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REVIEW

Potential of Hydrophilic Polymer Guargum as Pharmaceutical Excipient

VINITA V. KALE*, K. SREENEERANJ and JASMINE G. AWARI
Nagpur College of Pharmacy, Wanadongri, Hingna Road, Nagpur, India

Apart from active ingredients excipient(s) are an indispensable part of any formulation. One can broadly categorize the excipients into two classes—the major excipients and the minor excipients. The major excipients play a significant role in the development of formulation. The major excipients used vary according to different dosage forms. There are very few excipients that can be successfully used in more than one dosage form. In this review, the potential of guargum as major excipient in a variety of dosage forms has been discussed.

Guargum seeds have been well known in India since ancient times. The word guar is derived from the Sanskrit word "gua-ahar", which suggests it as food for cattle and has been used as such. It was considered to be the poor man's crop. But, during the last thirty-five years guar has gradually assumed greater importance as a cash crop due to the development of guargum as an important hydrophilic polymer[1]. The guargum is the powdered endosperm of seeds of *Cyamopsis tetragonolobus* (family: Leguminosae), an annual plant[2]. The contents of guargum are divided into water-soluble and water-insoluble parts[3]. The water soluble fraction consists of about 85% of the gum, which is known as 'guaran', a high molecular weight hydrocollide polysaccharide also called 'galactomannan'. The galactomannan is a three-dimensional polymeric molecule that contains the main chain of 1,4-linked-D-mannopyranosyl units to form a linear chain with single 1,6-linked-D-galactopyrynosyl residues attached to alternate mannose moieties[4]. This molecular structure gives properties that are intermediate between those typically associated with branched and linear hydrocolloids. The gum hydrates in cold water and is stable in acidic formulations. The galactose and mannose units contain hydroxyl groups, which can be subjected to modifications. Thus, derivatives of guar like guar acetate, guar benzoate and carboxy methyl guar[5–7] can be synthesized by alkylation with alkyl chlorides.

Guargum as pharmaceutical excipient

Drug substances are rarely administered as such. They are generally administered as a part of formulation. Thus, they are combined with one or more agent(s) (non-medical) that serve varied and specialized pharmaceutical func-

tions. With the use of these non-medicaments, called pharmaceutical excipients, different types of dosage forms can be designed. The pharmaceutical excipients solubilise, suspend, thicken, emulsify, stabilize, preserve, colour, flavour and fashion medicinal agents into efficacious and appealing dosage forms.

Several natural polymers are often preferred as excipients to synthetic polymers due to their non-toxicity, low cost and easy availability. The only disadvantage it has is that they usually contain the microorganisms that deteriorate the preparations. However, the Colony Forming Units (CFU) per gram of material were found to be zero in case of guargum[8] and also with carboxymethylated guargum[9]. The stability of the guargum was found to be adequate and Ahmed *et al.*[10] noticed reduction in the total count of cultures of *Salmonella typhosa, Escherichia coli, Staphylococcus aureus and Streptococcus faecalis*. Sakr[11] found that dry heat is the best way of disinfecting the swelling agents without decreasing the viscosity of their aqueous solutions.

Tablets and Binding Agents: Binders are solid materials used in the manufacture of solid dosage forms because of their adhesive and cohesive properties. The binders cause size enlargement and provide cohesiveness to powders thereby giving necessary binding strength to the granules and the tablets[12].

Tablet binders are generally hydrophilic substances such as sugars or polymers of natural origin or synthetic. The binders used in tablets are of sugar category like sucrose, glucose or sorbitol or of natural origin category like acacia, alginic acid, gelatin, starch, pregelatinised starch or semi-crystalline cellulose or of synthetic and semi-synthetic type like sodium carboxymethyl cellulose, methyl cellulose, hydroxypropyl methyl cellulose, ethyl cellulose, polyethylene glycol or povidone.

