



Locust Bean Gum and its Role as Polymer in Pharmaceutical Industry

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ABSTRACT

Locust bean gum come from a natural sources and are biocompatible, biopolymers have drawn attention from the pharmaceutical industry. Aside from this, some intriguing qualities are their accessibility and lower financial load. Among the biopolymers with a variety of uses in the food industry and medicine delivery systems is locust bean gum. Traditionally, the only uses for locust bean gum were as a binder, thickening, and suspending/emulsifying agent. Recently, locust bean gum has gained attention as a possible polymer or excipient for creating innovative drug delivery methods.. The use of locust bean gum in tissue engineering, transdermal drug delivery systems, microcapsules, microspheres, and polymeric films is discussed in this article. By carefully referencing published research on locust bean gum, we have also detailed its physical characteristics, chemical makeup, and structure.

Keywords: Biopolymer, Locust bean gum, Pharmaceutical, Drug delivery

1. Introduction

A galactomannan polysaccharide with a high molecular weight (about 310,000 g/mol) is locust bean gum. It is made from the seeds of *Ceratonia Siliqua*, a member of the Leguminosae family and commonly referred to as the carob tree. The Mediterranean region is where it is most frequently found [1]. Because of its affordability, accessibility, and low toxicity, LBG is regarded as a natural gum that distinguishes itself from other industrial polymers. Although it is structurally and chemically similar to guar gum, it is very different. LBG solutions do not generate gels on their own, but they are soluble in water and enhance gels created by other hydrocolloids such as xanthan and carrageenan [2].

Among the many components of the carob fruit, which also include sugars and medicinal substances, polysaccharides are found in both the carob fiber and the carob bean gum. The fruit's sugars and dietary fibers assist prevent diabetes, heart disease, and gastrointestinal diseases, while its polyphenols are strong antioxidants. Recent claims of carob products' potential health advantages are a result of these characteristics. Many years ago, carob mucilage, commonly known as locust bean gum, was extensively studied for its colloidal qualities. At the end of the 1800s, it was critically described [3,4].

LBG is generally utilized as an additive (E410) in the food and beverage sector, most commonly as an emulsifier, thickening, stabilizing, and gelling agent because texture is an essential intangible food attribute. This polysaccharide has been used in a variety of other industries, including as the petroleum, paper, textile, cosmetic, and pharmaceutical sectors. In fact, certain non-starch polysaccharides produced from plants, like LBG, show great promise for developing drug delivery systems that offer site-specific and/or customizable drug release. Hydrogels made from natural gums has its application in tissue engineering, hygiene products, water purification, wound dressing, and agriculture.

2. Structure & Chemical Composition

Locust bean gum (LBG), a polysaccharide of vegetal origin belonging to the galactomannan family, is created when α -(1-6)-galactose randomly branches β -(1-4)-mannose backbones (**Figure 1**). The mannose:galactose ratios, usually determined by the Blakeney method, differ for each type of galactomannan depending on where they come from. The ratios found range from 1 to 1 to 10 to 1 for a variety of gums, including fenugreek gum 1:1, guar gum 2:1, tara gum 3:1, LBG 4:1, cassia gum 5:1, etc. The fine structure of LBG was originally clarified by Baker et al. in 1975 using an alkaline degradation approach, however Dea et al. clarify that its discovery and investigation go back considerably further [5].

However, there are methods of characterisation which are available. These consist of methylation, enzymatic hydrolysis, ¹³C NMR, hydrolysis, periodate oxidation, and the formation of sulfonyl derivatives. The LBG pods generally comprises of an endosperm (about 42%), germ layer (approximately 25%), and seed coat (approximately 30%) comprise a carob bean pod [6]. The moisture content of the residual bulk is around 8%. Galactomannan makes up roughly 85% of a pod's chemical composition, followed by water (about 8%), protein (about 5%), and trace amounts of ash, fiber, and fat (about 1% each).

