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Research Article

Extraction and Evaluation of *Lepidium Sativum* and Flax Seeds Mucilage as a Pharmaceutical Granulation Binder

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ABSTRACT

The powders hold together by a binder to form granule. Some excipients of natural origins are currently available as an alternative over the synthetic ones in pharmaceutical formulation. The aim of this study was to isolate the mucilage from different plant seeds and compare them to evaluate the binding effects. In present study an effort was made to investigate the efficacy of mucilage obtained from *Lepidium sativum* and flax seeds as granules excipient. The mucilage was extracted from selected seeds by conventional method by precipitation of soaked and blended seeds in acetone. The dried mucilages were subjected to several phytochemical and physicochemical properties. Granules were formulated by wet granulation method by using extracted mucilage as a binding agent and comparison was made against the granules prepared with standard binder as PVP. The granules evaluated by various physical properties such as (bulk and tapped densities, Hausner's ratio, Carr's index, angle of repose and friability). The results showed that the granules prepared from extracted mucilage as a binder had good flow and mechanical properties, all evaluated parameters were within the permissible limits. Thus, mucilage could be used as an alternative binding agent in pharmaceutical granules.

INTRODUCTION

Medicinal plants are one of the most important sources for providing medicines and providing natural additives that contribute to placing medicines in effective pharmaceutical preparations as excellent pharmaceutical aids as well as excipients.

In recent times, botanicals have gained very great importance due to their huge and widespread pharmaceutical uses as a binding agent in tablets, thickening agent in liquids, and others. They are also used in other industrial fields such as the cosmetic industry, the paper industry and some types of paints.

There are many additives that are used in pharmaceutical preparations of plant origin, including starch, agar, alginate and gum, in addition to many colourings, flavourings and sweeteners. These plants originated additives are most commonly used in pharmaceutical preparations (Rashmi, et al., 2019). These natural additives that have been extracted from plants have a very effective role compared to the synthetic additives. Due to its valuable advantages and properties such as low cost, availability, eco-friendly extract, renewable resources, its palatability by the public and by patients and others, compared to its manufactured counterparts (kirti, et al., 2016).

Binders are agents added to solid pharmaceutical forms in order to give them the cohesion and bonding necessary to bind the solid particles together to form granules and to give them the necessary cohesion to bind these granules together under pressure to form tablets. In the wet granulation process, binders contribute to enlarging the size of the solid particles to form granules and thus contribute to improving the flow properties of the mixture during the

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manufacturing process (Mayur, et al., 2012, Neeta and Vaishali, 2014, Smita, et al., 2014). Natural binders such as mucilage are among the most commonly used additives in pharmaceutical preparations. Mucilage extracted from plants are usually hydrophilic in nature and form gel. They are the normal product of metabolism formed within cell (Alaa and Elnazeer, 2019, Vaishali and Neeta, 2014).

Mucilages are chemically heterogeneous compounds consisting mainly of polysaccharides made of simple sugars like arabinose, galactose, rhamnose and galacturonic acid. Since, they contain hydrophilic molecules so they combine with water to form large molecular aggregates. Mostly, mucilages are used as pharmaceutical additives in different dosage formulations with wide range of applications such as thickening, binding, disintegrating agent, suspending and emulsifying agent in biphasic liquid dosage forms, stabilizing and gelling agents. Mucilages may also be used as an adjuvant in sustained as well as controlled release dosage form. (Neela et al., 2014 and Moumita et al., 2017).

