REVIEW ARTICLE

Natural Gums Emphasized Grafting Technique: Applications and Perspectives in Floating Drug Delivery System

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Abstract

Polymers play a very pompous role in each and every morsel of lives. Intentionally or unintentionally, each and every personality at present depends on the polymer to get together various requirements. According to their characteristics, polymers are even not accomplishing the bid if it is abundant at times. Due to advancement in polymer science, it is vital in the future prospective as they can improve the range of applications in the floating drug delivery system. Due to modification of various techniques in the floating drug delivery system, the grafting of polymers has gained much more aggravated for the production of new monomers to transport polymeric materials from one region to another region in the body. In short, the modification is crucial to face and stand against various challenges because it is hard to obtain new polymers. Sometimes, harmonization of properties is required which can be achieved via modification of polymers. The modification is needed to fetch precise properties to material which is to be modified such as enhanced stability, compatibility, flexibility, and rigidity. This review highlights the various grafting technique which will help for the grafting modification by the use of natural gums in floating drug delivery.

Key words: Cross-linking, drug delivery, grafting, natural gums, pharmaceutical applications, polymers

INTRODUCTION

Human beings are gifted with a wide variety of materials by surrounding nature for balancing the healthiness of all living things straightforwardly or in a roundabout way. Polymers, especially of natural origin, such as various gums and mucilage are broadly handled natural resources for existing and novel drug delivery systems with rising attention in the use of polymers and excipients of natural basis; the pharmaceutical sector has conformity to employ most of them in various dosage forms. In the last few years, polymers obtained from plant source have suggested marvelous awareness owing to their varied pharmaceutical applications such as binder, diluents, disintegrates in tablets, protective colloids in suspension, gelling agent in gels, thickeners in oral liquids, and bases in suppositories; moreover, polymers are implemented in paints, textiles, paper making, and cosmetics. In general, natural gums are measured to be pathological yield obtained from mechanical damage to plant part or an inauspicious condition, like deficiency or by break down of cell walls while mucilages are metabolic products of the plants produced inside the cell and/or formed with no injury to plants. Gums as pathological products, dissolve in water but mucilages as physiological products, form slimy masses with water.[1] Guar gum, xanthan gum, locust bean gum (LBG), ghatti gum, cashew gum (CG), tamarind seed (TS) gum, karaya gum, mango gum, and gellan gum are some examples of natural gums. Mucilages are present in diverse parts of the plant body including leaves (senna), in barks (slippery elm), epidermal cells of seed coats (linseed and psyllium), middle lamellae (aloe), and roots (marshmallow). Both gums and mucilages are plant hydrocolloids containing hydrophilic molecules which result in viscous solutions and gel on contact with water.[2] These naturally existing gums

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can be modified to get specially made materials to compete with the synthetic products and for drug delivery systems. Modification of natural polymers by graft copolymerization render them into the intelligent biomaterials in controlled as well as sustained release applications as subject natural polymers (polysaccharides) may be unsuitable in controlled and sustained release drug delivery owing to their considerable swelling as well as quick enzymatic humiliation in physiological fluids. Demand is mounting continuously for these substances and new resources are being urbanized frequently. Due to geographical and environmental variation, India has usually been a fine source for such products surrounded by other Asian countries.[3,4]

Benefits of natural gums

1. Natural gums are biodegradable and renewable sources having no adverse effects on human being
2. They are greatly biocompatible and non-toxic in nature
3. They are low in cost and easily available
4. They are obtained from edible sources
5. They show better patient tolerance and public acceptance.

Drawbacks of synthetic polymers

Synthetic polymers have several disadvantages such as toxicity, poor patient compliance, and high cost. Synthesis of such polymers may affect environment during their synthesis. Skin irritation and eye irritation have been reported in workers dealing with synthesis of polymers such as methyl methacrylate (MMA) and poly (MMA).[3] Development of subcutaneous granulomas at the site of injection by povidone is observed. There is also a fact that povidone may accumulate in organs subsequent to intramuscular injections.[5] Carbomer-934P showed low oral toxicity during toxicity studies at a dose up to 8 g/kg. Dust of carbomer also causes eye and respiratory tract irritation along with inflammation of mucous membrane.[6]

Subcutaneously injected 5% polyvinyl alcohol aqueous solution in rats showed symptoms of anemia and infiltration of various organs and tissues.[7] Certain drawbacks have been shown by some biodegradable polymers like poor biocompatibility and swift loss of mechanical properties throughout degradation. Polyglycolides, polylactides, and their copolymers show systemic and/or local reactions owing to acidic degradation products. Mild inflammatory responses in rat implant have been seen while using poly (propylene fumarate).[4]

In current years, to design extended release dosage forms, natural gums have been widely used. Natural gums are generally hydrophilic carbohydrate polymers having high molecular weight and usually composed of monosaccharide units attached by glycosidic bonds. Gums are water soluble and swell in contact with water or disperse in cold water forming a viscous jelly like solution. Natural gums form three-dimensional monomeric networks, therefore, trapping water, drug and other excipients in it. Thus, the drug release can be extended to the desired level. However, these natural gums have certain disadvantages such as susceptibility to microbial contamination because of its moisture content, batch to batch variation because of geographical and environmental effect, uncontrolled rate of hydration, and reduced viscosity on storage. To overcome disadvantages of natural gums and synthetic polymers, gums can be tailored or modified in desired compound via different ways not only to overcome their drawbacks but also to modulate the site of drug release and it's kinetic, and also to makes them superior to their synthetic counterparts.[7,4]

CONCEPT OF GRAFTING

"Physisorption," "grafting" and "crosslinking" are techniques implemented for description of association of monomers and polymers. Term physisorption is correlated to physical attractive forces, and this process is reversible in nature. This process is a result of self-assembly comprising polymeric surfactants or end-functionalized polymers on the solid surface, while grafting is irreversible and involves covalent attachment. Grafting can be skilled either by "grafting to" or "grafting from" approach. In "grafting to" approach, functionalized monomers react with the backbone polymer resulting in the formation of grafted polymer. In contrast, "grafting from" is resulted by reacting the substrate with suitable method for generation of immobilized initiators followed by polymerization.

