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REVIEW

Advanced Dosage Form Design: Role of Modified Natural Gums

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Gums are naturally occurring segments in plants, which are cheap and abundant. Natural gums and their derivatives are widely used in a pharmaceutical dosage form. These natural materials possess several advantages over synthetic ones being chemically inert, non-toxic, low cost and biodegradable. However, quick degradation in the body, poor mechanical properties and low solubility are few disadvantages. To overcome these disadvantages, natural gums are modified by applying different chemical modification procedures. The modification of gums is done *via* various methods such as changing functional groups of gum, cross-linking with ions, grafting with polymers, sulfation, phosphorylation and thiolation. Modification of gums results in some superior properties which can be used in drug delivery applications. For example, change in crystallinity, improved solubility, stability, and improved mechanical properties are of use in development of modified drug delivery systems. Modified gums help to achieve pH dependent delivery and sustained delivery along with improved release kinetics of the drug. Current review covers various types of modifications in general and research literature on various medications of different gums (locust bean gum, cashew gum, moringa gum, xanthan gum, *etc*.). The modified natural gums and their derivatives can be the prospective carriers in the controlled drug delivery of drugs.

Keywords: Natural Gums, Modification, Cross-linking, Grafting, Sulfation, Sustained release.

INTRODUCTION

Gums are natural polysaccharides [1] and pathological products, which easily dissolves in water, also called as hydrocolloids [2,3]. Gums are produced when the plants are injured or growing under unfavourable conditions. Therefore, it is said that gums are abnormal products of plant metabolism and process is named as "gummosis". Gums are soluble or partly soluble in water and insoluble in alcohol and most of the organic solvents [4,5]. Gums are grouped into three categories: (a) **Natural gums**: It is found in the natural state and obtained from tree exudates, extracted from seeds of some legumes or seaweed hydrocolloids. These are polysaccharides consisting of multiple sugar units linked together to create large molecules such as arabinose, glucose, galactose, mannose, uronic acids and xylose (*e.g.* gum arabica, guar gum and tragacanth); (b) **Modified gums**: These are chemically modified natural gums or are derivatives of naturally occurring materials such as cellulose (*e.g.* carboxymethyl cellulose); and (c) **Synthetic gums**: These are completely synthesized products (*e.g.* polyvinyl pyrrolidone, polyethylene oxide).

Natural gums are promising biodegradable polymeric materials. They have found a great use in the pharmaceutical industries over synthetic materials due to their non-toxic, ease of availability, low cost and biodegradability properties [6]. Polymers have been successfully employed in the formulation of solid, semi-solid and liquid dosage forms and are especially useful in the design of modified release drug delivery systems. They are explored as an emulsifier, adhesives, suspending agent and binding agents. Guar gum, locust bean gum, xanthan gum,

ghatti gum, tamarind seed gum, cashew gum, karaya gum, gellan gum, mango gum are some of the examples, which can be used as excipients in manufacturing of dosage forms [1,7]. Most of the natural gums are associated with certain problems such as pH dependent solubility, change in viscosity on storage, uncontrollable swelling and microbial contamination. Chemical modifications of gums can be carried out to minimize these problems [3] and can compete with synthetic gums for drug delivery applications [8]. Modification of gums can develop polymers with desirable properties for selected industrial applications [9]. Natural polymers have become a thrust area in majority of investigations in drug delivery systems [10]. Modified gums have a variety of applications in pharmacy such as in medicines for their demulcent properties for cough suppression [11]. These are used in dental ingredients and other adhesives. It can be used as bulk laxatives [12]. The hydrophilic polymers are useful as tablet binders, emulsifiers, disintegrant, suspending agents, stabilizing agents, gelling agents, thickening agents, film-forming agents in transdermal and periodontal films, buccal tablets as well as sustaining agents in matrix tablets and coating agents in microcapsules [13].

Techniques for modification of natural gums: Natural gums are modified with chemicals to give them new properties for broader applications. Sometimes, modification can produce a very specific effect because of the novel properties of new structure [14]. Various techniques are used for modifications of natural gums in drug delivery such as carboxymethylation, grafting, cross-linking, sulfation, phosphorylation and thiolation, which are discussed as follows:

Carboxymethylation technique: This technique is widely used to increase hydrophilicity by making the gum more soluble in aqueous systems [15,16]. It involves covalent attachment of $–CH_2COOH$ moiety at the 6^{th} position of hexose by replacing –OH moiety [17] and leads to formation of polyelectrolyte, which helps to increase solubility of the gum [18]. It releases the drug at a specific pH and protects the drug from degradation at acidic pH. This technique is utilized in the modification of gum kondagogu, xanthan gum, guar gum and cassia tora gum, chitosan and tamarind kernel powder [19]. This modification leads to increased hydrophilicity and aqueous solubility of gums, increased transparency of gum solutions. Various steps in carboxymethylation process are shown in Fig. 1.

