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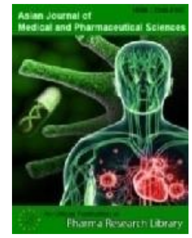

Review Article Open Access

A Novel Review on Natural Polymers used in Formulation of Pharmaceutical Dosage Forms

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A B S T R A C T

All pharmaceutical dosage forms contain many additives besides the active ingredients to assist manufacturing and to obtain the desired effect to the pharmaceutical active ingredients. The advances in drug delivery have simultaneously urged the discovery of novel excipients which are safe and fulfil specific functions and directly or indirectly influence the rate and extent of release and or absorption. Earlier used natural excipients are carrageenan, thaumatin, lard, shilajit, aerosil, myrobalan and storax. Use of these natural excipients to deliver the bioactive agents has been hampered by the synthetic materials. Excipients are any component other than the active substances intentionally added to formulation of a dosage form. Novel drug delivery systems are developed to address the challenges of drug development such as bioavailability, permeability, and poor solubility. This review discusses about the majority of these plant-derived polymeric compounds, their sources extraction procedure, chemical constituents, uses and so delivery system recent investigations.

Keywords: Plants, gums, mucilage, Natural Polymeric materials, Pharmaceutical excipients, Biodegradable

A R T I C L E I N F O

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1. Introduction

Drugs are hardly administered as such but are almost always formulated into a suitable dosage form with the aid of excipients, which serve various functions such as binding, lubricating, gelling, suspending, flavoring, sweetening and bulking agent among others. The International Pharmaceutical Excipients Council defines excipients as substances, other than the active drug substances of finished dosage form, which have been appropriately evaluated for safety and are included in a drug delivery system to either aid the processing of the drug delivery system during its manufacture; protect, support or enhance stability, bioavailability, or patient acceptability; assist in product identification; or enhance any other attributes of the overall safety and effectiveness of the drug delivery system during storage or use . Excipients play a critical role in the creation of medicines, helping to preserve the efficacy, safety, and stability of active pharmaceutical ingredients (APIs) and ensuring that they deliver their promised benefits to the patients. Optimal use of excipients can provide pharmaceutical manufacturers with cost-savings in drug development, enhanced functionality and help in drug formulations innovation.

What Is a Polymer

Have you ever ridden a bicycle or even a motorcycle? An essential part of the bike is the chain, which drives the back wheel. Chains are widely used in machinery and even jewellery, such as a bracelet or necklace. All chains share in common a structure made of links. These links are repeated units with similar or identical structure joined in some way. Think of a long train with many similar cars. Linked chains are also important in chemistry. A polymer is a chain of repeated units. The word comes from the Greek, polu meaning 'many' and meros meaning 'share.' The units that make up polymers are called monomers. The unit of most natural polymers is typically an 'organic molecule', therefore containing carbon - the stuff you, me and all living things are made of.

2. Types of Polymers

Polymers form by the process of polymerization, where monomers link together to form the chain, like linking pearls on a string. Polymerization usually occurs only in the presence of a catalyst. The units of polymers can be simple or complex. The length of a polymer chain can be long or short. Chemists recognize two main categories of polymers, addition polymers and condensation polymers. Addition polymerization happens because of an addition reaction where monomers bond together without losing any atoms. This happens with monomers that have double bonds, typically unsaturated carbon molecules. (A saturated compound only has single bonds.) During the reaction, the double bonds open, allowing the monomers to form a long continuous chain. The chemical industry uses addition polymerization widely for creating synthetic polymers, many of which are not biodegradable. Condensation polymerization occurs when monomers join together but lose some molecules as by-products. This happens when monomers react that have two functional groups, or a distinct group of atoms within a molecule. The molecule lost is often water, which will condense if conditions are right - hence the name.

