

# Exploring Guar Gum: Dietary Adjunct to Novel Drug Delivery Systems

Priyanka Purohit and Brahmeshwar Mishra\*

Department of Pharmaceutics, Indian Institute of Technology, Banaras Hindu University, Varanasi-221005.

## Abstract:

Guar gum is the complex polysaccharides composed of galactomannans and is obtained from the endosperm of the seed of the guar plant, *Cyamopsis tetragonaloba* (L) Taub. (syn. *Cyamopsis psoraloides*). The hydroxyl groups in polymer is responsible for gelling, emulsifying, film forming etc, properties which make it a suitable excipient in many industries like cosmetics, food, medical and drug delivery. This review aims to describe the recent developments of guar gum based drug delivery system. The medicinal and therapeutic properties of soluble dietary fiber of guar gum is reported to improve the serum biochemical profile of human and non-human primates, reduce total serum cholesterol and the management of glycemic indices and obesity. Due to its fascinating properties it is used as a rheological modifier in food, pharmaceutical, paper, textile and other industrial and commercial sectors. Guar gum has high drug loading capacity, biocompatibility and biodegradability which are the key points to design a drug delivery system effectively.

**Key Words:** Guar gum, Biodegradable, Controlled drug delivery system.

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**Author For Correspondence:** Dr. Brahmeshwar Mishra; Department of Pharmaceutics, Indian Institute of Technology, Banaras Hindu University, Varanasi-221005, Mobile: 09415811824, E-mail: [bmishrabhu@rediffmail.com](mailto:bmishrabhu@rediffmail.com)

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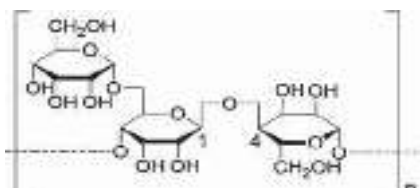
## INTRODUCTION

Polysaccharides are essential biomacromolecules for life, and play an important role in cell-to-cell communication, cell adhesion, and molecular recognition in the immune system. Polysaccharides are composed of many monosaccharide residues that are joined one to the other by O-glycosidic linkages. Natural polysaccharides (biological origin) are of more interest because of their non-toxicity, environmental safety, biodegradability, biocompatibility, renewability, cheaper prices and availability factors. Its unique multitasking behaviour makes it an important part of various industries like food, pharmaceuticals, cosmetics, textile, paper, paint, adhesive etc. Natural gums are hydrophilic polysaccharides derived from plants or microbial sources. They are classified as plant exudate gum, seed gum, microbial gum or marine gums depending upon the origin. Seed gums like guar gum, tamarind gum, locust bean gum etc., are obtained from the embryos of some seeds, where they are actually stored as food reserve (Reddy K et al., 2011).

### Physicochemical properties of Guar gum

Guar gum (GG) consists of high molecular weight (approximately 50,000-8,000,000) polysaccharides

composed of galactomannans and is obtained from the endosperm of the seed of the guar plant, *Cyamopsis tetragonaloba* (L) Taub. (syn. *Cyamopsis psoraloides*). Galactomannans are reserve polysaccharides consisting mainly of the monosaccharide's mannose and galactose units. The mannose elements form a linear chain consisting of (1→4)-β-D-mannopyranosyl residues, with (1→6) linked α-D-galactopyranosyl residues as side chain at varying distances. They are insoluble in organic solvents except formamide. At very low concentrations with water, it forms colloidal solutions of high viscosity. The galactose side chains attached to mannose backbone interact with the surrounding water molecules resulting into intermolecular chain entanglement which increases viscosity. As concentration of guar gum increases in water, the entanglement increases further to induces gelling or thickening. 1% aqueous dispersion of good quality guar gum may possess viscosity as high as 10,000 cps (Parija S et al., 2001). Guar gum solution is susceptible to microbial degradation. The unpreserved solution should be used within 24 h or else must be preserved with some preservatives.



**Figure 1: Chemical structure of guar gum**

An excessive number of –OH groups help the natural gums to be soluble in water, but the –OH moieties are unable to form strong ionic interactions with counter ions. So, they cannot be used directly for controlled drug delivery. Therefore, modification is required. Modification of hydrophilic backbone of this biopolymer diversifies and enhances its applications and functionality.

