Natural Gums and Mucilage’s in NDDS: Applications and Recent approaches

Umeshkumar M. Deogade*, Vilas N. Deshmukh, Dinesh M. Sakarkar

Department of Industrial Pharmacy, Sudhakarrao Naik Institute of Pharmacy, Pusad Dist. Yavatmal, Maharashtra (India) 445204

*Corres. author: umeshdevd@gmail.com
Mobile No: 09665740879

Abstract: Nature has provided us a wide variety of materials to help improve and sustain the health of all living things either directly or indirectly. In recent years there has been an important development in different dosage forms for existing and newly designed drugs and natural products, and semi-synthetic as well as synthetic excipients often need to be used for a variety of purposes. Gums and mucilages are widely used natural materials 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 their formulations. 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 reported origin. In the present review we have discussed gums and mucilages, as a potent candidate to be used in various pharmaceutical formulations as a potential candidate for New Drug Delivery System (NDDS). 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. In this review, we describe the developments in natural gums and mucilages for use in the pharmaceutical sciences.

Key words: Natural gum, Mucilage, Natural polymer, Pharmaceutical excipient, Natural polysaccharide, NDDS.

Introduction

Mother nature has gifted India with great variety of flora and fauna. For centuries man has made effective use of materials of natural origin in the medical and pharmaceutical field. Today, the whole world is increasingly interested in natural drugs and excipients. In recent years, plant derived polymers have evoked 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. These 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, soothing action and non irritant nature.

Furthermore, they can be modified to obtain tailor made materials for drug delivery systems allowing them to compete with the synthetic products that are commercially available. Many kinds of natural gums are used in the food industry and are regarded as safe for human consumption. It should be noted that many ‘old’ materials are still popular today after almost a century of efforts to replace them. It is usual to strike a balance between economics and performance in the face of commercial realities.
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.\textsuperscript{15}

What are gums and mucilages?

Gums are considered to be pathological products formed following injury to the plant or owing to unfavourable conditions, such as drought, by a breakdown of cell walls (extra cellular formation; gummnosis) while, mucilages are generally normal products of metabolism, formed within the cell (intracellular formation) and/or are produced without injury to the plant.

Gums readily dissolve in water, whereas, mucilage form slimy masses. Gums are pathological products, whereas mucilages are physiological products.\textsuperscript{8} Acacia, tragacanth, and guar gum are examples of gums while mucilages are often found in different parts of plants. For example, in the epidermal cells of leaves (senna), in seed coats (linseed, psyllium), roots (marshmallow), barks (slippery elm) and middle lamella (aloë).\textsuperscript{7}

Gums and mucilages have certain similarities—both are plant hydrocolloids. They are also translucent amorphous substances and polymers of a monosaccharide or mixed monosaccharides and many of them are combined with uronic acids. Gums and mucilages have similar constituents and on hydrolysis yield a mixture of sugars and uronic acids. Gums and mucilages contain hydrophilic molecules, which can combine with water to form viscous solutions or gels. The nature of the compounds involved influences the properties of different gums. Linear polysaccharides occupy more space and are more viscous than highly branched compounds of the same molecular weight. The branched compounds form gels more easily and are more stable because extensive interaction along the chains is not possible.

Disadvantages of synthetic polymers in pharmaceutical sciences

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

Acute and chronic adverse effects (skin and eye irritation) have been observed in workers handling the related substances methyl methacrylate and poly-(methyl methacrylate) (PMMA).\textsuperscript{8} 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.\textsuperscript{9} 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.\textsuperscript{10}

Studies in rats have shown that 5% polyvinyl alcohol aqueous solution injected subcutaneously can cause anemia and can infiltrate various organs and tissues.\textsuperscript{11} 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.\textsuperscript{12}

Advantages of natural gums and mucilages in pharmaceutical sciences

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

a) 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).

b) Biocompatible and non-toxic—Chemically, nearly all of these plant materials are carbohydrates composed of repeating sugar (monosaccharides) units. Hence, they are non-toxic.

c) 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.

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

e) Local availability (especially in developing countries)—In developing countries, governments promote the production of plant like guar gum and tragacanth because of the wide applications in a variety of industries.

f) 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.

g) Edible sources—Most gums and mucilages are obtained from edible sources.

Disadvantages of Natural Gums and Mucilages

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

b) 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.

c) 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.

