Use Of Natural Polymers Over Synthetic Polymers In Tablet Formulations: A Review

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ABSTRACT

The oral route is the most popular route of administration for numerous drugs because it is considered as the safest, most preferred and less economical. Active ingredients and excipients are the two main ingredients of any pharmaceutical formulation. Excipients help in the manufacturing of dosage form as well as improve physicochemical parameters of the dosage form. Polymers play a vital role in any dosage form as excipients. Polymers are utilized in drug delivery to provide weight, consistency and besides, they are multi-functional providing stability, drug release, targeting, enhanced bioavailability, and patient acceptability. A polymer is a large molecule (macromolecules) composed of repeating structural units. These subunits are typically connected by covalent chemical bonds. They are broadly classified into three categories viz. natural polymers, semi-synthetic and synthetic polymers. Natural polymers are more advantageous than synthetic polymers as they are economical, non-toxic and abundantly available in nature. Natural polymers can be used to formulate dosage forms where the drug is designed to release a pre-determined rate. They can be widely used in pharmaceutical dosage forms as binders, matrix formers or drug release modifiers, film coating formers, thickeners or viscosity enhancers, stabilizers, disintegrants, solubilizers, emulsifiers, suspending agents, gelling agents, and bioadhesives.

KEYWORDS: Natural polymers, oral dosage form, excipients, cost-effective.

INTRODUCTION

Polymers are a large class of high molecular weight compounds consisting of many small molecules (called monomers) that can be linked together to form long chains. Thus, they are known as macromolecules. A typical polymer may include tens of thousands of monomers[1,2]. In Greek, the word poly means 'many' and meros means 'units or parts'. They consist of different functional groups[3,4]. Natural polymers are materials of large molecular weights from natural origins such as plants, micro-organisms, and animals. In comparison to synthetic, natural polymers remain attractive primarily because they are inexpensive, readily available, capable of a multitude of chemical modifications and potentially biodegradable and compatible due to their origin. Natural polymers possess ample scope in drug, food and cosmetic industries. Natural polymers are biogenic and their biological properties such as cell recognition and interactions, enzymatic degradability, semblance to the extracellular matrix and their chemical flexibility make them materials of choice for drug delivery. Natural polymers are used in pharmaceutical formulations in the manufacture of solid monolithic matrix systems, implants, films, beads, microparticles, nanoparticles, and injectable systems as well as viscous liquid formulations. Within these dosage forms, polymeric materials are widely used as binders, matrix formers or drug release modifiers, film coating formers, thickeners or viscosity enhancers, stabilizers, disintegrants, solubilizers, emulsifiers, suspending agents, gelling agents, and bioadhesives[2,5].

CLASSIFICATION OF POLYMERS

Polymers can be classified as:

1. Natural polymers
2. Synthetic polymers
3. Semi-synthetic polymers

Natural polymers: These polymers are found in nature generally from plants and animal sources. Such as proteins, cellulose, starch, resins, etc.

Semi-synthetic polymers: These polymers are obtained from natural polymers by simple chemical treatment to change the physical properties of natural polymers like silicones, vulcanized rubber, cellulose acetate (rayon), etc.

Synthetic polymers: The fibers which are synthesized in the laboratory by polymerization of simple chemical molecules are called synthetic polymers. Synthetic polymers such as Nylon, polyethylene, polystyrene, synthetic rubber, PVC, Teflon, polyamides, etc.

CHARACTERISTICS OF AN IDEAL PHARMACEUTICAL EXCIPIENTS [6]

Pharmaceutical excipient should have certain characteristics. Natural polymeric substances should have to fulfill these characteristics to be successful as a pharmaceutical excipient.
These are as follows:

1. Pharmacologically inert but pharmaceutically active.
2. Nontoxic and non-irritant.
3. No interaction with drugs or with other substances present in the formulation and packaging.
4. Cost-effective and readily available.
5. Ease of handling.
6. Feasible.

ADVANTAGES OF NATURAL POLYMERS [7,8]

i. **Biodegradable**: Biodegradable as they are naturally available, and they are produced by all living organisms.
ii. **Biocompatible and non-toxic**: Basically, all of these plant materials are reiterating sugar polysaccharides.
iii. **Low cost:** They are cheaper to utilize as natural sources. The production cost is less compared with synthetic material. India and many other developing countries are dependent on agriculture, and there are substantial amounts of money invested in agriculture.
iv. **Environmental-friendly processing:** There are many types of natural compounds obtained from different plant sources that are widely utilized in the pharmaceutical industry and collected in immensely large quantities due to the simple production processes involved.
v. **Local availability (especially in developing countries):** In India and homogeneous developing countries, there is a promotion for the production of plants as pharmaceutical excipients being done by government, and it withal provides the facilities for bulk production, like gum and mucilages because of their wide applications in industries.
vi. **Patient tolerance as well as public acceptance:** There is less chance of side and adverse effects with natural materials compared with a synthetic one.

