

Application of natural gum as a binder in modern drug delivery

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Introduction

A very nice gift has been presented by the Mother Nature to us that a broad range of materials helps to improve and preserve the health of all living things either directly or indirectly. For centuries, man has made efficient use of materials of natural source in the medical and pharmaceutical field. Today, the whole world is increasingly paying attention 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.¹ Natural gums and mucilages are naturally occurring components in plants, which are essentially cheap and plentiful, are widely employed as natural excipients for conventional and novel dosage forms and shows potential to be biodegradable polymeric materials. With the increasing interest in polymers of natural origin, the pharmaceutical world has compliance to utilize most of them in the formulations. In recent years, there has been a incredible growth in natural products, which are essential to be used for a variety of purposes.² Many studies has been conducted in the fields including food technology and pharmaceuticals using gums and mucilages. The predictable use of excipients in drug formulations was to act as inert vehicles to provide the required weight, consistency and volume for the correct administration of the active ingredient, but in modern pharmaceutical dosage forms they often fulfil multi-functional roles such as modifying release, enhancement of the stability and bioavailability of the active ingredient, upgrading of patient acceptability and ensure simplicity of manufacture. A large number of plant-based pharmaceutical excipients are available today. Several researchers have explored the usefulness of plant-based materials as pharmaceutical excipients like binder, disintegrating agent, emulsifying agent etc. Capability to produce a wide range of material based on their properties and molecular weight, natural polymers became a thrust area in majority of investigations in drug delivery systems. Natural gums and mucilages can also be modified to meet the requirements of drug delivery systems and thus can compete with the synthetic excipients available in the market.³ The aim of this article is to highlight the natural gums and mucilages as natural binding agent in various pharmaceutical dosage form.

Binding agent

Binding agent or binders are employed to convey the cohesiveness to the granules. Binders are added to the tablet formulation to impart plasticity as well as increases inter-particulate bonding strength in the tablet that ensure the tablet remains intact after compression. To hold various powders together to form a tablet, binder is added either in dry mix or mix in granulating liquid and form matrix with fillers and drug embedded in it. On drying solid binder forms glue which holds the particles together, the wet binder is the most important ingredient

Kiranmoy Karmakar

Bachelor of Pharmacy, West Bengal University of Technology, India

Correspondence: Kiranmoy Karmakar, Bachelor of Pharmacy, West Bengal University of Technology, West Bengal, India, Email Kiranmoy2@gmail.com

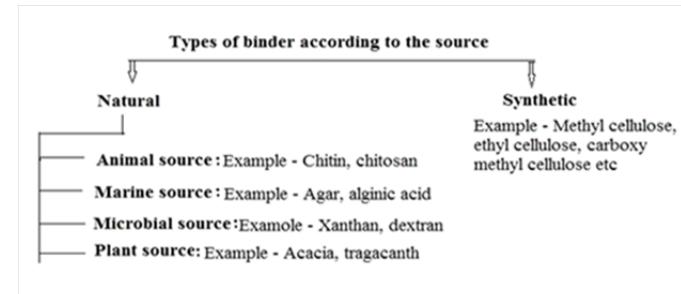
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in the wet granulation process, most binders are hydrophilic & most times soluble in water. Different starches like rice, potato, maize, corn, wheat, tapioca starch and gums like ferula gummosa boiss, gum olibanum, beilschmiedia seed gum, okra gum, aegle marmelod gum, gum cordial, okra gum and cassia roxburghii seeds gum and plant fruit like date palm fruit and orange peel pectin shows good potency as a natural binding agent. They also holds some other properties like filler, disintegrant, thickening agent and are safe and economical than synthetic polymers like PVP.