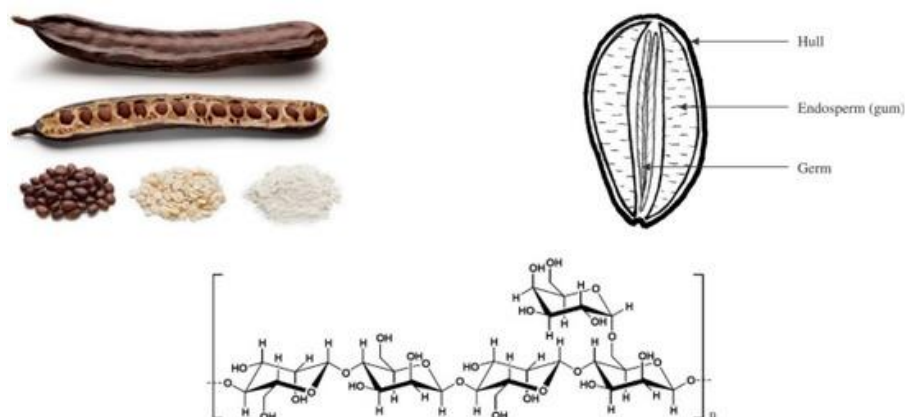


Figure 1. Carob Pod and Locust bean gum

3. Physicochemical Properties

3.1 Physical Appearance

Locust bean gum ranges in color from off-white to yellow-green. It has no taste or smell, but application of heat along with water gives a leguminous flavor [9].

3.2 Solubility

The solubility of LBG is mainly in water when it is heated at temperature range of 80 to 90 degrees celsius. This further results in the generation of a viscous solution. In case of cold water, locust bean gum is poorly soluble and forms a gel by imbining the water in its structure. However, the solubility of organic solvents is minimal.

3.3 Viscosity

The 1% solution of locust bean gum has a viscosity ranging from 3000-3500 cps.

3.4 pH

A 1% solution of locust bean gum has a pH of roughly 5.3, although a range of 3–11 is taken into consideration because of the influence of various factors on pH [10].

4. Pharmaceutical Applications

A remarkable range of polymer materials with intriguing applications in the biomedical sector can be found in nature. This is primarily due to the fact that they serve a variety of purposes in their native habitats. For instance, proteins serve as catalysts and structural components, while polysaccharides are crucial for membranes and cell communication. There are no better materials for the present trend of mimicking nature than those found in the natural world. The arrangement of monomers. Compared to synthetic materials, these natural materials provide significant advantages. Their mechanical characteristics are similar to those of natural tissues, and they are more adept at cell adhesion. In addition, they are relatively inexpensive, easily accessible, non-toxic, biodegradable, and, with a few exceptions, biocompatible [11]. But it's also important to take into account some important constraints. These include the polymers' varying sources and suppliers, as well as a greater risk of immunogenicity. Finding novel methods to chemically alter polysaccharides is a significant factor fueling interest in them. This enables the development of novel biological processes and the modification of existing characteristics to suit certain requirements. The biological activity of polysaccharides is also becoming more widely acknowledged for use in human applications. Polysaccharides are becoming increasingly prevalent in the biomedical industry. All things considered, polysaccharides play crucial roles as binder, disintegrant, suspending, emulsifying agent, and film forming in tablet coating [12]. Additionally, it has a variety of uses in the creation of polymeric beads, microspheres, microcapsules, and modified tablets. Besides this, the approach of tissue engineering has also been investigated using locust bean gum [13]. The graphical depiction of LBG's medicinal uses is highlighted in **Figure 2**.

