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Original Article

EVALUATION AND OPTIMIZATION OF *LEPIDIUM SATIVUM* SEED MUCILAGE AS BINDER IN TABLET FORMULATION

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ABSTRACT

Objective: The study elaborates isolation of mucilage from *Lepidium sativum* seeds and explores it as a tablet binder.

Methods: The mucilage from seed was extracted by precipitation of soaked and blended seed in acetone. The mucilage was evaluated for its binding properties in tablets prepared by wet granulation and direct compression method. The prepared tablets were evaluated for hardness, thickness, friability, disintegrating time and *in-vitro* drug release and compared with established binder like starch, PVP K-30, HPMC, MCC.

Results: The results of isolated mucilage from *Lepidium sativum* seeds as a binder were very promising. The results indicated that mucilage is required in concentration as low as 2% for wet granulation and 4% for direct compression to give equivalent binding effect.

Conclusion: *Lepidium sativum* seed mucilage [LSM] shows promising potential for its application as a binder in the tablet formulation. Low concentration of LSM as binder would also help to reduce cost of formulation.

Keywords: *Lepidium sativum* mucilage, Binder, Natural excipients.

INTRODUCTION

Agents used to impart cohesive quantities to the powdered material are referred to as binders or granulators. They impart cohesiveness to the tablet formulation that ensures the intactness of the tablet after compression, as well as improve the free- flowing quality by the formulation of granules of desired hardness and size [1]. Mucilages are polyuronides consisting of sugar and uronic acid units. They are usually formed from the cell wall or deposited on it in outer layers. They swell in water and form sticky and viscous solution[2]. These plant based material have been utilized as viscosity enhancers, stabilizers, disintegrants[3], solubilisers, emulsifiers [4], suspending agents [5], gelling agents [6] and bioadhesives, binders in different pharmaceutical dosage forms like matrix controlled system, film coating agents, buccal films, microspheres, nanoparticles, viscous liquid formulations like ophthalmic solutions, suspensions, implants and their applicability and efficacy has been proven[7-9].

Lepidium sativum (garden cress) is an annual herb, belonging to *Brassicaceae* family. It is a fast growing, edible plant botanically related to watercress and mustard and sharing their peppery, tangy flavor and aroma. Seeds, leaves and roots are economically important, however, the crop is mainly cultivated for seeds. In some regions garden cress is known as garden pepper cress, pepper grass or pepperwort. It is also known as asalio or chandrasur in India and it is an important medicinal crop in India. Garden cress is a perennial plant, and an important green vegetable consumed by human beings, most typically as a garnish or as a leaf vegetable [10].They show various properties such as anti-asthmatic, ant scorbutic, aperients, diuretic, stimulant, chemo protective effects, anti-diabetic, anti-hypertensive, fracture healing, hepatoprotective activity, pesticidal activity, antidiarrheal activity etc [11,12].

Different seed mucilage has been evaluated for binding property. M. Kamble et al evaluated binding property of *Ocimum tenuiflorum* [13], A. Waghmare et al evaluated binding property of flax seed mucilage [14], N. Patel evaluated binding property of *Cydonia vulgaris*[15]. Binding property of *Eulophia campestris* [16], *Prosopis juliflora* [17] etc has also been evaluated. But there is need of plant based polymers which are safe, stable, economics in production, and shows more promising binding property which can be used in less concentration. No significant work has been reported on *Lepidium sativum* for its use as a tablet binder. Hence the present study is concerned to explore *Lepidium sativum* seed mucilage [LSM] for its binding property by formulating tablet prepared by wet granulation, direct compression method.

MATERIALS AND METHODS

Seed of *Lepidium sativum* were collected from the local market, Nagpur, Maharashtra. The plant material (seeds) was authenticated with the help of herbarium sheet by Dr. N. M. Dongarwar, Department of Botany, R. T. M. Nagpur University, Nagpur. The specimen numbers given to the authenticated herbarium sheet were 9890. Voucher specimen of the plant is deposited in the Department of Botany, R. T. M. Nagpur University, Nagpur. Etoricoxib was obtained from ZIM Laboratories (Nagpur, India), as a gift sample. All the other materials used in the study were of analytical grade.

