Asian Journal of Biomaterial Research 2017; 3(6):1-10

Review Article

Application Of Fenugreek Seed Gum: In Novel Drug Delivery

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Received: 15 Nov 2017 Revised: 19 Nov 2017 Accepted: 24 Nov 2017

Abstract

Aim: To prepare review on application of fenugreek seed gum: in novel drug delivery **Method:** Various research paper were collected and compilation of study reported in these paper were presented in this review. **Results:** Fenugreek gum, have polysaccharide galactomannans chemical constituents. Polysaccharides play most important roles in pharmaceutical formulation fields as thickening, gelling, emulsifying, and suspending agents. The isolation of fenugreek gum are done with water/dilute alkali; so that the product yield comes different 13.6 to 38%, production of gum depends on the fenugreek seed variety and extraction methods. Fenugreek gum is widely grown; therefore its sustainable supply is well sure and cost economic crop. **Conclusion**: We express all the significant aspects of Fenugreek seed gum, contributing for its role in biopharmaceutical applications.

Key Words: Controlled release, gelling capacity, fenugreek gum, polysaccharides

Introduction

Trigonellafoenum-graecum(Family Leguminosae) is called methika in Ayurveda and used as medicine for the cure of wounds, abscesses, arthritis, diabetic, bronchitis and digestive disorders etc Fenugreek is assumed to be native to the Mediterranean region [Anonymous 1992, Shukla et al., 2011], T. foenum-graecum, is a 60 cm tall annual leguminous plant local to southern Europe and western Asia, and has a long history used as a gastronomic and medicinal herb since earliest times. The plant is cultivated in northern Africa, the Mediterranean, western Asia, northern India, and currently in Canada [Brummer et al., 2003]. Fenugreek has been reported other properties like anti-ulcer action, anti-bacterial, anti-helminthic, antioxidant activity, anti-fertility effects baldness and anti-nociceptive effects. India is the higher fenugreek producing country all over the world. [Farnsworth et al., 1966, Shukla et al., 2011]. The fenugreek pod is about 3–10 cm long and 1 cm wide and contains 10–20 seeds with each about 2–3 mm. The seed has a

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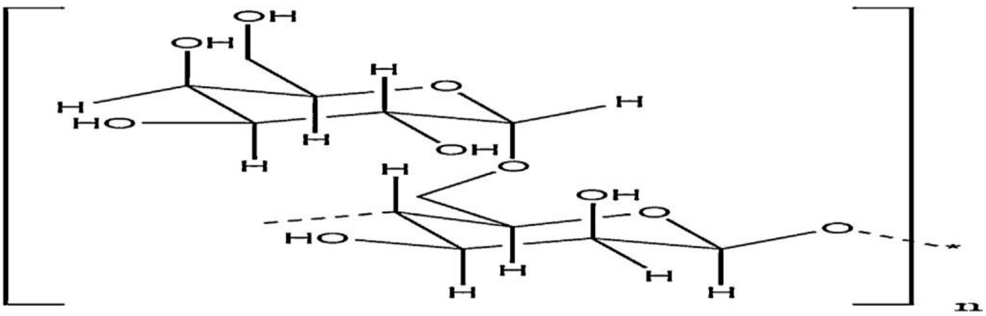
strong aroma and in bitter in taste. Fenugreek polysaccharide contains a few sugars other than mannose and galactose. Mannose (M), Galactose (G) in fenugreek gum. The fenugreek gum has the fenugreek, Lucerne (Medicago sativa) and clover (Trifolium pratense), have less common galactomannans, have 48% galactose. The molecular weight of fenugreek gum is 30,000 Da, corresponding to an average presence of 180–190 monosaccharides (mannose + galactose) units in a highest galactose (48%; M/G, 1.02:1) in its, and its molecule have linear mannan backbone, α 1→6 linked single galactose grafts with nearly all the mannose groups of the main chain part, as well molecule. On an average, the linear mannan backbone of fenugreek polysaccharide is built up of 90–95, β, 1→4 linked mannopyranosyl units and each backbone monomer carries and α 1→6 linked galactopyranosyl group (Fig. 1).