Grafting technique: In this technique, a monomer unit is attached to another functionalized polymer which forms grafted polymer. Acrylic derivatives or their subordinates have been utilized in such modification and resulted in improved swelling, drug discharging and film-forming properties. Some of the gums such as xanthan gum, arabic gum and acacia gum is modified by using grafting technique [20]. Grafting leads to increased stability, compatibility and inflexibility, biodegrad-

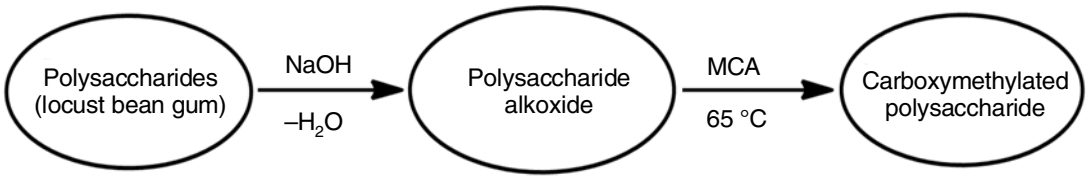

Fig. 1. Diagrammatic representation of carboxymethylation process

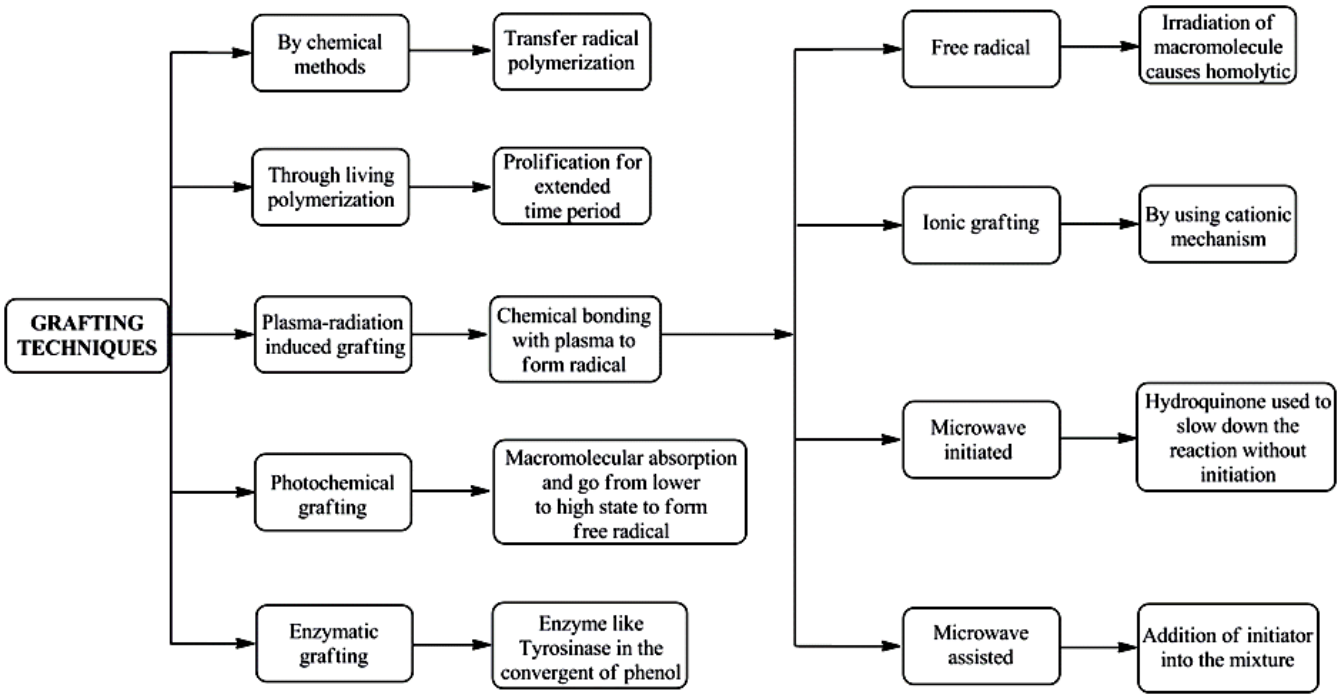

Fig. 2. Various types of grafting techniques

ability, non-toxic, alter discharge of drug. Grafting of gums *via* various methods is shown in Fig. 2.

Cross-linking technique: This technique is use to create ionic and covalent bonds between two polysaccharide chains by the addition of cross-linking agent. For example, addition of unpolymerized or partially polymerized gum with specific crosslinker results in formation of bonds in chemical reaction. This bond formation directly depends upon the ratio of cross-linker used. This technique is used to modify guar gum, gellan gum and cashew gum [21]. Increased quality and mass of gum, prevents oxidation, versatility are some of the advantages offered by the cross linking technique in modification of gums.

