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### LOCUST BEAN GUM: A PROMISING MATERIAL IN ORAL DRUG DELIVERY SYSTEM

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### **Keywords:**

Locust bean gum, Carob bean gum, Oral drug delivery, Pharmaceutical application, Natural polymers

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ABSTRACT: The increasing demand for natural polymers has fuelled substantial investment in research and development within the pharmaceutical and biotech sectors. Natural polymers, lauded for their biocompatibility, biodegradability, and safety, offer versatile advantages and among these, polysaccharides and proteins stand out. One class of natural polymers, gums, obtained primarily from plants, is gaining prominence in pharmaceuticals, biotechnology, and food industries. Notable examples include Xanthan gum, Guar gum, Locust bean gum (LBG), and Tara gum, all sharing the galactomannan compound at their core. LBG exhibits a range of physical and chemical properties that make it a valuable candidate for drug delivery systems. This natural biopolymer, with its unique characteristics, presents a compelling case for incorporation into oral drug delivery systems. The chemical composition of LBG makes it well-suited for interaction with other natural polymers. This interaction can lead to the development of novel drug delivery systems with controlled-release, improved solubility, and enhanced bioavailability. LBG's compatibility with various natural polymers offers a wide array of possibilities for formulation enhancement. Pharmaceutical applications of LBG encompass matrix-forming tablets, orodispersible tablets, enhanced drug solubility, mucoadhesive and buccal drug delivery systems, microparticles, and nanoparticles. The scope of LBG is promising, with potential applications in food, pharmaceuticals, cosmetics, and sustainable packaging solutions. In conclusion, the integration of LBG into oral drug delivery systems exemplifies its versatility and potential to transform pharmaceutical formulations. LBG aligns with the growing preference for natural and effective solutions across multiple industries, offering an exciting avenue for future research and development.

**INTRODUCTION:** The demand for natural polymers is constantly increasing, which is why pharmaceutical companies and Biotech start-ups are investing huge amounts of money in the research and development of natural polymer-based drug delivery systems <sup>1</sup>.



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Natural polymers are well known for their biocompatibility, biodegradability, non-toxic nature, and other factors like easy availability, economics, and being easily modifiable <sup>2, 3, 4</sup>.

Polysaccharides, proteins, peptides, polyisoprenes, polyesters, and lignin are a few common examples of such natural polymers <sup>5</sup>. Among them, polysaccharides and proteins are much more favourable due to their similarity with the extracellular matrix, and the formulation made by these natural polymers is less invasive <sup>6</sup>. There are various polysaccharides that are used in pharmaceutical and drug formulation; natural gums

are one of those polysaccharides, which are abundant in nature and easy to process. Gums are mainly obtained from a plant source; they are derived from the endosperm of plants, and they help in the germination of the seed. Gums are generally collected from plant species like Anacardiaceae. Leguminosae, Sterculiaceae, Combretaceae, Meliaceae, etc. Some common gums that are used in pharmaceuticals, Biotech, and Food are Xanthan gum, Guar gum, Locust bean gum, Tara gum, Tamarind, etc. Most of the abovementioned gums share the compound galactomannan in their basic structure, which again consists of two monosaccharides, namely mannose and galactose. Gums form mostly in stems or bark, and less gum can be obtained from other parts like roots and leaves. Plants produce gum using gummosis, which is the process of converting or disintegrating plant tissue into gum. Gummosis occurs either from injury or from a fungal or bacterial attack <sup>7, 8</sup>.

Gums can be implemented in a formulation in various ways, i.e., as a binder, they can increase the formation of granules and produce a stable formulation. Gums readily absorb water, and when used as a disintegrant, the formulation can swell five times when mixed with water, which helps in dissolution. Not only do gums absorb water they can also retain the absorbed water and form gel. This property of gum is utilized in sustained-release formulations and as a gelling agent. Some gums can be used as coating agents, entrapping drug molecules to form microspheres that show sustained action. Natural gums are very versatile, cost-effective, and safe to make formulations with 9, 10

Most institutions are trying to implement these natural gums into oral drug delivery systems. The oral drug delivery system is the most widely accepted drug delivery route <sup>11</sup>. Oral drug delivery has come a long way, where nowadays there is various novel drug delivery method, which can show targeting, sustained, delayed, and controlled action by various mechanism like floating, mucoadhesion, nanoparticles, microparticles, *etc* <sup>12</sup>. By using these natural gums over synthetic polymers, we can develop more safe and biocompatible formulations <sup>13, 14</sup>. Locust bean gum is also a natural gum that has great potential in the

oral drug delivery system which we will discuss in this review.

