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ISOLATION AND EVALUATION OF FENUGREEK, FLAXSEED MUCILAGES AND ITS USE AS A PHARMACEUTICAL BINDER

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Abstract

The objective of the present investigation was to evaluate the binder effects of mucilage isolated from flaxseed (*Linum Usitatissimum L.*) and fenugreek seed (*Trigonella foenum graceum L.*). Flax is an annual plant of the linaceae family and fenugreek is an annual herb of leguminosae family. These plants have been used since very long time for their medicinal values. Both these plants contain natural polysaccharides which have been employed as food and pharmaceutical excipients because of their biocompatibility, biodegradability, easy availability and low cost. Fenugreek seeds and flax seeds produce high viscosity mucilage at low concentration levels. The binding properties of the mucilage isolated were investigated using lactose granules with different binder concentrations levels of 3% $^{w}/_{v}$, 5% $^{w}/_{v}$, 7% $^{w}/_{v}$ and 10% $^{w}/_{v}$. The results were compared with regularly used binders such as starch paste, PVP and 1:1 concentration of both FXM and FNM. The Physical properties of the granules (bulk density, tapped density, Carr's index, flow rate, angle of repose, friability, compressibility) and tablets (weight variation, hardness, thickness, tablet wetting time, water absorption ratio, friability and disintegration time) were assessed. Tablets at 7 % $^{w}/_{v}$ binder concentration showed good results as compared to starch, PVP and 1:1 of 7% $^{w}/_{v}$ total FXM and FNM. The comparative results showed good tableting properties revealing the use of natural polysaccharide based binders for preparation of uncoated tablet dosage form.

Keywords: Binder, *Linum Usitatissimm*, Mucilage, Polyvinylpyrrolidone k30 (PVP 30), Starch, *Trigonella foenumgraecum.*

Introduction:

Binders are adhesives that are added to solid dosage formulations. The primary role of binders is to provide the cohesiveness essential for the bonding of the solid particles under compaction to form a tablet. In a wet granulation process, binders promote size enlargement to produce granules and thus improve flowability of the blend during the manufacturing process. Binders may also improve the hardness of the tablets by enhancing intragranular as well as intergranular forces.[1] A number of plant gums/ hydrocolloids have been used as binding agents, suspending or emulsifying agents in both solid and liquid dosage forms[2,3,4]. They have been utilized in variety of formulations like gastroretentive, colon specific drug delivery system etc.[5][6]

The plant *Trigonella foenum graecum Linn*. (Leguminaceae) is an aromatic annual herb [7]. It is also known as fenugreek in English. Fenugreek has been used in treating colic flatulence, dysentery, diarrhea, dyspepsia with loss of appetite, chronic cough, dropsy, enlargement of liver and spleen, rickets, gout, and diabetes. It is also used as gastro protective, antiurolithiatic activity, diuretic, antidandruff agent, anti-inflammatory agent and as antioxidant. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds).

Flaxseed, also known as linseed, is derived from the flax plant (*Linum usitatissimum*), of the family Linaceae, which is cultivated worldwide for its fiber and oil. Flaxseed contains 6% mucilage or soluble fibers, insoluble fibers 18%, 25% proteins, and 30-40% oil, with alpha-linolenic acid (ALA) making up about 50-60% of the total fatty acids [8]. The lignan constituent of flaxseed (but not its oil) possesses *in vitro* anti-oxidant and possible estrogen receptor agonist/antagonist properties, prompting hypotheses on its utility in the treatment of breast cancer, prostate cancer inflammatory bowel disease, lupus nephritis and type 2 diabetes[9,10].

Materials and Methods

The fenugreek seeds (*Trigonella foenum graceum L*.) and flaxseeds (*Linum Usitatissimum*) used in study were procured from a local market in Mumbai, India. The seeds were authenticated by Professor Harshad Pandit, Khalsa College, Mumbai. Polyvinylpyrolidine (PVP), starch, Acetone, absolute alcohol used were of high grade purity obtained from S.D. FINE Chemicals, Mumbai. Freshly prepared double distilled water was used throughout the experiment. The isolation of mucilage of fenugreek seeds (FNM) and flax seeds (FXM) was done by method developed at our laboratory.

