Formulation and Evaluation of Paracetamol Tablets using Fenugreek Seed Mucilage as Natural Disintegrant

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***Abstract*— Fenugreek, or Trigonella Foenum-graceum in scientific parlance, is a herbaceous plant of the leguminous family that originated in Western Asia. Since it was one of the first plants to be cultivated, it has been extensively utilized for food, food additives, and traditional medicine in every area where it has been planted. Mucilage, a naturally occurring gooey material found in many seed coverings, is present in high concentrations in the seeds. The aim of the current investigation was to separate and examine the fenugreek seed mucilage's suitability as natural disintegrant for creating fast dissolving drug delivery (FDTs) of the chosen model medication, paracetamol. The tablets were prepared using the Direct Compression method using 0.5, 1 and 1.5 % w/w concentrations of fenugreek seed mucilage. Pre-compressional studies were conducted and it was found that the flow properties of all the formulations were within limits. The evaluation test showed that the formulated formulation having 1.0% disintegrants shows the best activity on tablets.**

***Index Terms*—Direct Compression, Fenugreek seed mucilage, Flow properties, Paracetamol.**

I. INTRODUCTION

The oral route is the most recommended and practical method of administration since it has many benefits, including correct dose, patient compliance, convenience of administration, and great versatility[1]. For many patients, one significant disadvantage of these dose forms is their inability to be easily swallowed, even with ready access to water. Dysphasia, or difficulty swallowing, is a widespread issue affecting people of all ages, although it is particularly prevalent in the old and young due to physiological changes that are specific to these populations[2]. One important novel drug delivery method that is gaining popularity fast is fast dissolving drug delivery. Its objective is to create a convenient dosage form for administration in order to improve patient outcomes and safety[3]. The additions known as excipients are the substances that change the active chemicals in pharmaceuticals into dosage forms that may be given to patients. To satisfy the requirements of both sophisticated tablet manufacturing and traditional drug administration systems, new and enhanced excipients are constantly being created[4]. Plant-based products are an eco-friendly substitute for synthetic ones due to their affordability, accessibility within the community, and reduced cost when compared to imported synthetic goods. Herbs are renewable, non-polluting resources that can be used to produce cheaper pharmaceuticals over time. Plant-based materials have been investigated by several researchers for their potential use as pharmaceutical excipients[5]-[7]. The field of drug delivery has made extensive use of natural materials like gums and mucilage because of their accessibility, affordability, eco-friendliness, emollient and non-irritating nature, non- toxicity, ability to undergo a wide range of chemical modifications, potential for degradation, and compatibility because of their natural origins[8]-[10]. Mucilage does not dissolve in water, but when it comes into contact with liquids, it becomes a sticky, viscous substance. When exposed to liquids, fenugreek seeds swell up and become slippery, just like other materials that contain mucilage. Instead of being absorbed by the body, the resulting soft mass travels through the intestines and causes contractions of the intestinal muscles[11]. The aim of the current investigation was to separate and examine the fenugreek seed mucilage's suitability as a disintegrant for creating FDTs of the chosen model medication, paracetamol.

II. MATERIALS AND METHODS

A. Chemicals

The required materials and chemicals were provided by the department of pharmaceutics, SUCP, Hyderabad.

B. Plant Seeds

The Fenugreek seeds were purchased from the local market which were authenticated by SUCP, Hyderabad.

C. Extraction and Isolation of Fenugreek seed mucilage

250 grams of fenugreek seeds were soaked in double-distilled water at room temperature. After that, they were boiled in a water bath with enough double-distilled water while being stirred, until a slurry was formed. In order to settle out any undissolved components, the slurry was then cooled and refrigerated for the entire night. After decanting out the upper clear solution, a 30-minute centrifugation at 1000 rpm was performed. On a water bath, the supernatant was separated and concentrated to one- third of its initial volume at a temperature of 50–55º C. The solution was added to three volumes of acetone while stirring continuously after it had cooled to room temperature. The precipitate was dried after being repeatedly washed with acetone[12].

