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Review Article

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A Novel Review on Natural Polymers Used In Formulation of Pharmaceutical Dosage Forms

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Abstract

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 fulfill 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 as excipients in novel drug.

Key words: Plants, gums, mucilage, sustained release, novel drug delivery systems.

Introduction

Excipients were defined as 'the substance used as a medium for giving a medicament', that is to say with simply the functions of an inert support of the active principle or principles. The specific application of natural polysaccharide polymers in pharmaceutical formulations include to aid in 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 attribute of the overall safety, effectiveness or delivery of the drug during storage or use. Today we have several pharmaceutical excipients of plant origin, like starch, agar, alginates, carrageenan, guar gum, xanthan gum, gelatin, pectin, acacia, tragacanth, and cellulose. These natural excipients find applications in the pharmaceutical industry as binding agents, disintegrates, sustaining agents, protective's, colloids, thickening agents, suspending agents, emulsifiers, gelling agents, bases in suppositories, stabilizers, and coating material. A large number of plant-based pharmaceutical excipients are available today. Many researchers have explored the usefulness of plant-based materials as pharmaceutical excipients. Ability 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 can also be modified to meet the requirements of drug delivery systems and thus can compete with the Natural gums and mucilage is composed of many constituents. In several cases, the polysaccharides, resins or the tannins present in the gum are responsible for imparting release retardant properties to the dosage form. Gums are obtained from various parts of the plants. This review gives an insight of plant based novel drug release-retarding materials which have been recently studied as carriers not only in the conventional sustained release dosage forms but also in buccal drug delivery systems, gastro retentive systems and microcapsules be extracted from the leaf or bark.

Table-1: Shows some sources from natural origin.

From animals	From vegetables	From minerals
Beeswax,	Kokum butter,	Bentonite,
Cochineal,	Pectin,	Kieselghur,
Gelatin,	Starch,	Kaolin,
Honey,	Peppermint,	Paraffins,
Lactose,	Cardamon,	Talc,
Spermaciti,	Vanilla,	Calamine,
Lanolin,	Turmeric,	Fuller's earth,
Musk,	Saffron	Asbestos

Table-2: Shows the different gums and mucilage can be classified as follows

Charge	Source	Semi synthetic	Shape	Chemical structure
Non –ionic seed gums: guar, locust bean, tamarind xanthan, amylose, arabinanas, cellose, and galactomannans. Anionic gums: Arabic, karaya, tragacant, gellan, agar, align, carrageenans, pectin acid.	Marine(sea weed)origin/algal gums:agar,carrageenans,alginic acid,laminarin Plant origin: a)shrub s/trees exudates gum Arabica,gum, ghatti gum,karayagum,tragacanth, khaya and albizia gum. b) seed gums- guar gum,locust bean gum,starch, amylase. c) extracts- pectin,larch gum. d)tuber and roots-potato starch Animal origin: chitin and chitosan, chondroitin sulphate, hyaluronic acid.	Starch derivatives:hetastarch,acetate,phosphates starch Cellulose derivatives: carboxylmethyl cellulose(cmc)hydroxyl ethyl cellulose hydroxyl propyl methyl cellulose(HP MC) Methylcellulose e(mc) Microcrystalli necellose(MCC)	Linear:algins ,amylose, cellose,pectin. Branched :(a)short-branches-xanthan,xylan,glactomanan. b) Branchon-branch-amylopectin, gum Arabic, tragacanth.	Homoglycans:amylose,arabinanas, cellose Diheteroglycans:aligns,carragennans ,galactomanns. Tri-heteroglycans:arabinoxylans,gellan, Xanthan Tri-heteroglycans:arabinoxylans,gellan, xanthan. Tera-heteroglycans:gu m Arabic,psyllium, xanthan. Penta- heteroglycans: ghatti gum, tragacanth.