## **Locust Bean Gum (LBG):**

Source: Locust bean gum or LBG is a natural gum that is obtained from the carob tree and extracted from the seed, more specifically from the endosperm. Carob, or *Ceratonia siliqua* Linn., of the Fabaceae family is mostly found in the Mediterranean region and also in a few regions of North Africa, South America, and Asia. Locust bean gum, or Carob bean gum, is very much used in the Food industry as a thickening agent and stabilizer, but more so, it has potential in the drug delivery and formulation of dosage forms <sup>15</sup>. It has huge market and there are many marketed LBG as shown in **Table 1**.

TABLE 1: VARIOUS MARKETED LOCUST BEAN GUM BRANDS AND THEIR PRODUCT

Brand	Product
Carob SA (Spain)	Carobex
Nexira (France)	FibroGum
Cargill (United States)	Cargill Locust Bean
	Gum
TIC Gums (United States)	TIC Locust Bean Gum
Kerry Group (Ireland)	Kerry Locust Bean Gum
Altrafine Gums (India)	Altrafine Locust Bean
	Gum
DuPont Nutrition &	Suprocar
Biosciences (United States)	
AVT Natural Gum (India)	AVT Locust Bean Gum
Manish Agro Industries	Manish Locust Bean
(India)	Gum

**Processing of Carob Beans:** Carob seeds composed of 80-85% galactomannan, 10-12% moisture and other components like albumin, globulin, glutelin etc. The endosperm is processed using hull cracking, shifting, milling, clarifying, and drying Fig. 1. The husk of the carob seed is relatively hard to break and is done using acid peeling or thermal peeling. In acid peeling, dilute sulfuric acid is introduced, and the temperature is constantly increased to remove the husk. The endosperm is isolated by washing and brushing. The kernel is peeled and dried to separate the germ from the endosperm. The endosperm is then further crushed to obtain whitish carob bean gum. In thermal mechanical peeling, the seed is roasted in a rotating furnace and the endosperm is collected. The endosperm is then milled and sieved to get a dark-colored carob bean gum <sup>16</sup>.

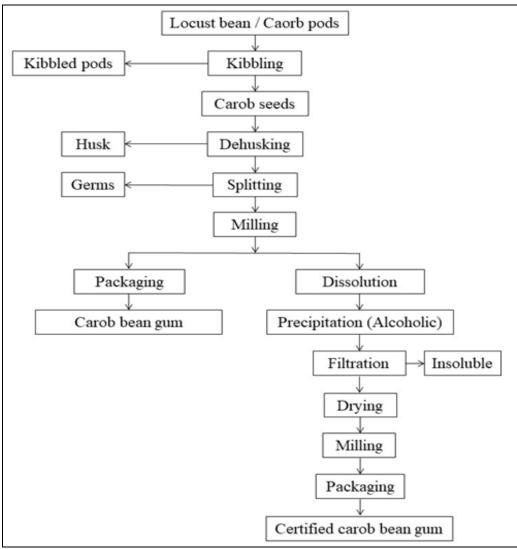


FIG. 1: FLOW CHART FOR PROCESSING OF CAROB BEAN GUM

Physical Properties of LBG: LBG is available in powder form, which varies from off-white to pale yellow colour. The texture of the prepared powder is smooth with good flow property <sup>17</sup>. LBG is very much soluble in both hot and cold water. When come in contact with water LBG produces gel-like solution which is viscous in nature <sup>18</sup>. LBG has the ability to increase viscosity in low concentrations <sup>19</sup>. LBG readily absorbs water and can hold significant amount of water <sup>20</sup>. LBG can be used to prepare film which has water retention and barrier properties. LBG is stable under moderate heating and retains its properties <sup>21</sup>. LBG is compatible with a vast range of ingredients across all industries like food, pharmaceutical, biotechnology, *etc* <sup>22</sup>.

**LBG Chemical Properties:** Galactomannans **Fig. 2** are the fundamental component of LBG. Galactomannans are long-chain polysaccharides with mannose and galactose units in a ratio of 4:1.