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

Classification of gums and mucilages

Gums and mucilages are present in high quantities in 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 and mucilages can be classified as follows.

I. According to the charge

a) Non-ionic seed gums: guar, locust bean, tamarind, xanthan, amylose, arabinans, cellulose, galactomannans.

b) Anionic gums: arabic, karaya, tragacant, gellan, agar, algin, carrageenans, pectic acid.

II. According to the source

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

b) Plant origin: i. Shrubs/tree exudates—gum arabica, gum ghatti, gum karaya, gum tragacanth, khayaandalbizia gums
   ii. Seed gums—guar gum, locust bean gum, starch, amylose, cellulose
   iii. Extracts—pectin, larch gum
   iv. Tubers and roots—potato starch

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

d) Microbial origin (bacterial and fungal): xanthan, dextran, curdian, pullulan, zanflo, emulsan, Baker’s yeast glycan, schizophyllan, lentinan, krestin, scleroglucan.

III. Semi-synthetic

a) Starch derivatives—hetastarch, starch acetate, starch phosphates.

b) Cellulose derivatives—carboxy methyl cellulose (CMC), hydroxyethylcellulose, hydroxypropyl methylcellulose (HPMC), methylcellulose (MC), microcrystalline cellulose (MCC).

IV. According to shape

a) Linear: algins, amylose, cellulose, pectins.

b) Branched: i. Short branches—xanthan, xylan, galactomannan;
   ii. Branch-on-branch—amylopectin, gumarabic, tragacanth.

V. According to monomeric units in chemical structure

a) Homoglycans—amylose, arabinans, cellulose;

b) Diheteroglycans—algins, carragennans, galactomannans;

c) Tri-heteroglycans—arabinoxylans, gellan, xanthan;

d) Tetra-heteroglycans—gum arabic, psyllium seed gum;

e) Penta-heteroglycans—ghatti gum, tragacantha.

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 safer for human consumption. However, there is growing concern about the safety of pharmaceutical excipients derived from natural sources. Plant gums and exudates are now screened for their uses 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. A newer use 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 fulfill. Gums and mucilages have the following applications.

a) Applications in the food industry
Gums and mucilages have a variety of applications in the food industry\(^\text{21}\). Different gums have different uses like water retention and stabilization (guar and locust bean gum), stabilizers for ice-cream, meat products and instant pudding (carrageenan), dairy, confectionary and meat products (agar), confectionary, beverages, backed product, and sauces (gum arabic, tragacanth, pectins, alginate, and xanthan gum).

b) Pharmaceutical applications
Gums and mucilages have a variety of 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, 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. Various gums and mucilages with their common names, biological sources, family and applications are listed in Table 1. Table 2 lists the different applications of gums and mucilages in novel drug delivery systems.

c) Industrial application
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).

