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MINI REVIEW

Physiochemical and Pharmaceutical Properties of Guar Gum Derivatives

DURE NAJAF IQBAL and ERUM AKBAR HUSSAIN*
Department of Chemistry, Lahore College for Women University, Jail Road, Lahore, Pakistan
Tel: (92)(42)9203801-9/245; E-mail: dure_najaf80@yahoo.com; erum.hussain@gmail.com

Despite the vast importance of green chemistry synthesis and characterization of environmental friendly modified natural polymers is the need of time. These natural polysaccharides eliminate the danger to health and environment. Guar gum is one of the important naturally occurring polymer which has wide applications due to its rheological modifying properties in medicinal, pharmaceutical, food, textile and scores of other industrial and commercial sectors. There has been wide study on physiochemical and pharmaceutical properties of guar gum. But study on modified guar gum and its derivatives is quite lacking. The unmodified guar gum has certain drawbacks like lack of clarity and free flowing properties, fall in viscosity and turbidity on prolonged stay *etc*. These draw backs can be overcome by modifying and derivatization of guar gum and can be used in multidiscipline fields. In this review article the authors have summarized different physiochemical and pharmaceutical properties of guar gum and its derivatives.

Key Words: Guar gum, Green chemistry, Physiochemical, Pharmaceutical properties.

INTRODUCTION

Guar gum is a natural water soluble nonionic polysaccharide, isolated from the seeds of cyamopsis tetragonolobus (Linn, family leguminous). This plant is cultivated for centuries in India and Pakistan .Extraction technology of guar gum was commercialized. In USA in 1953. Guar gum belongs to the galactomannan family and its structure is shown in Fig. 1.

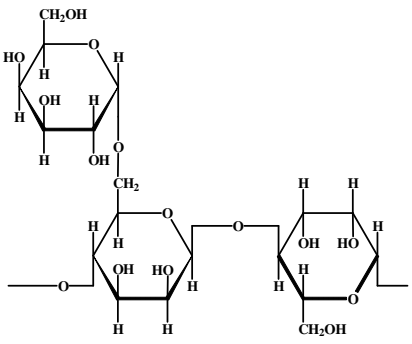

Fig. 1. Structure of guar gum

Guar gum has the ability to produce highly viscous, pseudoplastic aqueous solutions even at low concentrations due to high molecular weight (up to 2 MDa) and due to the presence of extended repeating unit formed by hydrogen bonding. This feature allows guar gum to be soluble and gelling even in cold in water. Chemically guar gum has a linear chain of (1 → 4)-linked β-D-mannopyranosyl units with (1 → 6)-linked α-D-galactopyranosyl residues as side chains with mannose: galactose ratio is approximately 2:1.

Guar gum and pharmaceutical application: Modified guar gum is widely used in pharmaceutical application due to its viscosity increasing properties. The therapeutic effect of guar gum is due to its ability to swell rapidly in aqueous media to form viscous dispersions or gels. When inhaled, guar gum gets adsorbed in the stomach and halts or alters absorption of glucose, cholesterol and possibly drugs.

Guar gum and its derivatives are used as binders and disintegrators in tablets to add cohesiveness to drug powder. Today guar gum is also used as a controlled-release agent for drugs due to its high hydration rate (swelling in aqueous media). It also used as thickener and stabilizer in pharmaceutical formulations. When mixed with different ingredients in formulation of tablets it forms a protective layer and consequently, drug comes out from the guar gum tablet in a sustained manner, achieving the desired kinetics effect and masks its unpleasant taste and odour of drug and improves its stability and drug releasing properties.

The role of guar gum and its derivatives to control blood sugar is well known in diabetes which is a chronic disease and occurs when the pancreas do not produce enough insulin or when the body cannot effectively use the insulin it produces. This leads to an increased concentration of glucose in the blood (hyperglycemia). The World Health Organization (WHO) estimates that more than 180 million people worldwide have diabetes. This number is likely to more than double by 2030. Dietary fiber decreases postprandial plasma glucose, insulin and triglyceride concentrations and has a clinically relevant hypocholesterolaemic effect.

Guar gum is also helpful in weight reduction and cancer therapy especially in colorectal cancer which is the most common form of cancer due to intestinal disorder.