Molecular weight- The molecular weight of LBG ranges from 200,000 to 300,000 Daltons. LBG is very hydrophilic in nature, and it can absorb and retain large amounts of water <sup>23</sup>. LBG has a linear mannose chain with a galactose side chain in regular intervals <sup>24</sup>. This branching provides LBG with gel-forming and viscous properties <sup>25</sup>. LBG can be modified using acetylation, where the hydroxyl group of the galactose unit gets esterified with acetyl group. Acetylated LBG shows more gelling properties <sup>26</sup>. LBG is stable across the pH range, from acidic to basic condition. It retains its functional properties in normal pH conditions of various industries <sup>27</sup>.

LBG is comparatively stable in normal and processing condition. LBG can be degraded by enzymes like  $\beta$ -mannanase, which hydrolyze the mannose-galactose bonds and LBG loses its functional properties  $^{28}$ .

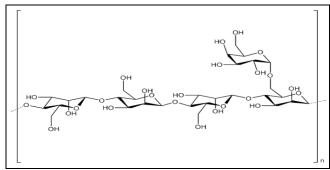


FIG. 2: STRUCTURE OF GALACTOMANNAN

Advantages of using LBG as a Pharmaceutical **Ingredient:** LBG grows abundantly Mediterranean regions and can provide consistent supply, therefore It is a reliable and cost-effective alternative <sup>29</sup>. LBG is highly soluble and can quickly dissolve in aqueous medium, which allows easy preparation, efficient drug incorporation, and a good release pattern <sup>30</sup>. LBG has been used in the food industry for a long period of time and it is generally recognized as safe (GRAS) by regularity authorities like FDA, therefore it is safe to use and non-toxic. Overall LBG has many properties like increasing viscosity, stability, mucoadhesion, and film-forming properties which make LBG an ideal candidate for pharmaceutical products <sup>31</sup>.

Interaction of Locust Bean Gum with Other Natural Polymers: Chitosan-Locust Bean Gum Interaction: Locust bean gum can interact with Chitosan, a biopolymer made from chitin, through electrostatic interactions between the positively charged amino groups of chitosan and the negatively charged carboxyl groups of locust bean Through this interaction. nanoparticles, or hydrogels with improved mechanical properties and long-lasting drug-release capabilities may be created 32, 33, 34

Alginate-Locust Bean Gum Interaction: Alginate, a naturally occurring polysaccharide obtained from brown seaweeds, can combine with locust bean gum to generate interpolymeric complexes. Alginate's negatively charged carboxyl groups and locust bean gums positively charged amino groups interact through ionic gelation. Hydrogels or microspheres with better stability and controlled drug release qualities may be created as a result of this complexation <sup>35, 36, 37</sup>.

**Xanthan Gum-Locust Bean Gum Interaction:** A microbial polysaccharide called xanthan gum can

interact with locust bean gum through hydrogen bonding and physical entanglement <sup>38, 39, 40</sup>. These two polymers can combine to create composite hydrogels with improved stability, rheological properties, and drug-release characteristics <sup>41, 42, 43</sup>.

**Gelatin-Locust Bean Gum Interaction:** Through hydrogen bonds and electrostatic interactions, the collagen-derived protein gelatin can interact with locust bean gum 44, 45, 46. These two polymers can be combined to create composite films or microspheres that have better water vapor barrier qualities, mechanical strength, and drug encapsulation capabilities 47, 48.

**Carrageenan-Locust Bean Gum Interaction:** Through ionic gelation and hydrogen bonding, the sulfated polysaccharide carrageenan, which is obtained from red seaweeds, can interact with locust bean gum <sup>49, 50, 51</sup>. Through this interaction, hydrogels or microspheres with improved gel strength, stability, and sustained drug-release qualities may be created <sup>52, 53, 54</sup>.

**Guar Gum-Locust Bean Gum Interaction:** Due to their comparable chemical compositions, locust bean gum, and guar gum can interact in a beneficial way. Both are mannose and galactose-containing galactomannans with comparable backbone architectures <sup>55, 56</sup>. These two polysaccharides can be joined to produce composite hydrogels or films that have better viscoelastic characteristics, thermal stability, and mechanical strength <sup>57, 58, 59</sup>.

