REVIEW
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# Natural gum: an option to prepare nanocarriers

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Seema Rohilla wrote the manuscript, Geetika Chawla proofread the manuscript, Deepak Prabhakar Bhagwat diagram and table and Ankur Rohilla conceptualized the study. All the authors have read and approved the final version of the manuscript.

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***Abbreviations***
GIT, gastrointestinal tract; TG, TG-g-PDMAEMA-PCL-mPEG; CUR, curcumin; MOF, metal-organic framework; PAGE, polyacrylamide gel electrophoresis.

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***Abstract***
The tree gum polysaccharide and their nanostructure are used eventually in various food and non-food industries. They attracted interest because of their makeup, non-toxicity and biological compatibility. They are currently being investigated as delivery systems for oral medicinal compounds. Natural gums have attracted more interest in the area of drug delivery systems due to their unique attributes. They are derived from bacteria, plants and algae. They are thought to be attractive prospective medication carriers as they have excellent biocompatibility and biodegradability. They swell in the intestine and are degraded by the colon microbiome. The original compounds are blended with other polymers to modify their properties as per requirements. Gums and gum-derived compounds can be used to prepare micro and nanoformulations that can deliver the drugs via different routes. In this review, We detailed and outlined the most recent studies on micro- and nanoparticles made from gums that have been extensively researched in pharmaceutical technology. This review focuses on the most crucial elements influencing the properties of micro- and nanoparticle systems and their applications as medication delivery systems.

**Keywords:** gum; nanocarriers; polymers; nanotechnology

### *Background*

Recently, the production of nanotechnology-based drug delivery formulations has significantly increased. Numerous studies have shown that the merging of pharmaceutical technology and nanotechnology has great potential to enhance the effectiveness of active chemicals for targeted applications [1]. Because of their colloidal size and molecular organization, medications based on nanotechnology offer greater benefits than traditional pharmaceutical forms [2]. These advantages include enhanced contact surface area, the ability to choose specific therapeutic zones, enhanced apparent solubility of active components, reduced dose, higher drug bioavailability, quicker and longer therapeutic action onset, and improved patient obedience [1, 2]. The introduction of nanotechnology into medicine has paved the way for the creation of nanometric systems.

Nanometric formulations, such as nanoparticles, nanoemulsions, electrospun nanofibres, polymeric micelles, and nano hydrogels, have effectively engaged in the biomedical and pharmaceutical fields. The two main issues, medication stability, solubility, and precise tissue targeting, may be encountered while using nanoformulations to treat cancer. Most nanoformulations were synthesized using synthetic ingredients that may be toxic to the environment and humans [3]. Nevertheless, natural materials are biodegradable and biocompatible. Thus, these natural extracts and gums seem more appropriate for nanometric formulation. Natural gums have unique physicochemical properties and are easily available with low-cost processing. These gums are polysaccharides and contain functional groups such as hydroxyl, sulfate, carboxyl, and amino groups. As a result, we may simply alter them using hydrophilic or hydrophobic groups or by polymerizing monomers to create custom drug delivery systems. Grafting is the technique used to alter the properties of these molecules. These drug delivery methods have greater stability and excellent loading and encapsulation capacities [4]. Natural gums made from plants and bacteria have a variety of intriguing qualities that could be helpful in different fields of medicine and pharmaceutical like drug delivery and tissue engineering.

Biocompatibility, sustainability, and low toxicity are essential for creating innovative materials that can be used as cell-implantation frameworks or as drug carriers for different biomedical fields. Most natural polysaccharides are recognized as safe, highly biocompatible substances that can produce porous nanocarriers. These nanocarriers are ideal for promoting cell division and growth as well as the entrapment of therapeutic agents and economics. They are found in abundance in plants and are comparatively effortless to acquire. Additionally, polysaccharides are very adaptable substances that are easily changed, either chemically or physically, by the addition of various components. This foundation allows for the creation of novel materials with fascinating features. Cross-linking, one of the most popular methods, aids in creating gels with characteristics distinct from those of the original molecule [5].