DISADVANTAGES OF NATURAL POLYMERS

i. **Microbial contamination**: During production, they are exposed to an external environment and hence, there are chances of microbial contamination. [3,6,8]
ii. **Batch to batch variation**: Synthetic manufacturing is a controlled procedure with fixed quantities of ingredients while the production of natural polymers is dependent on the environment and various physical factors. [6,9,10]
iii. **The 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. [3,8]
iv. **Heavy metal contamination:** There are chances of Heavy metal contamination often associated with herbal excipients. (8,10,11)

NATURAL POLYMERS USED AS PHARMACEUTICAL EXCIPIENT

1. Chitin and Chitosan

Chitin (β-(1→4)-N-acetyl-D-glucosamine) is a natural polysaccharide obtained from crab and shrimp shells. It possesses an amino group covalently linked to the acetyl group as compared to the liberate amino group in chitosan. Chitosan is produced commercially by deacetylation of chitin, which is the structural element in the exoskeleton of crustaceans (such as crabs and shrimp) and cell walls of fungi. Chitosan and their derivatives (N-trimethyl chitosan, mono-N-carboxymethyl chitosan) are safe and effective absorption enhancers to improve mucosal, nasal, peroral drug delivery of hydrophilic macromolecules such as peptide and protein drugs and heparins. Chitosan nanoparticles and microparticles are also suitable for controlled drug release. [7,8,13,17]

Fig.1: chitosan

2. Guar Gum

Guar gum is also called guaran, cluster bean, Calcutta lucern, Gum Cyamopsis, and Cyamopsis gum, Guarina, Glucotard, and Guyarem. Guar gum is the powder of the endosperm of the seeds of *Cyamopsistetragonolobus Linn.* (Leguminosae).Chemically, guar gum is a polysaccharide composed of the sugars galactose and mannose. The backbone is a linear chain of 1, 4-linked mannose residues to which galactose residues are 1, 6-linked at every second mannose, forming short side branches. Guar gum is more soluble than locust bean gum and is a better emulsifier as it has more galactose branch points. It degrades at extremes of pH and temperature (e.g. pH 3 at 50°C). It remains stable in solution over pH range 5-7. It is utilized as a thickener, stabilizer, and emulsifier. The bioadhesive and biodegradable property of guar gum make it the first choice for developing controlled and targeting drug delivery systems for the colon. Guar gum and its derivatives are used as a binder and disintegrate in tablets to add cohesiveness to drug powder. Guar gum is also used as a controlled release agent for the drug due to the high hydration rate. [2,3,8,7]

Fig.2: guar gum

3. Agar and treated agar

Agar or agar-agar is the dried gelatinous substance obtained from *Gelidium amansii* (Gelidaceae) and several other species of red algae like *Grailaria* (Gracilariaceae) and Pterocladia (Gelidaceae). Agar consists of a mixture of agarose and agaropectin. The agarose is a linear polymer that is made up of the repeating monomeric unit of agarobiose. Whereas, Agarobiose is a disaccharide made up of D-galactose and 3, 6 - anhydro-L-galactopyranose. Agaropectin is a heterogeneous mixture of smaller acidic molecules. Agar is used as Suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricant, tablet disintegrants, medium for bacterial culture, laxative. High gel vigor of agar makes it a potential candidate as a disintegrant. [2,3,14]

fig.3: agar

4. Fenugreek seed mucilage

Trigonella foenum-graceum commonly kenned as fenugreek is an herbaceous plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Like other mucilage- containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids. Hence, the study revealed that this natural disintegrant (fenugreek mucilage) showed more preponderant disintegrating property than the most widely used synthetic super-disintegrants like Ac-di-sol in the tablet formulations. (7,15)

Fig.4: fenugreek seed gum

5. Soy polysaccharide

It is a natural super disintegrant that does not contain any starch or sugar so it can be utilized in nutritional products. Halakatti et al. 2010 evaluated soy polysaccharide (a group of high molecular weight polysaccharides obtained from soybeans) as a disintegrant in tablets made by direct compression utilizing lactose and dicalcium phosphate dihydrate as fillers. (16) A cross-linked sodium carboxymethyl cellulose and corn starch were utilized as control disintegrants. Soy polysaccharide performs well as a disintegrating agent in direct compression formulations with results paralleling those of cross-linked CMC. (3,7,17,18)

Fig.5: soy polysaccharide

6. Locust bean gum

It is known as carob bean gum. It is a galactomannan vegetable gum extracted from the seeds of the carob tree (Ceretoniasiliqual) found in the Mediterranean region. Locust bean gum is utilized as a gelling and thickening agent in the food industry and utilized as a bioadhesive, and it enhances the solubility. The gum is a white to yellowish-white, odorless powder. It is insoluble in most organic solvents including ethanol. It is partially soluble in water at ambient temperature and soluble in hot water and needs heating to above 850 for 10 min for complete solubility. Locust bean gum consists of mannose and galactose sugar units at a ratio of 4:1. (7,8,19) fig.6: locust bean gum