Sulfation: Sulfated gums are modified by replacing hydroxyl group with sulphate moieties [21]. These sulphate polysaccharides are classified as L-series agarans and D-series carrageenans and galactans with α-galactose linkage. In sulfation technique, formaldehyde, dimethylformaldehyde, dimethyl sulphoxide and pyridine are widely used as solvents [22]. Konjac glucomannan gum, aegle marmelos gum and guar gum can be modified with this technique [23].

Phosphorylation: Phosphorylation includes the attachment of dihydrogen phosphate group at 2, 3, and 4-position of hexane [21]. It directly depends on the thermal reaction of polysaccharide with various phosphoric acid salts [24]. Phosphorylation helps to modify guar gum, xanthan gum, sesbania gum, durian seed gum and gum arabic.

Thiolation: Thiolation involves cross-linking between aryl group and thiol group occurred by the development of strong covalent bond [21]. It helps to improve drug permeation, inhibits efflux pump and increases mucoadhesiveness and *in situ* gelling properties. Thus, it is widely used in mucoadhesive drug delivery systems [25]. Thiolation technique helps to modify chitosan, pectin, gellan gum and gum karaya. Thiolation process leads to gelation properties, high stability, high biocompatibility, permeation enhancement and controlled drug release.

Role of modified natural gums in drug delivery

Guar gum in drug delivery: Guar gum is a water-soluble polysaccharide obtained from plant *Cyamopsis tetragonoloba*, a member of Leguminosae family. It comprises of a linear chain of 1,4-β-D-mannopyransoyl with 1,6-α-D-galactopyranosyl, mannopyranosyl, galactopyranose units. It is acquired by the agrochemical process from the endosperm of cluster bean [26]. It is utilized in industries since it can form hydrogen bonds with water. In the reaction of guar gum with complexing agent like organic titanates in the presence of chromium and aluminum salts, formation of thick gel with greater hydration rate. Guar gum is soluble in cold water and possesses binding, disintegration, suspending, thickening and stabilizing properties [27]. Various modifications of guar gum have been evidenced by researchers for application in modified release drug delivery. For example, guar gum succinate and sodium alginate beads were fabricated for colon targeted drug delivery and evaluated for pH-dependent swelling and drug release behaviour. The fabricated beads showed more swelling at pH 7.4 than at pH 1.2 and exhibited no cytotoxicity [28]. Another study utilized microwave radiations to modify guar gum using grafting co-polymerization reaction using different grades of polymer. Modified gum was evaluated for swelling at various temperatures and pH for the appropriate application in various segments of the gastrointestinal tract. The release of 5-amino salicylic acid was studied using these carriers for the treatment of inflammatory bowel disease [29]. Previous workers prepared esomeprazole nanoparticles using guar gum pH-sensitive copolymer for intestinal drug delivery. The copolymeric impact was synthesized using polyacrylamide and guar gum (PAAm-*g*-GG) (GG = guar gum) in alkaline hydrolysis. The drug loaded nanoparticles demonstrated a delayed release of the drug in the acidic environment [30]. Further, pH-sensitive pellets of glimepiride utilizing copolymer of polyacrylamide and guar gum (PAA-*g*-GG) by extrusion spheronization pelletization technique. The pAA-*g*-GG was set up with various concentrations of guar gum (1:2, 1:35 and 1:5). The amide group of graft copolymer was converted into carboxylic group. Microcrystalline cellulose was added during pelletization. Drug release was extended with increasing guar gum concentration upto 60 days at various temperatures. The modified polymeric complex facilitated pH sensitive drug delivery system for colon targeting [31]. Shruthi *et al*. [32] utilized silane modified nanoclay to prepare acrylic acid grafted guar gum nanocomposites *via* microwave irradiation technique. The superabsorbent nanocomposites loaded with 1.75% modified nanoclay was found to be optimal concentration for the removal of crystal violet dye [32]. Further sodium hydroxide activated guar gum blended with *n*-butyl glycidyl (BGE) to form 2-alkenyl-3-butoxypropyl guar gum (ABPG) and the resulting modified gum was incorporated into gel and characterized using RS6000 rheometer. The novel guar gum showed greater resistance and shear strength properties [33]. Praphakar *et al*. [34] reported an improved pH-responsive release of 5-fluorouracil (5-FU) loaded into guar gum united lysine-β-CD as a drug transporter. The *in vitro* evaluation demonstrated that there is significantly high drug release in acidic pH than basic pH, which was further indicated in cytotoxicity studies where cytotoxicity against KB cells with an IC_{50} estimation of 1.38 µg/mL was observed. Conclusive outcomes showed that KB cells enhance cell death with effective and successful activity on cancer treatment with inhibitory tumor cell activity [34].