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Common name</th>
<th>Botanical name</th>
<th>Family</th>
<th>Pharmaceutical Applications</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abelmoschus mucilage</td>
<td><em>Abelmoschus esculentus</em></td>
<td>Malvaceae</td>
<td>Binder in tablets, sustained release</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>Agar</td>
<td><em>Gelidium amansii</em></td>
<td>Gelidaceae</td>
<td>Suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricant, tablet</td>
<td>35</td>
</tr>
<tr>
<td>3</td>
<td>Albizia gum</td>
<td><em>Albizia zygia</em></td>
<td>Leguminoseae</td>
<td>Tablet binder</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>Aloe mucilage</td>
<td><em>Aloe species</em></td>
<td>Liliaceae</td>
<td>Gelling agent, sustained release agent</td>
<td>37</td>
</tr>
<tr>
<td>5</td>
<td>Asario mucilage</td>
<td><em>Lepidium sativum</em></td>
<td>Cruciferae</td>
<td>Suspending agent, emulsifying agent, controlled release tablet</td>
<td>38</td>
</tr>
<tr>
<td>6</td>
<td>Bavchi mucilage</td>
<td><em>Ocimum canum</em></td>
<td>Labiatae</td>
<td>Suspending agent, emulsifying agent</td>
<td>39</td>
</tr>
<tr>
<td>7</td>
<td>Carrageenan</td>
<td><em>Chondrus crypsus</em></td>
<td>Gigartinaceae</td>
<td>Gelling agent, stabilizer in emulsions and suspensions, in toothpaste, demulcent and laxative</td>
<td>40,41</td>
</tr>
<tr>
<td>No.</td>
<td>Name of Gum</td>
<td>Genus and Species</td>
<td>Family</td>
<td>Properties</td>
<td></td>
</tr>
<tr>
<td>-----</td>
<td>---------------------------------</td>
<td>--------------------------------------------</td>
<td>-----------------</td>
<td>---------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Cashew gum</td>
<td><em>Anacardium occidentale</em></td>
<td>Anacardiaceae</td>
<td>Suspending agent</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Cassia tora</td>
<td><em>Cassia tora Linn</em></td>
<td>Leguminosae</td>
<td>Binding agent</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Fenugreek mucilage</td>
<td><em>Trigonella Foenum graecum</em></td>
<td>Leguminosae</td>
<td>Gelling agent, tablet binder, sustaining agent, emollient and demulcent</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Guar gum</td>
<td><em>Cyamomopsis tetragonolobus</em></td>
<td>Leguminosae</td>
<td>Binding, disintegrant, thickening agent, emulsifier, laxative, sustained release agent</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Gum acacia</td>
<td><em>Acacia arabica</em></td>
<td>Leguminosae</td>
<td>Suspending agent, emulsifying agent, binder in tablets, demulcent and emollient in cosmetics</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Gum ghatti</td>
<td><em>Anogeissus latifolia</em></td>
<td>Combretaceae</td>
<td>Binder, emulsifier, suspending agent</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Gum tragacanth</td>
<td><em>Astragalus gummifer</em></td>
<td>Leguminosae</td>
<td>Suspending agent, emulsifying agent, demulcent, emollient in cosmetics and sustained release agent</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Hibiscus mucilage</td>
<td><em>Hibiscus esculentus Linn</em></td>
<td>Malvaceae</td>
<td>Emulsifying agent, sustained release agent, suspending agent</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Hibiscus mucilage</td>
<td><em>Hibiscus rosasinensis Linn</em></td>
<td>Malvaceae</td>
<td>Suspending agent, Sustained release agent</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Ispagol mucilage</td>
<td><em>Plantagopsyllium, Plantagoovata</em></td>
<td>Plantaginaceae</td>
<td>Cathartic, lubricant, demulcent, laxative, sustaining agent, binder, emulsifying and suspending agent</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Karaya gum</td>
<td><em>Sterculiaurens</em></td>
<td>Sterculiaceae</td>
<td>Suspending agent, emulsifying agent, dental adhesive, sustaining agent in tablets</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Khaya gum</td>
<td><em>Khayagrandifolia</em></td>
<td>Meliaceae</td>
<td>Binding agent</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>Leucaena seed gum</td>
<td><em>Leucaena leucocephata</em></td>
<td>Labiatae</td>
<td>Emulsifying agent, suspending agent, binder in tablets, disintegrating agent in tablets</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Ocimum seed mucilage</td>
<td><em>Ocimumgratissimum Linn</em></td>
<td>Labiatae</td>
<td>Suspending agent, binding agent</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Pectin</td>
<td><em>Citrus aurantium</em></td>
<td>Rutaceae</td>
<td>Thickening agent, suspending agent, protective agent</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Sodium alginate</td>
<td><em>Macrocytispyrifera</em></td>
<td>Lessoniaceae</td>
<td>Suspending agent, gelation for dental films, stabilizer</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Applications of gums and mucilages in Novel Drug Delivery Systems