7. Mangifera indica gum (MIG)

Mangifera indica is mango, and it belongs to the Anacardiaceae family. It is nontoxic and utilized as a disintegrant, binder, suspending agent, and emulsifying agent in different formulations. The gum powder is white to off white, and the powder was soluble in water and virtually insoluble in acetone chloroform, ether, methanol, and ethanol. It is facilely available, and gum is devoid of toxicity, and each component of the tree has pharmacological activity like diuretic, astringent, diabetes, asthma, diarrhea, urethritis, and scabies. (7,20)

Fig.7: mangifera indica gum

8. Plantago ovata seed mucilage

Psyllium or *ispaghula* is the prevalent name utilized for several members of the plant genus Plantago Mucilage of *Plantago ovata* has different characteristics like binding, disintegrating, and sustaining properties. It is used as an enteric coating material, tablet disintegrator and also used in sustained release drug formulations.(2,7,23) Psyllium husk was used in combination with other excipients such as hydroxypropyl methylcellulose to prepare a novel sustained release, swellable and bioadhesive gastro retentive drug delivery systems for ofloxacin. (3,21,22)

fig.8: plantago ovata seed mucilage

9. Starches

It is the principal form of carbohydrate reserve in green plants and especially present in seeds and underground organs. Starch occurs in the form of granules (starch grains), the shape and size of which are characteristic of the species, as is also the ratio of the content of the principal constituents, amylose, and amylopectin. Several starches are recognized for pharmaceutical use. These include maize (*Zea mays*), rice (*Oryza sativa*), wheat (*Triticum aestivum*), and potato (*Solanum tuberosum*). To deliver proteins or peptidic drugs orally, microcapsules containing a protein and a proteinase inhibitor were prepared. It is used as a binder, granulating agent, compression aids, etc. (3,12,21)

fig.9: starch

10. Alginates

Alginates are natural polysaccharide polymers isolated from the brown seaweed (Phaeophyceae) and marine algae such as *Laminariahyperborea*, *Ascophyllum nodosum, and Macrocystispyrifera*. They are hydrophilic, non-toxic, biodegradable, a linear polymer consisting of 1-4' linked-ß-D-mannuronic acid and β-L-glucuronic acid residues arranged as blocks of either type of unit or as a random sharing of each type. It is practically insoluble in ethanol (95%), ether, chloroform and slowly soluble in water, forming viscous colloidal solution. The gelling properties of alginate are used to prepare matrices, films, beads, pellets, microparticles, and nanoparticles. [2,3,8,24]

Fig.10: sodium alginate

11. Aegle Marmelos Gum (AMG)

It is obtained from the fruits of Aegle marmelos belongs to the category of super disintegrant than the croscarmellose sodium. The ripened fruit pulp is red in color with mucilaginous and astringent taste. The pulp contains carbohydrates, proteins, vitamin C, vitamin A, angelenine, marmeline, dictamine, O-methyl fordinol and isopentyl halfordinol. AMG is prepared by heat treatment technique. It increases the solubility of poorly soluble drugs. It increases glucose level and glycosylated hemoglobin in diabetic patients, decreases plasma insulin and liver glycogen in diabetic patient, decreases lipid peroxidation, stimulates macrophage functioning, and causes significant deviation in the GSH (glutathione) concentration in liver, kidney, stomach, and intestine. Purified, bael gum polysaccharide contains D-galactose (71%), D- galacturonic acid (7%), L-Rhamnose (6.5%), and L-arabinose (12.5%) [7,25] .

Fig.11: aegle marmelos gum (AMG)

12. Dehydrated Banana Powder (DBP)

Banana is additionally called plantain. DBP is yare from the variety of banana called Ethan and nenthran (nenthra vazha) and belongs to the family Musaceae. It contains vitamin A, so it is utilized in the treatment of gastric ulcer and diarrhea. It withal contains vitamin B6, which available in reducing the stress and solicitousness. It is a very good source of energy due to high carbohydrate content, and it contains potassium, which is responsible for more preponderant brain functioning. It is utilized as binder, diluent, and super disintegrant increase the solubility of poorly water soluble drug, decrease the disintegration time, and provide nutritional supplement. [7,26] .