Cashew gum in drug delivery: Cashew gum is the exudate from stem bark of *Anacardium occidentale*. Its atomic structure contains galactose, arabinose, rhamnose, glucose, glucuronic acid and other sugar deposits. It is hydrophilic and branched polysaccharide with higher sub-atomic mass [35]. It is biodegradable and biocompatible and is generally utilized as a binding agent, matrix-forming agent and floating bioadhesive in drug delivery systems [36]. Modification of cashew gum helps to accomplish its improved reactivity and can be viably used to formulate micro and nano-formulation for controlled release. It is utilized as suspending emulsifying agent in tableting for sustained drug delivery, mucoadhesive and gelling properties [37]. Lima *et al*. [38] utilized cashew gum polysaccharide for a self-composed nano-particulate delivery system, using acetylation reaction on cashew gum. A 2^3 factorial designs have been applied to study the effect of temperature and time on

yield and acetylation levels. A self-organized nano-particulate delivery system based on acetylated cashew gum with a size range 190-300 nm for long term release of amphotericin B. Bittencourt *et al*. [39] reported a film of dermaseptin 01 (DRS 01) and cashew gum to distinguish Lestmania cells and maintaining anti-leishmanial action. DRS01 peptide was conjugated with cashew gum on indium tin oxide by utilizing the layer-by-layer deposition technique. Conclusive outcome exhibits that thin film of dermaseptin 01shows anti-leishaminal action with carpet like mechanism.

Cruz *et al*. [40] mixed cashew gum polysaccharide (CGP) and polyvinyl alcohol (PVA) to create two film formulation of trypsin against *Platypodium elegans* and *Inga laurina* by using casting method. The CGP/PVA film proved better due to high rigidity, stretching and solid mechanical properties and 2 fold up higher movement and drug release after 720 min. The study confirmed that prepared film can be effectively utilized for immobilization. Jesus-Oliveira *et al*. [41] fabricated diclofenac diethylamine nanoparticles using acetylated cashew gum by nanoprecipitation and dialysis methods with improved stability and yield. The two techniques showed 60% entrapment with no cytotoxic impact on cell viability. Controlled release of drug with Fickian diffusion mechanism and 90% transdermal permeation was observed. Amaral-Rodrigues *et al*. [42] prepared chemically modified cashew gum using a solvent-free technique, by varying the concentration of phthalic anhydride and its reaction time. Silver nanoparticles were formulated using this gum, by the green route and conventional route and studied for antimicrobial activity. The phthalate cashew gum AgNPs showed superb antimicrobial properties against *S. aureus* and *E. coli* [42].

Araruna *et al*. [43] encapsulated epiisopiloturine in acetylated cashew gum nanoparticles to enhance the solubility and decreased the rate of drug release. The particles were spherical and highly stable in solution and showed drug incorporation at high levels, upto 55% efficiency. Simiarly, Abreu *et al*. [44] combined silver nanoparticles with cashew gum or carboxymethylated cashew gum through microwave-assisted method for antibacterial action against *S. aureus* and *E. coli* having promising antibacterial properties. Kaur *et al*. [45] reported use of modified cashew gum using *N*-isopropylacrylamide (NIPA) by radical polymerization in drug delivery. Epirubicin loaded nanoparticles in size range of 12-21 nm were prepared using CG-NIPA with 64% EE, 22% drug loading capacity and showed a controlled release oral drug delivery.

