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Studies on Vigna Mungo Mucilage as a pharmaceutical excipient

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ABSTRACT

The present work was aimed to isolate the mucilage using microwave assisted extraction technique and to evaluate its excipient properties. The yield was found to be 22.56g/kg. The drugs and the isolated mucilage powder were found to be compatible as confirmed by the IR spectral studies. The sedimentation rates of the prepared suspensions using a model drug metronidazole were similar to that of the marketed sample and they were easily redispersible and do not form a hard cake. The drug content of all the prepared suspension formulations was found to be in the range of 94.2-96.1%. The isolated mucilage was also studied for its binding nature using ibuprofen as a model drug. The prepared granules were free flowing and the compressed tablets showed good hardness and friability as compared with the starch and marketed product, thereby confirming the mechanical resistance of the tablets. The drug content of all the prepared tablet formulations was found to be between 93.0-99.45%. The rate of drug release from tablet formulations using mucilage as binder was fast when compared to formulations containing starch and marketed product. Formulation F4 (1:2 ratio) of the prepared ibuprofen tablets showed similar release profile in comparison with the marketed product. The drug release mechanism for the formulation F4 was predicted as first order model with the r^2 value of 0.9632.

Keywords: Mucilage, Metronidazole, Ibuprofen, Suspension, Binder.

INTRODUCTION

In recent years, plant mucilages have evoked tremendous interest due to their diverse applications in pharmacy, for formulation of both solid and liquid dosage forms[1]. Mucilages are pharmaceutically important polysaccharides with wide range of applications such as thickening, binding, disintegrating, suspending, gelling, emulsifying, stabilizing agents and also as release retardants[2]. They are normal products of metabolism formed with in the cell and they represent storage material that consists of sugar and uronic acid units[3,4]. Binders and suspending agents

from natural sources do hold advantages over the synthetic excipients, because of its inertness, cost, and availability. Because of its colloidal nature and viscosity, they can be used to suspend insoluble substances in liquids and help in preventing sedimentation in suspensions[5, 6]. Binders are agents used to impart cohesive qualities to the powdered material during the production of tablets[7]. With the increase in demand for natural mucilages, it has become necessary to isolate and evaluate the newer sources of mucilages to meet the needs. The seeds of Vigna mungo swell and form gelatinous mass when it comes in contact with water due to its hydrophilic nature[8]. Ibuprofen is a weekly acidic, non-steroidal anti-inflammatory drug having high permeability through stomach because it remains 99.9% unionized in stomach. It is well absorbed orally and its half life is 1.8-2 hours[9,10]. Metronidazole is antibiotic, amoebicide and antiprotozoal. Oral doses are rapidly absorbed from gastrointestinal tract. Its half life is 6.2 hours[11, 12]. The present study was undertaken to isolate a natural pharmaceutical excipient from Vigna mungo (black gram) which can be used as an effective suspending agent and tablet binder in pharmaceutical formulations.

EXPERIMENTAL SECTION

Metronidazole was purchased from Yarrow Chem Products Ltd., Mumbai. Ibuprofen was obtained as a gift sample from Eros Pharma, Bangalore. Black gram seeds were purchased from the local market. Dicalcium phosphate, starch, magnesium stearate, citric acid, methyl paraben, propyl paraben and purified talc were purchased from S.D. Fine Chemicals, Mumbai, India. All other chemicals used were of A.R grade.

Extraction of Vigna mungo (black gram) mucilage by microwave method

Black gram seeds were powdered in a mechanical blender for 5 min and soaked in distilled water for 24h in a beaker. The resulting mixture was subjected to microwave irradiation (Kenstar wave reflector system, Model no.OM-9918C) for 3min. Then the beaker was kept aside for 2h for complete release of mucilage into water. The mixture was squeezed through a muslin cloth. To the resulting viscous filtrate equal volume of ethanol was added to precipitate the mucilage. The obtained mucilage was collected, dried at 37^{o}C, powdered, sieved through sieve no.60 and stored in a dessicator till further use[13]. The dried mucilage powder was subjected to chemical tests to confirm its identity.

