Journal of Applied Pharmaceutical Research
Volume 5, Issue 4, Year of Publication 2017, Page 13 –21
DOI: 10.18231/2348-0335.2017.0010

Review Article

JOURNAL OF APPLIED PHARMACEUTICAL RESEARCH | ***JOAPR***

www.japtronline.com ***ISSN: 2348 – 0335***

REVIEW ON NATURAL GUMS AND MUCILAGE AND THEIR APPLICATION AS EXCIPIENT

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Article Information
Received: 27th March 2017
Revised: 18th June 2017
Accepted: 29th August 2017

Keywords
Natural gum, Mucilage, Natural polysaccharide, Pharmaceutical excipient

ABSTRACT
Natural mucilage's are included in novel drug delivered (NDDS) to multitask functions and in any cases directly or indirectly control the increase and rate of drug release. Substantial research efforts have been directed towards develop safe and efficient natural based mucilage particulate drug delivery systems., natural gums and mucilages and their isolation, purification, standardization and characterization characteristics along with their applications are covered. Recent trend towards the use of plant based and natural products demands the replacement of synthetic additives with natural ones. Today, the whole world is increasingly interested in natural drugs and excipients. These natural mucilages have advantages over synthetic ones since they are chemically inert, nontoxic, less expensive, and widely available.

INTRODUCTION

Natural plants play a vital role to preserve our health. In current time, the use of herbal products has increase tremendous in the western world as well as developed countries. India is one of the most medico-traditionally diverse countries in the world where the medicinal plant area is part of a time-honored tradition that is respected even today. Medicinal plants usage has been reported in the traditional systems of medicine such as Ayurveda, Unaniand Siddha [1].

The traditional use of excipients in drug formulations was to act as inert vehicle to provide necessary accurate weight, consistency and volume for the correct administration of the active ingredient, but in modern pharmaceutical dosage forms they often multi-functional roles such as modifying release, improvement of the stability and bioavailability of the active ingredient, enhancement of patient acceptability and ensure ease of manufacture.

In recent years, plant derived polymers have pharmaceutical applications such as diluent, binder, disintegrant in tablets, thickeners in oral liquids, protective colloids in suspensions, they are also used in cosmetics, paints and paper-making these

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polymers such as natural gums and mucilage are biocompatible, cheap and easily available and are preferred to semi synthetic and synthetic excipients because of their lack of toxicity, low cost, availability, in nature [2]

Gums and mucilage

Gums are considered to be pathological products formed following injury to the plant growing to unfavourable conditions, by a breakdown of cell walls (extra cellular formation; gummosis). Mucilage's are generally normal products of metabolism, formed within the cells of plants (intracellular formation). Gums readily dissolve in water, whereas, mucilage form slimy masses. Mucilage's are physiological products of plants [3]

Advantages of natural gums and mucilage [4]

The following are a number of the advantages of natural plant based materials:

- Local availability
- Biocompatible and non-toxic
- Environmental friendly processing
- Low cost
- Biodegradable

Disadvantages of natural gums and mucilages

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

Reduced viscosity (storage): Normally, gums and mucilages come into contact water there is an increase in the viscosity of the formulations. Due to the complex nature of gums and mucilage it has been found that after storage there is reduction in viscosity.

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 factors [5]

Natural Polymers

Natural Polymers in the solid, liquid and semi-solid dosages forms and are mainly useful in the design of modified release drug delivery systems. Both natural polymers and synthetic compound have been evolution extensively, but the use of natural polymers for pharmaceutical applications is attractive because they are economical, readily available, and capable of chemical modifications, potentially biodegradable and for few exceptions, also biocompatible. Increasing importance is the fact that plant resources are renewable and if cultivated or harvested in a sustainable [6]. The plant based polymers have been study for their application in different pharmaceutical dosage forms like, film coating agents, buccal films, microsphere, nanoparticle, natural polymers viscous solutions like ophthalmic solutions, suspensions, and their applicability and efficiency has been proven [7,8]