D. Physicochemical Characterization of Mucilage

i. Viscosity: 1 gram of finely ground, dried fenugreek mucilage was suspended in 75 milliliters of distilled water at least for 5hrs. The concentration of 1% w/v was achieved by adding 100 ml of distilled water. Using a Brookfield viscometer set to 37°C, the slurry was mechanically stirred for two hours to homogenize it[12].

ii. Swelling Index: Swelling index is the volume (in ml) occupied by 1g of the drug with the mucilage after 4 hours of swelling in an aqueous liquid. The powdered fenugreek mucilage's swelling index was calculated using the BP method. In a 25 ml ground glass stoppered cylinder graded in 0.5 divisions across a height of 120 to 130 mm, 1 gram of mucilage powder was added. This was filled with 25 ml of water, shaken briskly every 10mins for one hour, and let to stand for 24 hours. It was measured for how much volume the dissolving agent, including the adherent mucilage was occupied. Three assessments were averaged to get the Swelling index[13].

iii. Standard Calibration Curve: The paracetamol stock solution was diluted in phosphate buffer of pH 7.2 to get a series of dilutions: 10, 20, 30, 40, and 50 ug/ml. The Jasco 530 UV 1600 UV Visible spectrophotometer was used to measure the absorbance of these solutions. The absorbance was measured at 243 nm. A blank of phosphate buffer pH 7.2 was utilized.

E. Formulation of Paracetamol Tablets

The paracetamol tablets were prepared by the Direct Compression method using Fenugreek seed mucilage as 0.5, 1 and 1.5 % w/w concentrations. All ingredients were passed through mesh no.60 separately in order to achieve uniformity. Adequate quantity of the blend was then punched in a tablet punching machine. The proportions of ingredients used in the formulations are given in the table below.

Table I: Formula of formulations of Paracetamol

S. No.	Composition (mg)	F1	F2	F3
1	Paracetamol	250	250	250
2	Fenugreek seed mucilage	2	4	6
3	Starch Powder	2	2	2
4	Microcrystalline Cellulose (MCC)	90	88	86
5	Mannitol	50	50	50
6	Talc	3	3	3
7	Magnesium stearate	3	3	3
TOTAL		400	400	400

F. Evaluation[14]

i. Pre-compressional evaluation

iv. Angle of Repose: The following equation is calculated and changed to reflect the height (h) and radius ® of the pile that was created on the graph paper;

$$Tan(\theta) = height/radius$$

v. Carr's Index: The Carr's index of the powder was calculated using the following equation:

$$Compressibility = 100[(\rho T - \rho B)/\rho T]$$

Where, ρT=tapped density,
ρB=bulk density

vi. Hausner's Ratio: Good flow is indicated by a Hausner's ratio less than 1.25; readings between 1.25 and 1.5 guarantee that adding glidant would enhance flowability.

$$Hr = \rho t/\rho b$$

ii. Post-compressional evaluation

vii. Thickness: Vernier calipers were used to measure the thickness of 10 tablets. A tablet's thickness ought to be regulated to within ±5% of a standard value, contingent upon its dimensions.

viii. Hardness: For each formulation, the average of 20 tablets is assessed. Tablet hardness can be measured with the "PFIZER" or "Monsanto" hardness testers.

ix. Weight Variation: 20 tablets was weighed separately, and the average weight is derived from the total weight.

$$\%\, Weight\ variation = (Average\ weight - Individual\ Weight)/Individual\ Weight\ x\ 100$$

x. Friability Test: A sieve was filled with twenty tablets that were chosen at random. An air compressor or a soft brush was used to clear loose dust. Before being put in a friabilator, tablet samples were precisely weighed. Loose dust was once again taken out of the tablets after the predetermined number of turns. At last, a weight was taken of the tablets.

$$Friability = (W1 - W2/W1)\ x\ 100$$

Where, W1= weight of the tablets before the test
W2=weight of the tablet after the test

xi. Disintegration Test: The in vitro disintegration time was determined using a disintegration test device without a disk for six tablets. The disintegration medium consisted of 900 mL of distilled water that was kept at 37 °C and swirled at a speed of 30 r/min. The duration in seconds that the tablet required to entirely dissolve and leave no observable mass inside the apparatus was recorded.

xii. Dissolution Test: Using a USP type II paddle dissolver, the dissolution rate was measured in 900 mL of pH 6.8 phosphate buffer at 37°C and 75 r/min. At regular intervals, an aliquot of the dissolution medium was removed and replaced with an equal volume of freshly prepared dissolution media that had been pre-warmed to 37°C. After the samples were filtered, the drug content of paracetamol in each sample was measured using a Shimadzu UV spectrophotometer set to the proper dilution at 276 nm[15].

III. RESULTS

A. Pre-compressional Evaluation

The pre-compressional studies of the powder blend were carried out and the results are given in table 2.

Table II: Pre-compressional studies of the paracetamol tablet powder blend.

PROPERTIES	FSM DISINTEGRANT		
	F1	F2	F3
TAPPED DENITY (gm/cm3)	0.778	0.425	0.59
BULK DENSITY (gm/cm3)	0.665	0.375	0.48
CARR'S INDEX (%)	13.33	11.7	14.2
HAUSNER'S RATIO	1.09	1.13	1.15
ANGLE OF REPOSE	34.6	33.02	32.1

Pre-compressional studies were conducted and it was found that the flow properties of all the formulations was good. F2 was found to have excellent flow property while F1 & F3 had good-excellent flow property. The angle of repose and flow properties of F2 was excellent while other formulations F1 and F3 possessed good flow properties.