A grafted copolymer reflects macromolecular series with one or more species of block linked to main chain as side chains. One of the finest ways to employ polysaccharides for extended release drug delivery systems is offered by graft copolymerization of artificial polymers on polysaccharide backbone. Graft copolymerization is simple and used to alter the structure of natural polymers, and therefore, making them striking biomaterials in sustained and controlled release applications seeing as native polysaccharides may be unsuitable in such drug delivery systems owing to their considerable swelling and fast enzymatic degradation in the biological fluids.[8]

It is necessary to modify the properties of polymers as per tailor-made specifications intended for desired applications. There are quite a few ways to modify polymer properties such as blending, grafting, and curing. Blending involves physical mixture of two or more polymers to get required properties. Grafting involves covalent bonding of monomers on the polymer chain. Curing involves polymerization of an oligomer mixture to form a coating which adheres to substrate by physical forces followed by a soft finish by filling in the dell in surface.[9]

TECHNIQUES OF GRAFTING

Grafting initiated by chemical means

Grafting can be accomplished by chemical means via two main paths such as free radical and ionic. In chemical process, role of initiator to be used is extremely significant as it decides the fate of grafting process. Aside from common free-radical mechanism, atom transfer radical polymerization, and grafting in the melt are fascinating techniques for grafting.[9,10]

Grafting through living polymerization

In current years, "living polymerization" has urbanized to supply a possibility for grafting. According to Szwarc *et al*., most reasonable meaning of a living polymer is one which holds its ability to proliferate for extended time and grow to preferred highest size while their degree of extinction or chain transfer is still insignificant. Features of both the conventional free-radical and ionic polymerizations combine to express controlled free-radical polymerizations.[11] In the case of conventional free-radical polymerization, there is a requirement of constant initiation, with annihilation of growing chain radicals in coupling or disproportionate reactions, leading to unreactive polymers called dead polymers and basically time invariant degrees of polymerization and large molecular weight allocation. In living polymerization, it supplies living polymers with synchronized molecular weights and low polydispersities.[10,12-17]

Photochemical grafting

The grafting process is initiated as a result of formation of reactive free-radicals when chromophore on macromolecule absorbs light and undergoes in excitation state to form reactive free radical. If the absorption of light only is not sufficient, the process may be encouraged by addition of photosensitizers like benzoin ethyl ether, dyes like Na-2,7-anthraquinone sulfonate or acrylatedazo dye, aromatic ketones such as benzophenone, xanthone, or metal ions like $UO2^{2+}$. Hence, it can be stated that two approaches are involved in grafting process by photochemical technique namely: With or without a sensitizer.[18-20] Approach for "without sensitizer" involves formation of grafted polymer by the production of free radicals on backbone, which reacts with monomer free radical. Whereas, in "with sensitizer" approach, the radical sites needed for grafting are produced by the sensitizer which forms free radicals able to undergo diffusion to abstract hydrogen atoms from the base polymer.

Enzymatic grafting

It is a fairly newer technique. In this technique, enzyme begins the chemical or electrochemical grafting reaction. For instance, tyrosinase is able to convert phenol into reactive quinone, which further undergoes successive non-enzymatic reaction with chitosan.[21,22]

Plasma-radiation induced grafting

In this technique, plasma conditions achieved through sluggish discharge put forward the same potential as with ionizing radiation.[23,24] Electron-induced excitation, ionization, and dissociation are the main processes in plasmas. Rift of chemical bonds in polymeric structures takes place by accelerated electrons from plasma to form macromolecule radicals, which later on begin graft copolymerization.

Grafting initiated by radiation technique

Free-radical grafting

Free radicals on the polymer can be formed by irradiation of macromolecules which causes hemolytic fission. The use of an initiator is not necessary in radiation technique, but the medium is important. For example, if irradiation is performed in air, peroxides may form on polymer.[25-27] The life span of free radical relies on the nature of backbone polymer. Grafting by radiation technique generally takes place in three different ways:

1. Pre-irradiation
2. Peroxidation
3. Mutual irradiation.

In pre-irradiation approach, free radicals can be generated through the polymer backbone irradiation in vacuum or in the presence of inert gas followed by treating polymer substrate with monomer, in liquid or vapor state or as a solution in a suitable solvent. In peroxidation approach, trunk polymer is subjected to high-energy radiation to form hydroperoxides or diperoxides in the presence of air or oxygen, based on the nature of polymeric backbone and irradiation circumstances at higher temperature, stable peroxy products are treated with monomer and decomposition of peroxides to radicals initiate grafting.[28,29] For long periods, these intermediary peroxy products can be stored up prior to grafting. In mutual irradiation approach, polymer and monomers are irradiated at the same time to form free radicals and successive addition.[30-32]

As monomers are not exposed to radiation in pre-irradiation approach, the method is relatively free from formation of homopolymer and this is the clear advantage of this approach. Conversely, certain drawback of pre-irradiation approach is scission of base polymer because of its direct irradiation which may result in the formation of block copolymers.[33-35]

Ionic grafting

Grafting as well can proceed through an ionic mode. Some useful initiators in this purpose include alkali metal

suspensions in a Lewis base liquid, organ metallic compounds and sodium naphthalenide. For example, alkyl aluminum (R3Al) and backbone polymer in halide form (ACl) act together forming carbonium ions along the polymer chain, leading to copolymerization. The reaction proceeds through cationic mechanism.

$$ACl + R_3AL \rightarrow A+R_3\ Cl-$$

$$A+ + M \rightarrow AM+-M \rightarrow \text{graft co-polymer} \quad (1)$$

Cationic catalyst BF3 can be implemented for this purpose. An anionic mechanism also involved in the grafting process. For example, sodium ammonia or methoxide of alkali metals form alkoxide of polymer (PO-, Na+) which reacts with monomer to form graft copolymer.[36-40]

$$P\text{-}OH + NaOR \rightarrow PO\text{-}Na+ + ROH$$

$$PO- + M \rightarrow POM\text{--}M \rightarrow \text{graft co-polymer} \quad (2)$$

Microwave initiated grafting

In this technique, no initiators are used. Hydroquinones are used as a radical inhibitor to slow down the reactions of grafting while survival of free radicals in reaction mixture has not been confirmed by current instrumentation like electron spin resonance. Under microwave settings, heating results from the dipolar relaxation of solvent; especially water and because of localized rotation polar functional groups of polysaccharides.[41,42]

Microwave assisted grafting

In this technique, initiators are used and by addition of initiators to reaction mixture, ions are produced which improve the skill of aqueous reaction mixture to change microwave energy into heat energy. Under control of microwave dielectric heating, grafting reactions are facilitated by the production of free radicals from initiators.[42]

FACTORS AFFECTING GRAFTING

Nature of polymer backbone

The nature of polymer backbone, i.e., physical nature and chemical composition have important role in the process of grafting involving covalent connection between monomer and preformed polymeric backbone. Ng *et al.* have found that cellulose does not support grafting reactions in water due to its insolubility. Because of the vast size of polymeric chain bonding between amino residues in wool, cystine linkages, and intramolecular H-bonding may be accountable for determining and setting characteristics. In the presence of ultraviolet light, oxidative reactions are initiated and free radicals formed, leading finally to grafting if monomers are present.[43,44]