The seeds of fenugreek constituents are alkaloids, flavonoids, saponins, amino acids, tannins and some steroidal glycosides, proteins etc. Fenugreek gum is a product from a widely grown and therefore its sustainable supply is well sure. Besides, fenugreek seed also contains spicy oil, saponins and edible protein, thereby making it cost effective crop. Fenugreek gum is extracted from the endosperm or ground whole seed with water or dilute alkali, and the yield varies from 13.6 to 38%, depending on the variety/cultivar and extraction methods [Andrews et al., 1952]. Laboratory preparation involving pronase (a nonspecific protease isolated from Streptomyces griseus) treatments produces gum products of much higher purity with less than 0.6% protein contaminants [Brummer et al., 2003]. The molar ratio of galactose to mannose of fenugreek gum is approximately 1:1. A reported value of the molecular weight is 1.4 million, compared to 1.3 and 1.2 million for commercial guar and locust bean gum, respectively [Brummer et al., 2003]. The radius of gyration of fenugreek gum was 75 nm, which is in agreement with the range obtained by experiments and modeling for a gum with equal galactose and mannose contents and a molecular weight of 1.4 million [Brummer et al., 2001, Petkowicz et al., 1998]. Solution properties of fenugreek gum are typical of a random coil polymer. In rheological tests, fenugreek gum solutions exhibit pseudoplastic behavior at high shear rates. Mechanical spectra of locust bean, guar, and fenugreek gums with comparable molecular weights are similar in shape, but with slightly slighter moduli values for fenugreek gum. Fenugreek gum is a nongelling galactomannan and shows resistance against freeze-up–thaw treatments. In addition, little synergistic interaction was observed between fenugreek gum and other gums. In spite of numerous medicinal uses attributed to this plant, now it is leading source of the polysaccharide. Modern time Polymers are used to control the release of drugs from different dosage forms administered orally Natural polysaccharides are the choice of materials among the synthetic hydrophilic polymers because they are biodegradable, nontoxic and biocompatible [Singh et al., 2010]. Natural Fenugreek seed polysaccharide (FSP) is present in fenugreek gum; it is a hydrophilic

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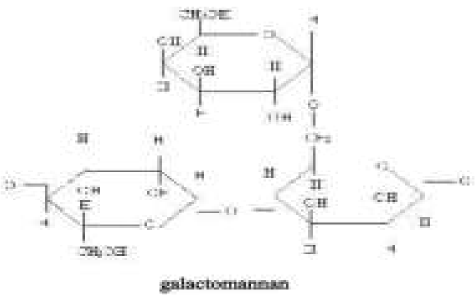
polymer and could be used as gelling, thickening, suspending and emulsifying agents. They have been using in various fields such as biomedical fields, tissue engineering as their different chemical structures and physical properties and using as drug vehicles for controlled release, to imaging techniques and associated diagnosis. As discussed by [Garti et al., 1996], There are four major herbal sources of galactomannans as locust bean (Ceratonia siliqua), guar (Cyamopsis tetragonoloba), Tara (Caesalpinia spinosa Kuntze), and fenugreek (Trigonella foenum-graecum) [Prajapati et al., 2013]. Fenugreek seed polysaccharide FSP is more capable than other hydro-colloids gums due to decreasing the interfacial free energy, its emulsions are self-possessed of tiny & uniform oil droplets (70% < 1μm). As a result, it is suggested to use FSP and GG blend for emulsion applications. FSP can provide emulsion stability and GG can further help in emulsion stability with greatly increasing the viscosity. In a general manner, polysaccharides play most important roles as thickening, gelling, and emulsifying, hydrating, and suspending agents, finding diverse applications in the above-mentioned areas [Rinaudo et al., 2008].

Factors That Make Prospective Polysaccharide In Drug Delivery According to whistler and BeMiller, investigated plant polysaccharides, or hydrocolloid is likely to be adopted for exploit like as

1. It is having good viscosity and gelling properties hence it may be used in large-scale
2. As regards to the cost factor, fenugreek is cheaper compared to other gum.
3. The supply of high quality of a product (gum), particularly when there is an increased world demand for it.
4. Its approval as a food, cosmetic, or drug additive by the suitable government agencies such as the U.S. Food and Drug Administration (FDA), Becomes a significant concern. In many cases, a physically modified, partially chemically derivatives gum provides better functionality compared to the natural gum from which it is derived.