Extraction of the mucilage from *Lepidium sativum* seeds [18]

100 g of *Lepidium sativum* seeds were soaked in 800 ml of distilled water for 12 hrs. The soaked seeds were blended for 15 min at about 2000 rpm. Blended seeds were then filtered through muslin cloth. Additional 200 ml water was added to the seeds and again blended and refiltered through muslin cloth to get maximum yield. To the filtrate [800 ml] equivalent amount of acetone was added to allow precipitation of mucilage. White supernatant coagulant mass separated after precipitation was filtered through the muslin cloth. Precipitated mucilage was dried in tray dryer [Labotech] at temperature not exceeding 60°c for 16 hr. Mucilage obtained was converted into powder by size reduction. Obtained powder was sieved using 80# sieve. The % yield, pH, and total microbial load [19] of mucilage were calculated.

Formulation of tablet

Wet granulation method

Mucilage solution of concentration 1%, 2%, 3% was prepared by dispersing the LSM in water. All the tablet ingredients were weighed and mixed geometrically. Dry mixing was carried out using mortar and pestle. Then the binder solutions [1%, 2%, and 3%] were added and mixed well to form a wet mass. The wet mass was then passed

through sieve No. 16 and dried at the temperature not exceeding 45°c in a hot air oven. These resultant granules were passed through sieve No. 22. Talc and magnesium stearate were uniformly mixed with above mixture and then evaluated for pre compression parameters. Tablets were compressed using 8 mm round flat punches with 6 tons compression pressures on 12 station tablet machines. The same method was followed in the preparation of tablets [B4, B5] using starch 2% w/w and PVP K-30 2% w/w concentration as a binder. The formulations of tablets are shown in Table 1.

Table 1: Formulation containing mucilage as binder (wet granulation).

Ingredients	B1 (1% LSM)	B2 (2% LSM)	B3 (3% LSM)	B4 (2% Starch)	B4 (2% PVP- K30)
Etoricoxib	120	120	120	120	120
LSM	1% (q. s)	2% (q. s)	3%(q. s)	-	-
Starch	-	-	-	2% (q. s)	-
PVP k-30	-	-	-	-	2%(q. s)
Lactose	156	156	156	156	156
SSG	12	12	12	12	12
Magnesium stearate	6	6	6	6	6
Talc	6	6	6	6	6
Total weight	300	300	300	300	300

Table 2: Formulation containing mucilage as a binder (direct compression)

Ingredient	D1(mucilage) 2%	D2(mucilage) 4%	D3(HPMC) 4%	D4(PVP k30) 4%	D5(MCC) 4%
Etoricoxib	120	120	120	120	120
LSM	4.4	8.8	-	-	-
HPMC	-	-	8.8	-	-
PVP k-30	-	-	-	8.8	-
MCC	-	-	-	-	8.8
Lactose	166.8	162.4	162.4	162.4	162.4
Magnesium state	4.4	4.4	4.4	4.4	4.4
Talc	4.4	4.4	4.4	4.4	4.4
Total weight	300	300	300	300	300

* All quantity are in mg

Direct compression method

All the powders were passed through 80# mesh sieve. Weighed quantity of drug and excipients was mixed thoroughly by blending for 15 min.

Tablets were compressed using 8 mm round flat punches on 12 station tablet machine. The formulations of tablets are shown in Table 2.

Evaluation of tablet

Drug mucilage compatibility study

The mucilage and Etoricoxib were mixed in 1:1 ratio. This mixture was mixed with KBr. The infra-red spectrum was recorded using FTIR (Shimadzu). The scanning range was 400 to 4000 cm^{-1}.

Evaluation of flow properties [20 -22]

Bulk and tapped densities

Pre-weighed, pre-sieved quantity of tablet powder and granules were poured into a graduated cylinder, and the volume was recorded. The bulk and tapped densities were calculated.

Carr's index and Hausner's ratio

Carr's index and Hausner's ratio were calculated from the bulk and tapped densities [23].

Angle of repose

The angle of repose was determined by the fixed height funnel method [24].

Post compression properties [20, 21, 25]

Uniformity of weight

20 tablets weighed were determined by using an electronic balance within ±1 mg. Determinations were made in triplicate.

Hardness

The hardness of the tablets was determined by diametric compression using a Hardness testing apparatus [Monsanto type]. Determinations were made in triplicate.

Friability

20 tablets were weighed and placed in Roche friabilator [Camp-bell Electronics, Mumbai]. Which were then operated for 1000 revolutions. The tablets were then dusted and reweighed. Percentage friability was calculated from the loss in weight.