Gum ghatti in drug delivery: Gum ghatti is a water soluble complex polysaccharide radiated from the bark of *Anogeissus latifolia* and shows pseudoplastic properties which become more prevalent with increasing concentration of gum ghatti [46]. It is sparingly soluble in water at >5% concentration and due to solubility restriction, makes it colloidal dispersion. Its rheological properties may change by applying strain; consistent shear may influence its emulsifying and gelling properties. It has gelling properties, a surface movement, which may prove its potential for pharmaceutical applications [47]. Various modifications have been reported of gum ghatti. For example, hydrogels of etherified gum ghatti loaded with ropinirole hydrochloride were reported for sustained oral drug delivery. Modification of gum ghatti through the carboxymethylation process resulted in round microbeads which were then embedded in hydrogel bases. About 80-90% drug release was achieved in 6 h at pH 6.8, with fickian diffusion and polymer relaxation mechanisms [48]. Singh *et al*. [4] evaluated the anticancer properties of guar gum and prepared hydrogels by the addition of monomer acrylamide and *N*,*N*-methylenebisacrylamide. The degree of crosslinking affected the equilibrium swelling ratio (ESR), which is correlated the release kinetics of drug [4]. Birajdar *et al*. [49] synthesized polyacrylamide and gum ghatti (PAAm-*g*-GGH) based cross-linked translucent gel for antipsychotic (quetiapine fumarate) drug delivery. Drug infiltration was extended with glutaraldehyde concentration and electric stimuli 2-8 mA. Along these lines, the histopathology study showed a reversible modification of skin under electric stimuli. Further interpenetrating networks (IPN) of GGH-*g*-poly(acrylic destructive aniline) were synthesized by Swart *et al*. [50] for colon targeted delivery of amoxicillin trihydrate and paracetamol. Interpenetrating networks (IPNs) were crosslinked with aniline through oxidative radical polymerization in acidic medium to form a hydrogel. Amoxicillin trihydrate showed surface phenomena and weak interaction whereas paracetamol shows chemical interaction with hydrogel matrices and both follow Fickian behaviour in different pH. Results revealed that drug release was lesser (20%) in acidic and neutral pH than basic pH which makes it progressively suitable for colon targeted delivery [50]. Hydrogel beads of diclofenac sodium were prepared using crosslinked polymers *i.e*. poly(acrylamide-gum ghatti) for enteric drug delivery [51]. Microwave irradiation time, initiator amount and constant gum ghatti amount affected drug release rate. *in vitro* Drug release showed that 20% of drug release at 1.2-5.5 pH for 3 h and 80% of drug was released in 6.8-7.4 pH for 8 h [51]. Bera *et al*. [52] reported alginate-arabic gum gel membrane coated with modified alginate-ghatti gum for mucoadhesive drug delivery. The drug release was extended up to 8 h and best fitted in Korsmeyer- Peppas and Case II transport models. Thus, coated alginate GGH-MMT system proved extended release behaviour [52].

Tragacanth gum in drug delivery: Tragacanth gum is acquired from the dried sap of *Astragalus tragacanth.* This polysaccharide is durable over wide ranges of pH and absorbs water because of its higher hydrophilicity [53]. It has the emulsifying capability, great thermal stability, excellent solvency and can deliver solutions with high viscosity in the presence of heat and acid with an extremely long period of usability [54].

Monjezi *et al*. [55] reported a quercetin loaded hydrogels of tragacanth gum (TG) and modified quaternary ammonium of tragacanth gum (OTG) with acrylic acid to exhibit better antimicrobial activities. Gupta *et al*. [56] synthesized TG-cl-poly-(lactic acid *co*-itaconic acid) by utilizing a microwave-assisted method. The prepared co-polymers showed high swelling *i.e.* 311.6% after 6 h at 25 ºC, however at 60 ºC, it shows 298.06% swelling after 3 h. Amoxicillin was loaded into fabricated gel systems which showed controlled release impact (96%) at pH 2.2 for 6 h, proved more efficient antibacterial activity against

S. aureus. Sahraei and Ghaemy [57] synthesized new composite hydrogels based on gum tragacanth carbohydrate and graphene oxide (GO). These hydrogels were utilized for heavy metal ions removal and the preparation of silver nanocomposite for antibacterial activity. Hemmati *et al*. [58] synthesized hydrogel of tragacanth gum and graphene oxide by utilizing sulfonic oxide, 2-acrylamine-2-methyl propane sulfonic acid and *N*,*N*-methylenebisacylamide. The hydrogel containing AgNPs effectively inhibit Gram-positive bacteria and increased the thermal stability of hydrogel. They [58] fabricated the microgels of tragacanth gum, poly(methyl methacrylate-*alt*-maleic anhydride-*g*-polycaprolactone) (MMA-*alt*-MA)-*g*-PCL-CCH. The model drug (quercetin) was loaded into the microgel which exhibited 40-80% drug release after 7 h. Similarly, Singh and Verma [59] utilized tragacanth gum and ciprofloxacin to form hydrogel for the improvement of diverticulitis. The drug release from the hydrogel followed Korsmeyer-Peppas model, non-Fickian diffusion system and also showed a pH-responsive swelling for site-specific drug delivery.