Lipidium sativum L. which is known as garden cress. It follows the Brassicaceae family, it is considered as one of the fast growing plants as it is found on a wide geographical area in many countries of the world. (Vaishali and Neeta, 2014) and The seeds contain proteins, fats, carbohydrates, and crude fibers. *Lipidium sativum* seeds contain 20–25% oil, and the main fatty acid is linolenic acid, 32–35%. They also contain natural antioxidants, Imidazole alkaloids (lepidine), monomeric alkaloids, (sinapic acid, and sinapine) are the most important in *Lipidium sativum* seeds. (Khalid et al., 2020). The preliminary phytochemical analysis of *Lepidium sativum* showed that it contained cardiac glycoside, phenolic, flavonoids, coumarins, glucosinolates, and amino-acids, mucilage, resins, saponins, sterols, tannins, volatile oils and triterpenes. (Ali et al., 2019). *Lipidium sativum* seeds considered as an important medicinal plant where it can be used as diuretic, aperient and aphrodisiac and used in the treatment of inflammation, bronchitis. (Omar et al., 2020). The seeds of *Lepidium sativum* were used as tonic, demulcent used to soothe acidity in the stomach, coating, and protecting the digestive tract, carminative, galatogogue, emmenagogue, to cure throat diseases, uterine tumor, nasal polyps and breast cancer. Seeds were supplemented with in the diet of lactating women to increase the milk secretion during the postnatal period. Seeds also applied conjointly applied as a poultice to pains, hurts, sprains, in the treatment of bacterial and fungal infections. The seeds were also used for the treatment of fracture healing in Saudi traditional medicine. In Turkish folk medicine, *Lepidium sativum* seeds were used to enhance digestion, and appetite. The mucilage in the outer seed was used as a substitute for tragacanth and gum Arabic. (Ali et al., 2019).

Flaxseed, also known as linseed (*Linum usitatissimum*), from the Linaceae family, which is cultivated all over the world for the purpose of extracting fiber and oil. (Alaa and Elnazeer, 2019). Flaxseed is well-known for the content of chemical compounds with specific biological activities including α-linolenic acid (ALA), lignans and other phytochemicals such as triterpenoids, steroids, glycosides, saponins, alkaloids, flavonoids, tannins, proteins, free amino acids, carbohydrate and vitamin C. Moreover, other bioactive compounds in flaxseed, such as phenolic acids and phytosterols, have also been implicated as positive mediators against cardiovascular diseases, insulin resistance, Type 2 diabetes and other degenerative diseases. It is also seemed to be effective in osteoporosis and mitigating the menopausal symptoms. (Madiha et al., 2018 and Qianchun et al., 2017). Flaxseed has long been recognized for its health benefits. The traditional and medicinal uses of flaxseed including relief of abdominal pains, constipation, stomach ulcer, skin inflammation, wounds, and gingival disorder. Flaxseeds are excellent source of omega-3 fatty acid, dietary fibers, unique proteins and phenolic acid. (Manisha et al., 2019).

As there are no previous reports comparing the properties of FSM and LSM as a pharmaceutical binder for granulation. Hence, the present study was aimed to isolate mucilage from garden cress (*lepidium Sativum*) seeds and flaxseed (*linum usitatissimum* L.) and compare their properties as a binder for granules preparation with each other as well as with standard binder such as PVP (Polyvinylpyrrolidone).

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MATERIALS AND METHODS

Plant Material

Lepidium sativum seeds and flaxseeds were collected from the local market in Tripoli, Libya. The collected seeds were authenticated in the herbarium of botany department, faculty of sciences.

Extraction of Seed Mucilage

Lipidium sativum and flaxseed mucilage (LSM&FXM) was extracted according to the method described by (Neeta and Vaishali, 2014). About 100 g of each seeds species were soaked in 800 ml of distilled water for 24 hr, the soaked seeds were blended for 35 min at about 2000 rpm by using KitchenAid 5KSB1585EER blender. The blended seeds were first filtered through 710# mesh to ease separation of large particles then through a muslin cloth. Additional 200 ml water was added to the blended seeds and again blended and filtered through muslin cloth to get maximum yield and to get rid of the coat residues. Equivalent amount of acetone was added to the filtrate (800ml) to allow precipitation of mucilage. A white supernatant coagulant mass separated by using muslin cloth. The precipitated white mass was spreaded on butter paper and allowed to dry on room temperature for 12 hr. The mucilage obtained was converted into a powder by size reduction using mortar and pestle, and powder was sieved using 180# sieve and weighed to calculate the yield through the following formula:

$$\%\ \text{yield} = \frac{\textit{Weight of the extracted mucilage}}{\textit{weight of seeds}} \times 100 \quad (1)$$

Physicochemical Characterization of Extracted Mucilage

The extracted mucilage was characterized by the following tests:

Organoleptic Characterization

Extracted mucilage was characterized for various parameters like color, odor, taste and texture.

Phytochemical Characterization

Aqueous solution of the extracted mucilage (1mg/ml) was used for chemical characterization. Tests for carbohydrates, alkaloids, starch, tannins, and non-reducing sugars were performed according to standard procedures described by Harborn (Harborn, 1984).