The researchers are trying to the new excipients for potential use as binding agent in tablet formulations continue to the interest. This is because different binding agents can be useful in achieving tablets with different mechanical strength and drug release properties for different pharmaceutical purpose. The choice of a suitable binder for a tablet formulation have need of extensive knowledge of the relative importance of binder properties for enhancing the strength of the tablet and also of the interactions between the various materials constituting a tablet.⁴

Types of binder

a. Classification on the basis of their resource



b. Classification on the basis of their function

Types of binder according to their function	
Solution binder	Dry binder
<p>This are dissolved in a suitable solvent (for example water or alcohol can be used in wet granulation processes).</p> <p>Examples - Gelatine, cellulose, cellulose derivatives, polyvinyl pyrrolidine, starch, sucrose and polyethylene glycol.</p>	<p>This are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula.</p> <p>Example - cellulose, methyl cellulose, polyvinyl pyrrolidine, and polyethylene glycol.</p>

According to De silva and Anderson (1995), binders can be grouped in three different classes

- Binders of protein origin (for example : Chitin and chitosan).
- Binders of carbohydrate origin (for example : Heta starch ,Potato starch).
- Binders with no nutritional assessment (for example : Cordia gum, Bhara gum).⁵⁻²⁰

Advantages of natural binder

- They can be used to variation of the drug release and thereby influences the absorption and bioavailability of the integrated drugs.
- Natural binders are broadly used in the pharmaceutical and food industry as excipients and additives due to their low toxicity, biodegradable, accessibility and inexpensive.
- They act as vehicles which convey the integrated drug to the absorption site and are expected to swear the stability of the incorporated drug, the precision and accuracy of the dosage, and also improve the organoleptic properties of the drugs where required in order to enhance patient loyalty.
- They should optimize the performances of dosage forms during manufacturing as well as when patients consume them.

Disadvantages of polymer binders

- Polymers binder can lead to processing problems such as rapid over granulation, tablet hardness increases & dissolution concert diminish.
- In case of polymer binders, addition of strong disintegrates usually required but these are huge expensive and have a negative effect on product stability.

Gum and mucilage

A fundamental consideration about gum is as the pathological products and can be produced into three distinct ways. A major point of view is the gummosis i.e. internal tissue disintegration of the plant. Secondly, formation of deep injury or cavity over the bark or stem leads to the creation of gum, and third is the bacteria or fungi attack.²¹⁻³⁵

In case of the mucilage, these leads to the intercellular formation caused by normal product of metabolism and produced without injury to the plant.

When both of this two (gum and mucilage) are allows to be mixed with water, gum gets readily dissolved where as mucilage forms a

slimy mass. This is the most common difference between gum and mucilage by which one can easily identified the sample.

Though gum and mucilage differs in their source of production and water solubility, they have some similarities also and they are as follows:

- Both are plant hydrocolloids
- Translucent amorphous substance
- Insoluble in oils or organic solvents such as ether, alcohol etc.
- Contains hydrophilic molecules that combines with water to form viscous solutions or gels
- Polymer of a monosaccharide or mixed monosaccharide
- On hydrolysis, they yields arabinose, galactose, mannose and glucouronic acid.³⁵⁻⁶⁰

Classification of natural gum and mucilage

Gums are present in elevated quantities in varieties of plants, animals, seaweeds, fungi and other microbial sources, where they act upon a number of structural and metabolic functions; plant sources make available the largest amounts. The different available Gums can be classified as follows:

According to the source

- Animal source: chitosan and chitin, chondroitin sulphate.
- Marine source: Agar, alginic acid, laminarin
- Microbial source(bacterial & fungal): Xanthan, dextran
- Plant source: Shrubs/tree exudates – example : gum Arabic, gum ghatti etc.

Seed gums – example : guar gum, locurt gum etc.
Extracts – example : pectin, larch gum etc.
Tuber and roots - example: potato starch etc.

According to the shape

- Linear : Example - Amylose, cellulose, pectin
- Branched : Short branch – Example - Xylan, xanthan
- Branch on branch – Example - Amylopectin, gum arabic

According to the charge

- Non-ionic: Example – Guar gum, xanthan gum, dextrin
- Anionic: Example – Alginic acid, pectin, karaya gum
- Cationic: Example – Chitosan, chitin, cationic guar gum
- Amphoteric: Example – Carboxymethyl chitosan, N-Hydroxyldicarboxyethyl chitosan
- Hydrophobic: Example – Cetylhydroxyethyl cellulose, polyquaternium

According to the monomeric units present in chemical structure

- Homoglycan: Example – Amylose, arabinose, cellulose
- Diheteroglycan: Example – Algin, carragenans, galactomannans
- Triheteroglycans: Example – Arabino xylans, gellan gum, xanthan gum