**Pectin-Locust Bean Gum Interaction:** Locust bean gum can interact with pectin, a complex polymer present in plant cell walls, *via* hydrogen bonds and electrostatic interactions <sup>60, 61</sup>. These polymers can be combined to create gels or emulsions that have better texture and stability. Particularly helpful in food and drug compositions is this connection <sup>62, 63</sup>.

Gum Arabic-Locust Bean Gum Interaction: Acacia gum, sometimes known as gum Arabic, is a naturally occurring secretion from these trees. Through hydrogen bonds and Van der Waals forces, it can communicate with locust bean gum. These two types of gums can be combined to produce stable emulsions and microencapsulation systems for a range of uses, such as taste encapsulation and medication delivery <sup>64, 65</sup>.

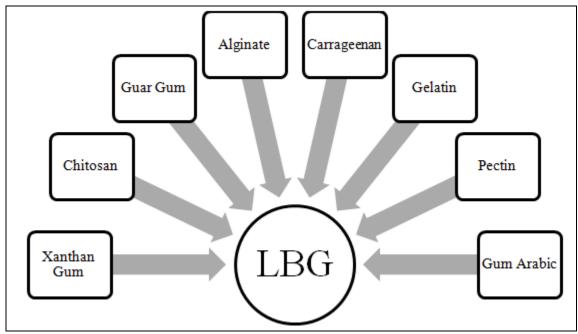


FIG. 3: FLOWCHART OF INTERCATION OF LBG WITH OTHER NATURAL POLYMERS

Pharmaceutical Application of Locust Bean Gum: Locust bean gum is a very versatile natural biopolymer that has many applications in food, cosmetics, and pharmaceuticals. Locust bean gum is a bioactive material with a hypolipidemic effect that helps decrease cholesterol synthesis. Locust bean gum has a wide range of utilizations, like binder, matrix former, drug release modifiers, coating material, thickening agent, viscosity

enhancers, stabilizers, disintegrators, solubilizers, emulsifiers, suspending agents, gelling agents, and bioadhesives. There are numerous studies and research going on to develop formulations based on Locust bean gum or modified Locust bean gum **Fig. 4**. Among these, the majority is related to oral delivery formulation, but ocular and topical formulation is also under research <sup>66</sup>.

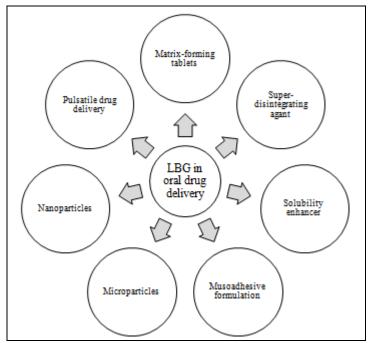


FIG. 4: APPLICATION OF LBG IN ORAL DRUG DELIVEY

**LBG in Oral Drug Delivery:** Oral drug delivery is the most commonly used approach for drug

administration. Oral administration is very easy and non-invasive; therefore, most of the pharmaceutical

industry is focused on developing new oral formulations or improving existing ones. Natural polymers are very useful in oral formulations due to their biocompatible properties. LBG can be introduced in different oral modified-release formulations.

**Matrix-forming Tablets:** Matrix forming tablets are formulation which incorporates a drug dispersed in a matrix made of polymers, sugars, or lipids <sup>67</sup>. Natural polymers are hugely integrated into controlled-release formulations; they help in the formation of matrix in these formulations and show controlled drug release <sup>68, 69, 70</sup>. LBG has good swelling properties and can be incorporated with other polymers. Since 1998, LBG has been used as an excipient in formulations like sodium diclofenac mini-matrix with a drug-to-polymer ratio of 1:1, which demonstrate faster non-Fickian erosion in intestinal Ph <sup>71</sup>.

Other studies, including LBG matrix tablets containing theophylline and myoglobin in comparison with guar gum, showed no effect of additional cross-linkers in LBG but a significant change in the guar gum-incorporated formulation. This phenomenon is due to the size of the side chain; LBG has a small side chain, and guar gum has a long side chain <sup>72</sup>.