Loss on Drying and Moisture Drying Content

Loss on drying was determined by accurately weighed the quantity of 1.5g of LSM and FXM powder at 105±5 ^{o}C in a hot air oven (LABSC, Germany), and the weight was checked an interval of 10 min, until a constant weight of the mucilage was obtained (Malviya, 2011). Loss on drying and moisture content were calculated by the following formulae:

$$\%\ \text{Loss on drying} = \frac{\textbf{initial weight} - \textbf{final weight}}{\textbf{initial weight}} \times 100 \quad (2)$$

$$\%\ \text{Moisture content} = \frac{\textbf{initial weight} - \textbf{final weight}}{\textbf{final weight}} \times 100 \quad (3)$$

PH Value of Mucilage

The pH of 1% w/v solution of mucilage in distilled water was determined using a digital pH meter (Jenway 3510, UK) at 25 ^{o}C (Lala PK., 1981).

Swelling Index and Swelling Capacity of Mucilage

Swelling index of polysaccharide was determined by using modified method reported by (Gauthami and Bhat, 1992). Accurately weighed 1 g of mucilage powder was transferred to a 50 ml stoppered measuring cylinder. The initial volume occupied by mucilage powder in the measuring cylinder was recorded (V1). The volume was made up to 50 ml mark with distilled water. The cylinder was stoppered, shaken thoroughly and then allowed to stand for 24 hr. at room temperature. The volume occupied by the mucilage sediment was measured after 24 hr. (V2).

Swelling index (SI) is expressed as a percentage and calculated using to the following equation:

$$\%SI = \frac{V2 - V1}{V1} \times 100 \quad (4)$$

The content from the measuring cylinder from the above test were filtered through a muslin cloth and the water was allowed to drain completely into a dry 50ml graduated cylinder. The volume of water collected was noted and the difference between the original volume of the mucilage and the volume drained was taken as water retained by sample and was referred as water retention capacity or water absorption capacity.

Surface Tension of Mucilage

Aqueous solutions of the binders 1% and 5% (w/v) were prepared by constant stirring for 2 hr. the

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experiment was performed at 25°C. Solutions were kept steady for 1 hr. to reach equilibrium before tests. The concentration of these solutions was also determined as m/v, where m is the mass of the binder liquid (g) and v is the binder liquid volume (ml). The surface tension (ST) of the solutions (mN/m) was determined by using the Du-Noüy ring tensiometer test method (KRÜSS GmbH K6, Germany). The ring method was performed as described by (Worapan et al., 2017). A platinum wire ring was immersed in the samples. The distance between the immersed ring and liquid surface was fixed at 4.5 mm to ensure a clean break of the meniscus on the immersed platinum ring. The immersed ring was pulled slowly through the liquid-air interface, where the tensiometer platform was moved in the opposite direction at the same time. The measured values can directly be read off the instrument in mN/m. The calibration was performed using distilled water (surface tension = 72.8 mN/m ± 0.05 at 25°C). Each measurement was performed three times and the average results of the surface tension and their corresponding standard deviation values are reported.

Conductivity of Mucilage

Dried LS and FX mucilages powder (1g and 5g) were dispersed in distilled water at room temperature to prepare 1 and 5% (w/v) dispersions, respectively. The dispersions were stirred using a magnetic stirrer (Jenway1200, Germany) for 2 hr. Then conductivity of these dispersions was measured using a calibrated conductivity meter (Jenway 4510, UK).

Relative Solubility of Mucilage

The method used by Tadese et al., 2014 was employed to determine the relative solubility of the mucilage in cold and hot distilled water, acetone, chloroform, and ethanol. Accordingly, 1g of the mucilage powder was added to 10 ml each of the above-mentioned solvents and left overnight. Five millilitres of the clear supernatants were taken in small preweighed evaporating dishes and heated to dryness over a thermostatic water bath (WATER BATH, HH-54) at 50°C for organic solvents and in an oven (Beschickug 100– 800, Germany) at 105°C for distilled water for 2hr.The weights of the dried residue with reference to the volume of the solutions were determined using an analytical balance (Mettler, type AE100S) and expressed as the percentage solubility of the mucilage in the solvents.