Xanthan gum in drug delivery: Xanthan gum is obtained from *Xanthomonas campestris* by fermentation procedure. Xanthan gum is a hetropolysaccharide utilized as a biopolymer. It is anionic due to presence of pyrolic acid and glucuronic acid. It mainly consists repeating unit of pentasaccharide formed by two two glucose units, two mannose units and one glucuronic acid unit [60] and exhibit amazing water solubility and great biocompatibility with better thermal stability because of the complex structure. Its production is done by microbial growth procedure [61]. Xanthan solution shows thickening properties with pseudoplastic behaviour, which is entirely steady over a wide range of temperatures and for controlled release of drug. It is utilized as a soluble polymer, wetting agent, stabilizer, gelling agent, viscosity enhancer and film-forming agent [62]. Xanthan gum has been modified by various methods to achieve drug delivery applications. For example, Singh *et al*. [63] synthesized amoxicillin loaded nanoparticles embedded into xanthan gum/acrylic acid for the controlled release of drugs. About 85% drug release was observed in acidic medium which follows the Koresmeyer-Peppas model and also the composites showed antioxidant activity for controlled release of amoxicilin. Sabba *et al*. [64] synthesized hydrogels of bovine serum albumin (BSA) using novel xanthan gum/poly(*N*-vinyl)imidazole as a protein carrier for controlled release drug delivery. Increased polymer concentration lead to increase in release of BSA and follows non-fickian or case II transport systems.

Park *et al*. [65] reported doxorubicin loaded carboxymethyl xanthan gum capped gold nanoparticles (CMXG) prepared through microwave light by altering in CMXG quantity and time. The *in vitro* release from nanoparticles was 4.6 fold than free doxorubicin. Rahdar *et al*. [66] formulated xanthan gum stabilized cerium oxide nanoparticles by the coprecipitation method. Cerium oxide nanoparticles (30 mg/kg) didn't show any huge impact on biochemical and antioxidant properties while CeO_2 nanoparticles 60 mg/kg portion decreases serum liver protein with improving serum catalysis and superoxide dismutase enzyme action and 120 mg/kg lead to inverse impact on biomedical parameters, antioxidant status and liver histology. Hanna and Saad [67] prepared ciprofloxacin loaded hydrogels based on *N*-trimethyl chitosan/sodium carboxymethyl xanthan gum and 96.1% *in vitro* drug release in phosphate buffer in 150 min was observed. The cytotoxicity of hydrogel analyzed on the human cell exhibit 97% cell viability at 50 µg/mL. Laffleur and Michalek [68] modified xanthan gum by chemical binding (amide bond) with L-cysteine (SH) for the drug delivery in saliva. Modified xanthan gum exhibited sufficient swelling, adhesion and higher water uptake than unmodified xanthan gum and showed a promising impact on treating sialorrhea.

Locust bean gum in drug delivery: It is obtained from the plant *Ceratonica siliqua* endosperm seeds by milling. It is slightly soluble in cold water and requires heat to achieve full hydration, solubilization and extreme thickness. Its structure comprises of galacto, D-mannoglycan, pentane proteins and cellulose [69]. It is utilized as a gelling agent, stabilizer, thickening agent and exhibited superior properties in drug delivery applications. In the pharmaceuticals, it is utilized as oral, buccal and colon drug delivery but also in ocular and topical formulations [70].

Modifications of locust bean gum (LBG) have been evidenced in several reports. For example, Boppana *et al*. [71] developed ketoprofen loaded polyacrylamide-*g*-LBG and sodium alginate based IPNs, under microwave irradiation using alkaline hydrolysis, for intestinal drug delivery. *in vitro* release revealed 90% drug release in phosphate pH (7.4) but only 10.6% in acidic pH. These IPNs proved effective in decreasing ulcer formation, erosion of gastric mucosa and haemorrhages. Similarly Braz *et al*. [72] prepared integrated locust bean gum nanoparticles *via* mild polyelectrolyte complexation between chitosan/sulphate-locust bean gum for oral immunization, which exhibited sufficient properties for the utilization of oral immunization because of positive and negative charges present on nanoparticles. Kaity and Ghosh [18] prepared sodium carboxymethyl ether reaction of locust bean gum for hydrophilic modification using monochloroacetic acid. The modifiedlocust bean gum was safe for external use without demonstrating any cytotoxic effects and biodegradability. Moreover, with poly(vinyl alcohol), this carboxymethylated gum was utilized to prepare the interpenetrating polymer network microspheres of buflomedil hydrochloride for controlled drug delivery for 12 h. Giri *et al*. [73] prepared graft copolymer of locust bean gum with acrylamide by utilizing microwave-assisted technique using potassium persulphate used as an initiator in an aqueous medium. This modified locust bean gum didnot show any toxic effect when it was given to mice for 14 days observation period.