Effect of monomer

The reactivity of the monomer is vital in grafting such as the nature of polymer backbone. Reactivity of monomers depends on various factors like polar and steric nature, swellability of backbone in the presence of monomers and concentration of monomers.[44,45]

Effect of solvent

The solvent is the carrier through which monomers are passed to the surrounding area of backbone in grafting mechanism. The criteria for assortment of suitable solvent relies on numerous parameters such as solubility of monomer in the solvent, swelling properties of backbone, miscibility of the solvents (if more than one is used) and generation of free radical in the presence of solvent. Nature of solvent plays important role in solubility of monomer and polymer. For example, alcohols are helpful solvents for grafting of styrene as they can swell the backbone proficiently and can dissolve styrene, so the monomer can simply diffuse in cellulosic structure. The degree of grafting reduces gradually with alcohol change from methanol to ethanol to isopropanol and then to t-butanol, owing to the slowly decreased swelling properties of alcohol, recognized to be corroborated by largeness of the alcohol molecules.[46,47]

Effect of initiator

The nature of initiator has a deep impact on the grafting process. Except radiation technique, all other chemical grafting techniques need an initiator, and hence, its nature, concentration, solubility and function should be considered. There are some initiators such as azobisisobutyronitrile (AIBN) and potassium persulfate ($K_2S_2O_8$). In the grafting of 2-hydroxy methacrylate on cellulose, AIBN provides reduced grafting and potassium persulfate ($K_2S_2O_8$) is not suitable as an initiator, as it degrades cellulose chain.[48]

Effect of temperature

Temperature is the key factor that controls the kinetics of graft copolymerization. With increasing temperature, grafting yield also increases until a limit is achieved. This may be attributed to faster monomeric diffusion in backbone which increases with the rising temperature and makes the progress of grafting smooth.[49] Sun *et al*. reported such behavior to produce free radicals on the base polymer with increasing temperature by increased thermal decomposition rate of initiator and the initiator efficiency resulting in increased polymer macro radical's concentration leading to enhanced graft polymerization. Rising temperature, at first enhances the grafting yield and helps the decomposition of peroxide.[50] On the other hand, as reported by Maldas,[51] in the case of acrylamide grafting

on cellulose acetate, grafting yield decreases gradually with the increase in temperature. The initial rise in grafting is the result of decomposition of peroxides formed due to irradiation of base polymer in air, making the necessary radicals accessible for grafting, and the following decrease is observed because of the increased molecular motion with rising temperature, ensuing in increased radical decay.[52]

Effect of additives on grafting

The presence of additives such as metal ions, acids, and inorganic salts affects the extent of graft copolymerization or grafting yield. Hence, the reaction among the monomer and backbone has to fight with any reactions among monomer and additives. Even if few additives may improve the monomer/backbone reaction to increase the grafting effectiveness, the reverse will be factual if reaction between monomer and additive is overriding (Table 1).[52,53]

CHARACTERIZATION TECHNIQUES FOR GRAFTED GUMS

Fourier transform infrared spectroscopy (FTIR)

The occurrence of specific functional groups in compounds can be examined by FTIR spectroscopy. For characterization, 0.5-1 mm thick films of natural gum and all graft copolymers can be prepared and analyzed by attenuated total reflectance-FTIR by means of transmittance mode.[54]

Solid state 13C nuclear magnetic resonance (NMR) spectroscopy

13C solid state NMR analysis of natural gum and grafted gum can be done by NMR spectrophotometer operating at 75 MHz. Around 300 mg of sample is required to insert in ceramic rotor of NMR spectrophotometer for its characterization.[54,55]

Table 1: Includes few examples of grafted gums with applications in drug delivery

Gums and mucilage	Grafting technique	Application (s)	References
LBG	Microwave assisted grafting	Sustained drug delivery	[54]
Gellan gum	Microwave assisted grafting	Sustained drug delivery	[55]
Cross-linked amylase	Grafting by chemical modification by substituting it in a one-step reaction	Disintegrating and binding agent	[56]
Cross-linked cellulose	Grafting by chemical modification by epichlorhydrine	Disintegrating and binding agent	[56]
Pectins	Grafting by chemical modification with acetyl chloride grafting by chemical modification with ethanolamine	Modified drug delivery, colonic drug delivery	[56]
CG	Grafting by free radical polymerization	Sustained drug delivery	[57]
Xanthan gum	Grafting by free radical initiation polymerization	Sustained drug delivery	[58]
Karaya gum	Grafting by heat treatment at various temperatures in hot air oven	Disintegrating agent	[59]
Agar and guar gum	Grafting by heat treatment at various temperatures in a hot air oven along with co-grinding of both	Disintegrating agent	[60]
Acacia gum	Grafting by chemical modification using epichlorhydrine	Disintegrating agent	[61-63]
Starch	Grafting by chemical modification of starch	Disintegrating and binding agent	[64-69]
Sesbania gum	Grafting by chemical modification with tartaric acid grafting by chemical modification with acetone: Chloroform mixture for gelling agent	Sustained release formulation, gelling agent	[70]
Guar gum	Grafting by chemical modification with glutaraldehyde grafting by chemical modification using isopropanol	Colonic delivery, film coating	[71-73]
TS gum	Grafting by chemical modification using epichlorohydrin	Sustained release formulation, rectal drug delivery	[74]
Okra gum	Grafting by conventional method	Controlled drug delivery	[75-77]

LBG: Locust bean gum, CG: Cashew gum

Powder X-ray diffraction (PXRD)

X-ray diffractometer is used to record PXRD of sample. The native gum and grafted gum can be studied. The X-ray source is generally Cu with wavelength 1.5406° A and Si (Li) PSD detector. The diffractometer basically run at a scanning speed of 2°/min, a chart speed of 2°/2 cm per 2 θ and an angular range fixed between 3° and 80°.[54]

Differential scanning calorimetry (DSC)

DSC instrument is used to obtain DSC thermograms of compounds. 3-5 mg samples are heated from 10°C to 300°C under nitrogen purge (50 ml/min) at a heating rate of 10°C/min.[55]

Elemental analysis

PCHN 2400 microanalyzer is used for the elemental analysis. The samples of native gum and all the graft copolymer can be examined for contents. The carbon, hydrogen, and nitrogen contents can be calculated.[54,55]

Viscosity measurement

A well programmed Brookfield viscometer is used to record the viscosity. 2% w/v aqueous solution of native gum and graft copolymer is sufficient for the viscosity study. Temperature can be maintained at 32.7°C. The samples are generally dissolved in water for native gum and heated at 80°C. The spindle, usually spindle no. S-01 is rotated at varying rpm and corresponding shear rate, shear stress and viscosities can be recorded.[55]