Table-3: Shows some natural gums and mucilage used in pharmaceuticals

Common name	Botanical name	Family	Pharmaceutical application
Agar	Gelidium amansii	Gelidaceae	Suspending agent, emulsifying agent, gelling agent in suppositories, surgical lubricant, tablet disintegrates, medium for bacteria culture, laxative.
Albizia gum	Albizia zygia	Leguminoseae	Tablet binder.
Aloe mucilage	Aloe species	Liliaceae	Gelling agent, sustained release agent.
Bavchi	Ocimum canum	Gigarginaceae	Suspending agent,emulsifying agent.
Cassia tora	Cassia tora linn	Leguminoseae	Binding agent.
Gum ghatti	Anogeissus latifolia	Leguminoseae	Binder,emulsifier,suspending agent.
Gum acacia	Acacia arabica	Combretaceae	Suspending agent,emulisyingagent, binder in tablets,demulcent and emollient in cosmetics
Gum tragacanth	Astragalus gummifer	Malvaceae	Suspending agent, emulisyingagent,demulcent,emollient in cometics and sustained release agent.
Khaya gum	Khaya grandifolia	Labiatae	Binding agent.
Satavari mucilage	Asparagus racemosus	aapocynaceae	Binding agent andsustaining agent in tablet.
Tamarind seed	Tamarindus indica	leguminoseae	Binding agent,emulsifier.
Gellan gum	Pseudomonas	elodea	Disintegrating agent.

Table-4: Applications of gums and mucilage's in NDDS

Common name	Botanical name	Family	Pharmaceuticalapplication
Bhara gum	Terminalia bellerica roxb	combretaceae	microencapsulation
Cordial gum	Cordial oblique willed	boraginaecae	Novel oral sustainedrelease matrix forming agent in tablets.
Cactus mucilage	Opuntia ficus -indica	---	Gelling agent in sustained drug deliverty.
Karaya gum	Sterculia urens	sterculiaceae	Mucoadhesive and buccoadhesive.
Locust bean gum	Ceratania siliqua	leguminoseae	Controlledrealase agent.
Mucunna gum	Mucuna flagillepes	papillionaceae	microsphere
Okara	Hibiscus esculents	malvaceae	Hydrophilic matrix for controlled realse drug delivery.
Sodium aliginate	Macrocytis pyrifera	lessoniaceae	Bioadhesive microspheres.nanoparticles,microencapsulation.

Polysaccharides

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. The seeds are processed in to gum by seed selection, seed coat removal, separation, hammer milling, grinding and sieving.

Tamarind gum is a polysaccharideomposed 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 xyloglucan has a (1 →4)-β-D-glucanbackbone that is partially substituted at the O-6 position of its glucopyranosyl residues with "-D-xylopyranose. Some of the xylose residues are-β-D-galactosylated atO-2. Magnetic microspheres of tamarind gum and chitosan were studied. The magnetic microspheres were prepared by suspension cross-linking technique. Microspheres formed were in the size range of 230 - 460 µm.The magnetic material used in the preparation of the microspheres was prepared by precipitation from $FeCl_3$ and $FeSO_4$ solution granulation technique were evaluated for its drug release characteristics. The result of this study demonstrated, that isolated TSP can be used as a drug release retardant. It was observed that the swelling index increased with the increase in concentration of TSP. Increase in polymer content resulted in a decrease in drug release from the tablets. The drug release was extended over a period of 12 hrs. And its followed zero order kinetics.

Hibiscus rosasinensis

Hibiscus rosa-sinensis Linn of the Malvaceae family is also known as the shoe-flower plant, China rose, and chines hibiscus. The fresh leaves of Hibiscus rosa-sinensis Linn are collected, washed with water to remove dirt and debris, and dried. The powdered leaves are soaked in water for 5-6 h,boiled for 30 min, and kept aside for 1 h for complete release of the mucilage into water. The material is squeezed from an eightfold muslin cloth bag to remove the marc from the solution. Acetone is added to the filtrate to precipitate the mucilage in a quantity of three times the volume of the total filtrate. The mucilage is separated, dried in an oven at a temperature < 50 °C, collected, dried-powdered, passed through a sieve (number 80), and stored for further use in In a study the use of its mucilage for the development of sustained release tablet has been reported . Matrix tablet containing dried mucilage and diclofenac sodium (DS) was prepared through direct compression techniques. It was found that mucilage can be used as release-retarding agent for 12 h, when the drug-mucilage ratio was 1:1.5.

Okra gum

Okra gum, obtained from the fruits of Hibiscus esculentus, is a polysaccharide consisting of D-galactose, L-rhamnose and L-galactouronic acid. Okra gum is used as a binder. In a study okra gum has been evaluated as a binder in paracetamol tablet formulations.These formulations containing okra gum as a binder showed a faster onset and higher amount of plastic deformation than those containing gelatin. The crushing strength and disintegration times of the tablets increased with increased binder concentration while their friability decreased. Although gelatin produced tablets with higher crushing strength, okra gum produced tablets with longer disintegration times than those containing gelatin.It was finally concluded from the results that okra gum maybe a useful hydrophilic matrixing agent in sustained drugdelivery devices.