Formulation of suspension

The required quantity of Vigna mungo mucilage powder as mentioned in Table 1 was taken in a mortar. Little quantity of water was added and triturated well. To this 500 mg of Metronidazole was added and triturated to form a paste. The preservatives, methyl and propyl paraben, citric acid, and vanillin flavor was added and further triturated to form a homogenous mixture. The mixture was transferred to a calibrated bottle and the volume was made up using sufficient quantity of distilled water.

Formulation of tablets

The tablets were prepared by wet granulation technique using varying concentrations of black gram mucilage as mentioned in Table 2 as a binding agent. To the mucilage powder dicalcium phosphate, ibuprofen and starch (previously passed through sieve no. 80) was added and granulated using alcohol as granulating agent. The wet mass was passed through sieve no 12 and the granules obtained were dried at 45^{0}C for 30mins. The dried granules were subjected to dry screening by passing through mesh no.16 superimposed on mesh no.24 and then the granules were lubricated with the mixture of talc and magnesium stearate. The granules were compressed

into tablets using 8mm concave punch in rotary tablet press (Rimek RSB-4 minipress, Cadmach).

Evaluation of prepared formulations

a) Phytochemical examination: Preliminary tests were performed to confirm the presence of mucilage. The chemical tests conducted were ruthenium red test, molisch test, and iodine test.

b) Loss on drying: 500mg of Vigna mungo mucilage powder was weighed and placed in a clean and neat china dish. It was kept in hot air oven at 105^{o}C for 1 hr. The china dish was removed from the oven and again the weight of the mucilage powder was determined. Loss on drying can be calculated by the following equation

%LOD = initial weight – final weight / initial weight X 100

c) pH of 1% solution: The pH of the mucilage solution was measured using a digital pH meter by dispersing the black gram mucilage in 25ml of distilled water.

d) Drug-excipient interaction studies: The pure drugs sample and the physical mixture of drugs and mucilage powder in the ratio 1:1 were subjected to I.R spectral studies using FTIR spectrophotometer (FTIR 8400 S, Shimadzu, Japan).

Evaluation of Suspensions

1) Sedimentation volume: Prepared suspensions were stored in a 50 ml measuring cylinder for 7 days at 35°C. Observations were made at every hr for 8 hrs and then every 24 hr for 7 days. The sedimentation volume, F, was then calculated using the following equation:

$$F = Vu/Vo$$

Where, Vu is the ultimate volume of the u sediment and Vo is the original volume of the of suspension.

2) Particle size analysis: The particle size distribution in the suspension was determined using optical microscope (Olympus LITE image). The suspensions were mixed thoroughly and a drop of the suspension was taken on a slide and spread into a thin film. A total of 100 particles are counted and their size is determined. The average particle size in micrometers was determined.

3) Redispersibility: Fixed volume of each suspension (50 ml) was kept in calibrated tubes which were stored at room temperature for various time intervals upto 45 days. At regular interval of 5 days, one tube was removed and shaken vigorously to redistribute the sediment and the presence of deposit if any was recorded.

4) Drug content: From the prepared suspension samples amount equivalent to 200mg of metronidazole was taken in a 100ml volumetric flask and the volume was made up to the mark with phosphate buffer (pH 7.4). The dispersion was vortexed, filtered, diluted suitably with buffer and the drug content was estimated at 223 nm using UV-VIS spectrophotometer (UV-1601, Shimadzu).

Evaluation of Tablets

1) Preformulation studies: The granules were studied for various micromeritic properties such as bulk density, tap density, Carr's index and Hausner's ratio (Electrolab Tap Density tester, USP,ETD-1020),

2) Post compression analysis: The prepared tablets were evaluated for weight variation test, test for hardness, disintegration time and friability.

3) Drug content determination: Ten tablets of each formulation were powdered. Powder equivalent to 200mg of ibuprofen was weighed and transferred to 100ml volumetric flask, initially about 50ml of phosphate buffer 7.4 was added and the flask was shaken thoroughly and the volume was made up to 100 ml with the buffer solution. The resulting solution was filtered, diluted and the drug content was estimated at 223 nm using UV spectrophotometer using phosphate buffer as blank.