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Common name</th>
<th>Botanical name</th>
<th>Family</th>
<th>Pharmaceutical applications</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acacia</td>
<td>Acacia Senegal</td>
<td>Leguminosae</td>
<td>Osmotic drug delivery</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>Bharam gum</td>
<td>Terminaliabellericaroxb</td>
<td>Combretaceae</td>
<td>Microencapsulation</td>
<td>77</td>
</tr>
<tr>
<td>3</td>
<td>Chitosan</td>
<td></td>
<td>---</td>
<td>Colonspecific drug delivery, microspheres, carrier for protein as nanoparticles</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>Cordia gum</td>
<td>Cordia oblique willed</td>
<td>Boraginaeae</td>
<td>Novel oral sustained release matrix forming agent in tablets</td>
<td>79</td>
</tr>
<tr>
<td>5</td>
<td>Cactus mucilage</td>
<td>Opuntia ficus-indica</td>
<td>---</td>
<td>Gelling agent in sustained drug delivery</td>
<td>80</td>
</tr>
<tr>
<td>6</td>
<td>Guar gum</td>
<td>Cyamompsistetragonolobus s</td>
<td>Leguminosae</td>
<td>Colontargeted drug delivery, cross-linked microspheres</td>
<td>81,82</td>
</tr>
<tr>
<td>7</td>
<td>Gellan gum</td>
<td>Pseudomonas elodea</td>
<td>---</td>
<td>Ophthalmic drug delivery, sustaining agent, beads, hydrogels, floating in-situ gelling, controlled release beads</td>
<td>83,84,85</td>
</tr>
<tr>
<td>8</td>
<td>Hakea</td>
<td>Hakeagibbosa</td>
<td>---</td>
<td>Sustainedrelease and peptide mucoadhesive for buccal delivery</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td>Ispagol</td>
<td>Plantagopsyllium, Plantagoovata</td>
<td>Plantaginaceae</td>
<td>Hydrogels, colon drug delivery, gastroretentive drug delivery</td>
<td>87,88</td>
</tr>
<tr>
<td>10</td>
<td>Karaya gum</td>
<td>Sterculiaurens</td>
<td>Sterculiaceae</td>
<td>Mucoadhesive and buccoadhesive</td>
<td>89</td>
</tr>
<tr>
<td>11</td>
<td>Locust bean gum</td>
<td>Ceratania silicia</td>
<td>Leguminosae</td>
<td>Controlled release agent</td>
<td>90</td>
</tr>
<tr>
<td>12</td>
<td>Mucuna gum</td>
<td>Mucuna flagillepes</td>
<td>Papillionaceae</td>
<td>Microspheres</td>
<td>91</td>
</tr>
</tbody>
</table>
Isolation and purification of gums and mucilages

Plant material is dried in sunlight (preferably) or in an oven at 105°C to retain its properties unchanged. Generally, chlorophyll or pigments are present in the plant which should be removed before isolating the mucilage. Plant material must be treated with petroleum ether and chloroform (to remove pigments and chlorophyll) and then with distilled water. Care should be taken when drying the final isolated/extracted mucilage. It must be dried at a very low temperature (not more than 50°C) or in a vacuum. The dried material is stored carefully in desiccators to prevent further moisture uptake or degradation.

Baveja et al., 22 and Wahie et al., 23 reported the following method for the isolation of mucilage.

The fresh plant materials were collected, washed with water to remove dirt and debris, and dried. Then, the powdered material was soaked in water for 5–6 h, boiled for 30 min, and allowed standing 1 h so that all the mucilage was released into the water. The material was then squeezed from an eight muslin bag to remove the marc from the solution. Following this, three volumes of acetone was added to the filtrate to precipitate the mucilage. The mucilage was separated, dried in an oven at a temperature less than 50°C, and the dried powder was passed through a No. 80 sieve and stored in a desiccator until required. The isolated mucilage from the plant was subjected to some preliminary confirmative testing.

Table No. 3 shows the preliminary confirmative test for dried mucilage 6, 15, 16.

Extraction is one of the most crucial procedures to achieve complete recovery of target compounds from plants. Recently, microwave energy has started to be used for the extraction of phytoconstituents from plants 24. It is a simple, fast, clean, eco-friendly and efficient method and saves energy, fuel and electricity.

Microwave extraction follows the same principle as maceration or percolation, but the speed of breaking up of the plant cells and tissues is much higher. Microwave assisted extraction methods require a shorter time and less solvent, and provide a higher extraction rate and better products at a lower cost. Plant material is powdered in a mechanical blender for 5 m and then soaked in distilled water for 24 h in a 1000 ml beaker. It is kept in a microwave oven along with a glass tube to prevent bumping when subjected to microwave irradiation. The beaker is removed from the oven and allowed to stand for 2 h to allow the mucilage to be released into the water. It is then processed in a similar way to the conventional procedure, weighed and stored.
Table 3. Preliminary confirmative test for dried mucilage