Locust bean gum

Locust Bean Gum (LBG) (also known as Carob Gum) is obtained from the refined endosperm of seeds from the carob tree Ceretonia Siliqua L. It is an evergreen tree of the legume family. Carob bean gum is obtained by removing and processing the endosperm from seeds of the carob tree processing of the ground endosperm is accomplished by dispersing the fine powder in boiling water and filtering to remove impurities. The gum is recovered by evaporating the solution and tray or roll drying. Locust bean gum (LBG) is a plant seed galactomannans,composed of a 1-4 linked!-D-mannan backbone with 1- 6-.47 linked "-D-galactose side groups. This neutral polymer is only slightly soluble in cold water; it requires heat to achieve full hydration, solubilization and maximum viscosity. The physic-chemical properties of galactomannans are strongly influenced by the galactose content. A controlled delivery system for propranolol hydrochloride(PPHCL) using the synergistic activity of LBG and xanthan gum (X) was studied. Granules of PPHCL were prepared by using different drug: gum ratios of X, LBG alone and a mixture of XLBG (X and LBG in 1: 1 ratios). The XLBGmatrices exhibited precise controlled release than the X and LBG matrices because of burst effect and fast release in case of X and LBG alone respectively and there was no chemical interaction between drug and polymers in the XLBG formulation as conformed by FTIR studies. The first-pass50 effect of PPHCL can be avoided by using this formulation.

Guar gum

Guar gum comes from the endosperm of the seed of the legume plant Cyamopsis tetragonolobus. Guar gum is prepared by first drying separating from the seeds. The gum is commercially extracted from the seeds essentially by a mechanical process of roasting, differential attrition, sieving and polishing. The seeds are broken and the germ is separated from the endosperm. Two halves of the endosperm are obtained from each seed and are known as undehusked Guar Splits.

Refined guar splits are obtained when the fine layer of fibrous material, which forms the husk, is removed and separated from the endosperm halves by polishing. The refined Guar Splits are then treated and finished into powders by a variety of routes and processing techniques depending upon the end product desired. 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- 42 branches. The refined Guar Splits are then treated and finished into powders by a variety of routes and processing techniques depending upon the end41 product desired. 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-42 branches. Guar gum is used and investigated as a thickener in cosmetics, sauces, as an agent in ice cream that prevents ice crystals from forming and as a fat substitute that adds the "mouth feel" of fat and binder or as disintegrator. Besides being used as a matrix former for sustained release tablets guar gum has been investigated as a carrier for Indomethacin for colon-specific drug delivery using in vitro methods Studies in pH 6.8 phosphate buffered saline (PBS)containing rat caecal contents have demonstrated the susceptibility of guar gum to the colonic bacterial enzyme action with consequent drug release. The pre-treatment of rats orally with 1 ml of 2% w/v aqueous dispersion of guar gum for 3 days induced enzymes specifically acting on guar gum there by increasing drug release. A further increase in drug release was observed with rat caecal contents obtained after 7days of pre-treatment. The presence of 4% w/v of caecal contents obtained after 3 days and 7 days of enzyme induction showed biphasic drug release curves. The results illustrate the usefulness of guar gum as a potential carrier for colon specific drug delivery.

Isapgulla Husk (Psyllium)

Psyllium seed husks, also known as ispaghula, isabgol, or simply as psyllium, are portions of the seeds of the plant Plant agoovate, (genus plant ago), a native of India and Pakistan. Gel forming fraction of the alkali-extractable polysaccharides is composed of arabinose, xylose and traces of other sugars they are soluble in water, expanding and becoming mucilaginous when wet. Seeds are used commercially for the production of mucilage. It is white fibrous material, hydrophilic in nature and forms a clear colorless mucilaginous gel by absorbing water. Psyllium seed husk is used as binder, disintegrant and release retardant. In an attempt, psyllium and acrylic acid based pH sensitive novel hydrogels using N, N methylenebisacrylamide (N, 0NMBAAm) as cross linker and ammonium per sulfate (APS)as initiator for model drugs (tetracycline hydrochloride, insulin and tyrosine), for the use in colon specific drug delivery was studied. The hydrogel was evaluated for the swelling mechanism and drug release mechanism from the polymeric networks. The effects of pH on the swelling kinetics and release pattern of drugs have been studied by varying the pH of the release medium. It has been observed that swelling and release of drugs from the hydrogels occurred through non-Fickian or anomalous diffusion mechanism in distilled water and pH 7.4 buffer. It shows that the rate of polymer chain relaxation and the rate of drug diffusion from these hydrogels are comparable.