What Polymers Occur Naturally

Most of the structures of living things are comprised of natural polymers. There are three main types. One, polynucleotides, which are chains of nucleotides. Two, polyamides, which are chains of proteins. And three, polysaccharides, which are chains of sugars. You probably already know at least one naturally-occurring polymer: DNA, or deoxyribonucleic acid. You wouldn't be here without it! The DNA molecule is made of monomers called nucleotides. The monomers are linked by a condensation reaction so that many nucleotides are linked in a chain to make the DNA polymer molecule, which is why it's called a polynucleotides.

3. Natural Polymeric Materials

Cellulose: In higher plants, cellulose is an essential structural component and represents the most abundant organic polymer. Cellulose is a linear unbranched polysaccharide consisting of β-1, 4-linked D-glucose units and many parallel cellulose molecules which form crystalline micro fibrils. The crystalline micro fibrils are mechanically strong and highly resistant to enzymatic attack and are aligned with each other to provide structure to the cell wall.

Hemicellulose:

Bound to the surface of cellulose microfibrils are complex polysaccharides which themselves do not form micro fibrils. These bound polysaccharides are called hemicelluloses and include xyloglycans, xylans, mannans and glucomannans, and β-(1→3, 1→4)-glucans [19]. They can be extracted from the plant cell wall with the aid of strong alkali.

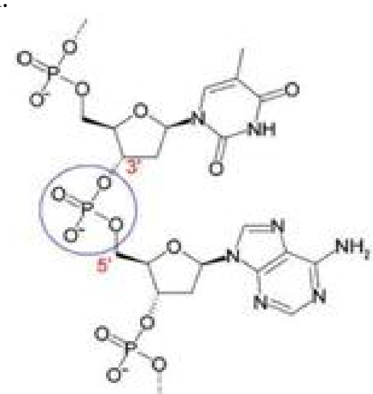

Figure 1: Hemicellulose

When you cut your nails or comb your hair, you are dealing with another naturally-occurring polymer, keratin. Keratin is among the most abundant proteins in humans. Keratin monomers are amino acids, which form the primary structure of all proteins, a second group of natural polymers. Proteins are condensation polymers made from amino acid monomers. One amino acid's -NH2 functional group reacts with the -COOH functional group of another amino acid, forming a peptide bond, -CO-NH-. The peptide bond is also called an amide bond, so proteins are also call

Pectins:

Pectins are non-starch, linear polysaccharides extracted from the plant cell walls. They are predominantly linear polymers of mainly (1–4)-linked D-galacturonic acid residues interrupted by 1,2- linked L-rhamnose residues with a few hundred to about one thousand building blocks per molecule, corresponding to an average molecular weight of about 50, 000 to about 180,000. Being soluble in water, pectin is not able to shield its drug load effectively during its passage through the stomach and small intestine. It was found that a coat of considerable thickness was required to protect the drug core in simulated *in vivo* conditions ed polyamides

Gums and mucilages:

Gums and mucilage are produced in various ways by the plant. These substances can be formed from middle lamella as in the algae; cell wall as in the seed epidermis, seed endodermis, cells in the bark; special secretory cells as in the squill; in the schizogenous sacs as in the young stem of *Rhamnuspurshiana*, or by lysiogenous metamorphosis of the cell walls as in tragacanth and acacia .To unlock this lesson you must be a Study.com Member. Create your account

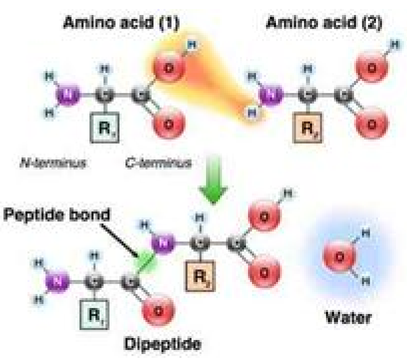

Figure 2: Seaweed polysaccharides

Alginates:

Alginates are natural polysaccharide polymers isolated from the brown sea weed (Phaeophyceae). Alginic acid can be converted into its salts, of which sodium alginate is the major form currently used. They are linear polymers consisting of D-mannuronic acid and L-guluronic acid residues arranged in blocks in the polymer chain. These homogeneous blocks (composed of either acid residue alone) are separated by blocks made of random or alternating units of mannuronic and guluronic acids. Alginates offer various applications in drug delivery, such as in matrix type alginate gel beads, in liposomes, in modulating gastrointestinal transit time, for local applications and to deliver the bio molecules in tissue engineering applicati.