Molecular weight analysis

Gel permeation chromatography technique is used for the molecular weight analysis of sample by a refractive index detector. A PL aquagel-OH mixed column (7.5 mm × 300 mm; 8 µm) is used with mobile phase containing 0.1% w/w sodium azide dissolved in de-ionized water. The flow rate of mobile phase and column temperature is kept at 0.5 ml/min and 30°C, respectively. Dextrans with molecular weights of 150,000, 410,000, 670,000, 1,400,000, and 2,000,000 Daltons are used as standards. 1 mg/ml of standard or sample solution is filtered through a cellulose nitrate membrane (pore diameter = 0.45 µm) before analysis. At least triplicates should be carried out for each batch of sample and the average results reported.[55,56]

Swelling study

Two different media can be used for equilibrium swelling measurements of both native gun and different grades of grafted ones. A small, formerly weighed amount of the material (W1) is immersed in 50 ml buffer (pH 1.2 and pH 6.8) and left to swell for 2 h. Afterward, the swollen quantity is recovered and excess water is removed vigilantly with tissue paper and reweighed (W2) to an accuracy of 0.01 mg on electronic microbalance.[55] The swelling characteristics of sample can be measured by the following equation:

$$\text{Swelling index} = W2 - W1/W1 \times 100 \quad (3)$$

Where, W2 and W1 are the swollen and dry weights of the native gum/grafted gum, respectively.

Acute oral toxicity study

Acute oral toxicity study of grafted gum can be performed as per Organization of Economic Co-operation and Development guideline. Five nulliparous and non-pregnant 5-week-old female mice (Swiss albino strain) are required for this study. Mice are required to house in polycarbonate cage with food and deionized reverse osmosis water at 20-25°C and 40-70% relative humidity in a 12 h light/dark series. A single dose of 2000 mg/kg body weight of grafted gum is administered by gavages using a stomach tube in the first animal. The same dose is administered in the remaining four animals after survival of the first animal. The animals should be kept under constant examination up to 4 h subsequent to dosing. The examination must continue up to 14 days. The mortality rate can be evaluated by visible inspection and reported, consequently.[55] Serum biochemical studies on 30th min, 4th h, 1st, 3rd, 7th and 14th day should be performed. The animals should then forfeit on the 15th day and histopathological studies on liver, kidney, lung, and stomach should be performed.[54,55]

OVERVIEW OF PATENTS FILLED FOR GRAFTING IN NOVEL DRUG DELIVERY

Many inventors have received patents on grafting, modification, and fields related to the same techniques. In 1964 Borunsky, received a patent (US3138564) on the process for grafting a monomer onto an oxidized polysaccharide. The invention relates to the grafting of polymerizable compounds on to pre-formed naturally occurring polymers. It also quoted that "grafting" means the addition of the polymerizable compounds as branches to the previously formed long chain molecules of said polymer. The invention is more particularly concerned with such preformed naturally occurring polymers which are at least partially water soluble although water insoluble naturally occurring polymers may also be used.[78] In 1968 Horowitz, received a patent (US3401049) on the method of grafting polymerizable monomer onto substrates and regulant article. This invention relates to the method whereby a polymer is "grafted to" an underlying non-metallic substrate such as cellophane, and fabrics by distributing bodies of silver or silver oxide *in situ* onto the surface of the

substrate in such manner that the bodies are bonded to the surface, and then a material to the substrate is polymerized. The material being polymerized is a composition such that the polymerization thereof is activated polymerization by silver or silver oxide particles in the surface of the substrate.[79] In 1969 Henry, received a patent (US3455853) on the method for preparing polysaccharide graft copolymers. The invention relates to graft copolymers of polysaccharides and synthetic polymers wherein an ion exchange site is the point of grafting between the polysaccharide and the synthetic polymer. These graft copolymers are prepared by ion exchanging a basic-nitrogen, cationic, organic azo compound with the polysaccharide to obtain the azo compound ionically bonded to carboxyl group of the polysaccharide.[80] In 2006 Gunn *et al*. received a patent (US20060029561) on polysaccharide graft copolymers and used it of them in personal care applications. It relates to grafting of polysaccharide polymer with a polymer having the ability of bonding to human hair and is useful in hair care compositions In 2009 De Angelis, received a patent (US7575904) on polymer grafting by polysaccharide synthases.[81] The invention relates to the process of polymer grafting by polysaccharide synthase and predominantly, polymer grafting by the use of hyaluronate synthase from *Pasteurella multocida*. The invention also includes coatings for biomaterials to provide protective properties to the biomaterial. Such coatings might be useful in electrical devices, catheters, sensors, and any device which may be considered for use in a mammal.[82] In 2010 Liu and Priou received a patent (US7838667) on grafting polymerization of guar and other polysaccharides by electron beams. This invention relates to the method of grafting galactomannantype polysaccharide polymers, preferably guar to a functional group by irradiation with high energy electron beams in the presence of an unsaturated monomercompressing the described functional group.[83]

In 1997 and 1999 Rong-Kun *et al.* received patent on crosslinked amylose and cellulose as a tablet excipient.[65]

In 2011 Petzold *et al.* received a patent (US20110053271) on irradiation induced grafting of polysaccharides to cell culture vessels. This invention relates to the method for grafting a polysaccharide to a surface of a cell culture. In addition to the grafting of polysaccharide to the surface, the ionizing radiation may serve to sterilize the article.[84] In 2011, Patil *et al.* received a patent (US007999040) for developing method for making graft copolymers from sodium poly (aspartate) and the resulting grafts copolymer. Graft copolymers at high variation with molecular weight up to millions can be prepared by implementing this method. Few examples of patent filled are as shown in Table 2.

APPLICATIONS OF GRAFTED GUMS

Natural gums have been modified to defeat specific downsides including unrestrained hydration rate, fall in viscosity while storage, thickening and microbial contamination. For the execution of polymeric materials in the field of pharmaceutical technology, many efforts have been made to alter physical and chemical properties of polymeric materials, and hence, their potential applicability in drug delivery. Many researchers in recent years have done research works with respect to grafting modification.