A batch 100gm of crushed fenugreek seeds was soaked in 500ml of double distilled water and boiled at 80^{o}C using water bath for 4 hours with occasion stirring or till thick mass was obtained. It was kept aside at room temperature for 4 hrs stirred intermittently and then kept aside overnight below 20^{0}C. The hydrated mucilage was separated by using muslin cloth. The mucilage was then precipitated with 300 ml of absolute alcohol. The precipitated mucilage was filtered using vacuum filtration. The separated mucilage was then dehydrated with 200ml of acetone. This treatment also removes any extracted oil present in hydrated mucilage. After filtration precipitated mass was dried in hot air oven at 50^{o}C for 12 hours. The dried mucilage was then powdered using mortar and pestle and passed through sieve #60. Flax seed mucilage also prepared as per the method mentioned above. The resultant dried mucilage were subjected to pharmacotechnical evaluation in order to assess and compare their potentiality as a tablet binder.[11]

The present investigation was designed to explore FNM and FXM as a natural source based binders. The granules were prepared with Lactose using wet granulation method. Aqueous binder solution of FNM in the concentration 3%, 5%, 7% and 10 % $^{w}/_{w}$ were prepared in freshly prepared double distilled water. All ingredients were dry mixed manually in mortar. Binder solution was slowly added into powder mixture and kneaded to make wet dough mass. The wet mass was granulated by passing them manually through a number 16# sieve. Granules were dried at 60 ºC in hot air oven. The granules were evaluated for fines percent, Particle size and Angle of Repose. The particle size distribution was determined by sieve analysis. Lactose granules were prepared using FXM as per mentioned above in the same concentration range. The property of the FNM and FXM granules were compared with industrially used binders like PVP-K30 and Starch. All the granules batches were subjected to detail pharmacotechnical evaluation and the results were compared.

Pharmaco Technical Evaluation Of Granules Of Dried Flaxseeds, Fenugreek Seeds Mucilage, PVP K30, and Starch: [12,13,14]

1. Bulk density (B_d)

The term bulk density refers to a measure used to describe a packing of particles. The bulk density of FNM and FXM was obtained by dividing the mass of a powder by the bulk volume in cm^3 (V). The standard method (USP) was adopted for measurement of bulk density of both dried powdered mucilage and following equation was used for calculation.

$$B_d = \frac{M}{V}$$

Where, M = weight of samples in grams, V= bulk volume of powder in cm^3

2. Tapped density(T_d)

The tapped density or poured density attained after mechanically tapping a container containing the powder sample. The standard method described in USP was followed and tapped density was calculated using equation given below:

$$T_d = \frac{M}{V_p}$$

Where, M = weight of samples in grams and V_p = final tapped volume of powder in cm^3

3. Carr's index

An indirect method of measuring powder flow from bulk densities was developed by Carr. A low Carr's index implies a good initial packing arrangement, with less volume of voids. As the value of these indices increases, the flow of the powder decreases. In general, however, Carr's index below 16% indicates good flowability while values above 35% indicate cohesiveness[14]. Carr's index of each sample was calculated according to equation given below:

$$CI = 100 \left(\frac{T_d - B_d}{T_d}\right)$$

4. Hausner's ratio

Hausner's ratio measures the powder ability to settle and permit an assessment of the relative importance of interparticulate interactions. Hausner's ratio is calculated as the ratio of bulk density to tapped density. The Hausner's ratio less than 1.25 indicates good flow; the values between 1.25 to 1.5 assure that adding glidant will improve flow ability.