LBG is already on the market as a tablet formulation known as TIMERx, along with Xanthan gum. TIMERx is manufactured by Penwest Pharmaceuticals which is a twice-a-day oxymorphone controlled release matrix formulation <sup>73</sup>. This is one of the examples of using LBG with other polysaccharides for improvement, which is due to synergies among the gums. Likewise, LBG and Xanthan can be incorporated into hydrogels with myoglobin to form tablets, but in this case, the diffusion is inhibited solely by LBG <sup>74</sup>.

**Super-disintegrating agents:** Many natural polymers show disintegrating property, LBG can be also incorporated into formulation as super-disintegrating agent. Fast disintegrating tablet of Amlodipine besylate was prepared using LBG and in showed 98% drug release within 30 min <sup>75</sup>.

Then there are orodispersible tablets, which are quick dissolving solid dosage forms which disperse in the mouth without help of water <sup>76</sup>. Hydrophilic

materials are suitable for preparing these types of formulation <sup>77</sup>. LBG can also act as a super disintegrant in orodispersible tablets. For example, orodispersible has been prepared tablet using LBG using direct compression method and compared them with formulation consisting croscarmellose sodium. After testing various parameter, they found the disintegrating pattern in better in the formulation where LBG is used. By swelling and increasing porosity LBG show super-disintegrating property and can be integrated into orodispersible formulation <sup>78</sup>.

Increase the Solubility of Poorly Soluble Drugs: Increasing solubility is one of the major areas which is being researched for the poorly soluble drugs <sup>79</sup>. There are solid dispersion using LBG and modified Locust bean gum (MLBG) to increase the solubility of Lovastatin an HMG CoA inhibiter which has low water solubility. They have developed solid dispersion using kneading method, spray drying method, solvent wetting method, and modified solvent evaporation method. Among the above methods for preparing solid dispersion modified solvent evaporation method resulted in better dissolution than others. And MLBG causes better release pattern than LBG due to the viscous nature of LBG <sup>80</sup>.

**Pulsatile Drug Delivery:** Pulsatile drug delivery is a unique delivery system where the time, amount and location are predetermined and controlled <sup>81,82</sup>. It is helpful in case of chronic disease like arthritis, asthma, hypertension, etc. Floating pulsatile drug delivery formulation containing quinapril hydrochloride was prepared using carboxymethyl locust bean gum and it showed drug release at right time and right amount <sup>83</sup>.

Mucoadhesive and Buccal Drug Delivery: Mucoadhesion is the phenomenon of the polymers binding to the mucus membrane and releasing the drug in a sustained and controlled manner 84. Buccal drug delivery also provides better bioavailability and bypasses hepatic first-pass metabolism and pre-systemic elimination Natural polymers have good mucoadhesive properties, and LBG also shows mucoadhesion. The formulation has been observed for mucoadhesive buccal tablets using LBG and Chitosan, which demonstrated high bioavailability

and mucoadhesion with an LBG and Chitosan ratio of 2:1. Other examples include bioadhesive oral controlled release tablets of theophylline, which show an increase in gum concentration will result in prolonged release but the bioadhesive strength remains the same <sup>86</sup>. It can also be incorporated as stabilizer in buccal formulations.

**Incorporation as a Microparticle:** Microparticles are formulations that are used as carriers and biomaterials. LBG can be formulated into microparticles to increase bioavailability and improve drug release. Studies have shown that LBG successfully produces microspheres microcapsules. For example, a controlled-release formulation of alginate-locust bean gum-based microcapsules of Lactobacillus rhamnosus the microcapsule was formed using alginate, which is cost-effective, biocompatible, and compatible with LBG and Xanthan gum. In the intestine, the formulation shows delayed release. Studies of LBG microspheres consisting of mesalamine ulcerative colitis have shown low drug release in the upper GI tract and target the colon region. By using ionic gelation, we can even produce alginate locust bean gum microspheres of diclofenac sodium, which show slow drug release <sup>87, 88</sup>.

Nanoparticles with LBG: Nanoparticles are small formulations that can deliver drugs more effectively and have better bioavailability than conventional dosage forms <sup>89</sup>. There are studies where LBG with Chitosan is used to formulate nanoparticles of aceclofenac interpenetrating network nanocomposites. The formulation shows good drug entrapment and drug release at an acidic pH <sup>90</sup>.