Classification of Mucilages and Gums

Gums and mucilages are present in high quantities in verities of like plants, animals, fungi and othermicrobial sources, where they perform a number ofstructural and metabolic functions; The different part availablegums and mucilages can be classified as follows [9-14]

According to the Charge

Non-ionic seed gums: tamarind, guar, locust bean, xanthan, arabinans, cellulose,

Anionic gums: tragacanth, arabic, karaya, gellan, agar, carrageenans, pectic acid

According to the Source

A) Marine Origin/ algae Gums: agar, carrageenans, alginic acid, laminarin

B) Plant Origin:

(1) shrubs/tree exudates — gum arabica, gum ghatti, gum karaya, gum tragacanth, khaya and albizia gums;

(2) seed gums—guar gum, locust bean gum, starch, amylose, cellulose;

(3)extracts- pectin, larch gum;

(4) tuber and roots—potato starch.

C) Animal Origin: chitin and chitosan, chondroitinsulfate, hyaluronic acid.

D) Microbial Origin (bacterial and fungal): xanthan, dextran, curdian, pullulan, zanflo emulsan, Baker's yeast glycan, schizophyllan, lentinan, krestin, sclera glucan.

Semi-Synthetic

Cellulose derivatives: carboxy methyl cellulose (CMC), hydroxyl ethylcellulose, hydroxypropyl methyl cellulose (HPMC), methyl cellulose (MC), micro crystalline cellulose (MCC), starch derivatives: starch acetate, starch phosphates

According to Shape

Linear: algins, amylose, cellulose, pectins.

Branched: (1) short branches—xanthan, xylan, galactomanan; (2) branch-on-branch- amylo pectin, gum Arabic [9 – 13]

1. GUM ARABICA/ GUM ACACIA

Acacia gum, Indian gum or gum Arabica is the dried from the stems and branches of *Acacia arabica* (Combretaceae).or Acacia Senegal (Leguminosae) [6,12,14,15] Synonyms are gum acacia; gum arabic; gummi arabicum; gummimimosae; and talha gum [10]. Acacia gum consists of a glycosidal acid of high molecular weight, which has been termed arabic acid, combined with potassium, calcium and magnesium. Structurally, gum arabic is a branched molecule with the main chain consisting of 1, 3-linked β-D galacto pyranosyl units for other carbohydrates such as arabinose, glucuronic acid and rhamnose also present [14,15]. It is used as a general stabilizer in emulsions and used asan osmotic suspending and expanding agent to prepare a monolithic osmotic tablet system, binding agent for tablets, cosmetics. Its demulcent properties are employed in various cough, diarrhoea and throat preparations. It has wide spread use in the food, drinks and other industries. Pharmaceutically, it is more applicable as a matrix microencapsulating agent for the enzyme, endoglucanase, which proofed to give slow release of the encapsulated enzyme and in addition increased its stability [16 – 21]

2. KARAYA GUM

Karaya gum, Indian tragacanth obtained from the Sterculiaurens (Sterculiaceae). It consists of hetero polysacchrides of sugars and uronic acid. It doesn't contain methoxyl groups.. Pharmaceutically, it is used as a Suspending agent, emulsifying agent, dental adhesive, stabilising and thickening agent. Karaya gum is widely used as bulk laxative matrix forming agent in sustain release tablets and Ithas also been used in food, paper and textile industries. [15,22,27–29]

3. AGAR

Agar is also known as Japanese Isinglass, It is the dried colloidal concentrate from a decoction of various red algae, Agar can be separated into two major polysaccharides named as agaropectin and agarose (a neutral gelling fraction) is responsible for gel strength of agar and is composed of (+) – galactose and 3, 6-anhydro-(–)-galactose moieties. It contains about 3.5% cellulose and 6% of nitrogen containing substance. Agaropectin is (a sulphated non-gelling fraction) responsible for the viscosity of agar solutions [7-9]. Pharmaceutically it is used as Suspending agent, gelling agent in suppositories, emulsifying agent, surgical lubricant, tablet disintegrates,, laxative. It also used in preparation of jellies [14,15]