Moringa gum in drug delivery: Moringa gum is obtained from *Moringa oleifera*. It comprises of L-arabinose, L-galactose, L-glucoronic acid, L-rhamnose, arabinose, xylose, rhamnose and a units of uronic acid [74]. It is modified by esterification of hydroxyl group with thioglycolic acid to form thiolated moringa gum [75]. Its hydroxyl group interacts with the mucus membrane and gives mucoadhesive properties. The swelling of gum yields sustained drug delivery. It is sparingly soluble in water but swells when interacts with water and form a thick solution. Moringa gum is utilized as a coating agent, gel former, binder, disintegrating agent, control release matrix for desired

properties such as mucoadhesion. Grewal *et al*. [76] modified moringa gum with thiolation process using thioglycolic acid. Metronidazole benzoate buccal tablets were formulated using thiolated moringa gum, which showed drug release for 24 h and followed zero-order release kinetics. Ahuja *et al*. [77] reported the microwave assisted graft copolymerization reaction on moringa gum using *N*-vinyl-2-pyrrolidine (NVP) and ammonium persulfate to yield moringa gum-*g*-poly(NVP). The grafting of *N*-vinyl-2-pyrrolidine on moringa gum decreases its crystallinity by making its surface smooth. Clotrimazole buccal tablets using grafted moring gum leads to sustained buccal delivery of drug than local moring gum. Similarly, Singh and Kumar [78] prepared hydrogels by copolymerization of *N*-vinyl imidazole and moringa gum. The hydrogels were loaded with levofloxacin (antibiotic drug) and evaluated for mucoadhesion and antioxidant property and blood compatibility. Polymer showed non-hemolytic mucoadhesive properties and antioxidant properties with pore size 12.09 nm and 9.13×10^{-5} mol cm^{-3} thickness.

Susbania gum in drug delivery: Susbania gum is obtained from the shrub of *Sesbania aculeate*. It is composed with β-1,4-glycosidic and α-1,6-glycosidic linkage with average molecular

TABLE-1
VARIOUS GUMS, THEIR MODIFICATIONS AND ROLE IN DRUG DELIVERY

Drug	Modification method	Polymer	Result	Ref.
Buflomedil hydrochloride	Carboxymethylation method	LBG	Controlled drug delivery	[18]
Glimepiride	Free radical polymerization	Polyacrylamide-*g*-GG	Colon targeted drug delivery	[22]
Ibuprofen	Graft copolymerization	GG-*g*-PMAC	Colon targeted drug delivery	[28]
5-Amino salicylic acid	Graft copolymerization	GG-*g*-P(HEMA)	Inflammatory bowel drug delivery	[29]
Esomerazole magnesium	Chemical modification method	GG	Delayed drug delivery	[30]
Nanoclay	Microwave irradiation	Acrylic acid-*g*-GG	Crystal dye removal	[32]
–	Chemical cross-linking	2-alkenyl-3-butoxypropyl GG	Improved rheological properties	[33]
5-Flouracil	Grafting method	GG-*g*-Lysine-beta-CD	Controlled release drug delivery	[34]
Amphotercin B	Self-organized method	CG	Long term stability	[38]
Dermaseptin 01	Layer-by-layer deposition Technology	CG	Anti- leishamanial action	[39]
Trypsin	Casting method	CG- PVA	Sustained release of drug	[31]
–	Chemical bonding	Phthalated CG	Antimicrobial drug delivery	[41]
Epiisapiloturine	Chemical bonding	Acetylated CG	Anti-inflammatory Drug delivery	[42]
–	Microwave assisted	Carboxymethylated CG/CG	Antibacterial drug delivery	[43]
Epirubicin	Graft copolymerization	Poly(N-isopropulacrylamid-grafted-CG)	Controlled drug delivery	[44]
Ropinirol hydrochloride	Carboxymethylation method	Etherified GG	Sustained oral drug delivery	[47]
Diclofenac	Motozato method	Acetylated CG	Transdermal drug delivery	[48]
Quetiapine jumarate	Free redical polymerization	Polyacrylamide-grafted-GG	Improved antipsychotic drug delivery	[49]
Amoxicilin tryhydrate + PCM	Graft co-polymerization method	GG-*g*-poly(acrylic acid-anilin)	Colon targeted drug delivery	[50]
Diclofenac sodium	Microwave assisted method	Poly(acrylamide-*g*-GG)	Entric drug delivery	[51]
Flurbiprofen	Crosslinking	Alginate/GG	Stomach drug delivery	[52]
Quercetin	Crosslinking method	QTG-AA	Better antimicrobial activity	[55]
Amoxicilin	Graft copolymerization	TG-cl-Pcla-co-IAI	Controlled drug delivery	[56]
Graphene oxide	Grafting method	TG	Better antibacterial activity	[57]
Quercetin	Grafting method	TG	Improved drug delivery	[58]
Ciprofloxacin	Polymerization method	TG	Site specific drug delivery	[59]
Amoxicillin	Free radical polymerization	XG-poly AA	Controlled release drug delivery	[63]
Imidazole	Carboxymethylation method	XG-CS	Controlled release drug delivery	[64]
Doxorubicin	Carboxymethylation method	Carboxymethyl XG	Buccal drug delivery	[65]
Cerium oxide	Microwave assisted method	XG	Improved drug release	[66]
Ciprofloxacin	Carboxymethylation method	XG-CS	Controlled release drug delivery	[67]
L-Cysteine	Chemical modification method	Modified XG	Buccal drug delivery	[68]
Ketoprofen	Microwave irridation method	PAAm-*g*-LBG	Intestinal drug delivery	[71]
Ovalbumin + HE extract	Carboxymethylation method	LBG	Oral drug delivery	[72]
Potassium persulphate	Microwave assisted method	LBG	Sustained release drug delivery	[73]
Metronidazole benzote	Thiolation method	Thiolated MG	Sustained release drug delivery	[76]
5-Flourouracil	Microwave assisted method	GG	Anticancer drug delivery	[40]
Ofloxacin	Carboxymethyaltion method	Carboxymethyl MG/CS	Sustained release drug delivery	[77]
Clotrimazole	Microwave assisted	MG-*g*-poly-N-vinyl-2-pyrrolide	Sustained release drug delivery	[75]
Metformin	Carboxymethylation method	Carboxymethyl SG	Sustained release drug delivery	[80]
–	Crosslinking method	SG	Sustained drug release	[81]
–	Microwave assisted method	SG	Antibacterial drug delivery	[82]
–	Graft copolymerization method	SG-*g*-PMA	Improved adhesion properties	[84]
N-Halamines	Electro-spining method	SG	Improved antibacterial activity	[85]