$$HR = \frac{V_0}{V_f}$$

Where, V_0: unsettled apparent volume, V_f: final tapped volume

5. Angle of Repose

Angle of repose has been defined as the maximum angle possible between the surface of pile of powder and horizontal plane. The angle of repose for the granules of each formulation was determined by the fixed height funnel method. The

angle of repose was calculated by substituting the values of the base radius 'r' and pile height 'h' in the following equation:

$$\tan \theta = \frac{h}{r}$$

$$\text{Therefore; } \theta = \tan^{-1}\left(\frac{h}{r}\right)$$

6. Determination of flow rate

Ten grams (10g) (*w*) of the granules were passed through dry glass funnel and allowed to flow through the funnel orifice. The time taken for the powder to flow through the orifice (*t*) was noted and the flow rate was computed as;

$$\frac{w}{t}$$

7. Friability

The granule strength was determined by friability test using the Roche friabilator (Erweka Germany). The apparatus was rotated at 25rpm for 4 min. A sample of 10 g (W_A) granules was placed in friability testing machine. After the drum movement stopped, the granules were sieved through a 60-mesh sieve and the residue remaining on the sieve was weighed (W_B). The friability was calculated using the following equation

$$F\% = \frac{W_{A-W_B}}{W_B} \times 100$$

8. Percent compressibility (%C)

It is an important measure that can be obtained from bulk density measurements. It is the simple test to evaluate the V_0 and V_f of powder and the rate at which it packed down. The following formula was used to compute the percent compressibility.

$$\frac{100(V_0 - V_f)}{V_0}$$

Where,

V_f = packed bulk density

V_0 = apparent bulk density

9. Particle size distribution [15]

Standard sieve method as per IP was adopted to study particle size distribution. Clean standard sieves were taken and arranged in such a manner that the coarsest sieve remains on the top and finest sieve remains on the bottom. Butter paper was placed at the bottom of arranged sieve set. 10 gm of the FSM granules were spread on top sieve. The set of sieve were rotated semicircular motion with intermediate jerking for 10 mins. Disassemble the sieve set. Separated powder was collected from each sieve and weighed separately. The oversize and undersize particles for each sieve was noted.

10. Characterization of FNM and FXM for adhesiveness.

The measuring device consists of two square shaped flat glass plates with thickness of 3 mm and two dimensions each 100 mm. The plates were placed in a water bath until their temperature reaches 25°C and quickly dried. Then a sample of 1 g of the dispersion was poured in four points of the lower plate and second plate was being carefully placed on. The appropriate weight equivalent to 100 g was then applied on and allowed to remain for 10 minutes. After removing the upper plate, the diameter of four regions was measured and the average diameter, d (cm) was placed on the following formula to obtain yield value, τ (N/m^2) of the binder.

$$\tau = \frac{2.943 \times 10^3}{d^3}$$

Characterizations of Tablets

1. Weight variation: Five tablets were selected randomly from each batch and weighed individually on electronic balance. The individual weight is then compared with the average weight for the weight variations.

2. Thickness and hardness: For each formulation of the tablet thickness was determined by the vernier caliper while the hardness of the tablet was determined using Pfizer hardness tester.

3. Tablet wetting time study: The experiment was designed to evaluate the water uptake rate by the tablet. 25 ml of water was placed in a Petri dish. The band of the filter paper, supported on the glass slide, was partially dipped in water. A tablet was placed on the surface of filter paper band. The uptake of water occurred from the lower surface of tablet. The time required for water to reach the centre of the upper surface of the tablet was noted.

3. Water absorption ratio: Test was done with the same procedure as that of wetting time. In this test, initial weight of the tablet was noted before placing it on the Petri dish. After complete wetting, the wet tablet was then weighed. Water absorption ratio, R was determined using equation,

$$R = \frac{W_b - W_a}{W_a} \times 100$$

W_a = weight of the tablet before absorption.

W_b = weight of the tablet after absorption.