Fig.12: dehydrated banana powder (DBP)

13. Pectin

Pectins are non-starch, linear polysaccharides present in the walls that surround growing and dividing plant cells. Pectin is widely found in plant tissues where it serves, in combination with cellulose, as intercellular structural substance (membranes, middle lamellae). It is soluble in water, insoluble in ethanol (95%) and other organic solvents. Pectin has been investigated as an excipient in many different types of dosage forms such as film coating of colon-specific drug delivery systems when mixed with ethyl cellulose, microparticulate delivery systems for ophthalmic preparations and matrix type transdermal patches. It has high potential as a hydrophilic polymeric material for controlled release matrix drug delivery systems, but its aqueous solubility contributes to premature and fast release of the drug from these matrices. Pectin hydrogels can be used as a binder in tablet formulations. [2,8,27,28]

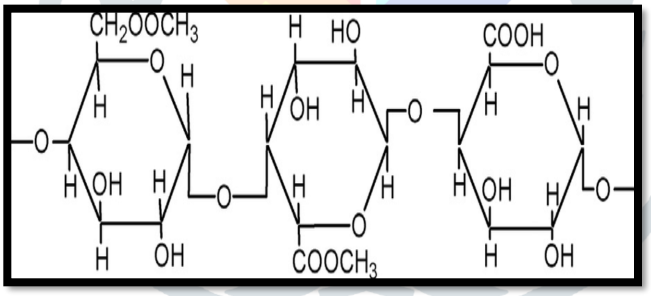

fig.13: chemical structure of pectin

Fig.14: pectin powder

14. Tamarind Gum

Tamarind xyloglucan is obtained from the endosperm of the seed of the tamarind tree, *Tamarindus indica*, a member of the evergreen family. Tamarind Gum, also known as Tamarind Kernel Powder (TKP) is extracted from the seeds. Tamarind gum is a polysaccharide composed of glucosyl : xylosyl : galactosyl in the ratio of 3:2:1 . Xyloglucan is a major structural polysaccharide in the primary cell walls of higher plants. Tamarind gum is Non-Newtonian and yield higher viscosities than most starches at equivalent concentrations. This has led to its application as stabilizer, thickener, gelling agent and binder in food and pharmaceutical industries. Other important properties of tamarind seed polysaccharide (TSP) have been identified recently. They include non-carcinogenicity, mucoadhesivity, biocompatibility, high drug holding capacity and high thermal stability. This has led to its application as excipient in hydrophilic drug delivery system. [36,37,38]

Fig.15: tamarind gum

15. Hibiscus Mucilage

The mucilage is extracted from the fresh leaves of *Hibiscus rosasinensis. Hibiscus rosasinensis*, belongs to Malvaceae family and commonly known as China rose. The dried Hibiscus rosa-sinensis leaves mucilage can be used as a matrix forming material for preparing sustained release matrix tablets. Mucilages are also utilized as thickeners, suspending agent, water retention agent, and disintegrants. [7, 16, 37, 39]

Fig.16: hibiscus mucilage

NATURAL POLYMERS AND ITS PHARMACEUTICAL APPLICATIONS

TABLE.1: A list of natural polymers approved by the FDA and its pharmaceutical applications are given below:

S.I	Natural polymers	Pharmaceutical applications
1	Pectin	Colon specific drug delivery, controlled release drug delivery, patch, and transdermal drug delivery, nanoparticle drug formulation. [2,6,27,28]
2	Cellulose	Binder, filler, diluents, thickening, and viscosity imparting agent, compressibility enhancer [29]
3	Hemi-cellulose	The stabilizer of the gel phase of tablet and release modifier [6,28]
4	Carrageenan	Gelling agent, stabilizer, demulcent, laxative [2,6,31]
5	Xanthan gum	Suspending agent, emulsifier, stabilizer, sustained release agent, pellets [2,3,8,32]
6	Grewia gum	Binder, tablet property enhancer, improved drug release [31,34]
7	Okra gum	Binder, suspending agent, control release, sustained release, film coating and bio-adhesive material [6,35,40]
8	Irvingiagabonensis	Binder, emulsifier, suspending agent [6,40]

9	Hakeagibbosa gum	Mucoadhesive, sustained-release property [6,40]
10	Gum ghatti	Binder, emulsifier, suspending agent [3,6,8]
11	Rosin	Microencapsulation, film former, coating material, sustained-release property, nanoparticle drug Delivery [3,6,8]
12	Cassia toragum	Binding agent [6,8]
13	Leucaena seed gum	Emulsifier, suspending agent, binder, disintegrating agent [6]
14	Albizia gum	Binder [6]
15	Mimosa pudica	Binder, disintegrating agent [6]

CONCLUSION

Polymers play a vital role in the design of various dosage forms. The natural polymers can be modified to meet the requirements of drug delivery systems. Apart from being used in conventional dosage forms, natural polymers have a wide range of applications in the design of novel drug delivery systems like gastro retentive dosage forms, bioadhesive systems, and microcapsules. There is a huge scope for research on new natural polymers obtained from plants and could be further exploited in the future as a novel natural polymer for the development of different drug delivery systems in the pharma industry.

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