- d. Tetrahetero glycans: Example – Gum arabic, psyllium seed gum
- e. Pentahetero glycans: Example – Gum ghatti, gum tragacanth

According to the preparation

- a. Semi synthetic :

Starch derivative – Example: Starch acetate, starch phosphate
Cellulose derivative – Example: Carboxymethyl cellulose, HPMC

- b. Synthetic: Example – Dextrin, scleroglucan

Disadvantages of synthetic polymer

Though the utility of synthetic polymers are increasing day by day, these shows certain disadvantages. These are as follows:

- a. The synthetic polymers are non recyclable, creates environmental pollution during synthesis, very high in cost, produces side effects and poor patient compliance.
- b. Certain processing difficulties can be created by the Polymer binder such as rapid over granulation, increase in tablet hardness and decrease in dissolution performance.
- c. Additions of strong disintegrating agent are needed with polymer binder which is very expensive and have a negative outcome on product stability.
- d. Studies in rats have shown that 5% polyvinyl alcohol aqueous solution when given in subcutaneous injection produces anaemia and can infiltrate various organs and tissues.
- e. Acute and chronic adverse effects (eye and skin irritation) have been observed in workers handling the related substances like methyl methacrylate and poly methyl methacrylate.
- f. An adverse reaction of povidone has been reported that the formation of granulomas at the site of injection when administered subcutaneously.⁶¹⁻⁶⁶

Advantage of natural gum and mucilage

In comparison to the synthetic polymer, natural polymer (gum and mucilage) posses a lot of advantages and these are as follows:

- a. **Biodegradable:** Biodegradable polymers that are widely available in nature are produced by all living organisms. They are from recyclable sources and have no side effects on human health.
- b. **Local availability:** In most of the developing countries, the production of plant such as tragacanth and guar gum are promoted by the government. This is because the application of this material increases day by day in various industries.
- c. **Low cost:** As these are widely distributed and available in nature, the production cost is less as compare to the synthetic one.
- d. **Biocompatible and nontoxic:** As nearly all the gum and mucilages that are obtained from plant resources, are composed of repeating monosaccharide units and are carbohydrates. Hence they are nontoxic and biocompatible.
- e. **Eco-friendly processing:** As the collection of the gum taking place seasonally from different sources and ease of production procedure, hence they are ecofriendly.
- f. **Patient tolerance:** These produces better patient tolerance as well as public acceptance because of their production from

natural source and less side effect as compare to the synthetic polymer.

Some drawbacks of natural gum and mucilage's

- a. 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.
- b. 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 .
- 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.
- d. Alteration in viscosity-When gums are gets in touch with water, the viscosity of the formulations is found to be greater than before. 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.
- e. Potential antigenicity- The nanospheres made up of heat denatured natural polymers can cause anaphylactic shock (Figure 1).

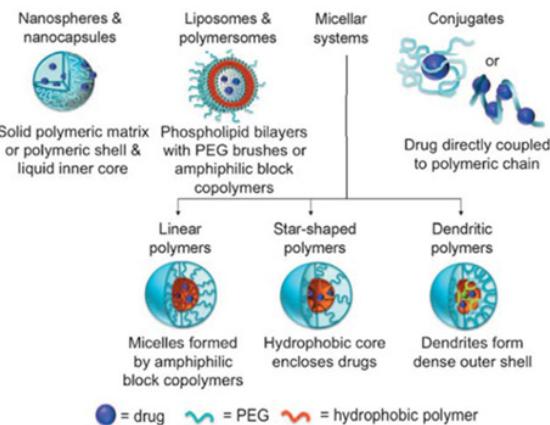


Figure 1 Mechanism of action of binder (Natural and Synthetic).

Natural gum and mucilage as binder

Most of the natural polymer (gum and mucilage) are formed by high molecular weight carbohydrates. They are biodegradable, biocompatible and non-hazardous polymers showing irregular physical-chemical properties and environmentally sustainable features. Carbohydrates represent the most abundant biological molecules, covering a large array of fundamental roles in living things: from the reserve and transport of energy, (starch and glycogen), to the development of structural components (cellulose in plants, chitin in animals), to the linking between intercellular walls (hemicellulose). The high molecular weight carbohydrates derived, are known as polysaccharides. They may be viewed as condensation polymers in which carbohydrates have been joined together by glycosidic linkage with the elimination of molecules of water.