4) *In-vitro* drug release: Drug release studies were carried out using USP dissolution rate test apparatus-II (Electro lab, Mumbai, India). The study was conducted at 37^{o}C and 50rpm. The dissolution medium used was 900ml of phosphate buffer pH 7.4 and study was carried up to 2 hours. 2ml of sample was withdrawn at different time intervals and replaced with fresh medium in order to maintain sink condition. The withdrawn samples were diluted suitably and drug content was estimated spectrophotometrically at 223nm.

RESULTS AND DISCUSSION

The black gram mucilage was extracted by microwave assisted extraction technique. The yield of mucilage was found to be 22.56g/kg of black gram seeds. On treatment of mucilage with ruthenium red, it showed red color confirming the presence of polysaccharide. A violet ring was formed at the junction of two liquids on reaction with molisch reagent confirming the presence of carbohydrates. The compatibility between the drug and isolated mucilage powder was found to be good as confirmed by the I.R spectral studies. Infrared spectra of pure drug metronidazole showed sharp peaks at 1076.21, 1477.37, 3217.04, 1431.08 cm^{-1} that confirmed the presence of C-N stretch, N=O, C-H, O-H and C-C stretch (Fig1). The I.R. spectra of physical mixture of metronidazole with mucilage powder showed peaks at same regions according to their functional groups, as compared with pure drug thereby proving the absence of incompatibility between the drug and the mucilage powder (Fig 2). The presence of peaks at 937cm^{-1},1419.51, 1716.53 cm^{-1} and 2950.29cm^{-1} confirmed the O-H bending, C-C stretch , C=O stretch and C-H stretching for the drug Ibuprofen (Fig 3). The physical mixture of Ibuprofen with mucilage powder confirmed that there was no interaction between the drug and the mucilage powder by exhibiting peaks at same wave number (Fig 4). The pH of 1% solution was found to be 7. The loss on drying of the isolated mucilage powder was found to be 16% and the average particles size of the mucilage powder was found to be 6.42µm. The results of characterization of isolated mucilage powder were shown in Table 3.

Table 1: Formulation of Metronidazole suspension

Ingredients (in mg)	Formulation Code			
	F1	F2	F3	F4
Metronidazole	500	500	500	500
Vigna mungo mucilage powder	250	500	750	1000
Citric acid	200	200	200	200
Methyl paraben	150	150	150	150
Propyl paraben	100	100	100	100
Vanillin flavor	5	5	5	5
Purified water Q.S to ml	50	50	50	50

Table 2: Formulation of Ibuprofen Tablets

Ingredients (in mg)	Formulation Code					
	F1	F2	F3	F4	F5	F6
Ibuprofen	200	200	200	200	200	200
Vigna mungo mucilage powder	10	20	30	40	X	X
Starch	X	X	X	X	20	40
Dicalcium Phosphate	82	72	62	52	72	52
Talc	5	5	5	5	5	5
Magnesium Stearate	3	3	3	3	3	3

Table 3: Mucilage powder characterization

S.No	Parameters	Observed values
1	Bulk density	0.551g/ml
2	Tapped density	0.760g/ml
3	Carr's index	27.5%
4	Hausner's ratio	1.379
5	Angle of repose	$36^{o}56^{1}$
6	Average particle size	6.42µm
7	Average rate of flow	10.33 sec
8	Loss on drying	16%
9	pH of 1% solution	7

Table 4: Pre-compression properties of the granules

Parameters	Formulations					
	F1	F2	F3	F4	F5	F6
Bulk density (g/ml)	0.371	0.405	0.417	0.388	0.357	0.401
Bulkiness	2.69	2.46	2.39	2.50	2.80	2.50
Tapped density (g/ml)	0.502	0.567	0.548	0.558	0.510	0.550
Carr's index (%)	26.09	28.57	23.90	30.01	30.0	27.20
Hausner's ratio	1.3	1.4	1.3	1.4	1.4	1.3
Angle of repose (θ)	12.17	13.49	7.43	7.23	8.51	10.0