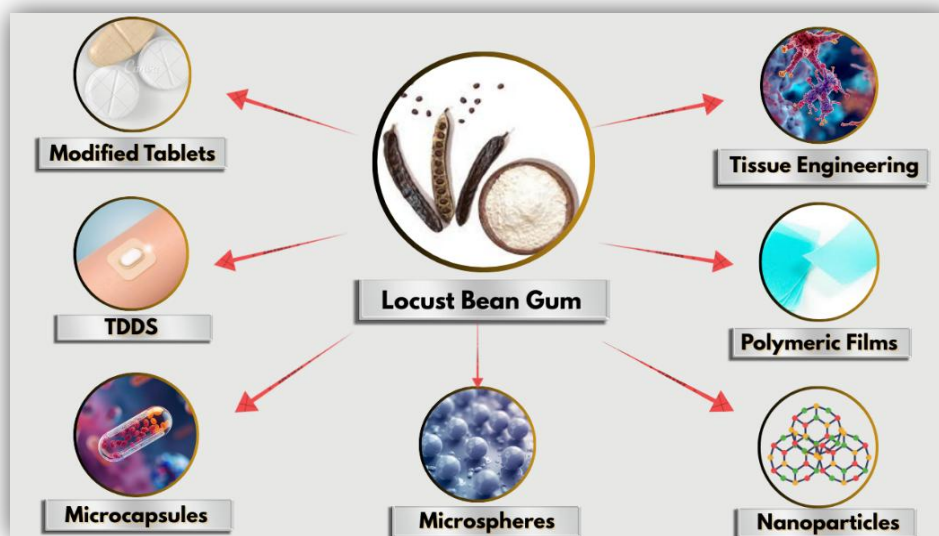


Figure 2. Pharmaceutical Applications of LBG

4.1 Development of Modified Tablets

As a matrix-forming substance in tablets, locust bean gum is mostly used in oral administration systems. The release of the medication from the matrix depends on the polysaccharides. The capacity of locust bean gum to swell helps regulate the release of drugs from the matrix tablets.

Ashok Kumar P et.al studied the ability of locust bean gum in controlling the drug release from a dosage form. The wet granulation process was used to create the Metformin HCl tablets. The gum from locust beans was employed as a matrix to control the rate. It was mixed with the medication Metformin HCl in six batches at varying ratios. From F1 to F6, the locust bean gum content was maintained in progressive order (10–40% w/w). The medication release profile was contrasted with that of the commercially available glycomet SR 600 tablet. The controlled release of the drug from the matrix was observed in batches F3, F4, F5, and F6 that contained a higher concentration of the polymer matrix (locust bean gum). On the other hand, F4's medication release profile was well-regulated and gradual. It closely matched the commercial product's drug release profile. Plotting the drug release profile of batches F3 through F6 using the Korsmeyer-Peppas equation revealed high linearity (R^2 : 0.997 to 0.996) and a relatively high slope (n) of > 0.5 , which seems to suggest a coupling of the erosion mechanism and diffusion, a phenomenon known as anomalous (non-Fickian) diffusion. Therefore, the mechanism of drug release from locust bean gum-based controlled release matrix tablets may be diffusion combined with erosion [14].

In order to improve the effect of regulating the drug release rate, the use of locust bean gum in modified tablets was also investigated in conjunction with the incorporation of additional polymers. The use of locust bean gum and chitosan in various ratios (2:3, 3:2, and 4:1) to create mucoadhesive buccal tablets containing propranolol HCl was investigated by Vijayaraghvan et al. A 5% ethyl cellulose coating was applied to the pills. With a 98% release in 60 minutes, the tablets prepared with a 2:3 ratio demonstrated the optimum mucoadhesivity and drug release. Sixteen healthy participants participated in a bioavailability research. The maximum bioavailability was shown by the tablets made with a 2:3 ratio of chitosan to locust bean gum. [15].

For matrix tablets, Venkataraju et al. also used xanthan and locust bean gum together. While locust bean gum is a nonionic polymer that is not dependent on pH for hydration, xanthan is an anionic, hydrophilic hetero-polysaccharide. Metoprolol matrix tablets were created using a combination of locust bean gum and xanthan in an effort to increase the drug's bioavailability by avoiding the first-pass effect. The mixture served as a matrix substance. In 45 minutes, tablets containing 7.5% polymer released 98% of the medication, but tablets containing 15% polymer released 45% of the medication at the same period. Tablets with good physical integrity, hardness, and mucoadhesion strength were created by the LBG/xanthan combinations. According to the drug release profile, the matrix system that contained both xanthan and locust bean gum released the drug more slowly than those that contained either substance alone [16]. In acidic conditions, xanthan-containing tablets exhibited burst release, whereas locust bean gum-containing tablets showed rapid erosion of the hydrated layer. In acidic conditions, there was no indication of burst release from the locust bean gum and xanthan combination in the matrix. These results implied that the interaction between locust bean gum and xanthan results in a regulated release.

4.2 Development of Transdermal Drug Delivery System

One strategy that offers a number of benefits over traditional drug administration methods is the transdermal drug delivery system. The fundamental strategy is to provide the medication through the epidermis. It differs from topical administration techniques in that the medicine enters the bloodstream directly. It increases the drug's bioavailability. This method makes it simple to administer several medications that are prone to pre-systemic first pass metabolism. As a rate-controlling matrix, the function of LBG in TDDS is investigated.

