared gums**
    - Biosynthetic gums Xanthan, scleroglucan, dextrins.
    - Starch and its derivatives, dextrins.
    - Cellulose derivatives.
  - ***Semi-synthetic***
    - **Starch derivatives** — Heta starch, Starch acetate, Sarch phosphates.
    - **Cellulose derivatives** — Carboxymethyl cellulose (CMC), Hydroxyethyl cellulose, Hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), Microcrystalline cellulose (MC).
  - ***According to shape***
  - Linear: Algins, Amylose, Cellulose, pectins.
  - Branched
    - Short branches—Xanthan, Xylan, Galactomannans;
    - Branch-on-branch—Amylopectin, Gum Arabic, Tragacanth.
- ***According to Manomeric units in chemical structure***
  - Homoglycans— Amylose, Arabinanas, Cellulose;
  - Diheteroglycans— Algins, Carragennans, Galactomannans;
  - Tri-heteroglycans—Arabinoxylans, Gellan, Xanthan;
  - Tetra-heteroglycans—Gum Arabic, Psyllium seed gum;
  - Penta-heteroglycans—Ghatti gum, Tragacanth.

Disadvantages of Synthetic Polymers in Pharmaceutical Sciences:

1. The synthetic polymers have certain disadvantages such as high cost, toxicity, environmental pollution during synthesis, non-renewable sources, side effects, and poor patient compliance.[4]

2. Acute and chronic adverse effects (skin and eye irritation) have been observed in workers handling the related substances methyl methacrylate and poly- (methyl methacrylate).[5]

3. Reports of adverse reactions to povidone primarily concern the formation of subcutaneous granulomas at the injection site produced by povidone. There is also evidence that povidone may accumulate in organs following intramuscular injections.[5]

4. Acute oral toxicity studies in animals have indicated that carbomer-934P has a low oral toxicity at a dose of up to 8 g/Kg. Carbomer dust is irritating to the eyes, mucous membranes and respiratory tract. So gloves, eye protection and dust respirator are recommended during handling.[6]

5. Studies in rats have shown that 5% polyvinyl alcohol aqueous solution injected subcutaneously can cause anemia and can infiltrate various organs and tissues.[7]

6. Some disadvantages of biodegradable polymers used in tissue engineering applications are their poor biocompatibility, release of acidic degradation products, poor processing ability and rapid loss of mechanical properties during degradation. It has been shown that poly glycolides, polylactides and their co-polymers have an acceptable biocompatibility but exhibit systemic or local reactions due to acidic degradation products. An initial mild inflammatory response has been reported when using poly-(propylene fumarate) in rat implant studies.[8]

Advantages of Natural Gums in pharmaceutical science

- 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).
- Biocompatible and non-toxic—chemically, nearly all of these plant materials are carbohydrates composed of repeating sugar (monosaccharide's) 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 that for synthetic material. India and many developing countries are dependent on agriculture.
- Environmental-friendly processing—Gums 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) —in developing countries, government promote the production of plant like Guar gum and Tragacanth because of the wide applications in a variety of industries.
- 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.
- Edible sources—Most gums are obtained from edible sources.[4]

Disadvantages of Natural Gums in pharmaceutical science

- Microbial contamination—the equilibrium moisture content present in the gums 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.
- Batch to batch variation—Synthetic manufacturing is a controlled procedure with fixed quantities of ingredients, while the production of gums is dependent on environmental and seasonal factors
- 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.
- Reduced viscosity on storage—normally, when gums come into contact with water there is an increase in the viscosity of the formulations. Due to the complex nature of Gums (monosaccharide's to polysaccharides and their derivatives), it has been found that after storage there is reduced in viscosity.[4]

Natural gums

Natural gums (gums obtained from plants) are hydrophilic carbohydrate polymers of high molecular weights, generally composed of monosaccharide units joined by glucocidic bonds. They are generally insoluble in oils or organic solvents such as hydrocarbons, ether, or alcohols. Gums are either water soluble or absorb water and swell up or disperse in cold water to give a viscous solution or jelly. On hydrolysis they yield arabinose, galactose, mannose and glucuronic acid.

Gums are produced by members of a large number of families but commercial exploitation is restricted to a few species of Leguminosae, Sterculiaceae and Combretaceae (Table 1). Gum is also extracted from seeds (Table 2), seaweeds (Table 3) microorganisms (Table 4), and *Aloe barbadensis* (aloe gum) wood chips of Larixoccidentalis (stractan), seed coats or barns of corn, wheat, oats, barley, rice and soybean (Hemicellulose). Resins occur in a wide range of plants. They are formed in the specialized structures called ducts. With the exception of Lac produced by the Lac insect (*Laccifer lacca*) all the natural resins are of plant origin.[9, 10]

Table 1: List of a few plants, which are commercially tapped for, gums with their product names