Table 2: Patents filed related to grafting modification

Patent no.	Inventor (s)	Publication date	Invention	References
US3138564	Borunsky	1964	Process for grafting a monomer onto an oxidized polysaccharide	[78]
US3401049	Horowitz	1968	Method of grafting polymerizable monomer onto substrates and regulant article	[79]
US3455853	Henry	1969	Method for preparing polysaccharide graft copolymers	[80]
US20060029561	Gunn *et al.*	2006	Polysaccharide graft copolymers and their use in personal care applications	[81]
US7575904	De Angelis	2009	Polymer grafting by polysaccharide synthases	[82]
US7838667	Liu and Priou	2010	Grafting polymerization of guar and other polysaccharides by electron beams	[83]
US5616343	Rong-Kun *et al.*	1998	Cross-linked amylose as a binder in tablet formulation	[65]
US5989589	Rong-Kun and Ashton	1975	Cross-linked cellulose as a tablet excipient	[66]
US20110053271	Petzold *et al.*	2011	Irradiation induced grafting of polysaccharide to cell culture vessels	[84]
US007999040	Patil *et al.*	2011	Method of making graft copolymers from sodium poly (aspartate) and the resulting graft copolymer	[85]

Deogade *et al.* mentioned grafting of natural gums to prepare tailor-made advanced polymers and their importance and applications.[56] TS gum with MMA was grafted by Shailaja *et al.* chemical method of grafting by ascorbic acid redox pair and potassium persulfate has been selected for grafting.

Physical characterization showed no fall of viscosity on storage, and controlled rate of hydration of grafted TS polysaccharide (TSP).[86] TSP from tamarind kernel powder was isolated by Ganesan *et al*. and investigated for sustained release of tablet granules of salicylic acid by means of two dissimilar grades of TSP, cross linked TSP and embedded with chemically synthesized ZnS nanocrystals. Formulation containing TSP and cross linked released drug in sustained manner, and there were no noteworthy changes in drug content and physical parameters.[87]

Graft copolymerization of acrylic acid on guar gum which is initiated by vanadium (V)-mercaptosuccinic acid redox pair was performed by Pandey *et al.* The most favorable reaction conditions giving maximum grafting ratio, efficiency and conversion have been studied.[88] Osemeahon *et al.* have developed sodium alginate and konkoli gum grafted polyacrylamide blend membrane. It was observed that grafting parameters such as acrylamide, ceric ammonium nitrate, konkoli gum, temperature and reaction time had notable influence on percent graft yield of the graft copolymer. Results showed the optimum grafting conditions required for copolymerization of acrylamide onto konkoli gum.[89] Varshosaz *et al.* have developed sustained release matrix tablets of extremely water soluble tramadol HCl using xanthan gum and guar gum as non-toxic, easily available, cheap and suitable hydrophilic matrix systems against broadly investigated hydrophilic matrices (i.e., hydroxypropyl methylcellulose [HPMC] or carboxymethyl cellulose).[90]

da Silva *et al.* have grafted acrylamide onto CG. The radical polymerization technique was used for synthesis of CG grafted polyacrylamide using potassium persulfate as redox initiator under N2 environment. Acrylamide concentration was varied, whereas concentration of initiator and polysaccharide was kept constant to prepare series of graft copolymers. Comparison between grafting parameters of reaction of variety of natural polysaccharides with polyacrylamide was done. A high percentage of acrylamide conversion (%C) and grafting efficiency (GE) (%E) were obtained for CG, also with a low acrylamide/CG ratio.[57] Mundargi *et al.* have prepared controlled release matrix tablets for antihypertensive drugs such as atenolol and carvedilol using acrylamide grafted xanthan gum. Tablets were manufactured using plain xanthan gum, grafted xanthan gum, and other excipients. With increasing grafting ratio, release time increased and swelling pointed out that xanthan gum showed the highest swelling compared to graft copolymers. The drug release via matrix tablets followed the non-Fickian (anomalous) trend.[58] Vijan *et al.* have synthesized acrylamide grafted gellan gum in microwave assisted free radical polymerization method using ceric ammonium nitrate as initiator. By varying in amount of

Table 3: Natural gums gaining importance for grafting

Gum	Botanical name	Family	Applications	References
Albizia gum	*A. zygia*	Leguminosae	Emulsifier, coating material	[66,67]
Almond gum	*P. amygdalus*	Rosaceae	Binder, emulsifier	[68]
Bhara gum	*T. bellerica*	Combretaceae	Microencapsulating agent	[69]
Cordia gum	*C. oblique*	Boraginaceae	Binder, emulsifier	[70]
Grewia gum	*G. mollis*	Tiliaceae	Binder, film forming agent	[71,72]
Gum copal	*B. bipinnata*	Burseraceae	Film forming agent	[73]
Gum dammar	*S. wiesneri*	Dipterocarpaceae	Microencapsulating agent	[74]
Hakea gum	*H. gibbosa*	Proteaceae	Mucoadhesive component	[75]
Honey locust gum	*G. triacanthos*	Leguminosae	Binder	[76]
Khaya gum	*K. grandifolia*	Meliaceae	Binder	[77]
Mango gum	*M. indica*	Anacardiaceae	Disintegrating agent	[91]
Mimosa scabrella gum	*M. scabrella*	Mimosaceae	Matrix forming agent	[92]
Moi gum	*L. coromandelica*	Anacardiaceae	Microencapsulating agent	[93]
Moringa oleifera gum	*M. oleifera*	Moringaceae	Binder	[94]
Mucuna gum	*M. flagillepes*	Papillionaceae	Microencapsulating agent	[95]
Neem gum	*A. indica*	Meliaceae	Binder	[96]
Olibanum gum	*B. serrate*	Burseraceae	Binder	[97]

A. zygia: Albizia zygia, P. amygdalus: Prunus amygdalus, T. bellerica: Terminalia bellerica, C. oblique: Cordia oblique, G. mollis: Grewia mollis, B. bipinnata: Bursera bipinnata, S. wiesneri: Shorea wiesneri, H. gibbosa: Hakea gibbosa, G. triacanthos: Gleditsia triacanthos, K. grandifolia: Khaya grandifolia, M. indica: Mangifera indica, M. scabrella: Mimosa scabrella, L. coromandelica: Lannea coromandelica, M. oleifera: Moringa oleifera, M. flagillepes: Mucuna flagillepes, A. indica: Azadirachta indica, B. serrate: Boswellia serrate

acrylamide, ceric ammonium nitrate and microwave irradiation time, a series of graft copolymers was prepared. Comparison of grafting parameters like GE, percent grafting and percent conversion was done. Three independent process variables were used to optimize synthetic parameters including amount of ceric ammonium nitrate, amount of acrylamide and microwave irradiation time. Elevated level of all these three variables had given higher grafting efficiency (GE%) of grafted gum. Tablets were prepared by incorporating anti-diabetic drug, metformin hydrochloride in grafted gum along with excipients.[55]

Kaity *et al.* have synthesized acrylamide grafted LBG by microwave irradiation in which ceric ammonium nitrate was used as initiator. It was later used to formulate controlled release matrix tablets of buflomedil hydrochloride. *In vitro* release profile of tablet showed that rate controlling property of acrylamide grafted LBG was parallel to that of HPMC-K15M. Some of the importance of natural gums are shown in Table 3.[54]

CONCLUSION

Polymers and their derivatives are budding in last few years as most widely used biomaterials in the area of drug delivery system. In recent times, immense snooping has been compensated to the modification of natural polymers to obtain new hybrid materials. Modified polymers can be used in designing a range of controlled and sustained drug release systems. Most of the exploration on natural polymers in various novel drug delivery systems plays around polysaccharides. Natural gums can also be modified to fight with and defeat some disadvantages of synthetic polymers to get tailor-made products for designing a much better drug delivery systems. Even if the use of traditional gums has continued, newly identified and isolated gums have been widely used and modified owing to their exceptional qualities. There is enormous scope for research on newer natural gums and mucilages and their grafting modification. In the present and upcoming future, it could be further exploited as ground-breaking modified natural polymers for the development of various drug delivery systems in pharma manufacturing business.