Along with carrageenan and montmorillonite, Ramanjot Kaur et al. investigated the activity of LBG in the creation of biocomposite film. Each of the four batches—carrageenan, carrageenan/LBG40, carrageenan/LBG100, and carrageenan/LBG/montmorillonite—was made using curcumin as a wound-healing agent. Carrageenan, carrageenan/LBG 40, and carrageenan/LBG 100 all had drug releases of $80.42 \pm 4.12\%$, $69.38 \pm 3.28\%$, and $63.94 \pm 3.1\%$ after 500 minutes, respectively. One potential explanation for the delayed drug release from the film could be the formation of the polymer matrix. After 500 minutes, the drug release from carrageenan/LBG 40/M was $56.39 \pm 1.74\%$. The inclusion of MMT considerably delays the release of the medication from transdermal films. This is because to the phenomenon of clay particle interpenetration, which causes the polymeric chain of LBG and carrageenan to relax. The medication was released according to a method that was controlled by erosion and diffusion. Additionally, compared to carrageenan alone, the wound-healing properties of carrageenan/LBG40 and carrageenan/LBG 40/MMT were faster. The regulated release of curcumin from carrageenan/LBG 40 and carrageenan/LBG 40/MMT was responsible for the faster wound healing. Therefore, in order to achieve the desired effect when designing transdermal delivery systems, LBG can be applied in combination with other natural and synthetic polysaccharides.

4.3 Development of Microcapsules

Microcapsules are hollow microparticles made up of a solid shell with a core-forming space that can hold compounds like medications and other comparable materials either permanently or temporarily.

For controlled medication release, Cheow and Hadinoto et al. created microcapsules containing *Lactobacillus rhamnosus* biofilm probiotics based on alginate-locust bean gum. The biofilm cells are protected from the stomach juice by capsules and released relatively little in the gastric region, allowing for a progressive and full release to the intestine. It has a high density and the necessary gastrointestinal release properties [18]. Because of the inherent biocompatibility of locust bean gum in drug delivery applications, alginate is used to encapsulate live bacterial cells. It is also inexpensive and can combine with either locust bean gum (LBG) or xanthan gum (XT) to form capsule matrices. Natural polysaccharides like LBG and XT are frequently utilized as thickeners, stabilizers, and emulsifiers [19]. The high affinities of LBG and XT for water molecules cause the capsule matrices to swell more. It is assumed that the viscous gel layer created by LBG and XT swelling condition slows down the beginning of capsule disintegration and causes a delayed release in the digestive area.

4.4 Development of Microspheres

Microspheres are tiny drug delivery systems made of polymers. Using hydrophilic polymers to create microspheres for regulated drug release has gained attention recently. They are widely accepted by regulatory agencies, provide flexibility in achieving desired drug release profiles, and are reasonably priced. One of the most commonly utilized naturally occurring biodegradable polymers in medication delivery systems is locust bean gum (LBG).

Alginate-locust bean gum interpenetrating network (IPN) microspheres were created by Jana et al. to deliver aceclofenac orally in a sustained-release fashion. They employed calcium ion ionotropic gelation. According to the Korsmeyer-Peppas model, in vitro research revealed that aceclofenac was released gradually over the course of eight hours. In vivo findings showed that carrageenan-induced rats exhibited potent anti-inflammatory effects for a considerable amount of time following oral treatment. These results imply that the continuous aceclofenac release provided by these microspheres is an efficient drug delivery method that can lower the frequency of dosage [20].

In the pharmaceutical industry, microparticles are a new method for delivering medications and other biomaterials. They slow down evaporation, prevent incompatibilities, change solubility, adjust flavor or odor, protect medications from oxidation, and assist solidify oils. Celecoxib, a COX-2 inhibitor, was encapsulated in locust bean gum and xanthan gum microparticles. In vitro studies showed that the drug release rate increased with higher concentrations of these gums. Over the course of six months, the microparticles' physical characteristics and drug content stayed constant across a range of temperatures. Following super case II transport mechanisms, the drug release was unaffected at gastric pH but slowed later at intestinal pH. This was true for all formulations.

4.5 Development of Nanoparticles

The LBG loaded silver nanoparticles have also been explored for the antibacterial activity. Ghassan H. Matar et al. studied the antibacterial activity of silver nanoparticles loaded with LBG/PVA hydrogel. The silver nanoparticles were prepared from the Fig leaf extract by using silver nitrate solution. The separate solution of LBG and PVA were prepared with AgNO_3 . Both the solutions were further mixed together. Later, this was subjected for the formation of the hydrogel membrane using gel casting method. This results in the formation of silver nanoparticles loaded with LBG/PVA hydrogel. It was examined for the antibacterial activity using minimum inhibitory concentration (MIC) method and disc diffusion method. The antibacterial test was done against gram positive (*S. aureus* and *E. faecalis*) and gram negative (*P. aeruginosa* and *K. pneumonia*) bacterial strains. The antibacterial activity LBG/PVA AgNP hydrogel was best amongst the compared chitosan/PVA loaded silver nanoparticles from literatures. The dimensions and form of silver nanoparticles may contribute significantly to their effectiveness in antibacterial applications [22].