Natural gums have a number of significant drawbacks and application-related challenges, in addition to their many advantages. For instance, natural gums can be amalgamated by different organisms. Their precise chemical configuration, physicochemical properties, and molecular mass may vary according to the origin of the compound, which may be a reason for concern. In contrast, gums derived from natural sources, such as plant exudates or seeds, typically contain some additional ingredients, such as proteins and minerals. Thus, the origin source or parameters of a product's manufacturing process affect the final product's characteristics. The quality of pharmaceutical dosage forms depends on the purity of both the active ingredients and the excipients. The impurities or challenges encountered during the purification process may restrict the use of natural polysaccharides in large-scale industrial drug manufacturing. Microbial contamination is the major drawback of polysaccharide gums [6]. A suitable chemical and/or physical amendment may create smart materials that can change their characteristics due to temperature, ionic strength, or pH alterations. These materials are particularly attractive pharmacologically because they can be employed as drug carriers that release active ingredients at targeted sites [7, 8]. In pharmaceutical technology, both anhydrous and hydrous forms of natural gum-based nanocarriers can be used as micro- and nanoparticles (micro- and nano-gels, respectively). They swelled in physiological fluids excreted in the gastrointestinal tract (GIT) and converted into their novel hydrogel state. The liberation of the drug in different parts of the GIT is based on the composition of the matrix and its characteristics. Most of the natural gums used in pharmaceutical technology, like guar or xanthan, are digested by glycosidase enzymes of the colon microbiome. The matrices prepared with the polymers can pass through the GIT without any physical and chemical decomposition and release the drug in the colon upon contact with bacterial enzymes. This characteristic makes natural polysaccharides an appealing element of in-depth research to create innovative dosage forms for the targeted drug administration to the colon [9, 10]. The unmodified natural gums have shown intensive swelling in physiological fluid due to unfavorable mechanical properties leading to erosion of the physical matrix in the GIT. Different techniques and combinations of hydrophobic matrix-forming agents must be used to alter their characteristics and drug release kinetics and to obtain a dosage form with desired characteristics [11]. Thus, natural gums play an imperative role in green nanotechnology, which combines nanotechnology with natural gum. Green nanotechnology cuddles the concept of green chemistry. Green chemistry reduced the use or production of perilous products in the design, fabrication and application of nanometric formulation. Natural gums can lower interfacial tension, and these qualities have been used to stabilize or reduce the use of synthetic materials in the preparation of nanoparticles. The desire to use natural polymers in pharmaceutical products has increased. Polysaccharides of gums are used in food, drug, and cosmetic industries as gelling, emulsifying, dissolving, stabilizing and thickening agents [8]. The microbes and seed coats of maize, seaweeds, oat, aloe, barley, rice, soybean, and wheat can extract natural gum (Table 1). Gums are used as carriers in nanoformulations because they are stable, inexpensive, renewable, hydrophilic, non-toxic, biocompatible, and biodegradable as compared to costly synthetic polymers that have troubles with environmental toxicity along with time-consuming synthetic processes [9]. This review article has highlighted distinct gums, their applications in nanoformulations, and different methods used to prepare nanoparticles with natural gums.

### *Classification*

Natural exudates (gums) are classified on the bases of their origin, structure and functional properties (Table 1) (Figure 1) [11]. The gums are complex acidic polysaccharides with three or more sugar moieties. The sugar moiety may be present as furanose or pyranose ring, which can change its configuration at glycosidic linkage. D-glucuronic acid and galacturonic acid are the acidic groups present in gums. Some gums also have minerals like Ca, Mg, Na, K, Fe, and P. So, the plant exudates gums are classified on the bases of the analogous configuration of related molecular species. Normally the difference is found at the side chain, in their nature and number that are attached to the sugar moiety.

According to reported literature, the structural classification depends on the core polysaccharides present in the gum. A branch of -D-galactopyranose residue serves as the core of some gums, while others have distinct branches with glycosidic linkages linked to the core [12]. The gum Arabic (A. Senegal) and Cashew gum (A. occidental) are examples that have galactopyranose residue and highly branched arabinose-galactan protein complex. Gum ghati (Anogeissus latifolia), apricot gum (Prunus armeniaca), and gum kondagogu (Cochlospermum gossypium) contain glucuronomannans

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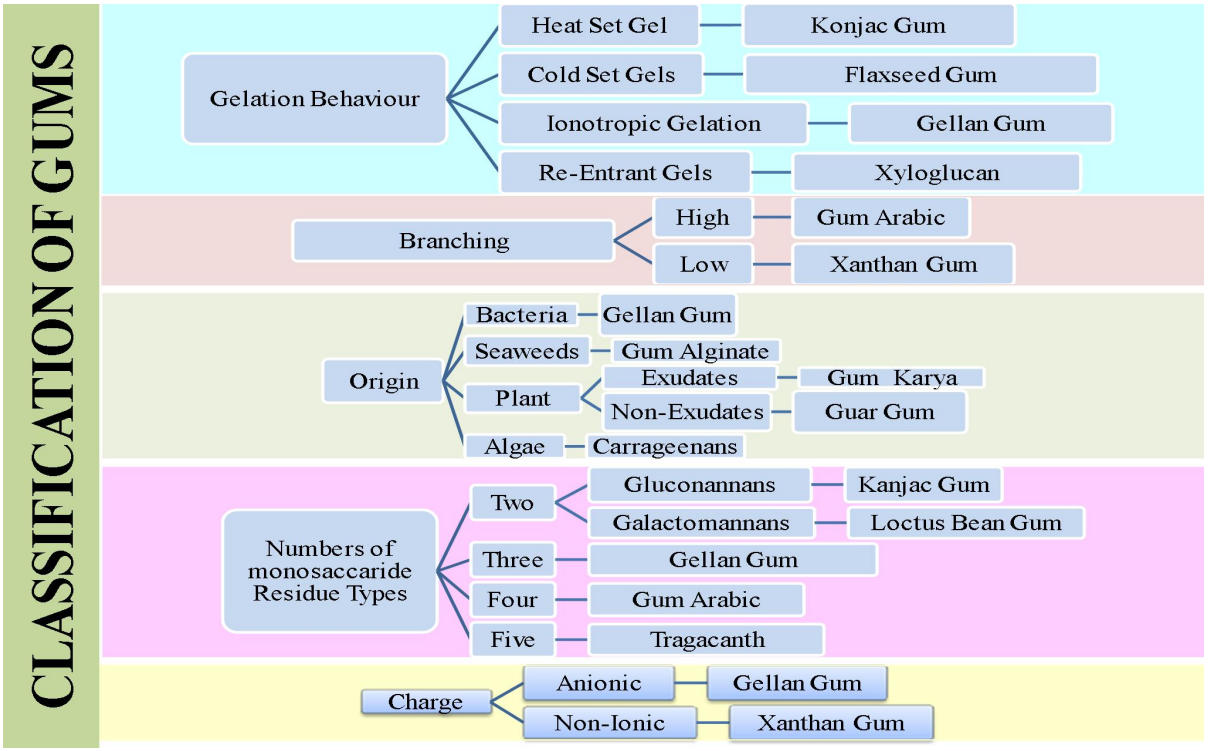