<table>
<thead>
<tr>
<th>Test</th>
<th>Observation</th>
<th>Inferences</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Molisch’s test:</strong></td>
<td>Purple green color observed at the junction of the two layers</td>
<td>Carbohydrate present</td>
</tr>
<tr>
<td>(100 mg dried mucilage powder + Molisch’s reagent + conc. H2SO4 on the side of a test tube)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ruthenium test:</strong></td>
<td>Pink color develops</td>
<td>Mucilage present</td>
</tr>
<tr>
<td>Take a small quantity of dried mucilage powder, mount it on a slide with ruthenium red solution, and observe it under microscope.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Iodine test:</strong></td>
<td>No color observed in solution</td>
<td>Polysaccharides present (starch is absent)</td>
</tr>
<tr>
<td>10 mg dried mucilage powder + 1 ml 0.2 N iodine solution.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Enzyme test:</strong></td>
<td>No blue color produced</td>
<td>Enzyme absent</td>
</tr>
<tr>
<td>Dissolve 100 mg dried mucilage powder in 20 ml-distilled water; add 0.5 ml of benzidine in alcohol (90%). Shake and allow to stand for few minutes</td>
<td></td>
<td>(Distinction between dried mucilage and acacia)</td>
</tr>
</tbody>
</table>

Characterization and standardization of gums and mucilages

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. For excipient analysis, analytical techniques can be classified according to the type of information generated.

a) **Structural**—Gums and mucilages are polysaccharides and contain sugars. So, confirmation of the different sugars is carried out by chromatography and structure elucidation can be carried out by NMR and mass spectroscopy.

b) **Purity**—To determine the purity of the selected gum and mucilage, tests for alkaloids, glycosides, carbohydrates, flavanoids, steroids, amino acids, terpenes, saponins, oils and fats, and tannins and phenols are carried out.

c) **Impurity profile**—Testing for impurities must be carried out using suitable analytical techniques.

d) **Physico-chemical properties**—Color, odor, shape, taste, touch, texture, solubility, pH, swelling index, loss on drying, hygroscopic nature, angle of repose, bulk and true densities, porosity and surface tension. Different ash values are also estimated. The microbial load and presence of specific pathogens are also determined. In vitro cytotoxicity is also determined. Gums and mucilages are highly viscous in nature. So, the rheological properties of excipients are important criteria for deciding their commercial use. The flow behavior of the samples is determined.

e) **Toxicity**—The acute toxicity of gums and mucilages is determined by the followings fixed-dose method as per OECD guideline No. 425. A sub-acute toxicity study, determination of the LD50 etc., is carried out in rats and guinepigs of both sexes.

Once analysis is complete, determination of the structure, composition and impurity profile enables a scientific dossier to be prepared describing the excipient. This information is of value for the regulatory dossier of the final pharmaceutical product that would contain the given excipient.

Finally, gums and mucilages are added to pharmaceutical formulations. So a compatibility study is important. The compatibility studies of gum/mucilage/drugs are performed using spectrophotometry/FTIR/DSC.

Pharmacopoeial standard specifications of gums and mucilages

Different pharmacopoeias, like USP, PhEur, and JP give pharmacopoeial standards for specific gums. The Pharmacopoeial standard for different gums is shown in Table No. 4.
Table 4. Pharmacopoeial specifications for gums

<table>
<thead>
<tr>
<th>Excipient</th>
<th>Test</th>
<th>Pharmacopoeia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acacia</td>
<td>Microbial limit, ash values</td>
<td>USP, JP, PhEur</td>
</tr>
<tr>
<td>Alginic acid</td>
<td>Microbial limit, pH, loss on drying</td>
<td>USP, PhEur</td>
</tr>
<tr>
<td>Carrageenan</td>
<td>Solubility, viscosity, loss on drying, ash value</td>
<td>USP</td>
</tr>
<tr>
<td>Dextrin</td>
<td>Loss on drying, residue on ignition, reducing sugars</td>
<td>USP, BP, JP</td>
</tr>
<tr>
<td>Gelatin</td>
<td>Isoelectric point, microbial limit, residue on ignition, loss on drying, total ash, jelly strength</td>
<td>USP, BP, JP</td>
</tr>
<tr>
<td>Guar gum</td>
<td>pH, microbial contamination, apparent viscosity, loss on drying, ash, galactomannans, organic volatile impurities</td>
<td>USP, PhEur</td>
</tr>
<tr>
<td>Lecithin</td>
<td>Water, arsenic, lead, acid value, heavy metals</td>
<td>USP</td>
</tr>
<tr>
<td>Sodium alginate</td>
<td>Microbial limit, appearance of solution, loss on drying, ash, heavy metals</td>
<td>USP, PhEur</td>
</tr>
<tr>
<td>Tragacanth</td>
<td>Microbial limits, flow time, lead, acacia and other soluble gums, heavy metals</td>
<td>USP, JP, PhEur</td>
</tr>
<tr>
<td>Xanthan gum</td>
<td>pH, viscosity, microbial limits, loss on drying, ash, heavy metals, organic volatile impurities</td>
<td>USP, PhEur</td>
</tr>
<tr>
<td>Gellan gum</td>
<td>pH, microbial limit, loss on drying, moisture content, specific gravity, solubility, bulk density</td>
<td>USP</td>
</tr>
</tbody>
</table>

Reasons for developing new excipients

For a number of reasons there has been an increase in interest in the development of new excipients/diluents.

