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Role of Citrus Concentrate in Extraction and Evaluation of Herbal Polymer

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Abstract

***Background**: The use of natural polymers as excipients in the pharmaceutical sector is expanding day by day. Low cost, safety issues, availability, and biodegradability are the main causes that make them differ from other sources. Natural sources have a wide range of varieties and characteristics. So, they can be used numerous times in pharmaceutical products as excipients to serve the desired purposes. **Aim**: To extract and evaluate the natural polymeric substances that can be used as excipients in pharmaceuticals from fenugreek seeds by using solvent extraction method. **Methods**: Trigonella foenum-graceum fenugreek mucilage is drive from the endosperm of the seeds it consists of galactose and mannose of it gives high viscosity in aqueous solution the fenugreek seeds used for thickening, stabilizing and emulsifying food agent. In this procedure we use grapefruit juice to treat with extract mucilage from fenugreek seeds which enhance its stability and bioavailability. Grapefruit juice increases the bioavailability of some orally administered drugs that are metabolized by CYP3A4 and normally undergo extensive presystemic extraction. **Results**: In addition, grapefruit juice it can decrease the oral absorption of a few drugs that rely on organic anion transporting polypeptide in the gastrointestinal tract for their uptake. The number of drugs shown to interact with grapefruit juice in vitro is far greater than the number of clinically relevant grapefruit juice drug interactions.*

Keywords: *Natural Polymer, use fenugreek seeds, solvent extraction process, mucilage treat with grapefruit juice.*

1. Introduction

Polymer is an essential part of any matrix drug delivery systems. Polymers are used for the various drug delivery systems, provide the thickness, consistency, and volume and also provide multifunctional stability, drug release, proper targeting, improved biological compatibility, and patient compliance. Study have been done for so many plants like the mucilage powder isolated from lady's finger (Abelmoschus esculents) stem that was effective in the clarification of sugarcane juice in the preparation of jiggery. [1] Trigonella *foenum-graceum* (Fenugreek) mucilage is derived from the endosperm of the seeds. It consists of galactose and mannose. It gives high viscosity in aqueous solution. The fenugreek gum is used for thickening, stabilizing and emulsifying food agents.

Fenugreek mucilage is less exploited in the food industry as compared to other gums such as guar and locust bean**.** [2]

In India, natural gums and mucilage are well known for their medicinal use. Certain plants contain natural polysaccharides which have been employed as food and pharmaceutical applications. Mucilage are physiological products, often found in different parts of plants. They are plant hydro colloids and have a variety of applications in the food industry. They have different uses like water retention and stabilization, stabilizers for ice-cream, meat products and instant pudding, dairy, confectionary and meat products, beverages, backed products, and sauces.[3] Polymers are widely used in the formulation of pharmaceutical and healthcare products. Applications include controlling drug release, providing site specific delivery of active pharmaceutical ingredients (APIs) & improving drug stability.

Polymers are commonly used in all major dosage forms including tablet, film, capsule, semi-solid, suspension, gel, and transdermal patch as well as in specialized delivery systems which are long-acting injections and biodegradable implants.

2. Materials And Methods

Source Of Natural Polymer (Fenugreek Seeds)

Trigonella Foenum-graceum, commonly known as Fenugreek, is an herbaceous plant of the leguminous family. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). Although it does not dissolve in water, mucilage forms a viscous tacky mass when exposed to fluids. Like other mucilage- containing substances, fenugreek seeds swell up 82 and become slick when they are exposed to fluids. The mucilage derived from the seeds of fenugreek, was investigated for use in matrix formulations containing propranolol hydrochloride. Methocel® K4M was used as a standard controlled release polymer for comparison purposes. A reduction in the release rate of propranolol hydrochloride was observed with increase in concentration of the mucilage in comparison to that observed with hypromellose matrices. [4] The rate of release of propranolol hydrochloride from fenugreek mucilage matrices was mainly controlled by the drug: mucilage ratio. Fenugreek mucilage at a concentration of about 66% w/w was found to be a better release retardant compared to hypromellose at equivalent content.

Fenugreek gum thicken ingested food to form a gel in stomach trapping fat, sugars and starch hydrolyzing, amylase enzymes to slow down sugar absorption. [5] Thus, it is good for obese and diabetic persons. The gel, which appears like 'fat' inside the body, signals the gallbladder to empty bile into the stomach. The gel then irreversibly traps lipid-emulsifying bile salts and prevents their re-absorption. Thus, emulsification and absorption of lipids including cholesterol results in lowering of blood lipids. This in turn reduces hypertension and chance of heart attack.