4. Friability

The tablets were carefully dedusted prior to testing. Accurately weigh the tablet sample, and place the tablets in the drum. Rotate the drum 100 times, and the tablets were removed. The tablets were then reweighed after removal of fines and the percentage of weight loss was calculated. A maximum mean weight loss from the three samples of not more than 1.0% is considered acceptable for most products.

$$F\% = \frac{W_{A-W_B}}{W_B} \times 100$$

5. Disintegration test

The disintegration time were measured using disintegration test apparatus as per the USP. One tablet were placed in each tube of the basket. The basket with the bottom surface made of a stainless-steel screen (mesh no.10) were immersed in water bah a 37± 2°C. The time required for complete disintegration of the tablet in each tube were determined using a stop watch.

Table-1: Comparative results of granules prepared using different binders.

Sr. No	Properties	FNM				FXM				FNM and FXM	Starch paste	PVP
		3%	5%	7%	10%	3%	5%	7%	10%	(1:1)	10%	10%
1	Bulk density(g/ml)	0.56	0.57	0.55	0.45	0.54	0.55	0.66	0.42	0.52	0.4	0.41

2	Tapped density(g/ml)	0.62	0.61	0.71	0.50	0.61	0.60	0.71	0.55	0.58	0.41	0.45
3	Carr's index	11.1	6.55	22.53	10	11.47	9.8	7.04	23.63	10.34	2.44	8.88
4	Hausner's ratio	1.3	1.07	1.29	1.11	1.14	1.11	1.07	1.30	1.11	1.02	1.0
5	Flow rate(sec)	12.0	10	10.0	10.0	10	12	8.0	15.0	10.0	10.0	12.0
6	Angle of repose	39.9	39.4	38.65	30.54	36.1	35.6	33.42	31.80	38.65	29.68	33.42
7	Friability (%)	0.3	0.2	0.2	0.1	0.2	0.3	0.1	0.2	0.1	0.2	0.3
8	Compressibility	10.71	6.8	22.22	11.11	12.43	10	6.66	30.95	10.52	4.0	8.33

Table-2: Comparative results of tablets prepared using different binders:

Properties	FNM				FXM				FNM and FXM	Starch paste	PVP
	3%	5%	7%	10%	3%	5%	7%	10%	(1:1)	10%	10%
Weight variation	151± 0.55	150± 0.60	152±0.70	150± 0.60	152± 0.40	151± 0.50	150± 0.63	150± 0.58	1510.22	150±0.55	151±0.30
Hardness (kg/cm^2)	7±0.2	7.5± 0.38	9±0.5	8±0.45	8±0.69	7.5± 0.58	7.85± 0.60	10± 0.10	8.0±0.34	8.0±0.20	7.5±0.10
Thickness (mm)	6.2± 0.20	6.0± 0.32	5.9± 0.25	6.1± 0.30	6.0± 0.23	6.2± 0.32	6.1± 0.42	6.0± 0.34	6.1±0.25	6.1±0.30	6.0±0.54
Tablet wetting time study (sec)	39	31	25.5	18	24	42	55	71	52	40	33
Water absorption ratio %	41	52.5	63.5	84	78.3	77.4	74.6	59.6	63.5	74.4	77.3

Friability %	0.65	0.33	0.21	0.54	0.46	0.32	0.26	0.43	0.25	0.91	0.95
Disintegration time (min)	3mins 30sec	2min s 30sec	1mins 55sec	55sec	11mins 30sec	13min	14mins 20 sec	22mins	8mins 55sec	13mins 30sec	18mins 15sec

Results and Discussion

Since last two decades a lot of work has been done in exploring and incorporating natural plant based polysaccharides in different capacity in pharmaceutical formulations. Natural polysaccharides and dried mucilage have been widely explored as emulsifying, suspending, binding, and disintegrating agent and as sustained-release matrix by the pharmaceutical industry.

The aim of the present work is to isolate mucilage from FN seeds and FX seeds and compare their properties as a binder with each other as well as with starch paste, PVP and 1:1 of optimized concentration of FXM and FNM. Mucilage from FN and FX was easily isolated using absolute alcohol and precipitated with acetone. A cost effective method was adopted for isolation of mucilage. The resultant dried mucilage were subjected to comparative evaluation of basic pharmacotechnical parameters in order to study their suitability as a tablet binder.