4. GHATTI GUM

Gum ghatti or Indian gum obtained from *Anogeissus latifolia* (Combretaceae) consists of calcium salt of a complex high molecular weight polysaccharide made up of sugars and uronic acid One of the polysaccharide acid, ghattic acid contains mainly arabinose, galactose, mannose. Pharmaceutically it is used as stabilizer, binder, thickener, emulsifier, and suspending agent it gives a stable oil in water emulsion and, used in formulation of oil soluble vitamin preparation. Gum is edible. In India it is administered to women after childbirth as a good tonic to health [9,22,30,31]

5. GUAR GUM

Guar gum is a seed gum produced from the powdered endosperm of the seeds of *Cyamopsis tetragonolobus* (Leguminoseae). Water soluble part consist mainly galactomannan which is composed of about 34.5% of galactose anhydride and about 63.4%of mannose anhydride. Pharmaceutically, it is used as carrier for oral extended release drug delivery. In colon targeted drug delivery it has high potential to serve as a carrier for oral controlled release matrix systems and as cross-linked microspheres. It is used as a binder, disintegrant, emulsifier, bulk laxative, appetite suppressant, and sustained release agent. Triacetate derivative of galactomannan from guar gum can be used to cast into strong, transparent, flexible films [9, 22,25,32-35]

8. TAMARIND GUM

Tamarind Gum, also known as Tamarind Kernel Powder (TKP).Tamarind gum obtained from seed polysaccharide *Tamarindus indica* (Leguminoseae) is composed of (1 4)-β-D-glucan backbone substituted with side chains of at the O-6 position of its glucopyranosyl residues with α-D-xylopyranose. Some of the xylose residues are β-D-galactosylated at O-2.Xyloglucan is a major structural polysaccharide in the primary cell walls of higher plants. gum is a polysaccharide composed of glucosyl:xylosyl:galactosyl in the ratio of 3:2:1. Pharmaceutically, it is applicable for Hydrogels, mucoadhesive drug delivery for ocular purposes, spheroids, nasal drug

delivery. It is used as binding agent, emulsifier, suspending agent, sustaining agent. The gel can be used as a thickening and stabilizing agent in food industry [36-38]

9. GELLAN GUM

It is an anionic deacetylatedexocellular polysaccharide secreted by *Pseudomonas elodea* with a tetrasaccharide repeating unit of one α -L-rhamnose, one β-D-glucuronic acid and two β-D-glucose. Chemical structure of the polysaccharide has been determined, one glucuronic acid residue, and one rhamnose residue. The exact molecular formula of gellan gum may vary slightly (e.g., depending on the degree to which the glucuronic acid is neutralized with various salts) [39,40]. Pharmaceutically aqueous solution of Gellan are used for ophthalmic preparation and for oral drug delivery and also in microspheres. Gellan gum is used in Ophthalmic drug delivery, as sustaining agent, beads, controlled release beads, hydrogels, floating in-situ gelling, disintegrating agent [41,42]

10. XANTHAN GUM

Xanthan gum is a complex microbial exopolysaccharide produced from glucose fermentation by *Xanthomonas campestris*. It also called as corn sugar gum, keltrol, polysaccharide B- 1459, rhodigel, vanzan NF [7].

The primary structure of xanthan consists of repeating pentasaccharide units consisting of two D-glucopyranosyl units, two D-mannopyranosyl units and one D-glucopyranosyl uronic acid .