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REFERENCES

1. Kottke KM, Edward MR. Tablet dosage forms. In: Banker GS, Rhodes CT, editors. Modern Pharmaceutics. New York: Marcel Dekker, Inc.; 2002. p. 287-333.
2. Alam AS, Parrott EL. Effect of aging on some physical properties of hydrochlorothiazide tablets. J Pharm Sci 1971;60:263-6.
3. Chang RK, Shukla AJ. Polymethacrylates. In: Raymond CR, Paul JS, Paul JW., editors. Handbook of Pharmaceutical Excipients. New York: Pharmaceutical Press and the American Pharmaceutical Association; 2003. p. 462-8.
4. Al-Tahami K, Singh J. Smart polymer based delivery systems for peptides and proteins. Recent Pat Drug Deliv Formul 2007;1:65-71.
5. Hizawa K, Inaba H, Nakanishi S, Otsuka H, Izumi K. Subcutaneous pseudosarcomatous polyvinylpyrrolidone granuloma. Am J Surg Pathol 1984;8:393-8.
6. Kolen JJ, McGinity JW, Wilber WR. Carbomer-934P. In: Raymond CR, Paul JS, Paul JW, editors. Handbook of Pharmaceutical Excipients. New York: Pharmaceutical Press and the American Pharmaceutical Association; 2003. p. 89-92.
7. Weller PJ, Owen SC. Polyvinyl alcohol. In: Raymond CR, Paul JS, Paul JW, editors. Handbook of Pharmaceutical Excipients. New York: The Pharmaceutical Press and the American Pharmaceutical Association; 2003. p. 491-2.
8. Zohuriaan MJ. Advances in chitin and chitosan modification through graft copolymerization: A comprehensive review. Iran Polym J 2005;14:235-65.
9. Soppimath KS, Aminabhavi TM, Dave AM, Kumbar SG, Rudzinski WE. Stimulus responsive smart hydrogels as novel drug delivery systems. Int J Pharm 2002;34:212-25.
10. Russell KE. Free radical graft polymerization and copolymerization at high temperatures. Progress Polym Sci 2002;27:1007-38.
11. Szwarc M. Living polymers: Their discovery, characterization and properties. J Polym Sci A 1998;36:9-15.
12. Stehling UM, Malmstrom EE, Waymouth RM, Hawker CJ. Synthesis of poly (olefin) graft copolymers by a combination of metallocene and living free radical polymerization techniques. Macromolecules 1998;31:4396-8.
13. Percec V, Barboiu B. Living radical polymerization of styrene initiated by arenesulfonyl chlorides and CuI (bpy) n Cl. Macromolecules 1995;28:7970-2.
14. Wang JS, Matyjaszewski K. Controlled 'living' radical polymerization. Atom transfer radical polymerization in the presence of transition-metal complexes. J Am Chem Soc 1995;117:5614-5.
15. Matyjaszewski K, Xia J. Atom transfer radical polymerization. Chem Rev 2001;101:2921-90.
16. Matyjaszewski K. Transition metal catalysis in controlled radical polymerization: Atom transfer radical Polymerization. Chem Eur J 1999;5:3095-102.
17. Coessens V, Pintauer T, Matyjaszewski K. Functional polymers by atom transfer radical polymerization. Progress Polym Sci 2001;26:337-77.
18. Kato M, Kamigaito M, Sawamoto M, Higashimura T.