Extraction Of Polymer by Solvent Extraction Method

The solvent used for the extraction of medicinal plants is also known as the menstruum. The choice of solvent depends on the type of plant, part of the plant to be extracted, nature of the bioactive compounds, and the availability of solvent. In general, polar solvents such as water, methanol, acetone and ethanol are used in extraction of polar compounds, whereas non-polar solvents such as hexane and dichloromethane are used in extraction of non-polar compounds. [6, 7, 8]. During liquid–liquid extraction, the conventional way is to select two miscible solvents such as water–dichloromethane, water–ether, and water–hexane. In all the combinations, water is present because of its high polarity and miscibility with organic solvent. The compound to be extracted using liquid–liquid extraction should be soluble in organic solvent but not in water to ease separation.[9] Furthermore, solvent used in extraction is classified according to their polarity, from n-hexane which is the least polar to water the most polar. The following are 5 various solvents of extractions arranged according to the order of increasing polarity. [10] Extraction is the first step to separate the desired natural products from the raw materials. Extraction methods include solvent extraction, distillation method, pressing and sublimation according to the extraction principle. Solvent extraction is the most widely used method.

The extraction of natural products progresses through the following stages:
(1) the solvent penetrates into the solid matrix. [11]

(2) the solute dissolves in the solvents [12]
(3) the solute is diffused out of the solid matrix [13]
(4) the extracted solutes are collected [14]

Any factor enhancing the diffusivity and solubility in the above steps will facilitate the extraction. The properties of the extraction solvent, the particle size of the raw materials, the solvent-to-solid ration, the extraction temperature and the extraction duration will affect the extraction efficiency. [15]

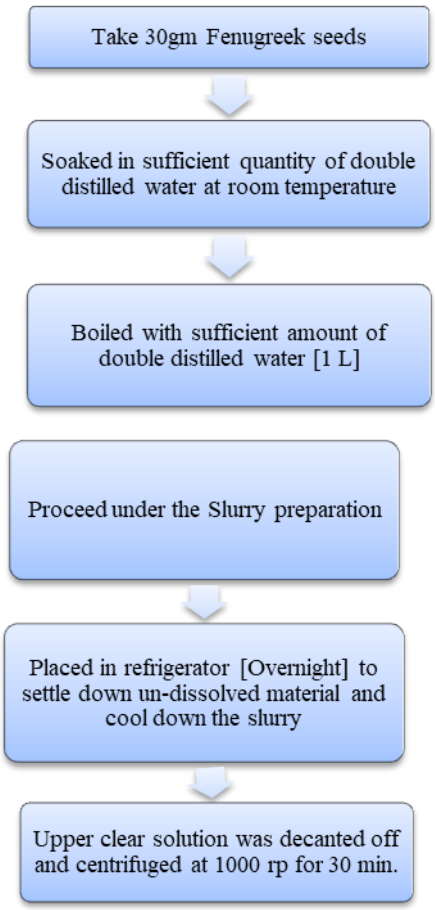
Experimental Design

Extraction of Fenugreek Seeds by Grape Fruit Juice

Fenugreek seeds were soaked in double distilled water at room temperature and then boiled with sufficient amounts of double distilled water under stirring condition in a water bath until slurry was prepared. Then the slurry was cooled and kept in the refrigerator overnight to settle out un-dissolved materials. Then the upper clear solution was decanted off and centrifuged at 1000 rpm for 30 minutes, the supernatant was separated and concentrated at 50-55^{0}C on a water bath to a third of its volume. Solution was poured into thrice volume of acetone by continuous stirring. The precipitate was washed repeatedly with acetone and dried in an oven at the temperature < 50 °C and the dried powder was stored in a desiccator until required.

Extracted mucilage was added to grape fruit juice (5 ml) and three experimental products such as T1, T2, and T3. Mucilage is added at the rate of 50mg, 75mg and 100mg in T1, T2, T3 respectively and a control sample is prepared without addition of mucilage [16]. To know the stable and required concentration of grapefruit juice in polymer which is used in the pharmaceutical formulation. [16]

Steps For Solvent Extraction with Grapefruit Juice [16]