Name of the source	**Family**	**Exudate/Product**
A. senegal (L.) Willd.	Leguminosae	Gum Arabic
Acacia seyal Del.	Leguminosae	Gum Arabic
Anogiessuslatifolia Wall.	Combretaceae	Gum ghatti
Astragalus gummifer	Leguminosae	Gum tragacanth
Astragalus microcephalus Willd.	Leguminosae	Gum tragacanth
Azadirachta indica A. Juss.	Meliaceae	Neem gum
Cochlospermum gossypium L.	Cochlospermaceae	Gum karaya Lannea
Lannea coromandelica	Anacardiaceae	Joel or Jingan gum
*Sterculia urens*Roxb.	Sterculiaceae	Gum karaya

Table 2: List of plants which yield seed gum

Plant names	**Family**	**Product**
Ceratonia siliqua L. (Carob tree)	Leguminosae	Locust bean gum
Cyamopsis tetragonolobus (L.) Taub.	Leguminosae	Guar gum
Plantago psyllium L	Plantaginaceae	Pysillum seed
Linum usitatissimum L.	Linaceae	Flax seed
Abelmoschus esculentus (Pods)	Malvaceae	Okra gum
Tamerindus indica	Leguminosae	Tamarind gum

Table 3: List of a few seaweeds used as sources of gum

Plant names (Red Algae, Rhodophyceae)	**Product**
Chondrus crispus	Carrageenan
C. ocellatus	Carrageenan
Gigartina stellate	Carrageenan
G. mamillosa	Carrageenan
G. acicularis	Carrageenan
G. radula	Carrageenan
G. pistillata	Carrageenan
Eucheuma spinosum	Carrageenan or Agar
E. muricatum	Carrageenan or Agar
E. cottonii	Carrageenan or Agar
E. edule	Carrageenan or Agar
Gelidium amansii	Agar
G. cartilagineum	Agar
G. latifolium	Agar
P. densa	Agar
P. lucida	Agar
Ahnfeltia plicata	Agar

Furcellaria fastigiata	Furcellaran
Brown algae (Phyophyceae)	
Macrocystis pyrifera	Alginate
M. integrifolia	Alginate
Laminaria digitata	Alginate
L. cloustoni	Alginate
L. sacchariana	Alginate
F. serratus	Alginate
F. spiralis	Alginate

Table 4: Biosynthetic gums (microbial gum)

Name of the organism	**Product**
Xanthomonas compestris	Xanthan
Pseudomonas elodea	Gellan
Leuconostoc mesenteroides	Dextran
Aureobasidium pullulans	Pullulan
Hansenula holstii (Yeast)	Phosphomannan - Y.2448
Sclerotium rolfsii (Fungus)	Scleroglucan

Pharmaceutical Application of gums

Gums possess a complex, branched polymeric structure because of which they exhibit high cohesive and adhesive properties such properties used in pharmaceutical preparation. Hence gums find diverse application in pharmacy. They are ingredients in dental and other adhesive and as bulk laxative. These polymers are useful as tablets binder, disintegrating agent, emulsifier, suspending agent, thickener, gelling agent, stabilizing agent protective colloids in suspension and sustain agent in tablets. They act as adjuvant in some pharmaceutical formulation.[4, 11]

Table 5: Gums used as binder in tablets formulation

Common name	**Botanical name**	**Family**	**Pharmacutical application**	**Refrence**
Agar	*Gelidium amansii*	Gelidaceac	Suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricant, tablet disintegrates, medium for bacterial culture, laxative	12
Albizia gum	Albizia zygia	Leguminoseae	Tablets binder	13
carragennan	*Chondrus cryspus*	Gigarginaceae	Gelling agent, stabilizer in emulsions and suspensions, in toothpaste, demulcent and laxative	14,15,16
Cashew gum	*Anacardium occidentale*	Anacardiaceae	Suspending agent	17,18
Cassia tora	*Cassia tora* Linn	Leguminosae	Binding agent	19
Guar gum	*Cyamompsis tetraganolobus*	Leguminosae	Binder, disintegrant, thickening agent, emulsifier, laxative, sustained release agent	20,21,22,23

Gum acacia	*Acacia arabica*	Leguminosae	Suspending agent, emulsifying agent, binder in tablets, demulcent and emollient in cosmetics	24
Gum ghatti	*Anogeissus latifolia*	Combretacea	Binder, emulsifier, suspending agent	25
Gum tragacanth	*Astragalus gummifer*	Leguminosae	Suspending agent, emulsifying agent, demulcent, emollient in cosmetics and sustained release agent	26
Karaya gum	*Sterculia urens*	Sterculiaceae	Suspending agent, emulsifying agent, dental adhesive, sustaining agent in tablets, bulk laxative	27, 28
Khaya gum	*Khaya grandifolia*	Meliaceae	Binding agent	29
Leucaena seed gum	*Leucaena leucocephata*		Emulsifying agent, suspending agent, binder in tablets, disintegrating agent in tablets	30, 31, 32, 33, 34
Sodium alginate	*Macrocytis pyrifera*	Lessoniaceae	Suspending agent, gelation for dental films, stabilizer, sustained release agent, tablet coating	35, 36, 37, 38
Tamarind seed polysaccharide	*Tamarindus indica*	Leguminosae	Binding agent, emulsifier, Suspending agent, sustaining agent	39
Xanthan gum	*Xanthomonas lempestris*		Suspending agent, emulsifier, stabilizer in toothpaste and ointments, sustained release agent	40, 41
Gellan gum	*Pseudomonas elodea*		Disintegrating agent,	42