B. Post-compressional Evaluation

The post-compressional studies of the prepared paracetamol tablets were carried out and the results are given in table 3.

Table III: Post-compressional studies of the prepared paracetamol tablets

S. No.	Formulation	Hardness (Kg/cm²)	Thickness (mm)	Friability (%)	Weight variation (mg)
1	F1	3.7	4.84 ± 0.04	0.60%	398
2	F2	4	4.03 ± 0.02	0.70%	400.4
3	F3	4.5	4.72 ± 0.04	0.90%	401.8

Hardness test resulted that all the paracetamol tablets are within the limit. The difference between

thickness values of all 3 formulations varied from 4.03-4.84 mm. Weight variation results for all 20 tablets are within the standards in accordance with USP i.e., the weight of NMT 2 tablets out of twenty differ from the average weight by NMT ±7.5%. Friability test results for paracetamol tablets were within the specified limits. From the above results we can conclude that the physical properties of formulated paracetamol tablets are within limits and among the 3 batches of fenugreek seed mucilage, the formulation having 1.0% disintegrant was found to have a better effect on tablets.

C. Disintegration Studies

The disintegration test was performed and it was found that with an increase in disintegrant conc. there was a decrease in the disintegration time of tablets. Therefore, formulation having 1.5% disintegrant conc. of the tablet weight (F3) disintegrated faster than other formulations. Formulation F2 gave the best among the 3 formulations. All 3 formulations were within the disintegration limits.

Table IV: Disintegration studies of the different formulations

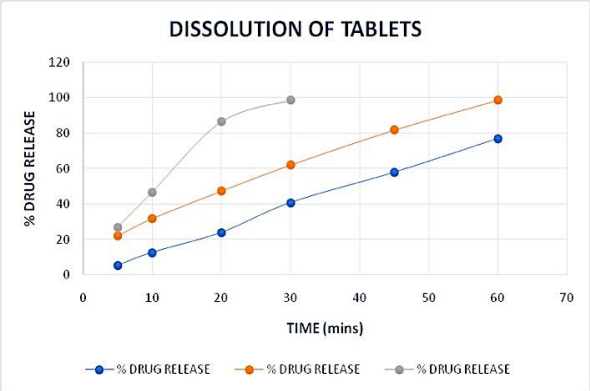
FORMULATION	AVG.WT. [6TABSLETS]	TIME OF DISINTEGRATION
F1	397mg	10mins 08sec
F2	398.5mg	7mins 43sec
F3	401.2mg	4mins 26sec

D. *In-vitro* Dissolution Studies

Table V: In-vitro dissolution studies of different formulations

TIME (mins)	% DRUG RELEASE		
	F1	F2	F3
5	5.35	22	26.83
10	12.65	31.8	46.72
20	23.96	47.3	86.52
30	40.78	62	98.67
45	57.9	81.7	-
60	76.98	99.2	-

The graph was plotted with % Drug Release against Time for all 3 formulations. As per the graph, formulation f2 showed a linear graph with 99% drug release.



IV. CONCLUSION

Paracetamol tablet is an analgesic & antipyretic drug commonly used to treat pain and reduce fever. This study includes the effect of binders taken in different ratios. Disintegrants are the agents that promotes break-up of the tablets into smaller fragments, thereby affecting the drug release pattern of the tablets. In our study, the paracetamol tablets were prepared using the direct compression technique. Among the 3 formulations, it was found that the formulation F2 was more stable and had better flow properties. The evaluation test showed that the natural disintegrant fenugreek seed mucilage shows the best activity at 1.0% disintegrant concentration. The *in-vitro* dissolution study was conducted and it was found that formulations F3 do not fit the criteria as it gets dissolved within 30mins and hence are not suitable. Formulation F2 is best compared to other formulations as it was released within 60mins which is most significant as per the standards.

V. FUTURE PROSPECTIVES

Fenugreek Seed Mucilage is an inexpensive and effective natural excipient that can be used as an alternative in pharmaceutical preparations. To meet increasing demands, it is necessary to explore new sources. Fenugreek also exhibits the anti-inflammatory and anti-oxidant activities which can be used along with paracetamol to reduce pain and inflammation. As fenugreek seeds have high mucilage content, it can also be used as a binding agent or a suspending agent along with disintegrant activity if used in appropriate concentrations.

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