Sterculia foetida

Sterculia is a genus colloquially termed as tropical chestnuts,(Sterculia foetida) . It contains a mixture of D-galactose, Lrhamnoseand D-galactouronic acid. The galactouronic acid units are the branching points of the molecule. In an independent investigation Sterculia foetida gum as a hydrophilic matrix polymer for controlled release preparation was evaluated. Different formulation aspects considered were: gum concentration (10–40%), particle size (75–420 µm)and type of fillers. Tablets prepared with Sterculia foetidagum were compared with tablets prepared with Hydroxymethyl cellulose K15M. The release rate profiles were evaluated through different kinetic equations: zero-order, first-order, Higuchi, Hixon-Crowell and Korsemeyer andPeppas models. Suitable matrix release profile was obtained at 40% gum concentration. Higher sustained release profiles were obtained for Sterculia foetida gum particles in size range of 76– 125 µm. The in vitro release profiles indicated that tablets prepared from Sterculia foetida gum had higherretarding capacity than tablets prepared with hydroxyl methyl cellulose K15M prepared tablets.

Honey locust gum

It is known botanically as Gleditsia triacanthos, and belongs to the order Leguminosea (suborder Mimoseae). The gum isobtained from the seeds of the plant. The seed contains proteins, fats, carbohydrates and fibers. Honey locust gum (HLG) was used to produce matrix tablets at different concentrations (5% and 10%) by wet granulation method. Theophylline was chosen as a model drug. The matrix tablets containing hydroxyethylcellulose andhydroxypropyl methylcellulose as sustaining polymers at the same concentrations were prepared and a commercial sustained release (CSR) tablet containing 200 mg theophylline was examined for HLG performance. No significant difference in in-vitro studies was found betweenCSR tablet and the matrix tablet containing 10% HLG.

Tara Gum

Tara gum is obtained from the endosperm of seed ofCaesalpinia spinosa, commonly known as tara. It is small tree of the family Leguminosae or Fabaceae. Tara gum is a white, nearly odorless powder. It is produced by separating and grinding the endosperm of the mature black color seeds.[45] The major component of the gum is a galactomannanpolymer similar to the main components of guar and locust bean gums, consist of a linear main chain of (1-4) D-mannopyranoseunits with D-galactopyranose units attached by (1-6) linkages. The ratio of mannose to galactosein Tara gum is 3:1 produce highly viscous solutions, even at 1% concentration. Tara gum requires heating to disrupt aggregation and full dissolution, whereas guar gum is soluble in cold water .Tara gum is used as a thickening agent and stabilizer in a wide range of food applications around the world. The use of taragum as a controlled release carrier in the formulation of gastro retentive controlled release tablets and emulsions for drugs like metformin hydrochloride, ciprofloxacin hydrochloridenimodipine, nifedipine, carvedilol, clozapine has been claimed in patents.

Khaya gum

Khaya gum is a polysaccharide obtained from the incised trunk of the tree Khaya grandifolia (family Malvaceae). It is known to contain highly branched polysaccharides consistingof D galactose, L-rhamnose, D-galacturonic acid and 4-O- methyl-D-glucoronic acid. Khaya gum has been shown to be used.

Aloe Mucilage

Many compounds with diverse structures have been isolated from both the central parenchyma tissue of Aloe mucilage is obtained from the leaves of Aloebarbadensis Miller. Aloe Vera leaves and the exudate arising from the cells adjacent to the vascular bundles. The bitter yellow exudate contains 1,8 dihydroxyanthraquinone derivatives and their glycosides . The aloe parenchyma tissue or pulp has been shown to contain proteins, lipids, amino acids, vitamins, enzymes, inorganic compounds and small organic compounds in addition to the different carbohydrates. Many investigators have identified partially acetylated mannan (oracemannan) as the primary polysaccharide of the gel, while others found pectic substance as the primary polysaccharide. Dried A. Vera leaf gel (acetone precipitated component of the pulp) was directly compressed in different ratios with a model drug to form matrix type tablets, including ratios of 1:0.5, 1:1, 1:1.5 and 1:2. These matrix systems showed good swelling properties that increased with an increase of aloe gel concentration in the formulation. The directly compressed matrix type tablets also showed modified release behavior with 35.45% and 30.70% of the dose released during the first hour and the remaining of the dose was released over a 6 hour period for those formulations containing the lower ratios of gel to drug, namely 1:0.5 and 1:1. The formulation that contained the highest ratio of gel to drug, namely 1:2exhibited only a 23.25% drug release during the first hour with the remaining of the dose being released over an 8 hour period. The dried A Vera gel polysaccharide component therefore showed excellent potential to be used as an excipient in the formulation of direct compressible sustained- release matrix type tab.