ACTIVE CONSTITUENTS OF FENUGREEK SEED POLYSACCARIDES

Fenugreek seed contains saponins that are changed in the gastrointestinal tract into sapogenins. This plant including; Sarsapogenin, Yuccagenin, Smilagenin [Elnaz et al., 2010]. Fenugreek seeds contain 50% fiber (30-percent soluble fiber and 20-percent insoluble fiber) that can slow the rate of postprandial glucose absorption [Ethan et al., 2003]. Fenugreek seeds contains other phytoconstituents as oils, alkaloids, amino acids (lysine, arginine, tryptophan, threonine, valine, and methionine) mucilages galactomannan, vitamins A, C, D, B1 and, minerals calcium, iron and zinc [Elnaz et al., 2010].



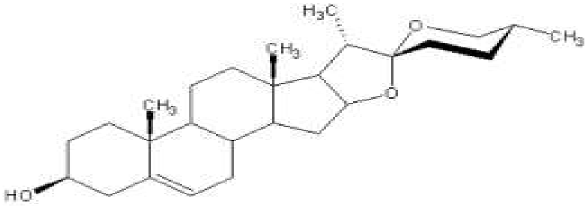


Fig. 1. Galactomannan Fig. 2. Diosgenin

MANUFACTURING OF FENUGREEK POLYSACCHARIDE GUM

For the isolation of fenugreek polysaccharide, the water extraction method generally adopted by the manufacturer. Due to it is more aqueous soluble.

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But wet-extraction methods are generally adopted from the general laboratory method of extraction of a water-soluble seed polysaccharide. The methods generally consist of course powdering of the whole seed, followed by petroleum ether and ethanol extractions of the powder to remove fatty and flavoring oils, pigments, saponins, bitter-tasting components, other low molecular weight substances. This is followed by hot- water extraction dissolves the soluble galactomannan polysaccharides, leaving behind insoluble celosics from the husk and most of the germ proteins. The insoluble part removes by filtration or centrifugation. From the clarifier, the galactomannan polysaccharide is precipitated by adding alcohol up to 60% concentration, which is the filtered and dried. Re-dissolving of crude polysaccharide in water followed second alcohol precipitation yielded purer gum product. Alcohol used in the process was recovered by fractional distillation and reused. Dry processing of fenugreek seed yields gum (25%) of much higher viscosity compared to the wet process (20%). This difference might be due to the fact that any hydrolytic breakdown of the polymer molecules taking place in the hot-water extraction process largely reduced in the dry process. Hence need to adopt dry processing for commercial manufacturing of fenugreek gum.

PHYSICAL PROPERTIES AND RHELOGY OF FENUGREEK GUM

Purified fenugreek gum is a nearly colourless or slightly cream-coloured powder, which can have characteristics, faint smell of fenugreek seed. It has a bland taste. Commercially available fenugreek galactomannan (gum) is easily dispersed in water at room temperature to develop high viscosity, in the range 500-1500 cps at 1.0% concentration, as measured by the Brookfield viscometer at 20 rpm. Typically composition of commercially marked, pure and extra pure fenugreek gum powder given in table [Mathur et al., 2006].

Table.2 Percentage Composition of Commercial Fenugreek Galctomannan Powder

Constituent	Pure %	Extra Pure %
Total carbohydrates	75	85
Proteins	15	5
Lipids	0.4	0.2
Soluble galactomannan	60	75
Ash	1.0	0.5
Water dispersibility	Good	Complete
Smell	Faint	Negligible

Surface Activity of FSP

Fenugreek gum was reported to have significant surface activity and be able to produce stable oil-in-water emulsions with reasonably small droplet sizes (2–3 µm) [Huang et al., 2001]. In addition, physical separation of protein residues from the crude gum did not decrease the surface activity. It is, therefore, the surface activity is a natural property of the polysaccharide. However, a protease-treated fenugreek gum sample containing less than 0.6% protein (calculated from nitrogen content) exhibited a reduced surface activity. These differing results may solely indicate that the protease treatment is more valuable in eliminating residual proteins. Protein components in fenugreek gum may be tightly associated with polysaccharide chains and able of dominating some surface activity-related purposeful properties.

FENUGREEK SEED POLYSACCHARIDE IN NOVEL DRUG DELIVERY

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Emulsifying Property of Fenugreek gum Polysaccharides

The fenugreek gum acting as emulsifiers is quite different. Highly purified and protein fee fenugreek polysaccharides are as good an emulsifiers. Therefore, it has been suggested that a nearly complete galactose-grafted mannan backbone in fenugreek gum allows the fenugreek galactomannan molecule to have a fully extended conformation in solution. Such polysaccharide molecules are deposited on an emulsified oil droplet in water, protecting it against coalescence and flocculation. This emulsifying property of fenugreek gum coupled with its strong moisture-hold capacity opens the interesting possibility of using fenugreek gum in cosmetic products [Garti et al., 1997].