Some drugs show incompatibilities with many of the current range of excipients. For example, atenolol-PVP, atenolol-mg-stearate. One of the more common drug-excipient incompatibilities is the reaction between aldehydic sugars, such as lactose and primary and secondary amines, leading to the formation of Schiff bases. These complex series of reactions lead to browning and discoloration of the dosage form. Despite being a carrier of choice for dry powder aerosol formulations, lactose may need to be replaced with a different carrier, such as mannitol or sucrose, when formulating primary and secondary amines.

Mg-stearate is incompatible with aspirin, some vitamins and most alkaloidal salts.

There is a need for excipients that will allow faster manufacturing of formulations. For example, at the present time, in tablet dosage forms, new excipients having better compressibility at very high compression speeds are needed. Today, it is not unheard of to have tabletting equipment compressing 8000 to 10000 tablets per min. It is critical under these conditions to have an exceptionally efficient flowing granulation/powder blend. Many sugar-based excipients, such as maltose, mannitol, and sorbitol are not compressible in their natural state and need to be modified for use in direct compression tableting.

Some future developments may require new delivery systems. For example, new drug delivery systems for oral administration of biotechnology products need new excipients which will avoid the inconvenience of multiple daily injections. Progress in the development of peptides as therapeutic drugs has been impeded in part by their rapid excretion, resulting in short circulating lifetimes. This has generated considerable interest in improving the duration of action of drugs through conjugation with the water-soluble, biocompatible excipient, poly (ethylene glycol). Such conjugates have reduced enzymatic degradation rates and lengthened circulating lifetimes compared with the native compounds. There are six FDA-approved PEGylated products on the market, vouching for the safety and commercial viability of this technology. Other novel lipophilic carbohydrate excipients, termed oligosaccharide ester derivatives (OEDs), have been used to modify the pharmacokinetic profiles of drugs. This technology is quite flexible, offering the ability to formulate drug molecules with modified release characteristics and improved bioavailability. In other areas of technology, selected carbohydrate excipient, such as trehalose and sucrose to stabilize molecules in the dry state, thereby preventing their physical and chemical degradation at ambient temperatures and above. These patent-protected drug delivery technologies are suited to the delivery of macromolecules, such as proteins and peptides by the pulmonary, oral, and injectable routes.

Drug targeting systems, like liposome delivery systems, need newer excipient, because the existing excipients for liposomes are too expensive.
Modification of existing gums and mucilages

It should be noted that many “old” materials compete successfully today after almost a century of efforts to replace them. It is the usual balance of economics and performance that determines the commercial realities. Natural gums have been modified to overcome certain drawbacks, like uncontrolled rate of hydration, thickening, drop in viscosity on storage, and microbial contamination.

Since the implementation of polymeric materials in the field of pharmaceutical technology, numerous attempts have been made to modify their physical and chemical properties, and thus, their potential applicability in various areas of drug formulation.

Various methods are available to modify the state of molecular interaction between polymers. Basically, two methods are available as the physical method and chemical method.

**Physical method**—a molecular interaction between polymers can be achieved by exposure to dry heat, saturated steam, microwave technology, UV, and gamma radiation.

**Chemical method**—polymers are treated with chemicals like aldehydes, epichlorhydrin, borax or glutaraldehyde. Temperature is one of the most favourable methods of cross-linking because it avoids both the application of harsh chemical materials for large-scale production and the diversity of equipment and methods used in their application.

Table 5 shows examples of modified gum and mucilage.