Formulation of Granules

Wet Granulation Method

The present investigation was designed to explore LSM and FXM as a natural source-based binder. The granules were prepared with Lactose using wet granulation method. Aqueous binder solution of mucilage in the concentration 1% and 2.5% were prepared by dispersing the LSM and FXM in distilled water. All the granules ingredients were weighed and mixed geometrically. The powders were dry-mixed using mortar and pestle. The binder solutions were added slowly into powder mixture and mixed well to form a wet mass. The wet mass was then passed through `oscillating granulator (ERWEKA AR 400, US) and dried at the temperature not exceeding 45°C in hot air oven. The dried granules are passed through sieve to get uniform particle size and particles with size fraction 0.710µm were evaluated. The same method as per mentioned above in the same concentration range was followed in the preparation of granules using PVP as industrially binders. All the granules batches were subjected to detail physical evaluation and the results were compared. The granules formulations were shown in Table 1.

Table 1: Granules formulations containing different binder [wet granulation].

Ingredients	Formulation					
	F1	**F2**	**F3**	**F4**	**F5**	**F6**
Lactose	91.5%	90%	91.5%	90%	91.5%	90%
Water	7.5%	7.5%	7.5%	7.5%	7.5%	7.5%
PVP	1%	2.5%	-	-	-	-
LSM	-	-	1%	2.5%	-	-
FXM	-	-	-	-	1%	2.5%

Evaluation of Granules Flow Properties:

Bulk Density (Bd)

The term bulk density refers to a measure used to describe a packing of particles. The bulk density of granules with different binder was obtained by transferred pre-weighed quantities of granules into a 100 ml graduated measuring cylinder and the bulk volume (Vo) was recorded. The bulk density measurements adopted according to the standard test method (USP, 2007) for all granules formulations and the following equation was used for calculation:

$$Bd = \frac{m}{Vo} \qquad (5)$$

Where, M = weight of samples in grams, Vo = unsettled apparent volume (bulk volume) of granules in ml, of a graduated cylinder.

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Tapped Density (Td)

The tapped density or poured density attained after mechanically tapping a container containing the granules sample which was previously placed in the 100 mL graduated cylinder as described above. The cylinder was tapped by using tapped density tester (PHATMATEST, Germany). The volume (Vf) of the granules after tapping were recorded and the tapped density was determined according to the standard method described in USP (2007) was followed and tapped density was calculated using equation given below:

$$T_d = \frac{m}{Vf} \qquad (6)$$

Where, M = weight of samples in grams and Vf = final tapped volume of granules in ml, of a graduated cylinder.

Carr's Index (CI) and Hausner's Ratio (HR)

The bulk and tapped density data obtained from above test were used to calculate the Carr's compressibility index (Carr., 1965) and the Hausner's ratio (Hausner., 1967) to provide a measure of the flow properties and compressibility for each batch of granules by using below mentioned equations:

$$\%\ CI = \frac{Td - Bd}{Td} \times 100 \qquad (7)$$

$$HR = \frac{Td}{Bd} \qquad (8)$$

where Td is the tapped density and Bd is the bulk density

Angle of Repose

Angle of repose (θ) has been defined as the maximum angle possible between the surface of pile of sample and horizontal base. The angle of repose for each granule formulation was measured via the fixed height funnel method. The angle of repose was calculated from the ratio of pile height 'h' to the base radius 'r' in the following equations (Wells, 2002):

$$\tan \theta = \frac{h}{r} \qquad (9)$$

$$\text{Therefore; } \theta = \tan^{-1}\left(\frac{h}{r}\right) \qquad (10)$$

Evaluation of Granules Friability

The mechanical strength of granules can be determined by friability test using the drum Roche friabilator (Erweka Germany). The apparatus drum was rotated at 25 rpm for 4min. A sample of 10 g (Wi) granules was placed in the friabilator together with 200 glass beads of 4 mm diameter. After the drum movement stopped, the granules were sieved through a (250-1000 μm) sieve. the granules fraction retained on 250 μm was weighed (Wf) (Chaudhari and Chaudhari, 2012). The %friability was calculated using the following equation:

$$\%\ F = \frac{Wi - Wf}{Wf} \times 100 \qquad (11)$$

RESULTS AND DISCUSSION

Physicochemical Characterization of extracted Mucilage

Percentage yield

From the present experiment acetone was used as solvent for extraction of mucilage from the seeds of Flax Seeds and *Lepidium sativum*. The average yield of dried powdered of FSM was found to be 12% ± 1.32 and LSM was found to be 14.5% ±1.7 w/w, those values are higher than those previously reported (Barbary et al., 2009, Thammarat et al., 2014, Neeta and Vaishali, 2014). The yield of mucilage largely depends upon the extraction method, time and temperature (Barbary et al., 2009). The dried extracted mucilages were evaluated by their organoleptic, physicochemical and some physical parameter according to standard procedure.