4.6 Development of Polymeric Films

For decorative, protective, and utilitarian purposes, polymeric films are utilized as solid dosage forms. Usually, a spray method is used to apply these films, in which the substance is sprayed onto a solid surface. Hirsch et al. made locust bean gum films cross-linked with butanediol diglycidyl ether to

coat theophylline tablets. Drug administration in the colon was another application for these films. They have a significant capacity for swelling (between 300% and 500%) and were well-degraded by the microbiota in the colon. However, there were problems with the films' mechanical stability, particularly when the coating quantities increased. This implied that they were unsuitable for use in the manufacturing of colonic carriers [22].

Mostafavi et al created edible mix films using locust bean gum and tragacanth. Gum-tragacanth (GT) and locust bean gum (LBG) mixtures in different ratios were used to make these films. At various mixing ratios, a synergistic impact between the two biopolymers was seen. When applied to food items, blending the two polysaccharides improved their spreadability, decreased their surface tension, and strengthened the integrity of the coating. The gum blending ratio had no effect on the films' thickness, density, or retraction ratio. Nevertheless, the inclusion of LBG enhanced their mechanical, water-resistant, and transparent qualities. Based on these results, the combination of LBG and GT shows promise as a biodegradable food packaging material [23].

4.7 Tissue Engineering

There are numerous uses for tissue engineering. It entails the combination of cells, acellular biomaterials, medications, genes, or gene products that can be created, manufactured, and administered concurrently or sequentially with therapeutic agents. Tissue scaffolds are one way that tissue engineering is being used. Tissue scaffolds are highly porous, interconnected, three-dimensional structures. They provide support for cell seeding, which facilitates tissue remodeling, repair, or reconstruction. These scaffolds can be made synthetically or from natural sources. Based on how long they last, scaffolds are divided into two groups: temporary and permanent implants. During the organ's regeneration or repair, permanent scaffolds keep their strength and form. Temporary scaffolds, on the other hand, decompose when the tissue grows again.

Combining LBG with other biopolymers increases its potential. Researchers have looked into modified versions of LBG, which have demonstrated promising results in wound healing. Luis F.S. Araujo et. al explored the utilization of oxidized LBG and N-carboxyethyl chitosan based scaffold for wound healing. By using the Schiff base reaction, both of the biopolymer modifications were produced. Three batches of the NCEC/LBGO hydrogel scaffold were made: NCEC/LBGO10, NCEC/LBGO30, and NCEC/LBGO50 (LBGO10, 30, and 50 denote varying degrees of oxidation). Following a 24-hour rest period for crosslinking, the produced batches were lyophilized for drying. The ethanol infiltration method was used to assess the pore size of the produced scaffolds. A pore size that is comparable to overall porosity is essential to the healing process of wounds. It facilitates the vascularization, tissue development, and gas and nutrition exchange necessary for wound healing. Scaffolds with a higher degree of LBG oxidation were found to have larger pores. The average pore size was the smallest in NCEC/LBGO10 ($73 \pm 25 \mu\text{m}$), followed by NCEC/LBGO30 ($125 \pm 15 \mu\text{m}$) and NCEC/LBGO50 ($268 \pm 66 \mu\text{m}$). Male Swiss mice were used in the in vivo wound healing investigation. Surgical punches were used to injure the animals. For 14 days, three batches of scaffolds and saline solution (negative control) were applied topically to the injured animals.

5. Compatibility and Safety Profile

Natural polysaccharide LBG has good compatibility with other polysaccharides, such as carrageenan and xanthan gum [28]. Elasticity and gelling properties work in concert as a result. Additionally, it is a biodegradable polymer. The primary enzyme responsible for breaking down galactomannan, a major component of LBG, is mannanase and its derivatives. The human body does not manufacture the mannanase enzyme [29]. Nonetheless, these enzymes are often produced by the gut flora's microbiome [30]. The enzyme β -mannanase hydrolyzes the galactomannan moiety at the β -(1-4) linked mannan backbone to produce manno-oligosaccharides. The galactomannan is broken up into a single mannose chain by the enzyme β -mannosidase [31, 32]. Beside this, the enzyme α -galactosidase cleaves the galactose side chain from mannan backbone (Figure 2).