A brief overview of different physiochemical and pharmaceutical properties of guar gum and its derivatives is given in the proceeding sections. Takahashi *et al.*[1] hypothesized that intake of hydrolyzed guar gum reduces the postprandial blood glucose absorption in small intestine of rats. By infusion of partially hydrolyzed guar gum into the duodenum of rats This decreases the rate of glucose diffusion in the lumen, as a result decrease in postprandial blood glucose takes place.

Tiwari *et al.*[2] has prepared photopolymerized guar gum-methacrylate derivative having molecular weight ranges from 74-210 Da with different degree of methacrylation. These hydrogels exhibit excellent endothelial cell proliferation capacity just like that of matrigel control. The human endothelial cell line EA.hy926 was photo-encapsulated in the GG-MA hydrogels. Cells remained viable at low macromonomer concentrations, but cell viability decreased sequentially as the macromonomer concentration increased.

Kuo *et al.*[3] evaluated the role of partially hydrolyzed guar gum for prevention of $FeCl_3$-induced arterial thrombosis and hyperlipidemia in the high fat-diet fed hamsters. Based on their results, they concluded that PHGG supplement can increase antioxidant protein expression and thus decrease oxidative stress induced arterial injury.

Zhu *et al.*[4] prepared sulfonated degraded guar gum by reaction of guar gum with chlorosulfonic acid under different conditions. Structure of this modified guar was confirmed by infrared spectrometry. They concluded that about 2500 mg/L concentration of sulfated guar can reduce about 60-66 % cholesterol, about 76-89 % LDL and almost 100 % of fibrinogen.

Alam *et al*.[5] observed the role of partially hydrolyzed guar gum for the treatment of cholera in adults. It undergoes fermentation when added in the colon liberating fatty acids when added in oral rehydration solution and reduces diarrhea by giving different doses of oral rehydration solution and modified gum to 195 male patients they concluded that partially hydrolyzed guar gum reduces the severity of diarrhea in these patients.

Belo *et al*.[6] evaluated the effect of partially hydrolyzed guar gum for treatment of functional constipation among different hospitalized patient. They found it beneficial for reduction of functional constipation.

Foulks[7] studied the role of HP-guar as gelling agent in polyethylene glycol (PEG)400/propylene glycol9(PG) eye drops used for the treatment of dry eye diseases. A literature review prior to 2007 July was conducted and founded efficacy of HP-guar as gelling agents in PEG/PG eye drops.

Nakamura *et al*.[8] explored the role of dietary fiber especially partially hydrolyzed guar gum on transitory diarrhea caused by ingestion of malitol and lacitol (sugar substitute). Partially hydrolyzed guar gum (PHGG) effect was evaluated by ingestion of different dose of malitol to volunteers female until they experienced diarrhea. Then observation confirmed suppressive effect on diarrhea of partially hydrolyzed guar.

Chaurasia *et al.*[9] evaluated the effect of glutaraldehyde crooslinked guar gum containing methotrexate for treatment of colorectal cancer (colon cancer) colorectal cancer is the third most serious type of cancer having 665,000 deaths per year all around the world. They prepared guar gum microsphere crosslinked by emulsification with glutaraldehyde and then characterized for local release of drug in the colon which is necessary for the treatment of colorectal cancer. The research shows that this crosslinked guar has high entrapment efficiency along with methotrexate (MTX) investigation of *in vitro* drug release was tested by US pharmacopeia paddle type (type-2) dissolution rate test apparatus, which shows different drug release result by changing amount of guar gum and glutaraldehyde.

Stewart *et al*.[10] observed fruitful physiological effects of partially hydrolyzed guar gum (PHGG) to human health in this research they investigated the variation in intestinal fermentability by changing molecular weight of modified guar gum. For trial guar gum of four different molecular weights (15, 20, 400 and 1,100 kDa)

was fermented using a batch *in vitro* fermentation system. The result shows that the molecular weight of guar gum was positively influenced the acetate production and negatively influenced the propionate production. They conclude that 400 kDa guar gum is suitable for intestinal fermentability.

Sakata *et al.*[11] investigated that how much amount of partially hydrolyzed guar gum (PHGG) ingestion can enhances bowel movement and can stop risk of colorectal cancer. The result shows that intake of PHGG can increases the fecal moisture and texture. The result shows that benefit of bowel movements provided by the PHGG intake has variation among different patients.