Polymerization of methyl-methacrylate with: The carbon tetrachloride (triphenylphosphine) ruthenium (II) bis (2, 6-di-tert butyl phenoxide) initiating system possibility of living radical polymerization. Macromolecules 1995;28:1721-3.
19. Bellobono IR, Calgari S, Leonari MC, Selli E, Paglia ED. Photochemical grafting of acrylated. Azo dyes onto polymeric surfaces. Die Ang Makromol Chem 1981;100:135-46.
20. Kubota H, Suka IG, Kuroda S, Kondo T. Introduction of stimuli-responsive polymers into regenerated cellulose film by means of photo grafting. Eur Polym J 2001;37:1367-72.
21. Peng T, Cheng YL. PNIPAAm and PMAA cografted porous PE membranes: Living radical co-grafting mechanism and multi-stimuli responsive permeability. Polymer 2001;42:2091-100.
22. Chen T, Kumar G, Harries MT, Smith PJ, Payne GF. Enzymatic grafting of hexyloxyphenol of chitosan to alter surface and rheological properties. Biotechnol Bioeng 2000;70:564-73.
23. Uchida E, Uyama Y, Ikada YA. Novel method for graft polymerization onto poly (ethyleneerephthalate) film surface by UV-irradiation without degassing. J Appl Polym Sci 1990;41:677-87.
24. Wenzel A, Yamgishita H, Kitamoto D, Endo A, Haraya KT, Nakane T. Effect of preparation condition of photo induced graft filling polymerized membranes on pervaporation performance. J Membr Sci 2000;179:69-77.
25. Bhattacharya A, Das A, De A. Structural influence on grafting of acrylamide based monomers on cellulose acetate. Indian J Chem Technol 1998;5:135-8.
26. Chen J, Iwata H, Maekawa Y, Yoshida M, Tsubokawa N. Grafting of polyethylene by gradiation grafting onto conductive carbon black and application as novel gas and solute sensors. Radiation Phys Chem 2003;67:397-401.
27. Marmey P, Porte MC, Baquey C. PVDF multifilament yarns grafted with polystyrene induced by γ-irradiation: Influence of the grafting parameters on the mechanical properties. Nucl Instrum Methods B 2003;208:429-33.
28. Uflyand IE, Ilchenko IA, Sheinker VN, Savostyanov VS. Polymers containing metal chelate units. Post-graft polymerization of metal chelate monomers based on 1- phenyl-4-methyl pent-4- ene-1, 3 dione. React Funct Polym 1992;17:289-96.
29. Yamaki T, Asano M, Maekawa Y, Morita Y, Suwa T, Chen J. Radiation grafting of styrene into cross-linked PTFE films and subsequent sulfonation for fuel cell applications. Radiation Phys Chem 2003;67:403-7.
30. Kaur I, Barsola R, Gupta A, Misra BN. Graft copolymerization of acrylonitrile and methacrylonitrile onto gelatin by mutual irradiation method. J Appl Polym Sci 1994;54:1131-9.
31. Kaur I, Misra BN, Chauhan MS, Chauhan S, Gupta A. Viscometric, conductometric and ultrasonic studies of gelatin-gpolyacrylamide composite. J Appl Polym Sci 1996;59:389-97.
32. Bhattacharyya SN, Maldas D, Pandey VK. Radiation induced graft copolymerization of N- vinyl carbazole and methylmethacrylate onto cellulose acetate film. J Polym Sci 1986;24:2507-15.
33. Kaur I, Misra BN, Barsola R, Singla K. Viscometric studies of starch-g-polyacrylamide. J Appl Polym Sci 2003;47:1165-74.
34. Basu S, Bhattacharya A, Mondal PC, Bhattacharyya SN. Spectroscopic evidence for grafting of N-vinyl carbazole on cellulose acetate film. J Polym Sci Polym Chem 1994;32:2251-5.
35. Aich S, Bhattacharya A, Basu S. Fluroscence polarization of Nvinyl carbazole on cellulose acetate film and electron transfer with 1, 4 dicyanobenzene. Radiation Phys Chem 1997;50:347-54.
36. Aich S, Sengupta T, Bhattacharya A, Basu S. Magnetic field effect on an exciplex between N-vinyl carbazole grafted on cellulose acetate film and 1,4 dicyanobenzene. J Polym Sci Polym Chem 1999;37:3910-5.
37. Pepenzhik MA, Virnik AD, Rogovin ZA. Synthesis of graft cellulose copolymers and calcium salt of poly (acrylic acid). Vysokomol Soedin Ser B 1969;11:245-50.
38. Mishra BN, Dogra R, Mehta IK. Grafting onto cellulose V Effect of complexing agents on Fenton's reagent (Fe^{+2}-H2O2) initiated grafting of poly (ethyl acrylate). J Polym Sci Polym Chem 1980;18:749-52.
39. Mishra BN, Mehta IK, Khetrapal RC. Grafting onto cellulose. Graft copolymerization of poly (ethylacrylate) onto cellulose by use of redox initiators. Comparison of initiator reactivities. J Polym Sci Polym Chem 1984;22:2767-75.
40. Prasanth KV, Tharanathan RN. Studies on graft copolymerization of chitosan with synthetic monomers. Carbohydr Polym 2003;54:43-51.
41. Assay NB. Effect of mineral and organic acids on radiation grafting of styrene onto polyethylene. J Appl Polym Sci 1949;42:885-9.
42. Kumar R, Setia A, Mahadevan N. Grafting modification of the polysaccharide by the use of microwave irradiation - A review. Int J Rec Adv Pharm Res 2012;2:45-53.
43. Xie W, Xu P, Liu WW. Preparation and antibacterial activity of a water-soluble chitosan derivative. Carbohydr Polym 2002;50:35-40.
44. Ng LT, Garnett JL, Zilic E, Nguyen D. Effect of monomer structure on radiation grafting of charge transfer complexes to synthetic and naturally occurring polymers. Radiation Phys Chem 2001;62:89-98.
45. Yasukawa T, Sasaki Y, Murukami K. Kinetics of radiation induced grafting reactions. II. Cellulose acetate-styrene systems. J Polym Sci Polym Chem 1973;11:2547-56.
46. Dilli S, Garnett JL. Radiation induced reactions with cellulose. III. Kinetics of styrene copolymerization in methanol. J Appl Polym Sci 1967;11:859-70.
47. Bhattacharyya SN, Maldas D. Radiation induced graft