The breakdown of galactomannan in the human body is caused by the combination of fermentation and enzymes [33]. The safety of LBG as an excipient becomes a crucial factor to take into account while creating the formulations. It is thought that some excipients can have an effect on the human body in addition to the therapeutic agent's action on the physiological system [35, 34]. Therefore, in the majority of cases, the excipient's therapeutic inactivity is essential. Since the LBG is a novel excipient, it needs to be thoroughly physiochemically characterized. This is important for comprehending LBG's toxicological rather than safety profile [36,37]. Several regulatory bodies worldwide have approved the use of LBG as a food additive. The Joint FAO/WHO Expert Committee on Food Additives has determined that it is a non-mutagenic and non-teratogenic polymer [38]. The LBG is deemed generally recognized as safe (GRAS) by the US FDA for use in the food sector. Additionally, the European Union (EU) has accepted it as a food additive [39]. Several regulated markets are still considering the use of LBG as a medicinal excipient. Nonetheless, the FSSAI and CDSCO in India acknowledge it as a food additive and medicinal excipient, respectively. LBG's promise in oral dosage forms is the only reason the US FDA has approved it [40, 41].

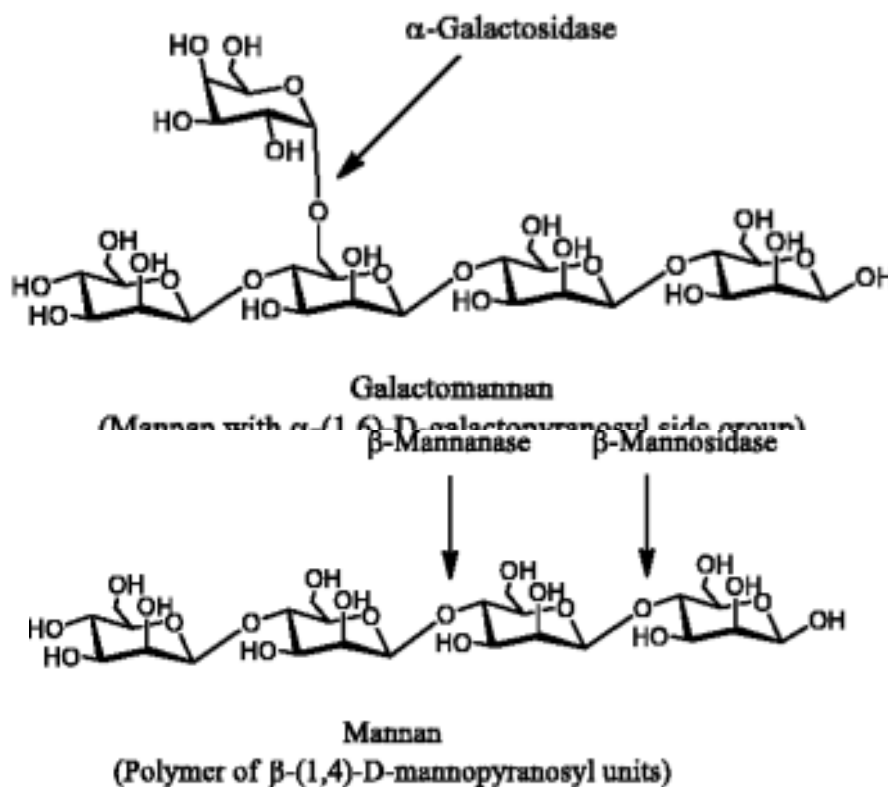


Figure 2. Degradation Pathway of Locust Bean Gum

6. Patents

The researchers across the globe have worked on the LBG due its known potential in pharmaceutical industry. There are patents filed for the various pharmaceutical application of locust bean gum. The **Table.1** provides the summary of patents on locust bean gum.