1. Application of gums in tablets formulation

Gums find its application in tablets formulation as a binder because of its adhesive nature. They impart cohesiveness to the powder mass and convert them into granules. They can also be used as disintegrates in tablets .the disintegrates property of gums due to absorb water and swell. They can swell up to 5 time their original volume this swelling lead to breakage of tablets into smaller particle which in turn improve dissolution rate. Example

- ✓ The binding agent Buteamonospermalam.gum act as binder in ibuprofen tablets.[43]
- ✓ The binding agent *Cassia roxbughii* seed as a binder in paracetamol tablets.[44]
- ✓ The binding agent *Magnifer indica* gums as binder in paracetamol tablets.[45]
- ✓ Cashew tree gums as binder in metronidazole tablets.[46]
- ✓ Ziprasidon tablets based on dissolutions and dissolution efficiency value of performance of gums is as follows gum karaya> acacia>olibanum>tragacanth>guar gum.[47]

2. Gums as emulsifying and suspending agent.

Gums act as emulsifying and suspending agent. They effectively stabilize the emulsion via interfacial absorption and subsequent formulation of condensed film of high tensile strength that resist coalescence of droplets. They stabilize oil/ water emulsion by forming strong multi molecular film round each oil globule thus retards the coalescence by hydrophilic barrier between oil and water phase.

Natural gums increase the hydration of the hydration layer around the suspended particle through hydrogen bonding and molecular interaction. Since this agent does not reduce the surface and interfacial tension, they function best in presence of the wetting agent. They also act as thickener and protective colloids. Natural gums are hydrophilic colloids which form dispersion with water and increase the viscosity of the continuous phase, so that solid particle suspended in it sufficient for long time to measure the uniform dose e.g. *Cordia gharaf* Gum.[48]

3. Gums as sustaining materials in dosage form.

Gums can be use for sustaining the drug release. They have been used in tablets, suspension as or as matrix system for sustaining the drug release. This polymer when come and contact with water get hydrate and form a gel the drug release from this gel will be usually diffusion controlled hence release will be sustained over a long period e.g. guar gums, xanthenes gums and karaya gums.[49]

4. Gums as coating agent.

Many gums act as coating agent, which can sustain the drug release, or can protect the drug from degradation in stomach as the number of coating increase the drug release is reduced e.g. Grewia Gum.[50]

5. Application of gums in microencapsulation.

The gums because of their coating ability find application in microencapsulation of drug particles for sustaining the drug release. Gums from *Acacia nilotica* delile, *Acaica senegal* wild and amizo gum has been studied for their microcapsulating properties using spray drying technique. Among these three *A. nilotica* is reported to be better microcapsulating agent e.g. gum kondagogu, gum Xanthan, gum guar.[51]

6. Application of gums as gelling agent.

Gums can form a gel either alone or in combination with other. Gelling is a result of numerous inter and intra molecular association to produce three dimensional network, within which water molecule are entrapped such association are brought about by Physical (pH change, altering temperature or chemical (addition of suitable reagent) treatment the mechanism of gelatin in acidic polysaccharides such as pectin is different. In this case the macromolecular chain is widely hydrogen bonded and as a result junction zone are formed between hydrogen bonded segments of chain. In Alginic acid, the gel formation occurs as result interaction with calcium ions. Galactomannan interact synergistically with xanthan gums and carrageenan to form as elastic gel e.g. locust bean gum.[52]

Application of gums in NDDS

Application of gums in NDDS is described in table 6.

Table: 6 Application of gums in novel drug delivery system

Common name	**Novel drug delivery system**	**Drug**	**Refrence**
Acacia	Osmotic drug delivery.	Water-insoluble naproxen.	53, 54
Bhara gum	Microencapsulation	Famotidine.	55
Cordia gum	Novel oral sustained release matrix forming agent in tablets. Suspension**.**	Diclofenac sodium. Paracetamol.	56 57
Guar gum	Colon targeted drug delivery, Cross-linked microspheres.	Albendazole Metronidazole methotrexate	58, 59 60
Gellan gums	Ophthalmic drug delivery, Beads, Floating in-situ gelling.	Timolol propranolol Amoxicillin	61 62 63
Karaya gums	Mucoadhesive and buccoadhesive.	Nicotine	64
Locust bean gum	Controlled release agent.	Nimodipine, Glipizide,	65 66
Sodium alginate	Bioadhvesive microspheres,	Gatifloxin. MetforminHCL	67 68
Tamarind gum	Mucoadhesive drug delivery. Sustained releases.	Diclofenac. Verapamil.HCL	69 70
Xanthan gum	Pellets. Controlled drug delivery system.	Diclofenac sodium. theophylline	71 72

Conclusion

Natural gums are promising biodegradable polymeric materials. Many studies have been carried out in fields, including food technology and pharmaceuticals using gums. Clearly gums have many advantages over synthetic materials. Various applications of gums have been established in the field of pharmaceuticals. 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, in the years to come, there will be continued interest in natural gums and their modifications aimed at the development of better materials for drug delivery.

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