Carageenans: The carrageenans are sulphated marine hydrocolloids obtained by extraction from seaweeds of the class Rhodophyceae, represented by *Chondruscrispus, Euchemaspinosum, Gigartinaskottsbergi, Gigartinastellata, Iradaealaminariodes.* These are red seaweeds growing abundantly along the Atlantic coasts of North America, Europe and the western Pacific coast of Koreaan and japan. Carrageenan is not assimilated by the human body. It provides only bulk but no nutrition. Carrageenan has been categorized into 3: kappa (κ), iota (ι) and lambda (λ). Lambda (λ-type) carrageenan produces viscous solutions but does not form gels. While the Kappa (κ-type) carrageenan forms a brittle gel, the iota (ι-type) carrageenan produces elastic gels. Studies have shown that the carrageenans are suitable in the formulation of controlled release tablets.

Gum agar: Gum agar is extracted from the red-purple marine algae of the Rhodophyceae class. The species include *Gelidiumcartilagineum, Gracilaria confervoides* which grow abundantly in the waters along the coast of Japan, New Zealand, South Africa, Southern California, Mexico, Chile, Morocco, and Portugal.

4. Microbial polysaccharides

Natural polysaccharide gums have also been obtained as carbohydrate fermentation products including Xanthan gum, produced in pure culture fermentation by the bacteria *Xanthomonascampestris*. It was originally obtained from the rutabaga plant. Gellan gum is a microbial polysaccharide obtained by fermentation by *Pseudomonas elodea*. Pullulan is an extracellular homo-polysaccharide of glucose produced by many species of the fungus *Aureobasidium, specifically A. pullulans.*

Xanthan gum:

Xanthan gum, a complex microbial exopolysaccharide produced from glucose fermentation by Xanthomonas campestrispv. Campestris, a plant bacterium. It has a molecular weight of about 2 million. The gum consists of D-glucosyl, D-mannosyl, and D-glucuronyl acid residues in a molar ratio of 2:2:1. It also contains O-acetyl and pyruvyl residues in variable proportions. Xanthan gum is an acidic polysaccharide gum of penta-saccharide subunits. The penta-saccharide subunits form a cellulose backbone with trisaccharide side-chains.

Gellan gum:

DeacylatedGellan gum (Gellan) is an anionic microbial polysaccharide, secreted from *Sphingomonas elodea*, consisting of repeating tetrasaccharide units of glucose, glucuronic acid and rhamnose residues in a 2:1:1 ratio: [→3)–β–D–glucose–(1→4)– β–D–glucuronic acid–(1→4)–β–D–glucose–(1→4)–α–L–rhamnose– (1→]. In the native polymer two acyl substituents, L-glyceryl at O(2) and acetyl at O(6), are present on the 3-linked glucose. On average, there is one glyceryl per repeating unit and one acetyl for every two repeating units. DeacylatedGellan gum is obtained by alkali treatment of the native polysaccharide.

Pullulan:

Insulin (Ins) spontaneously and easily complexed with the hydrogel nanoparticle of hydrophobized cholesterol-bearing pullulan (CHP) in water. The complexed nanoparticles (diameter 20–30 nm) thus obtained formed a very stable colloid. The thermal denaturation and subsequent aggregation of Ins were effectively suppressed upon complexation. The complexed Insulin was significantly protected from enzymatic degradation. Spontaneous dissociation of Insulin from the complex was barely observed, except in the presence of bovine serum albumin. The original physiological activity of complexed Insulin was preserved in vivo after i.v. injection. Figure 3 shows the microscopic view of pullulan in the solid and in the presence of water.