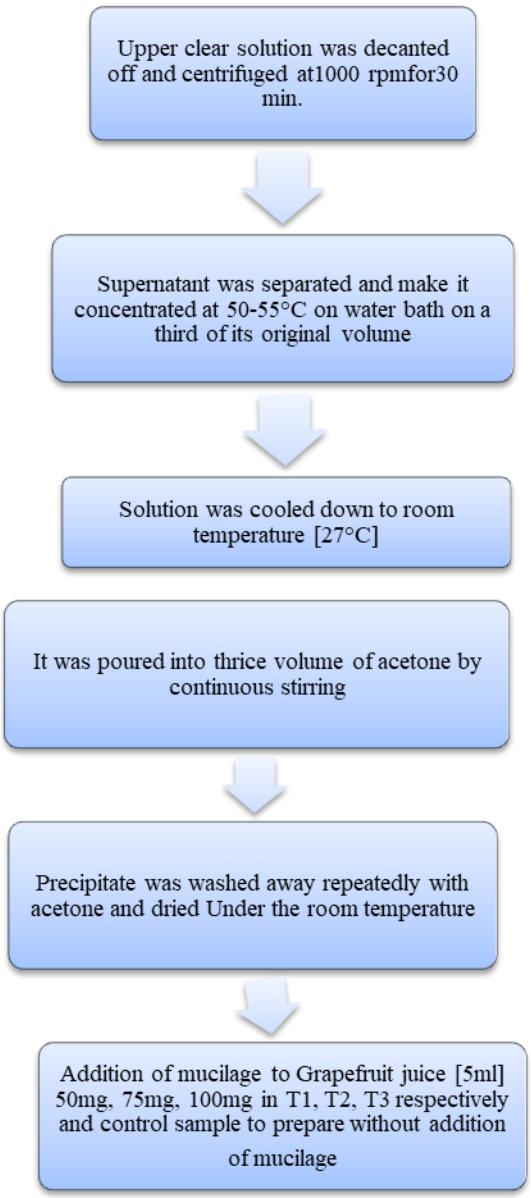


Figure 1: Solvent extraction with grapefruit juice

Islolation of Polymer (Mucilage)

To extract the mucilage from Fenugreek seeds and to evaluate it as a binder for pharmaceutical dosage forms. Present work reports extraction of mucilage from Fenugreek seeds. Fenugreek seed mucilage was extracted following the established methods with little modifications. Mucilage was isolated from Fenugreek seeds by extraction, soaking and boiling with double distilled water and precipitating by addition of acetone and also addition of grape juice and drying at 50-600 C under vacuum**.** [17] The percentage yield of mucilage was 20-25% w/w. The physicochemical characteristics of mucilage such as swelling index, solubility, loss on drying were studied and pH was found to be 7.2 which is near to neutral value. The mucilage was evaluated for its granulating and binding properties in tablets, using**.** [18**]**

Advantages of Mucilage in Pharmaceutical Formulation

- **Biodegradable**

Living organisms are the producers of all naturally available polymers, because of which these biodegradable materials have no harmful impact on humans or nature.

- **Biocompatible**

Since carbohydrates are the major part of these herbal materials, they are highly biocompatible.

- **Non-toxic**

The nature-friendly characteristic of mucilage makes it non-toxic and non-irritant

- **Better patient acceptance**

The chances of side effects occurring are the lowest in natural mucilage, as compared with synthetic ones.

- **Inexpensive**

Mucilage is obtained from natural sources, so it is always cheaper. Compared to that of synthetic material, the production cost is also lower.

Effects of Grapefruit Juice with Drugs

Administration of grapefruit juice can increase the plasma concentration of numerous drugs in humans and decrease the concentration of a few others. Such elevations of drug plasma concentrations have, on occasion, resulted in adverse clinical effects. Increased concentrations are primarily mediated by chemicals in grapefruit juice, which inhibit the CYP3A4 drug-metabolizing enzyme in the small intestines. This inhibition decreases the first-pass metabolism of drugs using the CYP3A4 intestinal system and increases the bioavailability and maximal plasma drug concentrations (Cmax) of the CYP3A4 substrates. The effect of grapefruit juice on drug metabolism is most pronounced in drugs with a high first-pass metabolism, in which it inhibits the first-pass metabolism of the CYP 3A4 substrates leading to an increase in Cmax and area under the concentration time curve (AUC).

Report suggested the use of grapefruit juice with a few specific drugs (eg, Fexofenadine, Digoxin) may lower plasma drug concentrations by inhibiting drug absorption catalyzed by the organic anion transporting polypeptide (OATP) [17,18].

Intake of grapefruit juice did not significantly alter the intravenous pharmacokinetics of Felodipine compared to control treatment, whereas after oral drug administration it did lead to an increase in the mean AUC and Cmax by 72% and 173%, respectively, and the mean absolute bioavailability was increased by 112%. The fraction of the oral Felodipine dose reaching the portal system was increased from 45% to 80% when intake of the drug was preceded by grapefruit juice ingestion. The pharmacokinetics of the primary metabolite of some drugs, was affected by the intake of juice, resulting in a 46% increase in Cmax. Juice intake immediately before oral felodipine resulted in more pronounced hemodynamic effects of the drug as measured by diastolic blood pressure and heart rate. [19].