**Figure 1 Classification of gums**

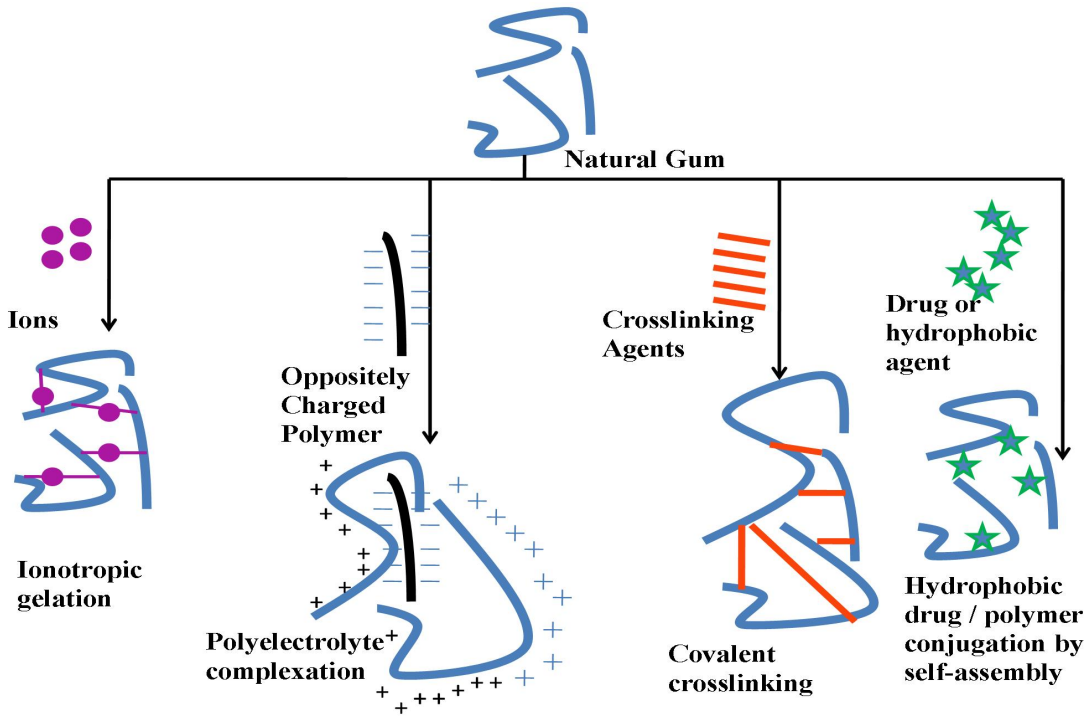


**Figure 2 Basic processes for particle formation**

groups and on hydrolysis with acid, they produced the residues of D-mannose and D-glucuronic acid. Sterculia genus gum karya (Sterculia urens), khaya genus, and gum tragacanth gums contain the galacturonorhamnan group [13].

This family is further subdivided into three categories. The gums contained D-galacturonic acid as the interior core and D-glucuronic acid as the side chain. The gums extracted from seeds have galactomannan group along with galactose and mannose monosaccharide as active ingredients e.g. locust bean gum (Ceratonia Siliqua), tara gum (Caesalpinia spinosa), tamarind gum (Tamarindus indica), fenugreek gum (Trigonella foenum-graecum), and guar gum (Cyamopsis tetragonoloba) [14].

***Micro- and nanoparticle fabrication methods: gelation mechanisms***

Depending on the physicochemical properties and chemical structure of gums, different manufacturing strategies have been employed to prepare micro- or nanoparticles using biopolymers. The basic mechanisms involved in particle formation are summarized in Figure 2.