Organoleptic Evaluation

The organoleptic evaluation can be done by visual inspection to establish the macroscopic identity, purity and thereby ensure quality of a particular sample and each of these characteristics are useful in judging the material related to excipient. The organoleptic properties of the extracted mucilage were shown in Table2.

Table 2: Organoleptic properties of extracted mucilage.

Properties	LSM	FXM
Appearance	Lustrous amorphous powder	Lustrous amorphous powder
Color	Dark brown	Light brown
Odor	Peppery	Nutty
Taste	Characteristic	Nutty
Texture	Smooth and sticky	Smooth

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Phytochemical Characterization

Phytochemical investigation of extracted mucilage showed the presence of carbohydrates and remaining phytoconstituents such as starch, alkaloids, non-reducing sugars were absent. Mucilage being polysaccharide, should only give positive result to the test for carbohydrates (Farooq U., et al., 2013). The results obtained are consistent with the confirmatory tests for mucilages from *Trigonella foenum graecum* L. and *Linum usitatissimum* showed presence of carbohydrates only (Suvakanta D., et al., 2014).

These results of qualitative tests can be considered as a proof for purity of extracted mucilage (Farooq U., et al., 2013, Rishabha M., and Giraj T. K., 2012 and Aileen M. and Inocencio Jr., 2019.) as revealed in Table 3.

Table 3: Chemical characterization of extracted mucilage

Test	Observation	
	LSM	FXM
Alkaloid	-	-
Starch	-	-
Carbohydrate	+	+
Non-reducing sugars	-	-

Present (+), Absent (–)

Loss on Drying and Moisture Content of mucilage powder

The US Pharmacopoeial limit for moisture content of natural gums and mucilages has been set at ≤15.0% (Rowe, et al., 2006). The moisture content was found to be 5.2% and 6%, also expressed as percentage loss on drying was found to be 5% and 5.5% for LSM and FXM respectively, values of each mucilage was does not exceed the regulatory limit. This indicated that each mucilage has lower moisture, this is required for safe storage of an excipient for industrial application. As higher moisture contents indicate a poor drying process can lead to subsequent deterioration in quality of the plant material which become suitable for microorganism's growth and affect the stability especially for dosage forms containing moisture-sensitive drugs (Rohokale, et al., 2012).

pH Value of Mucilage

The pH of the excipient is an important factor in determining its suitability in tablet formulations, since the stability and physiological activity of most preparations depends on the pH (Kalegowda P, et al., 2017) The pH of the extracted mucilage solution was found to be 6.5 and 5.8 of LSM and FXM respectively, which near to neutral pH. Hence, this mucilage would be minimizing irritation to GIT when used in uncoated tablet, this would be making mucilage suitable as a polymer carrier and used for formulations which are preferably stable at this pH (Malviya, et al., 2011 & Suvakanta D., et al., 2014).

Swelling Index and Swelling Capacity of Mucilage

Swelling is one of the primary characteristics for a hydrophilic polymer like a mucilage on coming in contact with water become hydrates and swells quickly and forming thick and viscous mixtures. Swelling index indicates the extent of granule hydration (Reyes, et al., 2007). Swelling capacity of a substance reflects the increase in volume of that substance following water absorption (Kasunmala, et al., 2017). Swelling index values of extracted mucilage in distilled water obtained were presented in Table 4 showed that FXM exhibited the highest value, while LSM gave the lowest value. The results obtained are not consistent by comparing with the findings in prior studies. the swelling index value of FXM showed higher than reported by (Shubham V., et al., 2014). On the contrary, LSM value lower than reported by (Vaishali and Neeta, 2014). Also, the water retention capacity of FXM was less, may be owing to mucilage extracted from FX had marked greater extent of swelling capacity as compared to mucilage extracted from LS. Higher degree of swelling indicated that the mucilage has excellent surface wettability and consequently, influence on the water penetration to form easily biodegradable biofilm matrices with higher hydrophilic nature due to their abundance of hydroxyl groups (Zhao, et al., 2009). Previous research has demonstrated that, the swelling property is useful for modifying the drug release by improving the pore characteristics of the excipient (Khullar, et al., 1998). Generally, mucilaginous materials with high swelling index could be performed well as binder, disintegrant and matrixing agent (Deore, and Khadabadi, 2008). Thus, the mucilage extracted from the LS and FX seeds with a significantly high swelling index, can be useful in achieving a potential use as binding agent in different pharmaceutical formulations.