The polymer backbone is made up of (1_4)-linked β-D-glucopyranosyl units, is identical to that of cellulose. To alternate D-glucosyl units at the O-3 position, at risaccharide side chain containing a D-glucuronosyl unit between two D-mannosyl units is attached. The terminal β-D-mannopyranosyl unit is glycosidically linked to the O-4 position of the β-D-glucopyranosyl uronic acid unit, which in turn is glycosidically linked to the O-2 position of a α-D mannopyranosyl unit. Approximately one-half of the terminal D-mannosyl units contain a pyruvic acid moiety as a 4, 6-cyclic acetal.

Finally, the non terminal D-mannosyl unit is stoichiometrically substituted at O-6 with an acetyl group. Pharmaceutically, it is applicable as sustained release agent, pellets, controlled drug delivery system. It is used as stabilizer for emulsions and suspensions. It is also used as suspending agent, emulsifier, stabilizer in tooth paste and ointments [42-46]

11. HAKEA GUM

Hakea gum is dried exudate from the plant *Hakea gibbosa* family Proteaceae. Gum exudates from this species contain L-arabinose and D-galactose linked as in gums that are acidic arabino galactans (type A). Molar proportions (%) of sugar constituents Glucuronic acid, Galactose, Arabinose, Mannose, Xylose is 12:43:32:5:8. Pharmaceutically, it is applicable for the formulation of buccal tablets, Sustained release and peptide muco-adhesive for buccal delivery [47-49]

12. MUCUNA GUM

This is obtained from *Mucuna flagillepes* (Papillionaceae). Mucuna composed of mainly D-galactose along with D-mannose and D-glucose. An investigation into the suitability of microspheres of glibenclamide with mucuna gum for oral delivery was studied, they shows good in vitro properties. Mucuna gum is good suspending agent, stabilizing agent in dosage formulations such as suspensions and emulsions, a good binder in tablets and a good candidate for bioadhesive drug delivery [50]

13. BALANGU GUM

Balangu gum obtained from *Lallemantia royleana* (Labiatae). Balangu seed gum (BSG) contains 61.74%carbohydrates, 0.87% proteins, 29.66% crude fiberand 8.33% ash. Because of high mucilage content, theseeds adsorb water quickly by hydration and produce a sticky, turbid and tasteless liquid, which can be used as a new source of food hydrocolloid in food formulations [51]

14. BEAL FRUIT

Gum is obtained from fruits of *Aegle marmelos* belonging to family Rutaceae. The pulp contains carbohydrates, proteins, vitamin C, vitamin A,angelenine, marmeline, dictamine, O-methyl fordinol and isopentyl half ordinol. The neutral oligosaccharides were characterized as 3-0-beta- D-galactopyranosyl- Larabinose, 5-0-beta-D-galactopyranosyl D-galacto pyranosyl-L-arabinose, & 3-0-beta-D-galacto pyranosyl- D-galactose, and the acidic oligosaccharides. *Aegle marmelos* gum is used as mucoadhesive in sustained release matrix tablet [52-54]

15. OKRA

The Okra gum obtained from the fresh fruits of the plant *Abelmoschus esculentus* belongs to the familyMalvaceae, is a polysaccharide consisting of Dgalactose, L-rhamnose and L-galacturonic acid with some fractions of glucose, mannose, arabinose andxylose. Okra has been used as food and it has been evaluated as a binder in paracetamol tablet formulation [55], control release [56], film coating [57],bio-adhesive [58] and suspending [59] agent. Okra gum maybe useful as hydrophilic matrixing agent in sustained drug delivery devices. Polymer for the development of a gastric floating dosage form [60].

Okra polysaccharide is also used as a microbially triggered material for Colon targeted tablet formulation and also as the carrier [60]

16. NEEM GUM

Neem gum is obtained from the trees of *Azadirachta indica* belongs to the family Meliaceae. Neem gum contains mannose, glucosamine, arabinose, galactose, fucose, xylose and glucose. [9] Pharmaceutically it used as binding agent.[61] in sustained release matrix tablets of Nimesulide using the fruit mucilage of *Azadirachta indica* was studied. [62]

17. ALOE MUCILAGE

Aloe mucilage is obtained from the leaves of *Aloe barbadensis Miller*. Aloe vera leaves and the exudates arising from the cells adjacent to the vascular bundles. The bitter yellow exudate contains 1, 8 dihydroxy anthraquinone derivatives and their glycosides [63].