**Table 1 List of Different Types of Gums**

| Source | Common name | Origin | Functional properties |
|---|---|---|---|
| Plant exudates | Cashew gum | A.occidenatele | Thickening, jellying, binding, suspending, emulsifying, and stabilizing agents, used in drug delivery [15]. |
| | Gum karya | Sterculia urens family sterculiaceae | Floating agent, adhesive, emulsifying agent, effect on diabetes, in preparation of soya protein isolate, hair dressing lotion [16] |
| | Gum tragacanth | Asiatic species of Astragalus Gum | Laxative, thickening agent and stabilizer, gum is highly heat and pH resistant [17] |
| | Gum Arabic | Wounded branch of A. Senegal | Food additive, Shelf-life enhancer, Microencapsulator, dental protective, antimicrobial agent, anti-inflammatory agent and anticoagulant, drug delivery agent |
| | Gum Ghati | An exudate of the Anogeissus Latifolia tree family Combretaceae | Emulsifying agent, forming hydrogel, used as flocculants in suspension because it more viscous to gum Arabic, controlled drug delivery of amoxicillin trihydrate, transdermal delivery of psychotic drug, Biodegradation and water retention of gum ghati hydrogel [18] |
| | Pectin | Pectin extracted from citrus peel like lemon, orange, lime and from apple pomace | Green synthesized cu-folic acid/pectin MOF nanofibre for drug delivery, pectin used as antioxidant , antibacterial, emulsifier [19,20] |
| | Gum Kondagogu | Gum kondagogu Cochlospermum gossy pium Bixaceae | Emulsifying, and metal-biosorption, reducing agent, stabilizing agent, Nanobiosensor, metal nanoparticle used for drug delivery [21] |
| Extracted from seed | Loctus Bean Gum | Ceratonia siliqua Leguminosae | Used for drug delivery for biopharmaceutical application, used as a polar binder for lithium ion batteries, used in food industry as a viscosity builder and stabilizer [22] |
| | Guar Gum | Cyamopsis tetragonoloba (legumi nosae family) | In textile industry used as pigment dispersing aid, used in beverage to increase viscosity and reduce calories, used water potable treatment (reduce turbidity) used in control drug delivery [23] |
| | Gum Tara | Caesalpinia spinosa (leguminosae) | Used in film that load curcumin, used as food additive [24] |
| | Basil Seed | Extracted from seed of basil (Ocimum basilicum | Used as stabilizer in ice cream, used as nanoparticles formation in food industry to stabilized emulsion [25] |
| | Tamarind Seed Gum | Seed of Tamarindus indica | Used as controlled drug delivery, nanofibre patch for clindamycin delivery, tropicamide loaded tamarind nanoaggregates [26,27] |
| Seaweed | Gum Alginate | Phaeophyceae, brown seaweeds. | Alginate hydrogel/gum Arabic/gelatine composite for antioxidant, drug delivery (citicoline) for brain [28] |
| | Gum Carageenan | Red seaweeds of the Gigartinaceae, Hypneaceae, Solieriace ae, Phyllophoraceae, and Furcellariaceae families | Used in food application, used in toothpaste stability, in cosmetic product, polyol-carageenan gum complex application, drug delivery application as stabilizer for nanoparticles drug formulation [29] |
| | Gum Agar | Hydrophillic collide produced by the genera and species (Gelidium, Gelidiella, Gracilaria) of the red-purple seaweads class Florideophyceae | Improved Tuna oil oxidative stability with coacervates of agar gum/gellan gum/whey protein [30] |
| Bacterial gum | Gum Xanthan | Xanthomonas campestris | Gelatine–xanthan gum complex used for edible oil industries as double emulsion, used for buccal application, use as a food stabilizer [31,32] |
| | Gellan Gum | Produced during aerobic fermentation of Sphingomonas elodea (earlier Pseudomonas elodea) | Regenerative medicine, used for seafood freshness, hydrogel bead for drug delivery, used in bone tissue engineering [33,34] |

**Ionic Crosslinking**

Some gums, like gellan gum or alginate, interacted with di- or trivalent cations through ionic crosslinking. It is assumed that the procedure is bidirectional and the crosslinking agents used are generally supposed as moderate, making the final goods biologically compatible. The conjugated polysaccharide chains grab the vital component. The interaction of cations with anionic parts of polysaccharides initiates the procedure of gel formations. According to egg-box model, the monocomplexes are formed in the initial stage and then converted into dimmers and multimers in further steps.

According to another theory, the crosslinked polymer chains are connected perpendicularly to form dimmers and formed tilted egg-box structure (Figure 2). At more than 40 °C temperatures, the polymer disbands in water and begins to form jumbled coils. These coils become helices as they cool and eventually coalesce to form a reconfigurable gel arrangement. The introduction of cations induced the creation of ionic bridges among the helices, forming stronger aggregates. This reaction is irreversible, as seen aggregates produced by cooling [35].

**Covalent Crosslinking**

Covalent crosslinking established a sturdy connection between adjoining polymer chains. This process is irrevocable, as the connections produced are generally insensitive to pH alterations [36]. At least two functional groups must be present in the suitable crosslinking agent that can interact with the hydroxyl groups of the gum particles. Glutaraldehyde and sodium trimetaphosphate are examples of the most commonly utilized compounds. The toxicity of dialdehydes restricted their applications in pharmaceutical technology. So, genipin or citric acids are used as substitutes due to their less harmful potential [37, 38].