Used as Suspending or Binding Agent

Indicated that the fenugreek seed mucilage has been used as a good suspending agent and was found to be superior compared to other gum like tragacanth, gum acacia, and bentonite in performance. The isolated mucilage from fenugreek (Trigonella foenum-graecum L.) seed has potential as a new suspending agent even as in low concentration. The present investigation is a primary platform to indicate the suitability of fenugreek seed mucilage as a suspending agent. The work can be further extended for evaluation of its suitability in other pharmaceutical applications considering the easy availability and cost-effectiveness of it. [Sabale et al., 2009, Amit et al., 2012]. Formulated and evaluate the paracetamol suspension with fenugreek. Concluded that it can be employed as a stabilizer of choice and high viscosity is desired especially in cosmetic, pharmaceutical and food industries [Senthil et al., 2011]. Like other mucilage containing substances, fenugreek seeds swell up and become slick when they are exposed to fluids [Petropoulos et al., 2002]. The ability of the husk to form mucilage, its binding properties in solid dosage forms were studied [Manoj et al., 2010]. Pharmaceutically fenugreek gum has been explored as a binder [Avachat et al., 2007], disintegrant [Kumar et al., 2009], solubility enhancer or as emulsifier [Sav et al., 2012, Sav et al., 2013].

Nanoemulsions were formulated in two steps. First, a less viscous, primary O/W emulsion was prepared using ultrasounds. In those emulsions, only isolate protein was used as an emulsifier agent, while the oily phase was olive oil. A stabilizer, fenugreek gum, was incorporated afterward in the primary formulations consequently in the secondary emulsions of increased viscosity. They showed increased viscoelastic properties and consistency leading to significantly increased stability compare to their coarse secondary emulsions produced by high shear mixing. Even the formulations with the lowest olive oil content investigated, 2.5% wt, presented an improved stability during a long-term storage of six months. Conclude that formulation for the macro- and nano/submicron emulsions may be used as suspending or stabilizer agent who increased stability and physical properties [Olga et al., 2016].

Controlled Release Formulation

Hydrophilic and gelling properties of these natural polymers play the chief role to control drug release for the extended period of time. Generally, hydrophilic polymer has always opted for the preparation of controlled release formulation of poor water soluble drug. Fenugreek gum (Trigonella Foenum-graceum), the leguminous family was used as extended release polymer in modified release matrices. The gelatinization and retrogradation behavior of cornstarch has been studied in the presence of fenugreek gum [Funami et al., 2008]. It was revealed from the study that addition of fenugreek gum inhibited the structural hardening of the composite system [Funami et al., 2008]. The octenyl succinate anhydride derivative of fenugreek gum (OSFG) was synthesized to initiate hydrophobic property and investigated for its drug release retarding property with reference to FG. The reaction was carried out under anhydrous conditions at different temperature (40–98 °C) using NaHCO3 as a gentle base catalyst, and the influences of three factors such as reagent/substrate concentration, reaction temperature and time on the degree of substitution of OSFG were studied. It was concluded that the developed formulations with OSFG have a release retarding property and can be used alone or in combination with other polymers for a controlled release [Sav et al., 2013].Sustain release formulation commonly preferred over conventional dosage form to attain constant therapeutic response for an extensive period of time. The major advantages of this formulation are reduced frequency of administration, maintained plasma drug level, devoid of dose dumping effect and reduced side effects [Gite et al., 2012].

Mucoadhesive Formulation

Suggested the fenugreek mucilage could be good carriers for controlled delivery of metformin HCL. Formulated calcium pectinate-fenugreek seed mucilage (FSM) mucoadhesive microshere beads containing metformin HCl was developed by ionic-gelation method. The swelling and mucoadhesivity of these beads were inclined by pH of the medium. The optimized beads showed batter mucoadhesive and significant hypoglycemic effect on alloxan-induced diabetic rats over a prolonged period after oral administration [Nayaka et al., 2013].

In Nasal Drug Delivery

A novel nasal drug delivery system of diazepam has been formulated with *Trigonella foenum-graecum*, used as natural mucoadhesive agent. Concluded that it could be feasible and economic polymer fit for the formulation of this type of delivery [Dutta et al., 2005].