Future Scope of Locust Bean Gum: The future prospects of locust bean gum (LBG), also known as carob gum, in the field of pharmaceuticals, are indeed promising and multi-faceted. LBG, due to its unique properties, is poised to play a pivotal role in advancing drug delivery systems across various routes. This versatile natural polymer exhibits gelling capabilities, mucoadhesive properties, biodegradability, and biocompatibility, attractive for oral making it an choice pharmaceutical formulations the contemporary landscape of pharmaceutical research and development, there is a growing emphasis on

designing drug delivery systems that offer sustained release, controlled release, targeted delivery, and personalized formulations. LBG's intrinsic characteristics position it as a valuable candidate for addressing these critical requirements. One of the foremost applications of LBG lies in its potential for sustaining drug release. Sustained release formulations are designed to release drugs gradually over an extended period, reducing the frequency of administration and improving patient compliance. LBG's gelling property can be harnessed to create matrices that control the release rate of drugs, ensuring a steady therapeutic effect. This approach holds great promise for managing chronic conditions and enhancing the overall patient experience 82.

Moreover, LBG's hydrophilic nature makes it an excellent choice for improving the solubility of poorly water-soluble drugs. Enhancing solubility of such drugs is a key challenge in pharmaceutical development, as it directly impacts their bioavailability. By incorporating LBG into formulations, researchers can enhance dissolution and ultimately increase the bioavailability of these challenging compounds. This not only improves the efficacy of the drugs but also opens up new possibilities for previously underutilized therapeutic agents <sup>93</sup>.

In the realm of mucosal drug delivery, LBG stands out as a superior mucoadhesive material. Mucoadhesion refers to the ability of a substance to adhere to mucosal surfaces in the body, such as the oral cavity or gastrointestinal tract. LBG, both as a standalone material and in combination with other polymers, exhibits remarkable mucoadhesive properties.

Researchers are actively exploring ways to optimize LBG's mucoadhesive characteristics, making it more amenable for mass production and widespread use. This advancement holds the potential to revolutionize drug delivery through buccal and sublingual routes, enabling rapid drug absorption and targeted therapy <sup>94</sup>. Furthermore, LBG can serve as an effective taste masking agent. Bitter taste is a common issue with certain drugs, often leading to poor patient compliance, especially in paediatric and geriatric populations.

LBG's gelling and masking properties can be harnessed to encapsulate bitter-tasting drugs, rendering them more palatable and increasing patient acceptance. This innovation contributes significantly to improving the overall medication experience and adherence 95. In the pursuit of comprehensive treatment strategies, LBG can also be formulated into combination Combining multiple drugs into a single dosage form simplifies medication regimens and enhances patient compliance. LBG's compatibility with various pharmaceutical agents makes it a valuable component in the development of combination therapies. This approach not only addresses complex medical conditions more effectively but also streamlines the drug administration process for patients <sup>96</sup>.

**CONCLUSION:** In conclusion, the study on the utilization of locust bean gum (LBG) in the oral drug delivery system highlights the significant potential of this natural polymer in pharmaceutical formulations. The escalating demand for natural polymers in drug delivery has spurred a wave of research and development, driven by their biocompatibility, biodegradability, safety, modifiability. Within this context, LBG stands out due to its unique properties and versatility.LBG has gained recognition for its role in various industries, notably the food sector, where it serves as a gelling and thickening agent. However, its application extends to pharmaceuticals, where it exhibits exceptional promise. The processing of LBG is a versatile powder with favourable physical and chemical characteristics. The molecular composition of LBG, rich in galactomannans, makes it conducive to interactions with other natural polymers, resulting in the development of novel drug delivery systems. LBG's involvement in oral drug delivery formulations showcases its efficacy in creating sustained-release systems, solubility, enhancing drug and enabling mucoadhesive and buccal delivery mechanisms. Additionally, its compatibility with nanoparticles demonstrates its role in advancing bioavailability and delivery efficiency. Looking ahead, the future scope for LBG is promising across multiple sectors. The pharmaceutical domain could see the development of novel drug delivery platforms and sustained-release formulations. Continued research into LBG's functional

properties could uncover new applications, thereby expanding its presence in diverse industries. In summary, the study of locust bean gum's integration into the oral drug delivery system underscores its versatility and potential to revolutionize pharmaceutical formulations, aligning with the growing preference for natural and effective solutions in various industries.

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