***In-vitro* disintegration test [25]**

The test was carried out on 6 tablets using tablet disintegration tester in distilled water at 37ºC ± 2ºC as a disintegration media and the time in second taken for complete disintegration of the time in taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

***In- vitro* dissolution profile [26, 27]**

To study the effect of binding agent on dissolution profile of drug *in-vitro* dissolution studies was carried out. Dissolution rate of Etoricoxib from various tablets was studied using USP XXIII six-station dissolution rate test apparatus [DISSO 2000, LABINDIA] with paddle stirrer. The dissolution rate was studied by placing tablet containing Etoricoxib in 900 ml 0.1 M HCl [pH 1.2] maintained at 37±0.5°c at 50 rpm. Sample of 5 ml was withdrawn at pre-determined intervals, filtered through whatman filter paper. 5 ml of fresh dissolution medium was added to the flask to maintain sink condition. The sample were diluted and estimated spectrophotometrically at 234 nm by using ELICO-167 Double beam UV spectrophotometer.

Accelerated stability study

Stability studies for optimized formulations were carried out. The tablet was wrapped in aluminum foil of thickness 0.04 mm and stored for three months at accelerated condition [temperature of 40°c±2°c and relative

humidity of 75±5% RH]. Hardness, thickness, weight variation, friability and disintegrating time were then estimated.

RESULTS AND DISCUSSION

Extraction of the mucilage from *Lepidium sativum* seeds

The mucilage was extracted by the method which was simple and cost effective. The percentage yield of mucilage was found to be 12% w/w. pH of mucilage 1% w/v dispersion in water was found to be 5.56. The microbial count for LSM was found to be 249 colonies and only 1 fungal count was observed during total microbial load study of LSM. Also there was no change observed in mucilage throughout a study period. In case of excipients from natural origin, the total aerobic count should not be more than 1000 cfu/g and total fungal count should not be more than 100 cfu/gm [28]**.** Result shows that the total microbial load of LSM was within the limit. And hence mucilage was stable and had the good shelf life.

Drug mucilage compatibility study

Compatibility testing between drug and LSM was carried out using FTIR. The spectra with results are shown in Fig. 1. The FTIR spectra showed that the drug and mucilage were compatible with each other.