Hakea Gum

Hakea gum a dried exudate from the plant Hakea gibbons family Proteaceae. Gum exudates from species have been shown to consist of L-arabinose and D-galactose linked as in gums that are acidic arabinogalactans (type A). Molar proportions (%) of sugar constituents Glucuronic acid, Galactose, Arabinose, Mannose, Xylose is 12:43:32:5:8. The exuded gum is only the force of detachment for the mucoadhesive buccaltablets increased as the amount of Hakea gum was increasedfollowing application to excised intestinal mucosa. Addition of sodium bicarbonate or tartaric acid, as well as higher amounts of CPM, did not affect the mucoadhesive bondstrength. These results demonstrate that the novel, naturalgum, H. gibbosa, may not only be used to sustain the release.

Konjac glucomannan

Konjac glucomannan, which is extracted from the tubers of Amorphophallus konjac, is very promising polysaccharide for incorporation into drug delivery systems. The konjacglucomannan molecule consists of D-glucose and Dmannoselinked by 13-1,4 linkage, and the ratio of mannose to glucose has been reported as 1.6:1, while there is someso act as bio adhesivepolymer partly soluble in waterletsbranching at the C-3 of the mannose unit. Since konjacglucomannan by itself forms very weak gels, it has been investigated as an effective excipient in controlled release drug delivery devices in combination with other polymers.

Resins

Gum Copal

Gum copal (GC) is a natural resinous material of plant Burs era bipinnata (family Burseraceae).Copal, a resinous material, is obtained from the plants of araucariaceae and caesalpinaceae. Medicinally, Copal is used in the

treatment of headache fever, burns and stomach ache. In dentistry, it is used as binding media in dental products and in treatment of micro, a subfamily of leguminoaceae .al structure leakage in teeth. Recently, Copal gum has been evaluated as13 matrix-formin.

Gum Damar

Gum damar (GD) is a whitish to yellowish natural gum of plant Shorea wiesneri (familyDipterocarpaceae). It contains about 40% alpha-resin (resin that dissolves in alcohol), 22% beta resin. 23% dammarol Diclofenacsodium was used as a model drug. Effect of gum concentration (10, 20 and 30% w/w with respect to total tablet weight) on in vitro drug release profile was examined. Matrix tablets with 30% w/w gum copal and gum damar showed sustained drug delivery beyond 10 h. Drug release from gum copal matrix tablets followed zero order kinetics while gumdamar (10 and 20% w/w) was found suitable to formulate the insoluble plastic matrix that releases the drug by diffusion. It was concluded that both gums possess substantial matrix forming property that could be used for sustained drug13 delivery.

Tannins

Bhara Gum

Gum Bhara is a yellowish natural gum of plant Terminaliabellerica roxb. Belonging to family combretaceae. Baheragum, extracted from the bark of Terminalia bellerica, is a waste material. Main chemical constituents are tannins which mainly include ß- sit sterol,Gallic acid, ellagic acid gall ate, galloyl glucose and chebulaginic acid .It has been mainly used as a demulcent and purgative. It is also used as an emulgent in cosmetic industries. Wide applications of bhara gum indicate their hydrophilic nature and compatibility with the physiologic environment .A new sustained release microencapsulated drug delivery system employing bhara gum has been proposed . The microcapsules were formulated by ionic gelation technique using famotidine as the model drug. The effect of different drug: bhara gum ratio on in vitro drug release profile was examined and compared with guar gum. Remaining all parameters was constant. Microcapsules employing bharagum exhibited slow release of famotidine over 10 hr. Fickianrelease was observed from most of the formulations with bhara gum. It was concluded that this gum possesses substantial release controlling properties that could be used for sustained drug delivery.

Conclusion

This article highlights the numerous uses of natural polymers in pharmacy and various fields; now-a-days natural polymers play a very important role in almost all kind of formulations. Majority of investigations on natural polymers in drug delivery systems center around polysaccharides. Though the use of traditional gums has continued, newer gums have been used some of them with exceptional qualities. Many other new gums viz. sesbenia gum, tara gum,etc. can be explored for their sustained release properties. These have found application not only in sustaining the release of the drugs but are also proving useful for development of gastro retentive dosage form, bio adhesive system, microcapsules etc.

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