#### Modifications of Guar gum

**Derivatization** : Various derivatives of guar gum like methylated, sulfated guar gum, carboxy methyl guar gum, o-carboxy methyl, o-hydroxy propyl guar gum (CMHPG), o-2-hydroxy-3-(trimethylammoniapropyl) guar gum (HTPG), o-carboxymethyl-o-2-hydroxy-3-(trimethylammoniapropyl) guar gum (CMHTPG), etc. have been prepared, characterized and examined for their applications. Carboxymethylation of gums increases their hydrophilicity and solution clarity and makes them more soluble in aqueous systems. Guar gum was derivatised with monochloroacetic acid to produce carboxymethyl guar gum (CMGG) (Thombare N et al., 2016).

**Cross-linking:** Being water soluble, it swells easily. So, there are more chances of entrapped drug leakage prior to arrival of the drug at its site of absorption. Cross-linking helps to reduce the excessive swelling of the gums. Hydrogels are cross-linked hydrophilic material, linear or branched polymers with the ability to absorb large quantities of water, or other aqueous solutions compared with general absorbing materials (Pourjavadi A et al., 2008). The straight chain guar gum molecules are randomly tied with each other by cross-linkers. Commonly used cross-linking agents are derivatives of methylene-bis-acrylamide, derivatives of ethylene-glycol-di(meth)acrylate, di-vinyl-benzene, glutaraldehyde, etc. These cross-linking agents have two active sites which undergo intermolecular bonding with hydroxyl groups of polymer chains to form closed loop like structure. When water is added to this material, the water is entrapped into cross-linked network which does not easily escape. This increases the water absorption and holding capacity of the hydrogels system (Doyle JP et al., 2006). Interpenetrating network (IPNs) microspheres of nifedipine were prepared by adding polyvinyl alcohol, guar gum and glutaraldehyde. The aldehyde groups of glutaraldehyde reacted with the hydroxyl groups of the polymers to form

acetal cross-links (Soppimath KS et al., 2000). Glutaraldehyde has been used extensively for cross-linking polymers containing hydroxyl groups. Cross-link density increases with increase in concentration of glutaraldehyde.

#### Guar gum in pharmacotherapy

Guar gum acts as a bulk forming laxative, promotes regular bowel movements, relieves constipation and related chronic functional bowel ailments like diverticulosis, Crohn's disease, colitis and irritable bowel syndrome (Iqbal DN et al., 2010). Partially hydrolyzed guar gum (PHGG) was added to oral rehydration solution (ORS) and reduced the severity of diarrhoea in adults (Alam NH et al., 2008), acute diarrhoea in children (Alam NH et al., 2000). PHGG was effective for improving somatic (gastrointestinal symptoms) and psychological (quality of life and psychological distress) symptoms for the short term (Parisi G et al., 2005). This dietary fibre proved to improve the serum biochemical profile of human and non-human primates, reducing total serum cholesterol, triglycerides, increasing the high density lipoprotein cholesterol level, and the management of glycemic indices and obesity. The reduction in intestinal cholesterol absorption may due to an increase in the faecal loss of bile acids and a reduction in the enterohepatic bile acid pool size which may stimulate the liver to produce more bile acids from cholesterol, thus reducing hepatic free cholesterol concentrations. The dietary supplementation of guar gum significantly reduced free and esterified cholesterol levels in guinea pig (Rideout TC et al., 2008). Guar gum and its derivatives are well established in suppressing diabetes. Guar gum, partially hydrolyzed guar gum (Dall'Alba V et al., 2013) and modified partially depolymerized guar meal (Brennan CD, et al., 1996) have shown the reduction of the postprandial rise in blood glucose and insulin concentrations. Now days, hydrophilic polysaccharides are in huge demand in the design of controlled drug delivery systems due to their flexibility to obtain a desirable drug release profile. Literature depicts that guar gum polysaccharide has been widely used in various forms such as oral controlled drug delivery systems, coatings, tablets matrix, hydrogels and nanoparticles. Guar gum is used as a binder, thickener, stabilizers, emulsifier, suspending agent, disintegrating agent in various formulations. The guar gum can be fabricated to get desired solubility, swelling and film forming ability.