Table 5: Post-compression analysis of the prepared tablets

Parameters	Formulations					
	F1	F2	F3	F4	F5	F6
Weight variation* (%)	0.28±0.02	0.29±0.02	0.30±0.02	0.30±01	0.30±0.02	0.29±0.02
Hardness* (kg/cm^2)	4.2±0.25	3.1±0.230	4.46±0.416	5.2±0.20	3.6±0.52	3.43±0.40
Friability* (%)	0.72±0.04	0.643±0.040	0.53±0.050	0.92±0.02	0.66±0.05	0.68±0.06
Disintegration time* (mins)	3.5±0.30	3.17±0.25	1.52±0.30	2.47±0.3	1.2±0.1	1.1±0.1
Drug content* (%)	96.83±0.8505	95.63±0.776	96.45±0.33	99.33±0.29	94.5±0.50	93.14±0.45

** Average of three determinations*

Four batches of suspension formulations were prepared using the isolated mucilage powder and were compared with a marketed product. The prepared suspensions were easily redispersible and do not form a hard cake. The average size of the particles in all the suspensions was found to be 14.5 µm. The drug content of all the formulations was in the range of 94.2-96.1%. On comparison of the sedimentation rates of the formulated suspensions and marketed product, no significant changes in the sedimentation behavior were observed.