Used As Disintegrating Agent

Studies reported that the extracted mucilage is a good pharmaceutical polymer, specifically a disintegrating agent [Kumar et al., 2009]. The fenugreek gum act as a good super disintegrating agent and it showed promising additive anti-inflammatory activity with diclofenac sodium M. has been investigated by [Uday et al., 2014].

In Tablet Formulation

The effect of lactose on the release of propranolol hydrochloride from matrices formulation with fenugreek mucilage was investigated. An increase in the concentration of the mucilage in matrices resulted in a decrease release rate of propranolol hydrochloride comparable to that observed with hypromellose matrices. The release rate of propranolol hydrochloride is successfully controlled with fenugreek mucilage .However, this is due to a reduction in tortuosity and increased pore size of channels caused by lactose through diffuses and therefore diffusion of water into the tablet [Ali et al., 2008]. Diclofenac sodium and propanolol took as a model drug and optimized the binding properties of husk using fenugreek husk dispersion and comparing the results against starch paste. They have reported that fenugreek husk dispersion was superior then starch paste for the formulation of tablet. It concluded that, could be a good granulating agent for tablet formulation in future [Avachat et al., 2007]. Investigated and found that fenugreek husk having good binding property [Nitalikar et al., 2003, Tavakoli et al., 2012]. Formulated and successfully evaluated the sildenafil Citrate fast dissolving tablet with using Fenugreek seed mucilage [Zafar Net al., 2014]. The floating tablets prepared with fenugreek gum as polymer showed satisfactory results with short floating lag time, long total floating time and controlled drug release up to 12 hrs Deepak [Khobragade et al., 2016]. Mucilage derived from the seeds of fenugreek, with matrix formulation of propranolol hydrochloride antihypertensive drug. Methocel K4M was used as a standard controlled release polymer for comparison [Ali N et al., 2008]. Gelling potentials of Fenugreek mucilage was evaluated [Gowthamrajan et al., 2002]. The husk from the seeds is isolated by reducing the size, and then suspending reduced seeds in chloroform for some time and then decanting. Successive extraction with chloroform removes the oily portion which is then air dried [Henry et al., 2002].

Novel alginate-fenugreek gum (FG) gel membrane coated hydroxypropyl methylcellulose (HPMC) based matrix tablets were developed for intragastric quetiapine fumarate (QF) delivery by combining floating and swelling mechanisms. The tablets were coated with Ca+2 ions and crosslinked with alginate-FG gel membrane by diffusion-controlled interfacial complexation technique. The biopolymeric-coated optimized matrices exhibited superior buoyancy, preferred swelling characteristics and slower drug release rate. Exposed the newly developed alginate-FG gel membrane coated HPMC matrices are suitable for intragastric delivery of QF over a prolonged period of time with better therapeutic benefits [Hriday et al., 2016].

In Nano Particles Formulation

The developed natural polymer based cefixime nanoparticles make easy to controlled drug release profile and better zone of inhibition with minimum concentration thereby improving the patient compliance [Shanmuganathan et al., 2016].

Conclusions

Excipients have traditionally been incorporated in drug formulations as inert substances whose role mainly relies on aiding the manufacturing process. However, in the last decades, they have been increasingly included in dosage forms to fulfill specialized function aimed at improving drug delivery. Fenugreek seed polysaccharide is used in biopharmaceutical applications with several distinct functions as controlled release excipient and tablet disintegrant. In most cases, the polysaccharide is associated with a second material, benefit from strong synergies, and fields of application are varied, comprising oral, buccal and controlled drug delivery, but also applications have been described. A significant amount of research remains too conducted to unveil the real potential the polysaccharide might possess. Considering the available works, it seems to be particularly interesting in the case of synergies established with other polysaccharides, namely xanthan gum and carrageenan etc.

Future perception and their applications

Various researchers suggested the fenugreek gum as a economic polysaccharide for the development of various types of pharmaceutical formulation like as emulsifiers, suspension, cosmetic, nanoparticles, tablet and various types of controlled release etc. It is easily available and can directly isolated from plant sources. So it is found in pure form. The fenugreek gum or polysaccharides have potential of ideal polysaccharide for drug delivery can be act as alternative of synthetic polymer in drug delivery in future. Although a detail investigation is required.

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