Table 4: Swelling index and water retention capacity of extracted mucilage (Mean ± SD, in triplicates)

Properties	LSM	FXM
Swelling index	189% ± 1.02	650% ± 0.98
Water retention capacity	15 ml/g ± 1.5	7.3 ml/g ± 0.7

Surface Tension of mucilage

Surface tension of the different solutions of LSM, FXM and PVP as function of their concentration were shown in Table 5. It was realized that the surface tension was increased with rise in the mucilage concentration, a similar observation has been reported for *Plantago major* seed mucilage (Alizadeh B., et al., 2017). Whereas, increasing the concentration of standard binder PVP solution reduced the surface tension. It has been reported that mucilage binder with lower surface tension value was necessary in order to enabled better penetration and wetting of polymer solution over the powder during wet massing and hence, results in producing of good quality of granule (Kulkarni,2010). Surface tension of mucilage binders are gaining importance in measurement of other physical characterization of granulation such as adhesion, cohesion, wetting, and spreading (Fell, 1988; Rowe, 1989).

Table 5: Surface tension of extracted mucilage (Mean ± SD, in triplicates).

Concentration (w/v)	Surface tension (mN/m)		
	LSM	FXM	PVP
1%	32± 0.65	34± 0.55	38± 0.05
5%	35.5± 0.80	35± 0.50	36± 0.10

Conductivity of Mucilage

The effect of different solution on electrical conductivity were presented in Table 6. Accordingly, by increasing mucilage concentration from 1 to 5% the electrical conductivity elevated for LSM, FXM and PVP solution. The increased electrical conductivity with increased concentration of the mucilage might be attributed to ionic structure of mucilage and the presence of uronic acids (Mohammadifar, et al., 2006). PVP is an uncharged {neutral} polymer therefore the electrical conductivity exhibited lower value compared with mucilage solution. Similar to previously reported on the conductivity of cactus mucilage (Gebresamuel and Gebremairaim, 2012). It was concluded that, therefore higher conductivity of any solution is a function of increase the amount of charge in electrolytes or ionic concentration (Shree, et al., 2014).

Solubility Test of Mucilage

The results of solubility of the extracted mucilage in different solvents were presented in Table 7. From the results, it is evident that both FXM and LSM were highly soluble in hot water, LSM was highly soluble in cold water, soluble in chloroform, poorly soluble in acetone and ethanol, this reveals that the structural network of the mucilage is composed of hydrophilic chains leading to low affinity for these organic solvents. These results are in agreement with the study done by (Ikoni J O., et al., 2013). While, FXM were partially soluble in cold water, soluble in chloroform, highly soluble in acetone and soluble in ethanol.

Table 6: Conductivity of extracted mucilage (Mean ± SD, in triplicates).

Concentration (w/v)	conductivity (µs)		
	LSM	FXM	PVP
1%	708 ± 1.01	636± 0.92	59 ± 0.08
5%	1989± 1.18	2016± 1.00	161.3± 0.05

Table 7: Solubility profile of extracted mucilage

Solvent	LSM	FXM
Cold water	70%	38%
Hot water	100%	73%
Chloroform	53%	57%
Acetone	16%	85%
Ethanol	11%	50%

Evaluation of Flow Properties of Granules

The extracted LS and FX mucilage was investigated for its binding properties in granules prepared by wet granulation technique and compared with established binder like PVP. The flow behaviour of the prepared granules was measured and results were presented in Table 8. All granules formulations were subjected for various evaluation parameters such as: (Carr's index, Hausner's ratio and Angle of repose) which indicate the flow properties of granules. The flow property of granules is necessary to be considered for solid dosage from technology. The bulk and tapped density provide an insight into the packing and arrangement of the particles and can dramatically affect the maximum packing achievable of the material (Okunlola and Odeku, 2009). The Carr's index and Hausner's ratio are measures of the propensity of compressibility of the material. As such, they are measures of the powder ability to settle and they help to assess of the relative importance of interparticulate interactions as they influence flowability.