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**Polyelectrolyte Complexation**

Complex coacervation is another name for this technique. This approach involves the employment of two opposite charges that interact with each other to form a complex. The proportion of anionic and cationic groups greatly influences the complex's characteristics. pH and the mixing succession of the specific components are the other significant aspects that influenced the characteristics of the consequential complexes (Figure 2) [39]. The literature demonstrated that the natural gums connected with chitosan are polycationic compounds [40]. This process may be utilized to prepare both microcapsules and solid microspheres with fluid core. In these formulations, the complex formed a shell around oil droplets and converted it into a microcapsule shell [41].

**Self-Assembly**

Self-assembly is shown when the hydrophobic moieties have been introduced in the structure to modify the gums. The amphiphilic molecule adopts a spatial configuration that allows it to conceal the non-polar moieties in the inner core of the particle while the polar domains stay at the exterior. They acted as a boundary between the lipophilic core and the lipophobic solvent in a polar environment. The process is instantaneous due to less interaction energy. The developed systems may be helpful in the administration of non-polar active substances as the core of particles is lipophilic Cholesterol [42, 43], fatty acids [44], and other substances can be employed in hydrophobic alterations [45]. Particle parameters like zeta potential, diameter and loading capacity can be amended by varying the length of the polymer chain and the content of the lipophilic remains [46].

**Polysaccharide/Drug Conjugation**

In this technique, the medication molecules are joined covalently to the backbone of the polysaccharide. The ligatures between the active component and the carrier gum need to be broken down to release the medicine in its native form for desired pharmacological effect. Therefore, a recyclable connector can be used to attach two halves of the conjugates. For instance, targeted chemotherapy could get benefit from the connecter's unique ability to cleave under certain situations. When the lipophilic active ingredients are linked with the backbone of hydrophilic gum, then the self-assembling process takes place automatically [47].

***Different nanoformulations derived from gum***

**Cashew gum-based nanometric formulation**

Cashew gum grafted with poly-lactide was used to stabilize the Pickering emulsion. It is obtained by spontaneous emulsification and loaded with amphotericin B drug against the disease leishmaniasis. Cashew gum-based emulsion is in a less amassed state than that observed in commercial Amphotericin B formulation [48, 49]. It is also used in a number of sustained and control delivery formulations. The observed data show that it can be chemically grafted and modified by oxidation, sulfation, carboxymethylation, acetylation, copolymerization with acrylamide, and cross-linking with epichlorohydrin [50]. The Synthesis of grafted gum-based nano-formulation and their relevance in drug delivery has been studied. Acetylated cashew gum-based self-assembled nanoparticle encapsulated indomethacin and their release profile depicted preliminary burs effect in the initial 2h pursued by a sustained release up to 72 hr. At the same time, the plan graft poly (DL-lactide-co-glcolide) has shown 84% release of indomethacin in 2h. Similarly, diclofenac diethylamine encapsulated nanoparticles were synthesized for control release and transdermal permeation. The controlled release rate was found to be up to 60% and the permeation rate was up to 90% [51].

**Tragacanth-based nanometric formulation**

Gum Tragacanth is a hardened exudate prepared from the branches and stems of Asian Astragalus Gum varieties. Tragacanth is a heterogeneous anionic polysaccharide having high molecular weight with traces of starch, proteins and cellulose. It is a highly branched and hydrophilic moiety that, on acid hydrolysis, fabricates into l-fructose, l-arabinose, d-glucose, d-galactose, d-xylose, l-rhamnose and d-galacturonic acid. Due to its extremely long shelf life and excellent stability against acidity, heat, and broad pH range, this gum is frequently employed as a stiffening agent, an emulsifying aid for bowel movement, and a stabilizer in the cosmetics, food, leather, textile, and healthcare sectors. It is one of the most effective gums

with the highest acid resistance employed in the preparation of acidic oil-in-water emulsions [17]. The tragacanth can be modified as gum by using acrylonitrile, itaconic acid, methyl methacrylate, acrylamide, and vinyl alcohol [52, 53]. Gum tragacanth is used to synthesize a number of nanometric formulations for targeted drug delivery after modification with vinyl alcohol. The itanoic acid grafted TG (TG-g-PDMAEMA-PCL-mPEG) nano hydrogel was used for control release of ampicillin. Grafted copolymers of TG were also used as pH-sensitive nanocarriers to deliver quercetin [54 – 56].

**Guar gum-based nanometric formulation**

Guar gum is derived from the drought-resistant plant cyamopsistetrago colobus (guar kernels) and belongs to the Leguminosae family. Guar gum is a chemical compound that contains a linear chain of (1→4)-linked β-D-mannopyranosyl units and (1→6)-linked α-D-galactopyranosyl motifs as auxiliary chains. It is used as a gelling agent, binding agent, thickening agent and disintegrating agent in pharmaceutical dosage forms [57]. It can also be grafted with different polymers like acrylonitrile, carboxymethyl, acrylic acid, polyacrylamide, and acrylic acid-co-acrylonitrile [58, 59]. Grafted gum-based nanometric formulations are beneficial to delivering microbes susceptible to the drug in the colon because of their colon susceptibility and high hydration rate. These drugs are degraded in highly acidic and alkaline pH and are stable between pH ranges 5–7 [60]. Because of its high stability at gastric pH, it can be used as a nanocarrier for oral vaccines against tuberculosis. The nanoparticles were investigated for protection from acid, uptake by Peyer's patches, and *in-vitro* antigen research. It was observed that the new nanocarrier formulations shielded the antigen from a harsh gastric environment and safely passed the medication through the gut area, and the vaccination produced a strong systemic immune response [61].