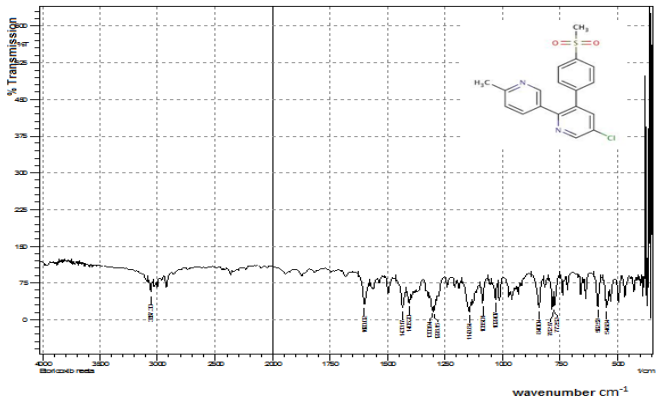

Fig. 1a: IR spectrum of Etoricoxib

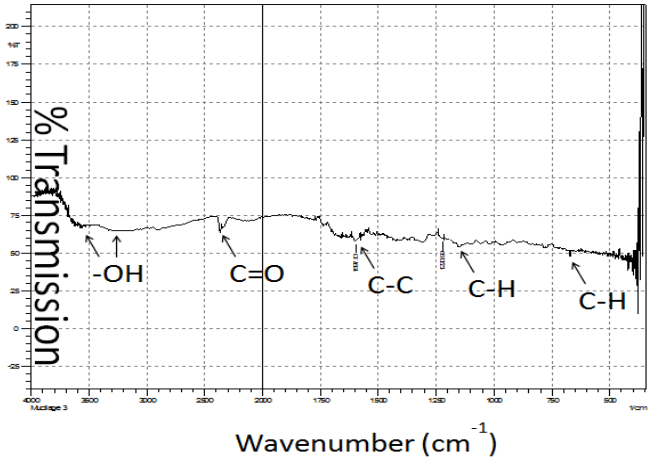

Fig. 1b: IR spectrum of LSM mucilage

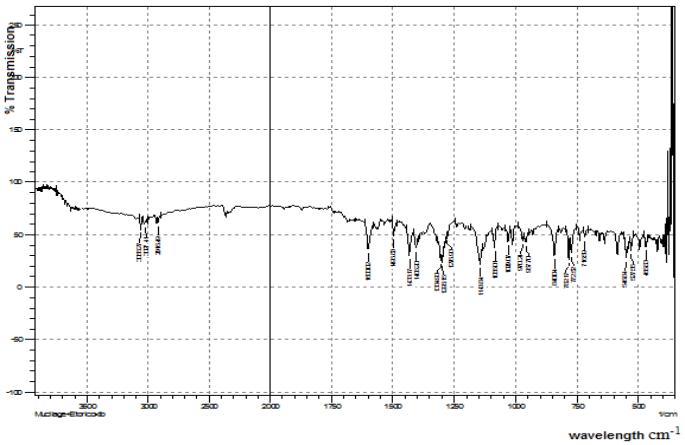

Fig. 1c: IR spectrum of Etoricoxib+LSM

Evaluation of flow properties

Lepidium sativum mucilage was investigated as a binder in tablet prepared by wet granulation method and its binding property was compared with established binder such as Starch, PVP K-30. The flow properties of the prepared granules [wet granulation] using LSM as tablet binder was studied and results are shown in Table 3. Angle of repose, Carr's index, and hausner ratio were selected as the flow indicating parameters.

They reflect the effect of bulk density, particle size, surface characters and moisture content of the powder flow [29]. Angle of repose of all formulation was found to between 29.70 to 30.52, bulk density in the range of 0.42 to 0.52, tapped density between 0.58 to 0.65, Carr's index% in range of 13.37 to 20.47, hausner ratio between 1.04 to 1.18. The above result shows that the prepared granules exhibited good flow property. LSM mucilage as tablet binder in direct compression method were evaluated and compared with established binder such as HPMC, PVP K-30, and MCC. Table 4 shows the results of evaluation of pre compression properties. Angle of repose of all the formulations was found to be in the range of 22.21 to 23.55. Bulk density in the range of 0.42 to 0.73 g/cc, tapped density between 0.82 to 0.95 g/cc, Carr's index in the range 18.61 to 24.69 %. Hausner ratio between 1.22 to 1.32. Indicating fair to passable flow properties for all the powder mixtures. Result indicated that use of LSM as a binder does not affect the flow property of powder.

Table 3: Pre compression parameters of granules B1-B5

S. No.	Formulation code	Angle of repose (θ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index %	Hausner Ratio
1.	B1	30.04±0.47	0.52±0.02	0.65±0.02	19.72±0.68	1.18±0.8
2.	B2	29.70±0.58	0.48±0.01	0.63±0.05	14.89±0.11	1.12±0.01
3.	B3	29.70±0.58	0.47±0.04	0.58±0.03	13.37±0.49	1.14±0.01
4.	B4	30.52±0.91	0.44±0.12	0.62±0.10	13.74±0.25	1.04±0.04
5.	B5	30.43±0.93	0.42±0.11	0.54±0.11	20.47±0.77	1.14±0.02

Table 4: pre compression parameter of powder D1-D5

S. No.	Formulation code	Angle of repose (θ)	Bulk density p_b (g/cm^3)	Tapped density p_T(g/cm^3)	Carr's index %	Hausner Ratio
1.	D1	22.38±0.8	0.42±0.04	0.825±0.06	23.97±0.7	1.22±0.4
2.	D2	23.17±0.2	0.69±0.02	0.92±0.03	24.69±0.4	1.32±0.02
3	D3	23.55±0.07	0.71±0.03	0.91±0.02	21.21±0.2	1.23±0.05
4	D4	23.2±0.5	0.71±0.02	0.91±0.02	18.61±0.5	1.23±0.05
3.	D5	22.21±0.2	0.73±0.01	0.95±0.03	24.08±0.4	1.31±0.01

Each value represent the mean ± standard deviation (n=3)

Post compression properties

After evaluation of pre compression parameters, tablets were compressed using rotary 12 station tablet machine (CEMACH). Compressed tablets were then evaluated for physical parameters like hardness, thickness, weight variation, friability. Post compression properties of formulated tablets using natural and synthetic binders as standard are shown in Table 5 and Table 6.

Average weight of tablets was found to be in the range of 302-304 mg. For all batches % deviation was observed within the limit. The average thickness of formulated tablet was found to be in the range of 4.15-4.36 mm within the limit. The friability values increases with decrease in binder concentration of LSM in both wet granulation and direct compression method as shown in Fig. 2 and Fig. 3. But over all friability values were less than specified limits (1%) which indicate tablets can withstand the mechanical shock during handling.