Effects of Natural Polymer with Gfj on Drugs/ Pharmaceutical Formulation

Many drugs are broken down (metabolized) with the help of a vital enzyme called CYP3A4 in the small intestine. Grapeofruit juice can block the action of intestinal CYP3A4, so instead of being metabolized, more of the drug enters the blood and stays in the body longer. The result: too much drug in your body. The amount of the CYP3A4 enzyme in the intestine varies from person to person. Some people have a lot of this enzyme and others just a little. So, grapefruit juice may affect people differently even when they take the same drug. Although scientists have known for several decades that grapefruit juice can cause too much of certain drugs in the body, more recent studies have found that the juice has the opposite effect on a few other drugs. [20]. Grape juice in natural polymer [Mucilage] that enhances its efficiency of process that decreases the disintegration and increases its bioavailability and decreases the drug releasing period of time. the long stay of the drug in the body with slow process of hepatic metabolism.

Evaluation of Mucilage

Organoleptic evaluation and % yield of isolated mucilage Prepared plant mucilage is evaluated for organoleptic properties to ensure the quality of product.

Percentage yield 10 gm of fenugreek seed was extracted and isolated. The isolated gum was then dried well and percentage yield was calculated by following formula.

$$\% \text{ Yield} = \frac{\text{Practical Yield x 100}}{\text{Theoretical Yield}}$$

- **Solubility**: Solubility of isolated mucilage is determined by dissolving the mucilage in various solvents.
- **pH**: pH of isolated mucilage (1%)
- **Swelling index**: In a measuring cylinder of 25 ml, 1 g mucilage is taken and dissolved in 25 ml of distilled water. This is shacked well in each 10 minute interval for the next 1 h and is allowed to stand for 3 hours. Swelling index is calculated using the following formula. [22]

$$\text{Swelling index} = \frac{(W2 - W1) \times 100}{W2}$$

- **Moisture content:** 1 g of mucilage sample is taken in a watch glass and this is placed in a hot air oven. The sample is then allowed to dry at 105°C and it is weighed in each 5-minute interval until it reaches a constant weight. [23]

The percent loss of moisture on drying is calculated using the following formula:

$$\text{LOD} = \text{weight of water in sampe} \times 100 \text{ weight of dry sample}$$

3. Results and Discussion

S. No.	Name of test	Results	
1.	**Percentage yield of polymer obtained**	**33.5%**	
2.	**Organoleptic evaluations**		
	Color	Light yellowish-brown	
	Odor	Odorless	
	Taste	Mucilaginous	
	Shape	Irregular	
	Touch and texture	Hard and rough	
3.	**pH of mucilage (1%w/v)**	4.8.5-0	
4.	**Solubility**	In warm water	Soluble
		Coldwater	Sparingly soluble
		Methanol acetone	Insoluble
5.	**Moisture content**	1.8 %	
6.	**Swelling index**	In water 76.32% In 0.1 N HCl 66.42 In Phosphate buffer 48.22	

The results obtained from analytical work, established that the treated fruit juice with fenugreek mucilage was as effective as enzymatic treatment for clarification of Grapefruit juice. Further using mucilage substances are cost effective. To enhance filtration process performance, pretreating with mucilage of fenugreek seeds before filtration, for the purpose of flocculating soluble polysaccharides responsible for high viscosity can be an effective pretreatment as pre-treatment with enzymes. Increasing the incubation time to 2hrs. The viscosity of the juice with mucilage treatment of Grapefruit juice had decreases. Incubation time also affects the viscosity. Grapefruit juice treated with mucilage, then there was a rise in TA (titratable acidity) compared with untreated Grapefruit juice.

The Grape fruit juices treated with different concentration of mucilage also, pH decreases with increasing incubation time. The present study may be extended to the other fruit extract used in mucilage.

4. Conclusion

The viscosity of the juice with mucilage treatment of Grapefruit juice had decreases. Incubation time also affects the viscosity. Grapefruit juice treated with mucilage, then there was a rise in TA (titratable acidity) compared with untreated Grapefruit juice.

The Grape fruit juices treated with different concentration of mucilage also, pH decreases with increasing incubation time. The present study may be extended to the other fruit extract used in mucilage to enhance the activity of the mucilage**.**

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