#### Guar gum in novel drug delivery system

##### Colon-specific drug delivery

Guar gum is used conveniently in hydrophilic matrix for oral controlled delivery of drugs due to resistance to

dissociation in acidic pH in stomach, gelling to reduce release of drug and susceptibility to enzymatic and microbial degradation in the large intestine. It is used by either compressing native guar into matrix tablets or chemical modification to reduce its swelling properties (Krishnaiah YSR et al., 1998). The colon targeted release of guar gum bound tablet was confirmed in healthy human volunteers with gamma scintigraphic study using technetium 99m-DTPA as tracer. The tablets were found to degrade in colon (Krishnaiah YSR et al., 1998). Matrix tablets of indomethacin and guar gum were found to maintain their integrity in 0.1M HCl for 2 h and in Sorensen's phosphate buffer (pH 7.4) for 3 h releasing only 21% of the drug in these 5 h. Matrix tablets of mebendazole with various proportions of guar gum were prepared. The results showed that matrix tablets containing either 20% or 30% of guar gum are most likely to provide targeting of mebendazole for local action in the colon (Krishnaiah YSR et al., 2003). Dexamethasone and budesonide matrix tablets were prepared by using 60.5% (w/w) of guar gum. The study concluded that the galactomannanase (0.1%) accelerated dissolution of dexamethasone and budesonide (Wong D, et al., 1997). The thermal sensitivity of thermoresponsive gels like poly-acrylic and poly (n-isopropyl-acrylamide) hydrogel were improved by adding guar gum (Li X et al., 2008). Poly(acrylamide)-graft-guar gum was synthesized by microwave initiated free radical grafting method as matrix for controlled release of 5-amino salicylic acid. Results proved that higher the percentage grafting, lower is the rate of drug release. Rate of release of the enclosed drug is low in acidic environment and is higher in neutral and alkaline environment, thus enhancing the possibility of further use of grafted guar gum matrix as a potential candidate for lower GIT targeted drug delivery (Sen G et al., 2010). Xanthan gum and guar gum were used to prepare rapidly disintegrating core tablets of 5-fluorouracil. Study reported that xanthan gum:guar gum mixture (10:20) coated tablets were able to deliver the drug to the colon (Sinha V et al., 2004). Another study showed that matrix tablets containing 50%, w/w guar gum were suitable for targeting of sennosides for local action in the colon (Momin M, et al., 2004). pH-sensitive colon targeted tablets of indomethacin were prepared by using film coating of guar gum and Eudragit FS30D. Pharmacokinetic study in beagle dogs shows delayed absorption of about 5 h and limited absorption fraction as a result of guar gum and Eudragit FS coating (Ji CM et al., 2007). Celecoxib loaded polysaccharide films of guar gum and chitosan were designed for treatment of colorectal cancer treatment. In vivo study suggested maximum

therapeutic efficiency may achieve by proposed adhesive, biodegradable polysaccharide composites (Haupt S et al., 2006). Chitosan and guar gum-gt-acrylamide (CH-GG-g-AAm) semi interpenetrating microspheres (semi IPNMs) were prepared using glutaraldehyde as a crosslinker. 5-fluorouracil (5-FU), an anticancer drug was successfully loaded in these semi IPNMs. In vitro release studies indicated the release of 5-FU more than 12 hours (Sekhar EC et al., 2011). For the treatment of irritable bowel syndrome (IBS), matrix tablet of ondasetron were prepared by guar gum and alginate. There was reduction of the visceral sensitivity and inhibition of motor activity in IBS (Tuğcu-Demiröz F et al., 2006). pH-enzyme sensitive colon-targeted theophylline microspheres were prepared with guar gum and Eudragit® for the prevention of episodic attack of asthma in early morning. The pH dependent solubility behaviour of Eudragit and gelling properties of guar gum was found to be responsible for delaying the release (Soni ML et al., 2011).

#### **Antihypertensive drug delivery systems**

Diltiazem hydrochloride and nifedipine loaded pH-sensitive microgels of poly-acrylamide-grafted guar gum (pAAm-g-GG) were prepared. Their release studies were performed in both the simulated gastric and intestinal pH conditions. Results showed a relatively quicker release in pH 7.4 buffers than observed in 0.1 N HCl (Soppimath KS et al., 2001). Matrix tablets of diltiazem hydrochloride, using various viscosity grades of guar gum were prepared. In vivo pharmacokinetic studies in healthy volunteers depicted that high viscosity tablets provided a slow and prolonged drug release when compared to D-SR tablets (Al-Saidan SM et al., 2005).