Gamal-Eldeen *et al.*[12] prepared the guar gum C-glycosylated derivative (GG) and its sulphated derivative (SGG) and observed their cancer chemopreventive and antiinflammatory properties. They reported that modified guar gum has potential to prevent cancer and must be taken as supplement in foods. Results conclude that this derivative of guar gum has ability to inhibited the carcinogen activator enzyme, cytochrome P450 1A (CYP1A) and also promote the carcinogen detoxification enzymes glutathione-S-transferases (GSTs).

De Cassia Freitas *et al.*[13] reported the effect of partially hydrolyzed guar gum towards intestinal iron absorption in rats with iron deficiency. Twenty four male wistar rats having iron deficiency anemia was divided in three groups and fed with partially hydrolyzed guar (100 Kg/day) diet, cellulose (100 kg/day) diet and without dietary fiber diet for each group, respectively. Maximum intestinal absorption of iron, regeneration of hemoglobin and hepatic levels of iron observed in first group fed on PHGG containing diet.

Das *et al.*[14] examined the effect of glutaraldehyde crosslinked guar gum for delivery of colon specific drug system. The ability of these hydrogel discs for drug loading capacity, buffer intake ability and drug release efficiency were investigated in different medium and pHs. They concluded that cross linking decreases the swelling (buffer intake) of guar gum. Per cent drug release capacity increased with increasing glutaraldehyde concentration.

Giannini *et al.*[15] investigated the role of dietary fibers especially partially hydrolyzed guar gum (PHGG) for the treatment of irritable bowl syndrome. Partially hydrolyzed guar gum found useful in constipation and diarrhea predominant forms of this syndrome. It reduces abdominal pain and improve patient's health life by increasing short chain fatty acids, in colon.

Parisi *et al.*[16] also observed useful effects of partially hydrolyzed guar gum for treatment of irritable bowl syndrome in an open clinical trial. The different dose of PHGG was given to different patients and their gastrointestinal symptoms (GSRS), physiochemical symptoms (HADS) and quality of life (SF-36) was observed in 6 months. Results shows beneficent effect of this modified guar gum on patient's health.

Suzuki *et al.*[17] concluded that guar gum hydrolysate (GGH) increases glucose intolerance and lower hypertriglyceridemia in rats fed with high-fructose diets. Possible mediators of these beneficial effects of GGH are due to the production of SCFAs (short chain fatty acids) by microbial fermentation of GGH in the large intestine.

Toti *et al.*[18] prepared copolymer of guar gum-polyacrylamide and investigated its grafting efficiency by Fourier transform infrared (FTIR) spectroscopy and scanning calorimetry. Tablets were prepared by incorporating an antihypertensive drug *viz.*, diltiazem hydrochloride. Effect of drug loading on release kinetics was evaluated. Nature of drug transport through the polymer matrices was studied by comparing with Higuchi, Hixson-Crowell and Kopcha equations. Results show that hydrolyzed pAAm-g-GG matrices are pH sensitive and can be used for intestinal drug delivery.

Narasimha *et al.*[19] investigated the role of carboxymethyl guar gum for drug delivery systems. For this purpose terbutaline sulfate (TS) was taken as model drug. The drug loading capacity of carboxymethyl guar gum films was observed at different pH range.

Soppirnath *et al.*[20] studied drug release ability of polyacrylamide-guar gum copolymer, crosslinked with glutaraldehyde. These guar gum hydrogel microspheres were incorporated with two antihypertensive drugs, verapamil hydrochloride (water-soluble) and nifedipine (water-insoluble) to investigate their controlled drug release capacity. *In vitro* study shows dependence of drug release on the extent of cross-linking of guar copolymer, concentration of drug, type of drug molecule and method of drug loading.

Soppimath *et al.*[21] experimented on modified guar gum by grafting with poly-acrylamide. This grafting converted amide group to carboxylic group. Degree of copolymerization was confirmed by FTIR. Drug loading capacity of theses modified guar microspheres were studied at different pH conditions. Diltiazem hydrochloride and nifedipine (both antihypertensive drugs) are used as model drugs and their release studies were observed in both the simulated gastric and intestinal pH conditions. The results show quick release in pH 7.4 buffer than observed in 0.1 N HCl.