The different macromolecular structures and chemical compositions of polysaccharides are responsible for the large array of their physical and biochemical applications. A wide range of polysaccharides, such as agar, alginic, chitin and pectin are able to hydrate in cold and hot

water, thus giving rise to both viscous solutions or dispersions and gels. The great interest with these polysaccharides in aquatic animal feed is strictly related to their gelling properties (Figure 2) (Table 1).

Table 1 Some common gum and mucilages and their application in pharmacy

Gum and mucilage	Botanical source	Family	Application in pharmacy	Reference
Almond gum	<i>Prunus communis</i>	Rosaceae	Suspending agent Thickening agent Stabilizer	37
Gum moringa	<i>Moringa olifera</i>	Moringaceae	Disintegrating agent	15
Okra mucilage	<i>Abelmoschus esculentus</i>	Malvaceae	Suspending agent Disintegrating agent	14,18,54
Aegle gum	<i>Aegle marmelos</i>	Rutaceae	Binder Thickening agent	20
Gum acacia	<i>Acacia catechu</i>	Leguminosae	Suspending agent Antioxidant Astringent	21
Tamarind gum	<i>Tamarindus indica</i>	Fabaceae	Gelling agent, Stabilizer, Binder	23
Prunus gum	<i>Prunus domestica</i>	Rosaceae	Binder, tonic	24
Gum ferula	<i>Ferula gummosa</i>	Apiaceae	Binder	27
Cassia roxburghii mucilage	<i>Cassia roxburghii</i>	Fabaceae	Binder Thickening agent	26, 31
Fenugreek mucilage	<i>Trigonella foenum-graenum</i>	Leguminosae	Solubilizing agent Binder	32
Brachystegia mucilage	<i>Brachystegia eurycoma</i>	Leguminosae-caesalpinoideae	Emulsifying agent Stabilizer Thickening agent	35
Ayoyo gum	<i>Cochorus olitorius</i>	Tiliaceae	Emulsifying agent Thickening agent Binder	42
Gum kondagogu	<i>Cochlospermum gossypium</i>	Bixaceae	Thickening agent Emulsifying agent	47
Cordia gum	<i>Cordia obliqua</i>	Boraginaceae	Binder Stabilizer	66
Gum odina	<i>Odina wodier</i>	Anacardiaceae	Binder Stabilizer	48
Cassia tora mucilage	<i>Cassia tora</i>	Caesalpiniaceae	Binder Disintegrating agent	60
Cassia fistula	<i>Cassia fistula</i>	Caesalpiniaceae	Granulating agent Binder	65

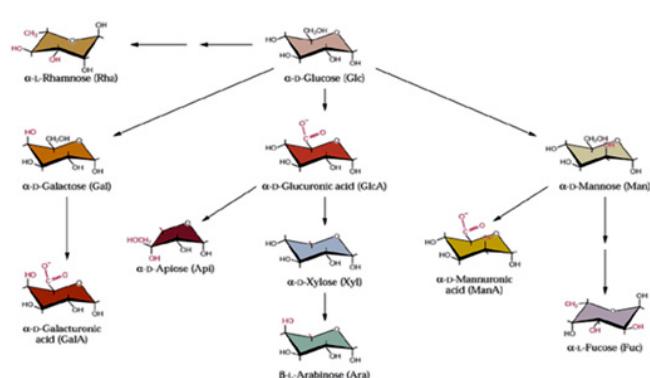


Figure 2 Natural gum and mucilage as binder.

Conclusion

There are great numbers of natural substances have been used in pharmaceutical preparations. Natural substances like gums, mucilage's, and also dried fruits can be used as binding agent. They have been shown good potential as binding agent as well as they hold some other properties like fillers, disintegrating agent, sustain releasing agent. Natural gums and mucilages exposed good binding property in wet granulation for the manufacturing of tablets; granules are stable and less friable in contrast with other binders. Natural binders are non-polluting renewable resources for sustainable supply of cheaper pharmaceutical excipients or product. Various applications of gums and mucilage's 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 resources for the formulation of novel drug delivery systems, biotechnological applications and other delivery systems.

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Conflicts of interest

The authors declare no conflict of interest.

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