Fig 1: I.R.Spectra of pure drug Metronidazole

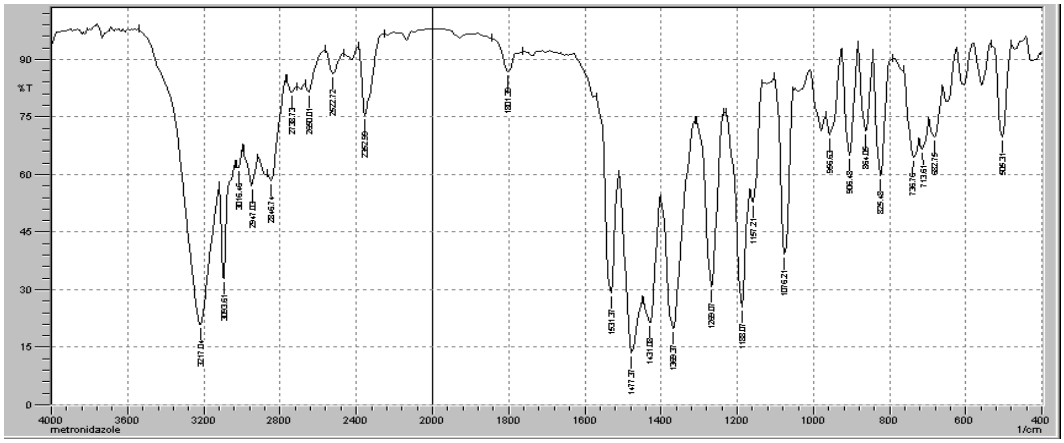


Fig 2: I.R.Spectra of mucilage powder with Metronidazole

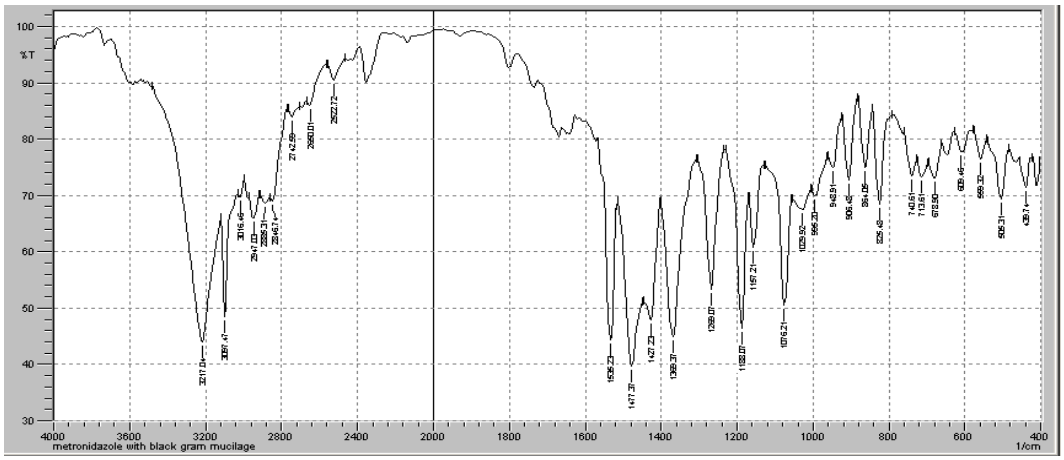
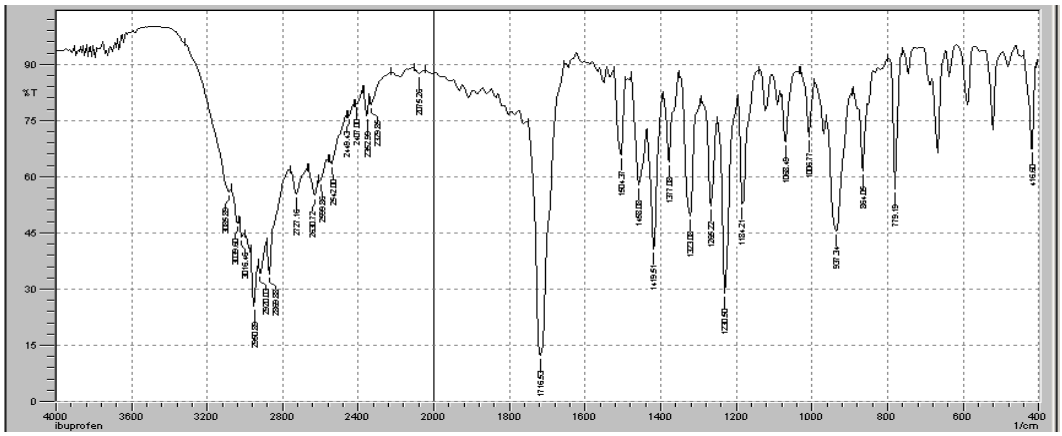


Fig 3: I.R.Spectra of pure drug Ibuprofen



Four batches of tablets were prepared using the isolated mucilage powder as binder and were compared with starch binder. A total of six batches were prepared. The results of pre-compression parameters indicated that the granules were found to be free flowing and exhibited better compressibility index (Table 4). The results of post-compression analysis were given in Table 5. The prepared tablets showed good hardness and friability as compared with the tablets prepared using starch binder which confirmed the mechanical resistance of the prepared tablets. Hardness of the tablets was found to be in the range of 3.1-5.2 kg / cm^2. All the tablet

formulations showed a drug content within the range of 93.14-99.33%. It was observed that rate of drug release from all tablet formulations containing mucilage was fast when compared to formulations containing starch binder.