5. Animal polysaccharides

Gums Exudates

Plants, which form the sources of exudate gums, when cut give a viscous, sticky fluid which exudes from the incision and tends to cover and seal the opening. Gum exudates are therefore believed to be produced by plants in order to seal-off infected sections of the plant and prevent loss of moisture due to physical injury or fungal attact. The fluid eventually dries to a brittle, translucent, glassy, hard mass. These gum exudates are secreted by various organs of the plant. They include tragacanth gum and acacia gum or gum Arabic.

Acacia gum:

Acacia gum or gum Arabic is the dried gummy exudate from the stems and branches of *Acacia Senega*l (Fam. Leguminosae) and other related African species of acacia. Gum arabic is a branched molecule of 1, 3-linked β-Dgalactopyranosyl units. It consists of monosaccharide sugarss such as arabinose, glucuronic acid and rhamnose. Studies recorded success with gum Arabic as a matrix microencapsulating agent for the enzyme, endoglucanase. In this study gum Arabic was shown to give slow release endogucanase from the formulation. In another study gum arabic was used as an osmotic suspending and expanding agent to prepare monolithic osmotic tablet systems. There was zero order release of the active for up to 12 hours at a pH of 6.8. Heterogeneity of *Acacia senegal* gum by sodium sulfate –induced precipitation has been studied

Tragacanth gum:

Gum tragacanth is a branched, heterogeneous, and anionic carbohydrate which consists of two major fractions: tragacanthin (water-soluble) and bassorin (water-swellable). It is not understood yet if the two polysaccharides are in a physical mixture or chemically bonded to each other, although easy separation procedures favor the former hypothesis. Bassorin and tragacanthin composition differ particularly in terms of their uronic acid and methoxyl content; it has been suggested that bassorin is a complex structure of polymethoxylated acids and on demethoxylation, probably yields tragacanthin.

Mucilage gums:

Many seeds contain polysaccharide food reserves which produce intracellular seed gums usually obtained by extraction from the seeds. Guar gum is obtained from the ground endosperms of the plant *Cyamopsistetragonolobus* (Fam. Leguminosae). Locust bean gum is obtained from the endosperms of the hard seeds of the locust bean tree (Carob tree), *Ceratoniasiliqua* (F: Caesalpiniaceae).

Locust bean gum:

It is also called carob gum, as it is derived from the seeds of the leguminous plant carob, *Ceratoniasiliqua* Linn (Fam. Caesalpiniaceae). Locust bean gum has an irregularly shaped molecule with branched β-1, 4-D-galactomannan units (See Figure 4 for molecular structure). This neutral polymer is only slightly soluble in cold water; it requires heat to achieve full hydration and maximum viscosity. Cross-linked galactomannan however led to water-insoluble film forming product-showing degradation in colonic microflora The colon-specific drug delivery systems based on polysaccharides, locust bean gum and chitosan in the ratio of 2:3, 3:2 and 4:1, were evaluated using *in vitro* and *in vivo* methods Core tablets containing mesalazine with average weight of 80mg were prepared by compressing the materials using 6-mm round, flat, and plain punches on a single station tablet machine. The formulated core tablets were compression coated with different quantities of locust bean gum and chitosan.

Guar gum:

Guar gum, obtained from the ground endosperms of Cyamposistetragonolobus, consists of chiefly high molecular weight hydrocolloidal polysaccharide, composed of galactan and mannan units combined through glycosidic linkages and shows degradation in the large intestine due the presence of microbial enzymes. The structure of guar gum is a linear chain of β-D-mannopyranosyl units linked (1→4) with single member α-D-galacto-pyranosyl units occurring as side branches.