copolymerization of mixtures of styrene and acrylamide onto cellulose acetate. I. Effect of solvents. J Polym Sci Polym Chem 1982;20:939-50.
48. Nishioka N, Matsumoto N, Kosai K. Homogeneous graft copolymerization of vinyl monomers onto cellulose in a dimethyl sufoxide-paraformaldehyde solvent system. Polymer 1983;15:153-8.
49. Sun T, Xu P, Liu Q, Xue J, Xie W. Graft copolymerization of methacrylic acid onto carboxymethyl chitosan. Eur Polym J 2003;39:189-92.
50. Samal S, Sahu G, Lenka S, Nayak PL. Graft copolymerization of methylmethacrylate onto silk using isoquinoline - sulphur dioxide charge transfer complex as the initiator. J Appl Polym Sci 1987;33:1853-8.
51. Maldas D. Radiation induced grafting of styrene and acrylamide on cellulose acetate from a binary mixture. Thesis, India: University of Calcutta; 1983. p. 47.
52. Chappas WJ, Silverman J. The effect of acid on the radiation induced grafting of styrene to polyethylene. Radiation Phys Chem 1979;14:847-52.
53. Hoffman AS, Ratner BD. The radiation grafting of acrylamide to polymer substrate in the presence of cupric ion. I. A preliminary study. Radiation Phys Chem 1979;14:831-40.
54. Kaity S, Isaac J, Mahesh Kumar P, Bose A, Wong TW, Ghosh A. Microwave assisted synthesis of acrylamide grafted locust bean gum and its application in drug delivery. Carbohydr Polym 2013;98:1083-94.
55. Vijan V, Kaity S, Biswas S, Isaac J, Ghosh A. Microwave assisted synthesis and characterization of acrylamide grafted gellan, application in drug delivery. Carbohydr Polym 2012;90:496-506.
56. Deogade UM, Deshmukh VN, Sakarkar DM. Natural gums and mucilage in NDDS: Application and recent approaches. Int J PharmTech Res 2012;4:799-814.
57. da Silva DA, Regina CM, Judith PA. Graft copolymerization of acrylamide onto cashew gum. Eur Polym J 2007;43:2620-9.
58. Mundargi RC, Patil SA, Aminabhavi TM. Evaluation of acrylamide-grafted-xanthan gum copolymer matrix tablets for oral controlled delivery of antihypertensive drugs. Carbohydr Polym 2007;69:130-41.
59. Babu GV, Himasankar K, Janaki Ram B. Studies on preparation and evaluation of modified form of gum Karaya. Indian J Pharm Sci 2002;64:244-9.
60. Jani GK, Goswami JM, Prajapati VD. Studies on formulation and evaluation of new super disintegrants for dispersible tablets. Int J Pharm Exc 2005;2:37-43.
61. Rama Rao N, Rao UM. Hypochlorate modified potato starch: A new potato starch derivative as potential tablet disintegrant. Int J Pharm Exc 2000;3:216-9.
62. Gohel MC, Patel SD, Shah NK. Evaluation of synthesized cross-linked tragacanth as a potential disintegrant. Indian J Pharm Sci 2010;59:113-8.
63. Trivedi BM, Patel PM, Patel LD. Cross linked gum acacia as a disintegrant. Indian J Pharm Sci 1986;48:188-90.
64. Baveja JM, Misra AN. Modified guar gum as a tablet disintegrant. Pharmazie 1997;52:856-9.
65. Rong-Kun C, Mirwais S, Michael L. Evaluation of the disintegrant properties for an experimental, cross linked polyalkylammonium polymer. Int J Pharm 1998;173:87-92.
66. Ashton WA, Jefferies M, Morley RG, Pass G, Phillips GO, Power DM. Physical properties and applications of aqueous solutions of *Albizia zygia* gum. J Sci Food Agric 1975;26:697-704.
67. National Academy of Sciences. Tropical Legumes Resources for the Future. Washington, DC: USA: National Academy for Sciences; 1979.
68. Sarojini S, Kunam SD, Manavalan R, Jayanthi B. Effect of natural gum as a binder in the formulation of diclofenac sodium tablets. Int J Pharm Sci Res 2010;1(3):55-60.
69. Nayak BS, Nayak UK, Patro KB, Rout PK. Design and evaluation of controlled release Bhara microcapsules of famotidine for oral use. Res J Pharm Tech 2008;1:433-6.
70. Dinda SC, Mukharjee B. Gum cordia - A new tablet binder and emulsifier. Acta Pharm Sci 2009;51:189-98.
71. Martins E, Christiana I, Olobayo K. Effect of grewia gum on the mechanical properties of paracetamol tablet formulations. Afr J Pharm Pharmacol 2008;2:1-6.
72. Ogaji I, Okafor IS. Potential of grewia gum as film coating agent: Some physicochemical properties of coated praziquantel tablets. Int J Pharm Res 2011;3:16-9.
73. Umekar MJ, Yeole PG. Characterization and evaluation of natural copal gum-resin as film forming material. Int J Green Pharm 2008;2:37-42.
74. Morkhade DM, Joshi SB. Evaluation of gum damar as a novel microencapsulating material for ibuprofen and diltiazem hydrochloride. Indian J Pharm Sci 2007;69:263-8.
75. Alur HH, Pather SI, Mitra AK, Johnston TP. Evaluation of the gum from *Hakea gibbosa* as a sustained-release and mucoadhesive component in buccal tablets. Pharm Dev Tech 1999;4:347-58.
76. Uner M, Altinkurt T. Evaluation of honey locust (*Gleditsia triacanthos* Linn.) gum as sustaining material in tablet dosage forms. Farmaco 2004;59:567-73.
77. Odeku OA, Itiola OA. Evaluation of the effects of khaya gum on the mechanical and properties of paracetamol tablets. Drug Dev Ind Pharm 2003;29:311-20.
78. Borunsky J. Process for grafting a monomer onto an oxidized polysaccharide. U.S. Patent 3,138,564, June 23, 1964.
79. Horowitz C. Method of grafting polymerizable monomer onto substrates and regulant article. U.S. Patent 3, 401, 049, September 10, 1968.
80. Henry GG. Method for preparing polysaccharide graft copolymers. U.S. Patent 3, 455, 853, July 15, 1969.
81. Gunn E, Liu Z, Priou C, Gabbianelli A, Warburton SA. Polysaccharide graft copolymers and their use in personal care applications. U.S. Patent 20060029561, February 09, 2006.
82. De Angelis PL. Polymer grafting by polysaccharide synthases. U.S. Patent 7,575,904, August 18, 2009.

83. Liu LZ, Priou C. Grafting polymerization of guar and other polysaccharides by electron beams. U.S. Patent 7,838,667, November 23, 2010.
84. Petzold ON, Ravichandran V, Senaratne W. Irradiation induced grafting of polysaccharides to cell culture vessels. U.S. Patent 20110053271, March 03, 2011.
85. Patil DR, Hills P, Fan LG, Fan JC, Yu J. Method of making graft copolymers from sodium poly (aspartate) and the resulting graft copolymer. U.S. Patent 007999040, August 16, 2011.
86. Shailaja T, Latha K, Sasibhushan P, Alkabab AM, Uhumwangho UM. A novel bioadhesive polymer: Grafting of tamarind seed polysaccharide and evaluation of its use in buccal delivery of metoprolol succinate. Pharm Lett 2012;4:487-508.
87. Ganesan K, Rajaram SK, Chinnathambi A. A sustained release of tablet granules associated with ZnS nanocrystals using tamarind seed polysaccharide. J Appl Pharm Sci 2013;3:44-7.
88. Pandey PK, Srivastava A, Tripathy J, Behari K. Graft copolymerization of acrylic acid on to guar gum initiated by vanadium (V)-mercapto succinic acid redox pair. Carbohydr Polym 2006;65:414-20.
89. Osemeahon SA, Barminas TJ, Aliyu BA, Nkafamiya II. Development of sodium alginate and konkoli gum grafted polyacrylamide blend membrane: Optimization of grafting condition. Afr J Biotech 2008;7:1309-13.
90. Varshosaz J, Tavakoli N, Kheirolahi F. Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of tramadol hydrochloride. AAPS PharmSciTech 2006;7:E24.
91. Ravi KN, Sachin R, Mirtyunjaya B. Evaluation of disintegrating properties of *Mangifera indica*. RGUHS J Pharm Sci 2011;1:11-20.
92. Vendruscolo CW, Andreazza IF, Ganter JL, Ferrero C, Bresolin TM. Xanthan and galactomannan (from *M. scabrella*) matrix tablets for oral controlled delivery of theophylline. Int J Pharm 2005;296:1-11.
93. Nayak BS, Nayak UK, Patro KB, Rout PK. Preparation and *in vitro* evaluation of lamivudine entrapped MOI microspheres for oral administration. Res J Pharm Tech 2008;1:437-41.
94. Panda D, Choudhury NS, Yedukondalu M, Si S, Gupta R. Evaluation of gum of *Moringa oleifera* as a binder and release retardant in tablet formulation. Indian J Pharm Sci 2008;70:614-8.
95. Anthony AA, Nwabunze OJ. Mucuna gum microspheres for oral delivery of glibenclamide: *In vitro* evaluation. Acta Pharm 2007;57:161-71.
96. Gangurde AB, Malode SS, Bhambar RS. Preliminary evaluation of neem gum as tablet binder. Indian J Pharm Educ Res 2008;42:344-7.
97. Prasanthi NL, Manikiran SS, Rao NR. *In vitro* drug release studies of ziprasidone from tablets using natural gums from biosphere. Arch Appl Sci Res 2011;3:513-9.

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