<table>
<thead>
<tr>
<th>Gums and mucilage</th>
<th>Modification technique</th>
<th>Application</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karaya gum</td>
<td>Heat Treatment at various temperatures in a hot air oven</td>
<td>Disintegrating agent</td>
<td>99</td>
</tr>
<tr>
<td>Agar and Guar gum</td>
<td>Heat Treatment at various temperatures in a hot air oven along with co-grinding of both materials.</td>
<td>Disintegrating agent</td>
<td>100</td>
</tr>
<tr>
<td>Hypochlorite potato starch</td>
<td>Chemical modification of potato starch carried out in presence of hypochloride</td>
<td>Disintegrating agent</td>
<td>101</td>
</tr>
<tr>
<td>Tragacanth</td>
<td>Chemical modification of tragacanth using epichlorhydrine</td>
<td>Disintegrating agent</td>
<td>102</td>
</tr>
<tr>
<td>Acacia gum</td>
<td>Chemical modification of acacia gum using epichlorhydrine</td>
<td>Disintegrating agent</td>
<td>103</td>
</tr>
<tr>
<td>Guar gum</td>
<td>Chemical modification of guar gum</td>
<td>Disintegrating agent</td>
<td>104</td>
</tr>
<tr>
<td>Cross-linked amylose</td>
<td>Chemical modification of amylase by substituting it in a one-step reaction.</td>
<td>Disintegrating and binding agent</td>
<td>105</td>
</tr>
<tr>
<td>Cross-linked cellulose</td>
<td>Chemical modification of cellulose by epichlorhydrine</td>
<td>Disintegrating and binding agent</td>
<td>106</td>
</tr>
<tr>
<td>Polyalkylamine</td>
<td>Chemical modification of polyalkylamine</td>
<td>Disintegrating agent</td>
<td>107</td>
</tr>
<tr>
<td>Cyclodextrin</td>
<td>Physical modification - co-drying of microcrystalline cellulose with cyclodextrin</td>
<td>Disintegrating agent</td>
<td>108</td>
</tr>
<tr>
<td>Starch</td>
<td>Physico-chemical treatment of to starch for modification</td>
<td>Disintegrating and binding agent</td>
<td>109</td>
</tr>
<tr>
<td>Sesbania gum</td>
<td>Chemical modification of Sesbania gum with tartaric acid for a sustained release formulation and chemical modification of gum with acetone: chloroform mixture for gelling agent</td>
<td>Sustained release formulation, gelling agent</td>
<td>110</td>
</tr>
<tr>
<td>Guar gum</td>
<td>Chemical modification of guar gum with glutaraldehyde for colonic delivery, chemical</td>
<td>Colonic delivery, film coating,</td>
<td>111,112, 113</td>
</tr>
<tr>
<td>Material</td>
<td>Modification</td>
<td>Application</td>
<td>Page</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>Tamarind powder</td>
<td>Chemical modification of tamarind powder using epichlorohydrin</td>
<td>Sustained release formulation, rectal drug delivery</td>
<td>114</td>
</tr>
<tr>
<td></td>
<td>and partial degradation of β-galactosidase for rectal drug delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psyllium</td>
<td>Chemical modification of psyllium was carried out to form N-hydroxymethyl</td>
<td>N-hydroxymethylacrylamide based hydrogels, oral insulin drug delivery</td>
<td>115,116</td>
</tr>
<tr>
<td></td>
<td>1 acrylamide based hydrogels, chemical modification with tartaric acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Okra fruits (pods) of</td>
<td>Chemical modification with acrylamide synthesis</td>
<td>Controlled drug delivery</td>
<td>117</td>
</tr>
<tr>
<td>Hibiscus esculentus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipomoea</td>
<td>Chemical modification of ipomoea with poly(acrylonitrile) grafted drug</td>
<td>Poly(acrylonitrile) grafted drug delivery</td>
<td>118</td>
</tr>
<tr>
<td>dasysperma,</td>
<td>delivery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ipomoea hederacea,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>and Ipomoea palmata</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pectins</td>
<td>Chemical modification of pectin with acetyl chloride in ethanol for</td>
<td>Modified drug delivery.</td>
<td>119</td>
</tr>
<tr>
<td></td>
<td>modified drug delivery, chemical modification with ethanolamine for</td>
<td>hydrogels, colonic drug delivery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>hydrogels and chemical modification of pectin for colonic drug delivery.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion**

Natural gums are promising biodegradable polymeric materials. Many studies have been carried out in fields including food technology and pharmaceuticals using gums and mucilages. It is clear that gums and mucilages have many advantages over synthetic materials. Various applications of gums and mucilages 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 systems.

**References**