Giaccari *et al.*[22] concluded that partially hydrolyzed guar gum is useful dietary supplement for treatment of irritable bowl syndrome due to its water solubility and gelling capacity in a clinical trial of 134 patients of both sexes suffering from this disease .They observed that use of PHGG is beneficial in this disease.

Watanabe *et al.*[23] investigated the effect of phosphorylated guar gum hydrolysate (P-GGH) on intestinal calcium absorption of overiectomized (OVX) rats. Rats were fed on P-GGH (50 g/Kg of diet) for 6 weeks. Results shows that in the condition of estrogen deficiency P-GGH may be useful for prevention of the reduction of intestinal calcium absorption and bone.

Kovacs *et al.*[24] reported the effect of modified guar on appetite and body weight loss. For this purpose 28 fatty male (age 19-56) were given semisolid meal along with modified guar gum in different amounts for a specified time period, as a result significant decrease in body weight taken place.

Ishihara *et al.*[25] investigated the effect of partially hydrolyzed guar gum (PHGG) for treatment of the colonization of *Salmonella enteritidis* (SE) in young and laying hens. They concluded that ingestion of different rent dose of PHGG decreases the *Salmonella enteritidis* (SE) due to improvement in the balance of intestinal micro-flora. Feed supplemented with 0.025 % PHGG was found the most effective.

Gliko-Kabir *et al.*[26] prepared a crosslinked low swelling guar gum (GG) hydrogel by reacting it with trisodium trimetaphosphate (STMP) and its function as a possible colon-specific drug carriers was analyzed in the rats. They concluded that crosslinked guar (biodegraded enzymatically) is an effective vehicle for colon specific drug delivery systems.

Alam *et al.*[27] evaluated the effect of partially hydrolyzed guar gum (Benefiber) on the rate of normal absorption of glucose, amino acid (arginine) and fat and their side effects was also investigated. Ten healthy male volunteers in a double blind trial were given to two different dietary supplements (with fibers ,without fibers) for a period of 2 weeks. The results of the study demonstrated that PHGG did not interfere with the normal absorption of glucose, amino acid and fat and shows no side effects so its use is safe for health.

Heini *et al.*[28] studied the effects of hydrolyzed guar gum on fasting and post-prandial hormone levels, respiratory quotient (RQ) and postprandial satiety during a controlled weight-loss program and found it useful for weight reduction.

Gatenby *et al.*[29] investigated the blood glucose, plasma insulin, C-peptide and gastric inhibitory polypeptide (GIP) of 14 patients of non-insulin dependent diabetes (NIDDM) after and before intake of modified partial depolymerized guar meal. Results indicated the reduction in the rise in blood glucose and plasma insulin with no effect on postprandial plasma C-peptide levels were observed.

Takahashi *et al.*[30] observed the effect of partially hydrolyzed guar gum (PHGG) on iron absorption in rats, in an iron balance test for 3 days administration of PHGG or GG caused an increase in iron absorption. The results confirmed that PHGG or its metabolites increase the bioavailability of dietary iron deficiency.

Takahashi *et al.*[30] confirmed the role of partially hydrolyzed guar gum (PHGG) for prevention of constipation in a trial on 15 constipated women for 3 weeks. Mostly reason for constipation is lack of dietary fibers in our diet. In the experiment female were taken an average diet of 9.7+/-0.1 g/day than weight, texture, moisture and bacterial flora of feces were observed. Results confirmed beneficial effect of PHGG for treatment of constipation.

Biesenbach *et al.*[31] used combination of pectin and guar gum for treatment of hyperlipidemia. They reported that the total-cholesterol levels and triglyceride concentrations in blood serum is lowered but HDL-cholesterol levels remained approximately the same in 15 female patients (52-70 yrs) having type-2 diabetes with hypercholesterolemia (total-chol > 240 mg/dl and LDL-chol > 130 mg/dl). So it is confirmed that PHGG is considered as safe and good to use as a food supplement products for lowering of lipids in patients suffering from hyperlipidemia.

Lampe *et al.*[32] observed effect of combination of enzymatically modified guar gum, maltodextrin and soy polysaccharides for 18 days trial to 11 healthy men. Improvement in gastrointestinal function was observed as a result of this treatment.

This review article is an effort to compile the research on modified guar gum which is water soluble, a non-digestible food ingredient that has potential to use in many pharmaceutical applications without any significant side effects.

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