Many investigators have identified partially acetylated mannan (or acemannan) as the primary polysaccharide of the gel, while others found pectin substance as the primary polysaccharide. Other polysaccharides such as arabinan, arabinorhamno galactan, galactan, galactogalacturan, gluco galactomannan, galacto gluco arabinomannan and glucuronic acid containing polysaccharides have been isolated from the Aloe vera inner leaf gel part [64].

A controlled delivery system of glibenclamide using aloe mucilage was studied [65]. Dried Avera gel polysaccharide component therefore showed excellent potential to be used as an excipient in the formulation of direct compressible sustained- release matrix type tablet.[66]

18. *HIBISCUS* MUCILAGE

Hibiscus rosa sinensis Linn of the Malvaceae family is also known as the shoe flower plant, China rose, and Chinese hibiscus. It contains L-rhamnose, D-galactose,D-galactouronic acid and D-glucuronic acid [67]. Pharmaceutically it is used for the development of sustained release tablet [68]. It is subjected to toxicity studies for its safety and preformulation studies for its suitability as a disintegrating agent [69]

19. CASSIA TORA MUCILAGE

Cassia tora mucilage derived from the seeds of *Cassia tora*, belongs to Caesalpiniaceae. It is locally known as charota [70]. Cassia is used as carminative and stimulant tonic. Cassia contains 1-2 %volatile cassia oil which is mainly responsible for the spicy aroma and taste. The primary chemical constituents of Cassia include cinnamaldehyde, gum, tannins, mannitol, coumarins and essential oils (aldehydes, eugenol, and pinene); it also contains sugars, resins and mucilage among other constituents. Seed mucilage of *Cassia tora* was evaluated as suspending agent and binding agent [71,72]

20. FENUGREEK MUCILAGE.

Mucilages obtained fromseeds of *Trigonella foenum-graceum* (family: *Leguminosae*). Its seeds contain a high percentage of mucilage and do not dissolve in water but form viscous tacky mass and swell up when exposed to fluids [73]. Gum contains mannose, galactose, and xylose. The mucilage obtained from fenugreek was found to be better release retardant compared to hypromellose at equivalent content [74].

21. OCIMUM MUCILAGE

Ocimum mucilage is obtained from the seeds of *Ocimum americanum* commonly called *Ocimumcanum* (family: *Lamiaceae*). Mucilage contains xylose, arabinose, rhamnose, and galacturonic acids [75]. The disintegration time for tablet formulations prepared using ocimum mucilage was less than tablets that were prepared by using starch as a disintegrant [76]. The mucilage was found to have disintegrating property.

APPLICATIONS OF GUMS AND MUCILAGES

Gums and mucilages 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 [77]. However, there is growing concern about the safety of

pharmaceutical excipients derived from natural sources. Plant gums and exudates are now screened for their use as pharmaceutical adjuvants. Mucilages of different origins are also used in conventional dosage forms of various drugs for their binding, thickening, stabilizing and humidifying properties in medicine. Newer uses of different gums and mucilages in cosmetics and textiles has 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 and mucilages have the following applications.

1. Applications in the food industry

Gums and mucilages have a variety of applications in the food industry [78]. 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).

2. Pharmaceutical applications

Gums and mucilages have a variety of applications in pharmacy. They are used in medicine for their demulcent properties for cough supression. 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, film forming agents in transdermal and periodontal films, buccal tablets as well as sustaining agents in matrix tablets and coating agents in microcapsules including those used for protein delivery

3. 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).

FINANCIAL ASSISTANCE

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

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