Guargum has been tested as a binder in tablet formulations. To obtain acceptable tablets it is necessary that proper concentration of binder should be incorporated. It was established that tablets made with 10% guargum had good uniformity and mechanical strength[13]. Also, the method of incorporating binders is equally important. The binders can be added either dry along with the diluents and then activated by addition of water or other solvents or added in solution to the bulking agent. The dissolution of the paracetamol tablets was affected by both the granulation and the mixing method[14].

It was observed that dry granulation gave better results with guargum. Also, tablets prepared with conventional slow mixing method had a higher solution rate than those prepared by high speed solid-solid mixing. However, the presence of small percentage of water in the dried granules was reported to be essential for the cohesiveness of the tablets[15].

In case of granule formulation diluents like calcium phosphate and lactose were found to interfere with cohesive force of guargum and granules dissolution. Moreover, it was established that calcium phosphate granules were more friable and more microporous than lactose granules. When the granules were compressed into the tablets, lactose tablets were less hard, more friable and more soluble. The disintegration and dissolution of calcium phosphate tablets was slow[16]. The

dissolution effectiveness of guargum tablets was found to be better for very slightly soluble drugs like ephedrine hydrochloride[17].

Colloids or thickeners or suspending agents: Colloids or suspensions are the preparations containing at least two components in any state of matter. The examples of colloidal agents used in preparations are aerosol liquid-gas or solid-gas; foams, gas-liquid; suspensions, solid-liquid; gels, solid; at high temperature, liquid; opals/glass, solid-solid; porous solids, solid-liquid-vapour. In this one component (usually insoluble) is dispersed into another. Thus, around insoluble component an interfacial tension always exists. Colloids and suspending agents, such as gelatin, natural gums and cellulose derivatives increase the strength of the hydrating layer formed around the suspended particle either by molecular interaction or by forming hydrogen bond.

Rheological behaviour of sodium carboxymethyl guargum (Na-CMG) was observed to be less pseudoplastic and to tend towards Newtonian flow. It was established that Na-CMG solution is more controllable as thickening agent and has viscosity building and emulsifying properties[8]. Na-CMG as thickening agent in the toothpaste was tested and found to produce optimal consistency[18].

Guargum was used in cariostatic dental preparations. William[19] successfully prepared aerosol of NaF microcapsule for dental spray. Guargum was used as suspending agent in the formulation of tetracycline HCl as reconstituting aqueous suspension[20]. A suspension of nitrofurantoin of guargum was tested for urine excretion of the drug. It was noted that although the gum due to increase in the viscosity slowed the absorption, its bioavailability was not affected and the required delay in excretion could be obtained[21].

Gel and gel-forming substances: In gels and jelly preparations the dispersed solid is dispersed in very large quantity of water. Several water-soluble polymers used as gel-forming agents are proteins, gellum gum, glycirhizin, guargum, hyaluronic acid and pectin form gels and are used in semisolid dosage forms including dental, dermatological, nasal, ophthalmic and rectal gels and jellies.

A jelly prepared by using guargum and pectin was used as a vehicle for oral application of pharmaceutical microcapsule for children and animals by Magnier[22]. Topical pharmaceutical bases were formulated by combining guargum with other polymers to apply to oral mucosa[23]. A tablet of guargum along with other antacid preparations was designed. The guargum in water formed a thixotropic gel, which remained at gastric pH, that adhered to gatric mucous membrane releasing antacid agent[24].

Baichwal *et al.*[25] prepared hydrophilic suppository base using homogeneous dispersion of guargum and drug in glycerol and hot agar solution. This formulation showed desired release over a period of time that followed matrix diffusion. Also, the guargum suppository had sufficient hardness and no signs of melting or change in shape after storing them at room temperature and 37°C for three months was observed.

Sustained release or controlled release oral formulations and hydrogels: In recent years, the use of control release technology in the formulation of pharmaceutical products has been increased because of several reasons. Administration of drugs as single dose, that releases the drug over extended period

of time, revealed enhanced clinical efficacy and better patient compliance. Various sustained release oral formulations, especially matrix forming tablets and capsules, were observed to prolong the dose interval of drug and thus found common place in the pharmaceutical industry.