The resultant FNM and FXM were subjected to their characterisation as an adhesive material using yield value determination. After following the reported method, the equivalent average diameter or yield value of FNM, FXM and starch binders solution was found to be 3.3±0.14 cm 1.64±0.21 and 0.85±0.05 cm respectively. These values indicate that mucilage of FN and FX spreads more easily than starch paste in the powder mass revealing that FNM and FXM has better nature of spreading over the particles and giving good adhesiveness to powder particles.

The flow properties and compressibility of a powder are essential in determining its suitability as direct compression excipients. The Hausner's and Carr's indices are considered as indirect measurement of powder flowability. The dried powdered mucilage of FN and FX were subjected for bulk density, tapped density, Carr's index, Hausner's ratio, angle of repose and flow rate.. Bulk density and tapped density was higher in FXM (bulk density 0.42 to 0.66 and tapped density 0.55 to 0.71 respectively) than a FNM (bulk density 0.45 to 0.57 and tapped density 0.50 to 0.71 respectively). The Carr's Index and Hausner's Ratio are measures of the propensity of a powder to be compressed. As such, they are

measures of the powder ability to settle and they permit an assessment of the relative importance of interparticulate interactions. In a free-flowing powder, such interactions are less significant, and the bulk and tapped densities will be closer in value. For poorer flowing materials, there are frequently greater interparticulate interactions, and a greater difference between the bulk and tapped densities will be observed. Hence, from the data depicted in result table reveals that FNM has better flow property based on its bulk density value and tapped density value. Carr's index was calculated according to the values prescribed in pharmacopoeia. It showed FXM has good flow than the FNM. (FXM 7 to 24 and FNM 10 to 22.5.respectively)

The compressibility index and angle of repose indicated that the powder is having good flow with moderate compressibility. The result of physicochemical characterization of FXM and FNM is reported in table 1. Since, the flow properties of the powder mixture are important for the uniformity of mass of the tablets, the flow of the powder mixture was analyzed before compression to tablets. Low Hausner ratio, compressibility index and angle of repose values indicated a fairly good flowability of powder mixture. The values of pre-compression parameters evaluated were within prescribed limits and indicated good free flowing property (Table 1).

The data obtained for post compression parameters such as hardness, weight variation, thickness, tablet wetting time study, water absorption ratio, friability and disintegration time are shown in Table 2. The hardness was found to be in the range of 7±0.12 to 10±0.10kg/cm^2 in all the formulations indicating good mechanical strength with an ability to withstand physical and mechanical stress conditions while handling. In all the formulations the friability value is less than 1% and meets the IP (Indian Pharmacopoeia) limits. All the tablets passed weight variation test as the % weight variation was within the pharmacopoeial limits. The weight of all the tablets was found to be uniform with low standard deviation values.

Since the dissolution process of a tablet depends upon the wetting followed by disintegration of the tablet, the measurement of wetting time may be used as another confirmative test for the evaluation of tablets. A significant decrease in the wetting times is seen with increase in the level of FNM and FXM concentration (3 to 10 %$^{w}/_{v}$).

The separated mucilage was evaluated for its performance as binder in tablets at various concentrations (3, 5, 7, 10 % $^{w}/_{v}$) and the optimum concentration found was 7 %. Its performance was compared with starch paste and PVP at

optimum concentration (10%) and it was found better than starch and PVP in tablet formulations with less disintegration time (1min 55 s) compared to that of starch paste (13mins 30 sec) and PVP (18mins 15sec).