Table 5: Post compression parameter of the tablet formulation B1-B

S. No.	Formulation Code	Thickness (mm)	weight variation (mg)	Disintegrating time
1.	B1	4.26±0.09	304±0.04	1 min35 sec
2.	B2	4.34±0.07	304±0.04	1 min52 sec
3.	B3	4.31±0.08	303±0.06	1 min55 sec
4.	B4	4.29±0.09	304±0.08	1 min40 sec
5.	B5	4.36±0.06	302±0.07	1 min33 sec

Each value represent the mean ± standard deviation (n=3)

Table 6: post compression parameters of tablet formulation D1-D2

S. No.	Formulation Code	Thickness (mm)	Weight variation (mg)	Disintegrating time
1.	**D1**	4.29±0.03	301±0.05	8 min 16 sec
2.	**D2**	4.28±0.06	304±0.08	5 min 25 sec
3.	**D3**	4.16±0.04	303±0.07	16 min 20 sec
4.	**D4**	4.24±0.12	304±0.05	15 min 50 sec
5.	**D5**	4.15±0.8	302±0.06	6 min 10 sec

Each value represent the mean ± standard deviation (n=3)

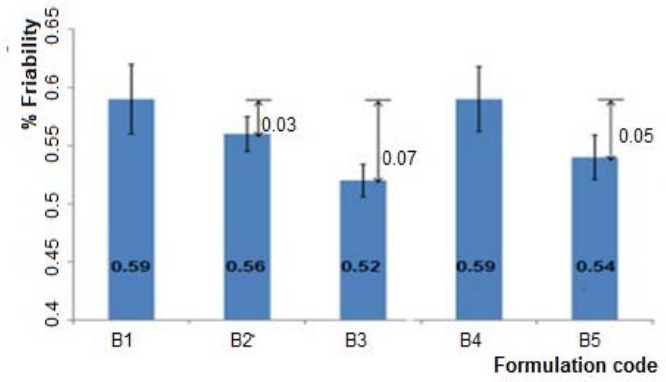

Fig. 2: Effect of binder on friability of tablet by wet granulation method.

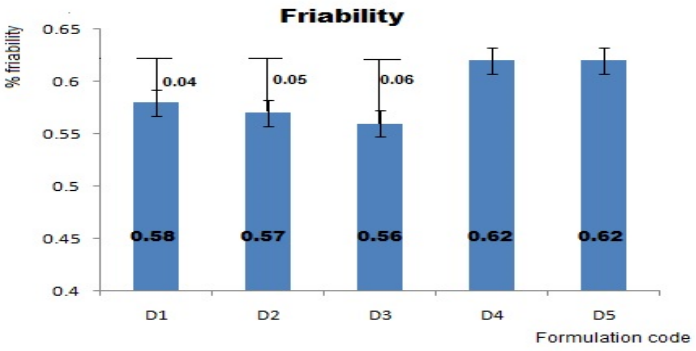

Fig. 3: Effect of binder on friability of tablet by direct compression method.

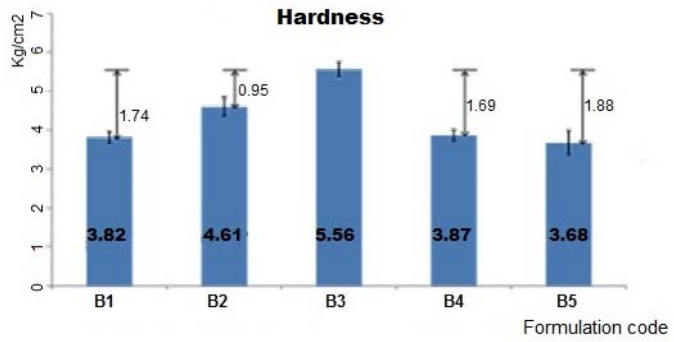

Fig. 4: Effect of hardness of tablet prepared by wet granulation method.