Hydrogels exhibit possible applications in controlled and novel drug delivery systems. A hydrogel is defined as a polymeric material which has the ability to swell in water, without dissolving, and to retain water within the structure[26]. It generally has two component systems—one being hydrophilic and insoluble, with three-dimensional network, and the other being water.

Conventional techniques followed for preparing sustained release formulations include coating the drug particles with substances that sustain its release or placing the drug in osmotic pump. Many of these techniques proved either expensive or very complicated to prepare. Thus, as an alternative, the use of swellable hydrogels as matrix materials had been investigated by several workers (Table-1).

TABLE-1
HYDROGELS USED FOR SUSTAINED RELEASE PREPARATIONS

Class	Polymers
Insoluble inert	Polyethylene
	Polyvinyl chloride
	Methylacrylate
	Methylacrylate copolymers
Insoluble, erodable	Carnauba wax
	Stearyl alcohol
	Stearic acid
	Polyethylene glycol
	Monostrearate
	Triglycerides
Hydrophilic	Methyl cellulose
	Hydroxyethyl collulose
	Hydroxypropyl methyl cellulose
	Sodiumcarboxymethyl cellulose
	Carboxy polyethylene galactomannose
	Sodium alginate

Several cellulose based formulations had been successfully formulated for sustained release of the drugs[27-29]. In the recent past, galactomannose hydrophilic polymers had received much attention as sustained release polymers. Ranga Rao *et al.*[30] had tested the potentiality of guargum as release-retarding material. Similarly, Bhalla *et al.*[31] suggested the use of guargum as sustaining material used alone or in combination with other reatarding polymers. Galactomann was found to be suitable for the formulation of hydrophilic matrix tablets[32-34].

The amount of hydrogel used was such that the therapeutic window of the drug in the blood could be maintained and the drug was released at a constant rate. It was shown that the drug release rate increased with decrease in the amount of guargum. On the contrary, release rate was decreased with decrease in the drug contents in the tablets[35]. Similarly, Henderson and Huber[36] observed that the extent of drug release and its rate in capsule formulation depended upon the concentration of the hydrophilic gum. Further, it was seen that the moisture content of granules prepared for sustained release tablets did not cause any change in the dissolution profile[37].

Sakr and Elsabbagh[17] studied the particle size distribution of the hydrocolloids that provide the desired sustained release profile. According to them, smaller particles disintegrate at a faster rate. Converse results, however, were reported by Kuherts[38] He suggested that the mean particle size of the gum should be 150 μ or less to obtain the desired sustain release profile. Altaf *et al.*[39] established the stability of guar based formulation under the stressed condiiton (40°C and 75% RH) for three months and found satisfactory. Guargum had a very high intrinsic viscosity but poor interaction coefficient. An attempt was made to improve its interaction coefficient by controlled hydrolysis using HCl acid by a few workers[40]. It was observed that interaction coefficient and dissolution profile of hydrolysed gum could be controlled.

Besides sustained release preparations some workers reported the potentiality of guargum in colon specific drug delivery, by performing scintigraphic studies on healthy human volunteers[41]. Guargum was modified to reduce its swelling properties by cross-linking with gluteraldehyde[42]. It was established that the cross-linked guargum resulted in biodegradable hydrogel, capable of retaining poorly water-soluble drugs, suitable for colon-specific drug delivery systems. A long lasting troche containing 3–6% guargum and 15.85% dry skim milk powder was found to be useful as a means of administration of medicament used in the treatment of oral cavity by sublingual or transdermal administration[43].

Conclusion

The above review suggests that guargum has wide applications as pharmaceutical excipients. There are only few substances that can be used in different dosage forms. Guargum is one of such agents that has the potential for use as pharmaceutical excipients in a variety of formulations.

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