weight. These are fibrous, pithy stems with long leaves and bear purple spotted beans [79]. It is insoluble in organic solvents and partially soluble in water. It is non-harmful, eco-friendly biopolymer and has possibility to alter drug release rate in sustained drug delivery. The gum is utilized as thickening agent and improves the quality of soil through nitrogen fixation process [80].

Ahuja *et al.* [79] modified susbania gum *via* carboxymethylation process using monochloroacetic acid in alkaline condition with 1.3 level of carboxymethyl substitution. Mucoadhesive beads were synthesized using the interaction of carboxymethyl groups with Ca^{2+} ions to get a sustained release of metformin. A 68% drug release was achieved in 12 h and release kinetics follows Higuchi model. Pal *et al*. [81] modified susbania gum by crosslinking with hydroxyl-propyl using ethanol. The crosslinked susbania gum has rougher surface than naive susbania gum. Tang *et al*. [82] performed the grafting of susbania gum using cationic monomer, diallyldimethyl ammonium chloride (DADMAC) through microwave assisted process. Grafting process show a positive charge on poly(DADMAC) to susbania gum which shows antibacterial property through agar medium. Further susbania gum was modified by altering the concentration of methylacrylate. Methylacrylate monomers were grafted with native susbania gum by Fenton's reagent. It showed that the graft modification for sesbania gum was simple and effective method to improve its sizing properties for polyester yarns and omit specific viscosity reduction [83]. Li *et al*. [84] synthesized sesbania gum-based polymeric *N*-halamines nanofibers were obtained through step-by-step controlled synthesis process. These nanofibers were characterized for their chemical properties, morphology and antibacterial activity. The cSG-PAN showed great antibacterial activity against *E. coli* and *S. aureus* with lesser toxic properties. The other various gums and their modifications have been summarized in Table-1.

Future prospective: As development of a new molecule is costly and time consuming process so now days trend is to develop modified release drug delivery systems of existing drugs. No doubt various synthetic polymers are of increasing use in development of modified drug delivery, the natural polymers/gums in modified form are of same level of interest in the development of pharmaceuticals with better release profiles. Modification of gums improves the flow property, crystallinity, solubility, and mechanical properties; decreases toxicity and make them of potential use in development of controlled release drug delivery. Another prospect is the use of these modified gums in food industry by exploiting their features for development of better food products. The gums which are used in food industry can be classified into three groups based on their sources: (i) plant-based food polymers, such as starch, dietary fibres and cereal protein, (ii) animal-based food polymers, such as meal protein, and (iii) microorganism-based food polymers, such as fungus polysaccharides. Thus, various future prospects associated with the use of natural gums with superior properties are of potential interest in upcoming era in pharmaceuticals as well as food industry. Moreover, the low cost of these natural excipients definitely will help in reducing the cost of developed products.

Conclusion

Modified natural gums are widely used in the development of controlled release drug delivery systems. In almost all modifications, two polymers are chemically crosslinked with each other to enhance the properties of drug. Modified gums help the drug release at particular site for specific action. Moreover, these are used to improve the antibacterial, antimicrobial and antifungal properties of the drug and also improve release kinetic of the drug. Protection of drug from degradation in acidic pH and tend to release the drug at alkaline pH thereby help in achieving drug release in specific segments of gastrointestinal tract. Modification helps to alter the release mechanism of drug by affecting swelling, flow properties, crystallinity of the drug and particle size of the drug for fast release kinetics.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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