**Gum alginate-based nanoparticles**

Curcumin (CUR) loaded alginate nanoparticles were synthesized for cancer therapy. In cancer therapy, drug targeting is the main issue. So, folic acid was used as a ligand for receptor binding. Folic acid was bound with the help of polyethylene glycol-polyethylene imine. Doxorubicin was encapsulated in sodium alginate nanoparticles as a doxorubicin-modified alginate complex for liver cancer treatment. The nanospheres of sodium alginate were prepared by self-assembly of sodium alginate in aqueous media containing $Ca^{2+}$ and $CO_3^{2-}$ to encapsulate the 5-fluorouracil drug. The same method was used to encapsulate methotrexate [62] and α-tocopherol [63]. Some other gums like xanthan gum, gellan gum [64], locus bean gum, moringa gum [65, 66], gum cordia, gum katara [67], gum arabic gum ghatti, and pectin were also grafted and used as nanocarrirers for drug delivery system [68, 69]. As per reported literature, some of these gums are predominantly used in green synthesis because of their high reducing properties, and some are used in nanoformulation as composite in combination with another polymer.

**Green synthesis of nanoparticles using different natural tree gum**

Plant gum exudates/polysaccharides act like a nano-yard because they reduce or oxidize the metal ion into metallic nanoparticles. The literature demonstrated that plant gum, besides the reducing agent, also acts as a capping and stabilizing agent. This property is due to the presence of carboxylic, hydroxyl group and carbonyl group in the gums structure that binds with metals like Ag, Au, Pd, Cu, and Zn and makes the stable metal nanoparticles. Several researchers synthesized metal nanoparticles by green synthesis using plant exudates such as gum acacia, gum karya, gum tragacanth, gum guar, gum arabic, gum ghati, xanthan gum, and gellan gum [70-72]. The silver nanoparticle has been developed by using aq. extract of gum olibanum. The water-soluble gum served the dual functional both as a stabilizing and reducing agent. IR and Raman spectra confirmed various functional groups on the gum surface. Thus, their capping on nanoparticles provides surface reactivity. The gum olibanum-based nanoparticles have more antibacterial properties than other chemogenic nanoparticles due to the higher value of zone of inhibition.

Green syntheses of copper oxide nanoparticles were performed using gum karya. The gum has various functional groups like hydroxyl and carboxylic groups that facilitate the formation of Cu(OH)2, which is hydrolyzed into the nanocrystalline structure of CuO [73]. Gellan gum has been utilized for the green synthesis of gold nanoparticles. These nanoparticles have shown great stability in addition to other electrolytes and pH. Carboxymethyl moringa gum with chitosan was used as a nanometric carrier to encapsulate ofloxacin. The result demonstrated the sustained release profile of the drug from these nanoparticles [74].

***Applications***

Plant-derived gums are polysaccharides extracted from different parts of the plant. One of the most popular gums, tragacanth, has been used therapeutically for a long time. Some tragacanth plants of the Fabaceae family (Genus Astragalus L.), such as Astragalus microcephalus Willd., Astragalus brachycalyx Fisch. ex Boiss, Astragalus gummifer Labill., etc., have several uses in the pharmaceutical and industrial sectors. The tragacanth gum, also known as “Katira” in Iran, has long been a common ingredient in both medicine and sweets. According to Iranian traditional medicine, it is commonly used as a general tonic, analgesic, and laxative to cure lip cracks and in the treatment of throat infections [75]. Herbal gums are frequently employed in the pharmaceutical sciences for wide goals, including stabilizing, binding, suspending, emulsifying, thickening, and for the sustained release of medications [76]. Different examples of plant-based gums are in Table 2. Applications of plant derived gums are as follows:

**To Improve the efficacy of the drug**

Khaya senegalensis (Desv.) was used by H. Ozoude et al. in 2020 to prepare metformin microspheres to examine the improvement in efficacy of metformin. The bark secretion from Khaya senegalensis (Maliaceae), known as Khaya gum, is used to prepare carriers able to transport the medicine. Gum from sodium alginate and Khaya senegalensis were mixed in a definite proportion to form a vesicle for formulation for controlled release of the drug [77, 78].

**As a binder**

In one investigation, the potential of steady dispersion of Prunus domestica L. and PAGE (Rosaceae) gum was compared by Seyedabadi et al. with hydroxypropyl methylcellulose (HPMC) and observed that Prunus domestica and PAGE gum in 1:1 ratio have higher release efficiencies and PAGE could be utilized in tablet formulations as a matrix [76]. In another study, Salarbashi et al. looked at the potential of PAGE and Prunus domestica gum synergistically as binders in tablet formulation. The outcomes demonstrated that the gums were used as a superior binder in preparation of uncoated tablets from PVP K30 [77].