Number of researchers has studied dried mucilage of FN seeds as disintegrant, suspending agent. Same way FX mucilage has also been used as mucoadhesive. As shown in table 2 disintegration time of FNM is less than 5 mins and hardness is between 7 to 9 Kg/ cm^2. These results are in accordance with previously reported data for FXM to be used as a rapid disintegrant as well as binder in a dispersible tablet. 1:1 of 7% total FXM and FNM shows disintegration time of 8 mins 55 sec which is less than FXM (14 mins and 20 sec respectively) the disintegration time was reduced in combination due to FNM.

Conclusion

The results obtained from the present investigation conclude following details. 7% FXM as binder gives best tableting property compared to starch 10% and PVP 10%. While tablet containing FNM showed improve disintegration suggesting its use as a disintegrating as well as binder. Combination of FXM and FNM in equal proportion is also a promising combination to get optimize hardness as well as disintegration of tablet.

References

1. Ehab Hamed, et al, Binders and Solvents, Handbook of Pharmaceutical Granulation Technology, published by Taylor & Francis Group.,109, 2006.
2. Ravi Kumar, Sachin R. Patil, M. B. Patil, Mahesh S. Paschapur, Mahalaxmi R "Isolation and evaluation of the emulsifying properties of tamarind seed polysaccharide on castor oil emulsion", *Scholars Research Library, Der Pharmacia Lettre*, 2 (1) 518-527, 2010.
3. Anroop B, Bhatnagar SP, Ghosh B, Parcha V. "Studies on Ocimum gratissimum seed mucilage: evaluation of suspending properties", *Indian J Pharm Sci.*; 67:206–9, 2005.
4. Ghule BV, Darwhekar GD, Jain DK, Yeole PG, "Evaluation of binding properties of Eulophia campestris Wall. Mucilage", *Indian J Pharm Sci.*;68:566–9, 2006.
5. Márcia R. de Moura,Fauze A.Aouada,Luiz H.C. Mattoso, "Preparation of Chitosan nanoparticles using methacrylic acid", *Journal of Colloid and Interface Science,* volume 321,Issue 2, 15, Pages 477–483, 2008.

6. Munira Momin and K. Pundarikakshudu, Studies On Formulation Development Of Colon Targeted Drug Delivery System For Sennosides. Journal of Pharmacy & Pharmaceutical Sciences. JPPS 7(3). Online - http://www.ualberta.ca/~csps/JPPS7(3)/Issue7(3).htm. December, 2004.

7. Trease GE, Evans MC. Editors, "Text book of Pharmacognosy", 15th ed., Balliere, tindall;London: 2002.

8. Trease G and Evans W. Drugs of biological origin. In: Trease and Evans, 11th ed. Bailliere Tindall. London; pp 319-320, 741- 1980.

9. Kokate CK, Purohit AP and Gokhale SB. Pharmacognosy, Nirali Prakashan. Pune, 15th,ed; pp: 98-102, 2005.

10. Bharadia PD, Patel MM, Patel GC, Patel GN. "A preliminary investigation on sesbania gum as a pharmaceutical excipient", *International Journal Pharma Excip*.3:99-102, 2004.

11. Pooja Abhang, Munira Momin, Mayur Inamdar, Snehal Kane, "Comparative evaluation of fenugreek and flaxseed as pharmaceutical excipients", International journal of Pharma world research, volume 3 issue 3, ISSN 0976-111X, 2012.

12. Staniforth, J.N. (1996). Powder flow. In: Aulton M. E. (Ed). Pharmaceutics- the science of dosage form design. Churchill Livingston, pp 600-615.

13. M. C. Gohel, A. F. Amin, Munira Momin, Seema Bazaz, M. K. panchal, "Preliminary investigations in matrix based tablet formulations of diclofenac sodium containing succinic acid treated guar gum." in Bollettino Chimico Farmaceutico 137(6) 1998.

14. United States of Pharmacopoeia Convention (USP), USP-24 NF-19, Rockville, USA, 1999.

15. Munira M Momin, Tejal A Mehta, "Practical manual for Pharmaceutical Engineering", B.S.Shah Prakashan. 2nd Ed ISBN NO.81-8416-090-9 Ahmadabad, Page 257, 2010.

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