Grewia gum:

Grewia genus is today placed by most authors in the Family Malvaceae, in the expanded sense as proposed in the Angiosperm Phylogeny Group (APG). Formerly it was placed in either the linden Family (Tiliaceae) or the Spermamanniaceae. However, these were both not monophylectic with respect to other Malvales. Grewia and similar genera have been merged into the Malvaceae. Together with the bulk of the former spermanniaceae, Grewia is in the Family Grewiodeae.

Okra gum:

Okra is a tall erect annual plant botanically known as Abelmoschusesculentus (Fam. Malvaceae). It is widely cultivated and grown in most tropical part of Nigeria. Okra has been used as food and soup in Africa and Asia and has been a subject of research in agriculture and food and therein the tribe Grewieae, of which it is the type genus.

Khaya gum: Khaya gum is obtained by extraction *Khayasenegalensis* and *Khayagrandifoliola* (F: Meliaceae). The comparative binding effects of khaya gum obtained from *Khayasenegalensis* and *Khayagrandifoliola* in paracetamol tablet formulation were evaluated. The mechanical properties of the tablets were assessed using the tensile strength (T), brittle fracture index (BFI) and friability (F) of the tablets while the drug release properties were assessed using disintegration and dissolution times. The tensile strength, disintegration and the dissolution times of tablets increased with the increase in binder concentration while F and BFI decreased. *K. senegalensis* gum produced strong tablets with long disintegration and dissolution times compared to *K. grandifoliola* gum.

Moringaoleifer gum:

A natural gum obtained from plant *Moringaoleifera* gum was extracted by using water as solvent and precipitated using acetone as non-solvent. Physical characteristics such as, solubility, swelling index, loss on drying, and pH were studied. Diclofenac sodium was used as model drug for the formulation of gels. Seven batches of drug loaded gels with concentration of mucilage ranging from 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, and 8.5 were formulated by using glycerin as plasticizer and methyl paraben as preservative. The pH, viscosity, and *in vitro* diffusion profiles were studied. The gels prepared with 8.0% of mucilage were found to be ideal and comparable with a commercial preparation.

Irvingiagabonensis:

Irvingiagabonensis (Aubry Lecomte ex O'Rorke) Baill. Commonly known as 'African mango' or 'bush mango' is a tree of 15-40 m, with a bole slightly buttressed. The plant is a wild forest tree with dark green foliage and yellow fragrant flowers and occurs in the wild lowland forest; 2-3 trees occur together and in some areas, it is reported to be widespread.

Hakeagibbosa gum:

The muco adhesive and sustained-release properties of the water-soluble gum obtained from Hakeagibbosa (hakea), for the formulation of buccal tablets. Flat-faced tablets containing hakea were formulated using chlorpheniramine maleate (CPM) as a model drug had been investigated. The research into and use of excipients from natural sources was reviewed and were discussed according to their classes. Natural polymeric excipients and their modifications have continued to dominate the research efforts of scientists in finding cheap, less expensive, biodegradable, ecofriendly excipients. Some of these excipients have obvious advantages over their synthetic counterparts in some specific delivery systems due to their inherent characteristics. If the current vigorous investigations on the use of natural polymeric materials are sustained and maintained, it is probable that there would be a breakthrough that will overcome some of the disadvantages of this class of potential pharmaceutical excipients that would change the landscape of the preferred pharmaceutical excipients for drug delivery in the future.

6. Conclusion

The research into and use of excipients from natural sources was reviewed and were discussed according to their classes. Natural polymeric excipients and their modifications have continued to dominate the research efforts of scientists in finding cheap, less expensive, biodegradable, ecofriendly excipients. Some of these excipients have obvious advantages over their synthetic counterparts in some specific delivery systems due to their inherent characteristics. If the current vigorous investigations on the use of natural polymeric materials are sustained and maintained, it is probable that there would be a breakthrough that will overcome some of the disadvantages of this class of potential pharmaceutical excipients that would change the landscape of the preferred pharmaceutical excipients for drug delivery in the future.

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