**As a Carrier to Encapsulate Drug**

Singh et al. prepared hydrogels using dietary tragacanth gum (TG) to address a pharmacokinetic flaw in methotrexate, an anticancer medication [79]. In one more study, Sharma et al. prepared hydrogel based on acacia gum using an aqueous polymerization technique and demonstrated that nanocomposite hydrogels are beneficial against bacterial infections due to their antibacterial potential [80].

**Investigation of Antibacterial Properties of a Mixture of Polymers and Guar Gums**

Iqbal et al. prepared a mixture of chitosan/poly (vinyl alcohol)/guar gum (CS/PVA/GG) to investigate their antimicrobial properties and swelling ratio. They observed that arranged mixtures displayed good antimicrobial activities against E. coli, P. Multocida, S. aureus, and B. subtilis [81].

**To Deliver Protein Drugs Via Oral Delivery System**

Freitas et al. used Sterculia striata to prepare gum-based formulation along with bio-polymers like chitosan, albumin, dextran sulfate, and calcium chloride as a cross-linking factor, and polyethylene glycol and polyxamer 188 as stabilizers to augment the bio-availability. Insulin formulations were prepared using ionotropic precursors and electrolytic complexes of opposite-charge biopolymers under pH-controlled conditions. Natural polysaccharides were checked for their potential in oral insulin administration because of their non-toxicity, degradability, effortless availability and economical price. Sterculia striata gum was used for the delivery of insulin, which has been observed as a suitable choice for the valuable delivery of these drugs [82].

**Targeted delivery**

Singh et al. prepared a polymer and guar gum-based matrix tablet of quercetin with sufficient mechanical strength to reveal *in vitro* targeted liberation of the drug mouth-to-colon [83]. Soleimani et al. reviewed that natural gums-based drug delivery systems have applications in the targeted delivery of medicines and different products to cure diseases [83].

**Stimuli-responsive natural gums-based drug delivery systems**

Stimuli-responsive carriers have solved the issue related to the early release of drugs and provided an intriguing option for the concept of multimodal targeting. Endogenous and exogenous are the two approaches to stimuli. Endogenous or internal stimuli include enzymes, ions, and redox potential, which are inimitable in tumor sections and can efficiently augment drug release [84]. In this approach, nanocarriers were prepared from vigilant materials so that they respond to precise endogenous stimuli and liberate enclosed drugs. In the exogenous approach, physical stimuli like temperature, light, electricity, ultrasound, and magnetic fields are applied to the target tissue [85]. The exogenous stimuli disrupted the structure of nanocarriers to release a drug in the desired tissue. Thus, the stimuli-responsive drug-delivery system prevented premature drug release [86]. For example, the pH-responsive carriers are structures that cause alterations in structure and characteristics in the influence of environmental pH. The pH-responsive polymers have the ability to ionize in acidic or basic residues based on the pH of the medium.

**Chewing Gums as a Drug Delivery Approach for Oral Health**

Active compounds from chewing gum are released on the basis of different parameters like gum base concentration, chewing speed, solubility of active content, and retention time in the mouth. They could transport chlorhexidine, calcium, antifungal compounds, and carbamide medicine like nitroglycerin, antihistamines, and methadone as drug carriers [87, 88].

**Table 2 Application of Different Plant Based Gums**

| Botanical Name/ Family | Substance (Common Name) | Pharmaceutical Application | Ref |
|---|---|---|---|
| Abelmoschus esculentus (L.) Moench/ Malvaceae | Okra gum | Controlled and Sustained-release tablets Suspending agent | [89] |
| Acacia nilotica (L.) Delile/Fabaceae | Gum acacia | Osmotic drug delivery Suspending agent, Binder Emulsifying agent Emollient, Demulcent | [90] |
| Albizia zygia (DC.) J.F.Macbr./ Fabaceae | Albizia gum | Coating materials in compression-coated tablets Emulsifier Tablet binder | [87] |
| Amorphophallus konjac K. Koch/Araceae | Konjac Glucomannan. | Gelling properties | [91] |
| Anacardium occidentale L./Anacardiaceae | Cashew gum | ↑Polymer ratio → ↓drug release to a larger extent Suspending agent ↑Disintegration time | [92] |
| Anogeissus latifolia (Roxb. ex DC.) Wall. ex Guillem. and Perr./Combretaceae | Gum ghati | Emulsifier Binder Suspending agent | [93] |
| Astragalus brachycalyx Fisch. ex Boiss.,A. ummifer Labill./Fabaceae | Tragacanth gum | Sustain release Emulsifying agent Suspending agent | [94-96] |
| Azadirachta indica A. Juss./Meliaceae | Neem Gum | Sustained release Binding property ↑Matrix tablet | [97] |
| Boswellia serrata Roxb. ex Colebr./Burseraceae | Olibanum Gum | Binding agent Sustained release | [98] |
| Caesalpinia spinosa (Molina) Kuntze/Fabaceae | Tara Gum | Controlled release carrier | [99] |
| Ceratonia siliqua L./Fabaceae | Locust bean gum (carob gum) | Controlled and targeted drug delivery to colon Mucoadhesive tablets Super disintegrants | [100] |
| Cordia myxa L./oraginaceae | Cordia gum | Oral sustained release matrix tablets | [101] |
| Cyamopsis tetragonoloba (L.) Taub./Fabaceae | Guar gum | Controlled drug delivery Sustained release Suspending agent | [92] |
| Firmiana simplex (L.) W.Wight/Malvaceae | Karaya gum | Gastric retentive dosage forms, ↑Dissolution rate of solid drug dispersions, Emulsifying agent, Suspending agent, Dental adhesive, Mucoadhesive,Buccoadhesive | [102] |
| Gleditsia triacanthos L./Fabaceae | Honey Locust Gum | Used in matrix tablets in 5% to 10% concentrations | [103] |
| Grewia mollis Juss./Malvaceae | Grewia gum | Controlled release dosage forms Suspending agent Binder,↑Fluidity granules, Film forming property | [104] |
| Hakea gibbosa Cav./Proteaceae | Hakea Gum | Binding agent, Sustained release | [105] |
| Khaya grandifoliola C.DC./Meliaceae | Khaya gum | Controlled drug release, Binding agent | [106] |