Fig 4: I.R.Spectra of mucilage powder with Ibuprofen

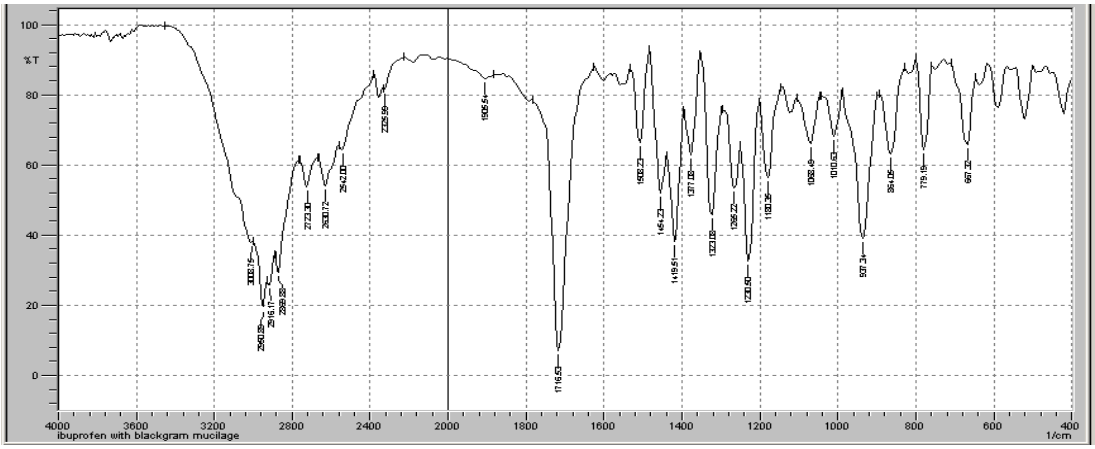


Fig 5: Cumulative % drug release of prepared tablet formulations

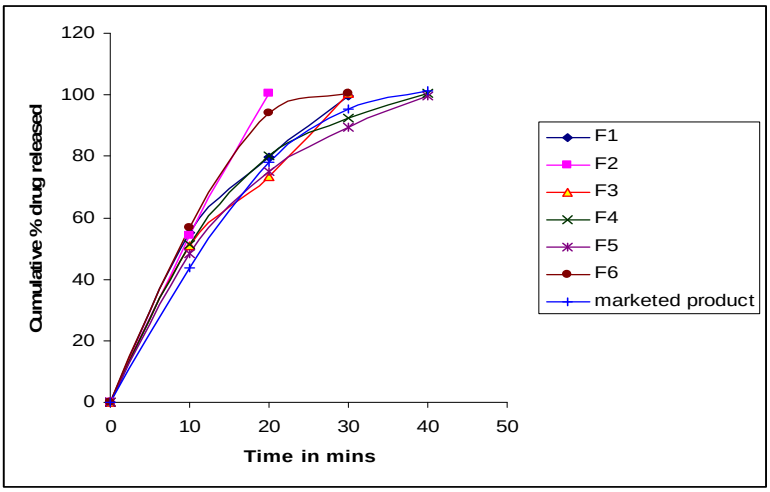
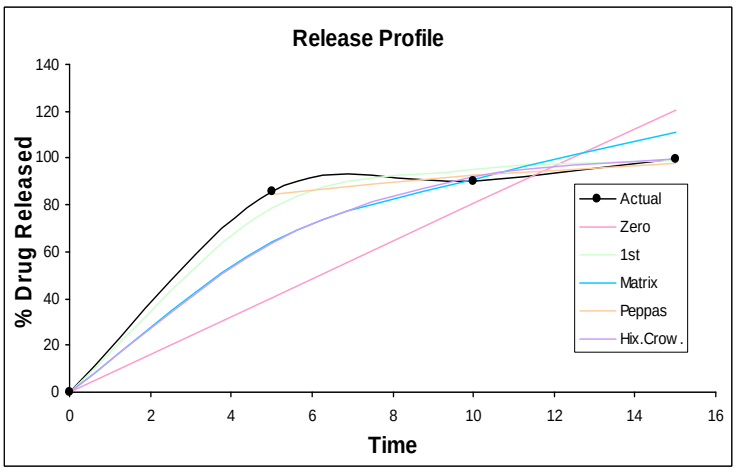


Fig 6: Drug release mechanism of the tablet formulation F4



Formulation F4 of the prepared tablets showed similar release profile in comparison with the marketed product. The drug release profile of all the formulations was shown in Fig.5. The drug release mechanism of formulation F4 was predicted (Fig.6) by PCP disso V3 software. The drug release mechanism was found to be by first order kinetics that was confirmed by the r^2 value of 0.9632.

CONCLUSION

Thus the present study suggested that mucilage can be isolated efficiently by using microwave irradiation from Vigna mungo (Black gram seeds) and can be used as an effective suspending agent and tablet binder in oral pharmaceutical formulations. But the feasibility of isolation of mucilage powder in pilot scale needs to be emphasized in future.

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