#### **Transdermal drug delivery systems**

It is an alternative route for administering medication via skin barrier by loading high dose of drug inside of a patch, which is applied on the skin for an extended period of time. The drug delivers into the blood by diffusion mechanism for a long period of time, maintaining the constant concentration of drug in the blood flow. Carboxymethyl guar gum was evaluated for its suitability of delivery of terbutaline sulfate in transdermal drug delivery systems. The results showed that the diffusion of terbutaline sulfate was relatively slower at pH 5 than at pH 10. That may be due to ionized/unionized state of drug (Murthy SN et al., 2004). Various types of acryloyl guar gum hydrogels were synthesized by the reaction of guar gum with acrylic acid, methacrylic acid, 2-hydroxyethyl methacrylate and 2-hydroxypropyl methacrylate. These hydrogels were used as transdermal drug delivery devices for l-tyrosine and 3,4-dihydroxy phenylalanine (l-DOPA) as the model pro-drugs. Release

studies showed that the release behaviour of these hydrogels was slow at pH 7.4. The results indicated that acryloyl guar gum hydrogels could be used as pro-drug delivery carriers for transdermal applications (Thakur S et al., 2009).

#### Protein drug delivery

Protein pharmaceuticals are mostly administered by injections rather than orally as they are unstable in nature. Peptides and protein drugs are readily degraded by the acidic environment of the stomach. So they should be protected from the harsh environment in the stomach. pH sensitive hydrogels have been fabricated by various synthetic or natural polymers for oral delivery of peptide or protein drugs. Cross-linked glutaraldehyde-alginate-guar gum pH sensitive hydrogel was prepared for the controlled delivery of protein drugs. The result showed that the presence of guar gum and glutaraldehyde cross-linking increases entrapment efficiency and prevents the rapid dissolution of alginate in higher pH of the intestine, which ensures a controlled release of the entrapped drug (George M et al., 2007).

#### Guar gum as nanoparticle carriers

A tamoxifen citrate, TMX loaded guar gum nanoparticles, GGNPs, crosslinked with glutaraldehyde were prepared for treatment of breast cancer. Cytotoxicity on Jurkat (human T-cell leukemia) cell lines as determined by cell growth inhibition after 48 hrs of incubation indicated that these nanoparticles were as efficient as the free drug. They exhibited sustained release of the drug and delayed apoptosis over a long period of time making it suitable for cancer treatment (Sarmah JK et al., 2012). Biologically synthesized silver nanoparticles (AgNP) were impregnated in biopolymer guar gum alkylamine (GGAA) for extended evaluations in punch wound models in rodents. Silver nanoparticles exerted positive and faster healing effects because of their antimicrobial properties (Ghosh AR et al., 2013). A lipase functionalized guar gum nanoparticles were prepared. The release kinetics depicted that the release was faster till 24 h and thereafter the release was very slow. This result suggests that guar gum based nanosized materials could be potentially used as drug delivery carrier applications (Soumya RS et al., 2010). Ag85A-loaded guar gum nanoparticles were prepared for oral vaccination against tuberculosis. The acid protection assay, Peyer's patch uptake study and in-vitro antigen study confirmed that the developed formulations can protect the antigen from harsh gastric environment and can safely deliver the antigen to the intestinal region. In vivo studies data indicated that the developed nanocarriers can induce a

strong mucosal as well as systemic immune response (Kaur M et al., 2015).

#### Conclusion

Pharmaceutical formulation developers always keep on trying to find ways of achieving better therapeutic efficacy of drugs by modifying the formulation technique, polymeric systems, etc. The formulators try to overcome the drawbacks associated with conventional dosage forms by utilizing tailor-made polymers synthesized specifically to solve the problems. The polymer of natural origin such as guar gum could be one such ideal candidate. However, a lot more scientific studies need to establish its relevance in developing various drug delivery systems. Guar gum and its derivatives are stable, safe and biodegradable. Due to these favourable properties, they are widely considered as potential target-specific drug delivery carriers. They as versatile excipients for a novel drug delivery system are an interesting challenge for future researches and have a wide potential in several pharmaceutical technologies.

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