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|---|---|---|---|
| Mangifera indica L./ Anacardiaceae | Mango Gum | Sustained release, Binding agent Disintegrating | [107] |
| Moringa oleifera Lam./ Moringaceae | Moringa oleifera Gum | Gelling property, Release retardant property Binder, Disintegrater, Emulsifier | [107] |
| Prunus dulcis (Mill.) D.A.Webb/Rosaceae | Almond Gum | Emulsifier, Thickener, Suspending agent, Adhesive agent, Stabilizing agent, ↑Drug release, Uncoated tablet dosage form | [108] |
| Shorea javanica Koord. and Valeton/ Dipterocarpaceae | Gum Damar | Sustained release | [109] |
| Tamarindus indica L./Fabaceae | Tamarind gum | Matrix tablets, ↓Drug release, Biodegradable carrier for colon specific release | [110] |
| Terminalia bellirica (Gaertn.) Roxb./Combretaceae | Bhara gum | Sustained release | [107] |
| Terminalia catappa L./Combretaceae | Terminalia catappa gum | Oral sustained release tablets | [107] |
| Terminalia randii Baker f./Combretaceae | Terminalia Gum | Binder | [111] |

***CHALLENGES AND FUTURE SCOPE***

The availability of natural gums varies based on the season and climate of regions. After processing, extractions along with purification are crucial steps [112]. The development and efficiency may also be impacted by morphological traits (such as seed coat), physical injury to seeds, and inappropriate gum disposal, posing a significant barrier to related expenses and the ability for production in large quantities. Another key process is storage, which influences the gum quality. Natural gums have gained attention as carrier material due to their cost, accessibility, effectiveness, and adaptability as compared to conventional carrier materials. Metallic nanoparticles extorted from plants are used for the identification and therapy of different illnesses with few adverse reactions [113, 114]. Soumya et al. prepared guar gum nanoparticles by nanoprecipitation and cross-linking methods to be used as carriers for different formulations [115]. Wang et al. highlighted the important insights and promoted further development in synthesis procedures, characterization techniques, and future applications of metallic nanoparticles by using various polysaccharides as the hosts to create metallic nanoparticles [116]. Sari et al. demonstrated the prospect of preparing nanocomposite materials with a polymeric matrix of gums allied with nanocarriers that have superior performance in drug delivery and can be delivered by different routes than the starting components. They also evaluated their permeability through topical barriers, drug delivery capacity, and biocompatibility [117]. Furthermore, natural gums have a broad perception for the preparation of metallic nanoparticles in pharmacy and consumer goods. Furthermore, the research offered a fairly optimistic future for natural gums in regenerative medicine and tissue engineering. As in tissue regeneration, natural gums provide a naturalistic 3D microenvironment due to their structural component. For the successful development of clinical products, there is still a need for an in-depth study of natural gums, cells, processing techniques, and biological environment, particularly in the fabrication of polymeric inks and/or bio-inks. Extensive research is needed for additive production of tissue scaffolds and/or tissue models for future tissue engineering and transplantation.

***Conclusion***

Natural gums and their derivatives are a broad and diverse category of substances with considerable potential for use in medication delivery and other fields. This review revealed the different ways to amend the characteristics of original compounds with their examples. A non-ionic compound is transformed into an anionic compound with the introduction of the carboxymethyl group. Gum-based micro- and nanosystems can be consumed via different routes, the oral route is the most admired one. Natural gums and their derivatives have the potential to modify the release rate of drugs as they engorge in water. Due to this reason, the dosage the form is administered in form of dried matrices that were converted into original micro- and nanogel forms at the target site. As discussed in the review, natural gums have good biocompatibility and biological degradation with few negative effects, are simple to change chemically, and may absorb water. Furthermore, the qualities of natural gums are variable and adaptable. Natural gums, therefore, provide structural compatibility that is extremely similar to the biological molecules found in living organisms (*in vivo*), lowering the possibility of an immune response. We concluded that green nanotechnology improves life quality and encourages environmentally friendly obligations, as well as ethical principles in the field of nanotechnology, but it also brings arduous work in the pharmaceutical sector.

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