Table 1. Patents

Patent No	Title	Description	Reference
US8603517B2	Buccal Drug Delivery	The active ingredient levels and pH of the lozenge remain constant throughout time. It consists of a matrix made of sugar alcohol and at least one gum (locust bean gum) intended for regulated buccal medication administration.	[41]
JP7072280B2	Anti-itch agent	The antipruritic agent in sustained delivery system comprises of mannitol, xanthan and locust bean gum for the sustained release of drug from gel matrix.	[42]
US8309122B2	Oxymorphone controlled release formulations	The invention pertains to a method of relieving pain by administering a controlled release pharmaceutical tablet containing oxymorphone which produces a mean minimum blood plasma level 12 to 24 hours after dosing, as well as the tablet producing the sustained pain relief. The pharmaceutical composition, wherein homopolysaccharide gum comprised of locust bean gum.	[43]

JP7366178B2	Intranasal pharmaceutical powder composition	Intranasal pharmaceutical powder comprising of active substance, one of the component from ph modifiers, thickeners, sugar alcohol or combinations. The locust bean gum is used as thickener.	[44]
US12201720B2	Pharmaceutical composition comprising GHB gastro-retentive raft forming systems having trigger pulse drug release	An orally administrable drug powder composition which forms a gastro-retentive RAFT having at least two trigger pulses is provided. The crosslinkable polysaccharide is a galactomannan selected from guar gum, fenugreek gum, or locust bean gum and the at least one cross-linking agent selected from borax, glutaraldehyde, and/or zirconium.	[45]
US10117812B2	Foamable composition combining a polar solvent and a hydrophobic carrier	A foamable pharmaceutical vehicle comprising of a polymeric agent selected from the group consisting of a locust bean gum, sodium caseinate, an egg albumin, a gelatin agar, a carrageenin gum, sodium alginate, a xanthan gum, a quince seed extract, a tragacanth gum, and a guar gum.	[46]
US10278928B2	Film-forming pharmaceutical composition for wound healing and method for preparing the same	It forms a film directly on the wound to increase the adhesion to the wound. The formed thin hydrophilic film protects the wound surface to prevent infection of the wound surface, retains the physiologically active substance useful for wound healing on the wound surface to promote the wound healing, and allow drugs to be continuously delivered to the wound surface. The additive is a thickener and the thickener is selected from among hydroxypropyl cellulose, hydroxyethyl cellulose, xanthan gum, locust bean gum, arabic gum, guar gum, carbomer, polyethylene oxide, poloxamer.	[47]

7. Clinical Trials

The clinical trials are essential tool to understand the safety, and also to elucidate the potential for human use. Several studies have been explored for the use of locust bean gum in clinical or in vivo studies to determine both safety and functional benefits. The Table 2. provides comprehensive overview of clinical trials on locust bean gum.

Table 2. Clinical Trials

Clinical Trial No	Title	Status	Reference
NCT04042454	To Assess the Safety and Tolerance of Infant Formula With Locust Bean Gum in Infants With Regurgitation (Solar)	NA	https://shorturl.at/wswE0
NCT06906965	Effect of the Imera Cultivar Carob in Postprandial Glycemia (IMERACAROBGLUC)	NA	https://shorturl.at/9cJMD
NCT04383639	Cocoa/Carob Polyphenols and Postprandial Changes in Type 2 Diabetes (CACAOBA)	NA	https://shorturl.at/80WE2
NCT02065076	Efficacy of Sodium Polystyrene Sulfonate in the Treatment of Hyperkalemia in Pre-dialysis Patients (SKIP)	Phase 4	https://tinyurl.com/52zpdnpa

8. Conclusion

A polymer belonging to the galactomannan group, locust bean gum is taken from the seeds of the carob tree (*C. siliqua*). The use of polysaccharide-based systems in medication delivery is expanding. Because of its thickening, gelling, and stabilizing qualities, locust bean gum has long been used as an excipient in pharmaceutical products. LBG shows synergistic effects with other gums and polymers like carrageenan and xanthan gum. Hence coalition of LBG with other polysaccharides aid in achieving desired objectives. There is an increasing need for more controlled drug administration, which has led to an increased need for custom-made polymers. Delivery systems such tablets, capsules, microspheres, gels, polymeric films, and beads are made with it. LBG-based formulations display sustained-release behavior and can enhance mucoadhesivity in some formulations. Researchers are investigating new applications of LBG in different types of delivery systems. Thus, more LBG-based delivery systems will likely emerge in the near future, enriching the versatility of LBG-based formulations in terms of their categories and functions. The wide range of applications and the increasing number of researchers studying locust bean gum, due to its unique qualities, have made significant contributions to many formulations and suggest that locust bean gum has great potential as a novel and flexible ingredient. It will likely become even more important in the future.

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