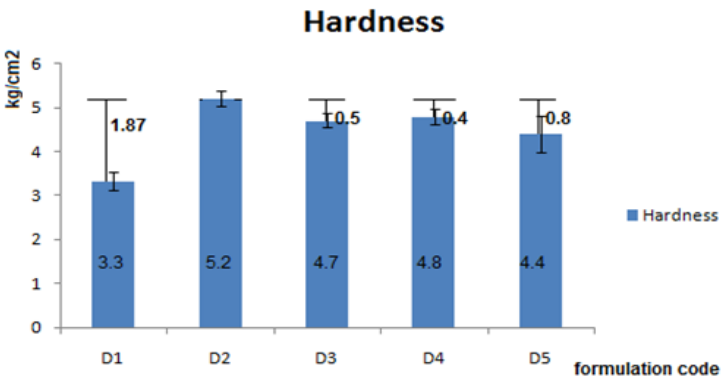

Fig. 5: Effect of binder on hardness of tablet prepared by direct compression method

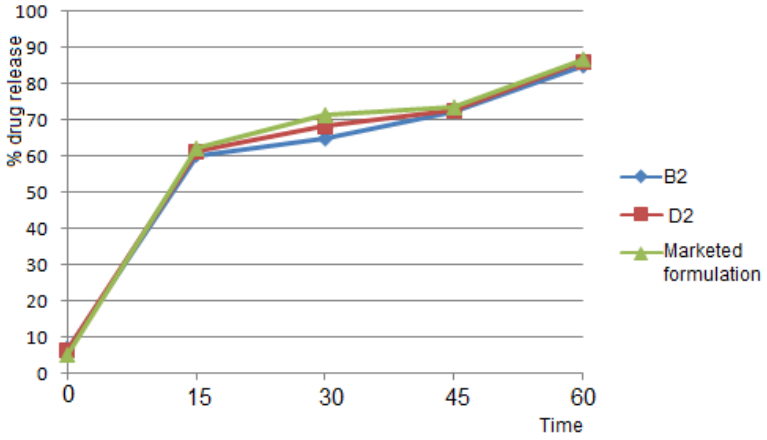

Fig. 6: *In- vitro* drug release of Etoricoxib B2, D2 and marketed tablet.

Hardness of tablets

The hardness of the tablet formulated by wet granulation method varies between 3.68-5.56 kg/cm^2. The hardness of the tablet increases with increase in percentage of LSM binding agent. Result shows that LSM binder is more effective binder compared to starch and PVP-K30. Also the amount of LSM binding solution required is comparatively less than other binder due to its viscous and sticky nature. LSM was used as a dry binder in formulation. The hardness of the tablet varies between 3.33-5.2 kg/cm^2. Hardness observed in formulation was acceptable and comparatively better hardness than HPMC, PVP- K30, MCC was observed as shown in Fig.4. The binder property of LSM mucilage in direct compression method was found less and required in more concentration than binding property of mucilage used in wet granulation method shown in Fig. 5. This may be due to the viscous and colloidal solution formed when mucilage was dispersed in water which enhances its binding property in the wet granulation.

***In-vitro* disintegration test**

As per IP monograph the disintegration time for uncoated tablet must be within 15 min. Disintegrating time for tablet formulated by wet granulation varied from 33 to 55 sec (Table 5). Whereas in direct compression tablet formulation disintegrating time for tablet without disintegrating agent varied from 4 min 10 sec to 5 min 25 sec. (Table 6) i. e. fast disintegration of tablets was observed when LSM mucilage was used as binder in dry state at 4% concentration. The result indicates that the LSM mucilage have ability to act as binder as well as disintegrating agent when used in dry state.

***In- vitro* dissolution profile**

The *in -vitro* dissolution profiles of Optimized 2% LSM mucilage as tablet binder tablet prepared by wet granulation technique and optimized 4% LSM mucilage as tablet binder in direct compression method were compared with that of marketed 120 mg Etoricoxib tablet. In vitro dissolution studies on the formulation were carried out in 0.1 N HCl. The dissolution profile is depicted in Fig. 6. From the result it was observed that above 80 % of drug was released in 60 min.

Accelerated stability study

Accelerated stability studies were carried out as per ICH guidelines. Optimized Formulation B2 and D2 did not show the change in color, texture and other physical parameters of tablet during the study period. This indicates that the prepared tablets are stable at accelerated storage conditions.

CONCLUSION

From the result, it can be concluded that *Lepidium sativum* mucilage is less susceptible to microorganism hence had the good shelf life and can be extracted easily by simple cost effective method with good % yield. LSM can be used as a binding agent in tablet formulation 2% concentration in wet granulation and 4% in direct compression for the preparation of uncoated tablets. Also the binding property increased and friability decreased with increase in concentration of LSM mucilage.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

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