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Table 1. Table 8: Evaluation of flow properties and friability of granules (Mean ± SD, in triplicates).

Formulation code	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's ratio	Car's index (%)	Angle of repose (θ)	Friability (%)
F1	0.38 ± 0.34	0.45 ± 0.33	1.16 ± 0.41	14.0 ± 0.38	32.6 ± 0.77	0.29 ± 0.89
F2	0.37 ± 0.25	0.44 ± 0.28	1.17 ± 0.01	15.01 ± 0.11	33.8 ± 0.22	0.17 ± 0.67
F3	0.41 ± 0.55	0.48 ± 0.28	1.17 ± 0.39	14.9 ± 0.67	33.4 ± 1.02	0.43 ± 1.11
F4	0.42 ± 0.43	0.48 ± 0.36	1.15 ± 0.33	12.5 ± 0.38	35 ± 0.90	0.28 ± 1.03
F5	0.41 ± 0.25	0.47 ± 0.29	1.17 ± 0.30	14.23 ± 0.41	31.7 ± 1.2	0.43 ± 1.06
F6	0.44 ± 0.11	0.50 ± 0.02	1.15 ± 0.11	12.9 ± 0.17	34.6 ± 0.89	0.22 ± 1.55

In a free-flowing material, such interactions are generally less significant, the bulk density and tapped density would be relatively similar in value, therefore, the Carr's index would be small. On the other hand, in a poor-flowing material, where there are larger interparticle interactions, so a greater difference between the bulk and tapped density would be observed, therefore, the Carr's index would be larger (USP, 2015).

The angle of repose is a characteristic related to interparticulate friction or resistance to movement between particles (Okafor, et al., 2001). From the results it was observed that bulk and tapped densities were slightly different in values, the LSM and FXM granules formulations had higher values of bulk density were found to be in between 0.41 to 0.44g/ml and tapped density 0.48 to 0.50g/ml, compared with granules prepared with standard binder PVP were found to be in between 0.37 to 0.38 g/ml and 0.44 to 0.45g/ml for bulk and tapped density respectively. Which indicates close packing arrangement and greater ability of granules reduction in volume. Carr's index% or Hausner's ratio with lower values indicate better flow properties than higher ones. LSM and FXM granules with 2.5% concentration showed lower values of Carr's index% and Hausner's ratio, while PVP granules showed higher values. Carr's index% of the granules formulated varied from 12.5 to 15.01 and Hausner's ratio varied from 1.15 to 1.1. Angle of repose values was found between 31.7 to 35^{o}. Based on the results obtained in table 8 reveals that all prepared granules formulations with different binder were within prescribed limits and rated as good in terms of its flow property based on its Hausner's ratio, Carr's index values (Carr RL., 1965) and angle of repose values (USP, 2010).

Evaluation of Friability of granules

The results of the friability tests of formulated granules using natural and synthetic binders are seen in Table 8. The most friable granules were produced using binder 1% of mucilage solution of LS and FX. However, for each binder a higher binder content reduced the granule friability, a larger fraction of the binder interacted with the granulation liquid and subsequently dried to form solid bridges after solidification (Djuric and Kleinebudde, 2010). As the lowest friability value was measured for granules prepared by 2.5% of mucilage solution. A binder was considered activated when the friability limit was achieved. PVP allowed production of granules with low friability value compared to the other binders. Overall, the percentage friability of all the formulation was found to be not more than 1% (within the pharmacopeial limit of <1%), which indicate all granules formulation considered mechanically strong enough can withstand stress during processing.

CONCLUSION

Mucilage was extracted from LS and FX seeds and characterized by various phytochemical and physicochemical properties based on specifications. Results showed that all the evaluated parameters for excipients was within the admissible limits. The binding properties of the extracted mucilage were compared with a standard binder such PVP in formulation development of granules by wet granulation method. Generally, all evaluated results of granules showed that the granules prepared with mucilage compared well with the standard binder granules for bulk, tapped density and angle of repose. All granules formulation showed good flowability and with increased binder concentration their percentage friability decreased. The conclusion can be drawn that the comparative study of extracted natural mucilage shows the promising intrinsic binding property comparing with synthetic binder. Low concentration of LSM and FXM as binder would also help for reducing formulation cost.

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