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Original Article

Investigating the Potential of *Lepidium sativum* Seed Mucilage as Binder in Tablet Formulation

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ABSTRACT

Introduction: The demand for natural excipients in pharmaceuticals has driven interest in plant-based materials. *Lepidium sativum* seed mucilage, a polysaccharide-rich and biocompatible compound, shows promise as a tablet binder for controlled drug delivery. This study evaluates its potential and optimization in tablet formulations. **Objectives:** This study aimed to assess *Lepidium sativum* seed mucilage as a natural binder, optimizing tablet formulations for pre- and post-compression parameters, drug release behavior, and release mechanisms. **Materials and Methods:** Mucilage was extracted and confirmed via FTIR spectroscopy. A Central Composite Design (CCD) optimized formulations based on pre-compression (bulk density, tapped density, angle of repose) and post-compression (hardness, friability, disintegration, drug content) parameters. *In vitro* dissolution studies assessed drug release, while kinetic modeling identified release mechanisms. **Results:** Batch F8 exhibited superior flow properties, uniformity, and high drug content. It's *in vitro* dissolution study showed 95.46% drug release over 12 hr, outperforming other formulations. Kinetic analysis confirmed a Higuchi model release, indicating diffusion-controlled drug release. Stability studies confirmed the robustness of the optimized formulation, establishing the potential of *Lepidium sativum* mucilage as a scalable, natural excipient for pharmaceutical applications. **Conclusion:** *Lepidium sativum* seed mucilage demonstrated excellent binding properties, supporting its role as a natural excipient for controlled drug delivery. Its potential for scalability and stability warrants further investigation.

Keywords: *Lepidium sativum*, Mucilage, QbD, DOE, Controlled Drug Delivery.

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INTRODUCTION

Binders, also known as granulators, are essential agents in the pharmaceutical industry, employed to impart cohesive qualities to powdered materials. (Bhattacharya *et al*., 2019) These agents ensure the structural integrity of tablets post-compression and enhance their free-flowing characteristics by forming granules of the preferred hardness and size (Ibezim *et al*., 2000) By improving the cohesiveness of tablet formulations, binders show a pivotal character in confirming the quality in addition to efficacy of pharmaceutical products (Kozakiewicz-Latała *et al*., 2022). Among the various natural and synthetic substances used as binders, mucilages have gained significant attention because of their multifunctional properties and natural origin (Tosif *et al*., 2022).

Mucilages are complex polysaccharides, classified as polyuronides, composed of sugar and uronic acid units (Shiam *et al*., 2025). These substances are derived from plant cell walls or are deposited on the cell walls' outer layers. In the presence of water, mucilages swell and form sticky, viscous solutions (Tekeshwar Kumar *et al*., 2012) This unique property has led to their utilization in various pharmaceutical applications. They enhance viscosity, stabilize, disintegrate, solubilize, emulsify, suspend, gel, and adhere bio actively (Tiwari and Kulmi, 2004). Mucilages are effective in numerous pharmaceutical forms like controlled-release systems, coatings, films, microspheres, nanoparticles, ophthalmic solutions, suspensions, and implants (Kamble *et al*., 2012). These plant-based materials' versatility and efficiency have positioned them as invaluable components in modern pharmaceutics (Layas *et al*., 2021).

Among the numerous sources of mucilages, plant-based materials have gained prominence because of their biocompatibility, biodegradability, and abundance. One such plant with immense potential in pharmaceutical applications is *Lepidium sativum*, commonly known as garden cress (Subodhkant *et al*., 2021). Garden cress, an annual herb of the Brassicaceae family, is fast-growing and shares a peppery flavor with watercress and mustard. While its seeds are the primary yield, its leaves and roots are also economically significant (Dhingra *et al*., 2021).

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Garden cress is widely known by different names across regions, for example garden pepper cress, pepper grass, or pepperwort. In India, it is referred to as asalio or chandrasur and holds an esteemed position as an important medicinal crop. This versatile plant is also valued as a green vegetable, typically consumed as a garnish or leaf vegetable, further emphasizing its nutritional and economic importance. Garden cress is not only a culinary ingredient but also a powerhouse of medicinal properties (Mali *et al*., 2022).

The pharmacological activities of garden cress are well-documented, showcasing its therapeutic potential. It exhibits a range of properties, including anti-asthmatic, antiscorbutic, aperient, diuretic, stimulant, chemoprotective, anti-diabetic, and anti-hypertensive effects. Additionally, the plant has demonstrated remarkable activities in fracture healing, hepatoprotection, pesticidal action, and antidiarrheal effects. These diverse therapeutic properties highlight the plant's potential in treating various medical conditions and underscore its significance in traditional and modern medicine (Subodhkant *et al*., 2021; Dhingra *et al*., 2021; Mali *et al*., 2022).

The seeds of *Lepidium sativum*, in particular, have garnered attention for their mucilaginous properties. When exposed to water, the seeds form a viscous gel, which can be harnessed as a natural binder in pharmaceutical formulations. The mucilage extracted from garden cress seeds compromises an economical, sustainable, and biocompatible substitute in the direction of synthetic binders. Moreover, its ability in the direction of enhances the mechanical strength of tablets while ensuring rapid disintegration and dissolution makes it an ideal candidate for use in various pharmaceutical products (Dhingra *et al*., 2021).

Beyond its binding properties, garden cress mucilage can function as a stabilizer, emulsifier, and viscosity enhancer. These attributes have been leveraged in the formulation of ophthalmic solutions, suspensions, and other viscous liquid formulations. Furthermore, its bioadhesive properties make it suitable for applications in buccal films and other mucoadhesive drug delivery systems. The plant's mucilage has also been incorporated into advanced drug delivery systems, for example microspheres and nanoparticles, further expanding its scope in pharmaceutical research and development (Mali *et al*., 2022).

This mucilage has emerged as a promising natural excipient in therapeutic preparations. Studies have presented its potential as a binder in granulation, producing granules with good flow and mechanical properties comparable to synthetic binders like PVP (Layas *et al*., 2021). The mucilage, extracted by precipitation in acetone, forms a transparent gel around the seed when soaked in water and consists mainly of polysaccharides (Subodhkant *et al*., 2021). It has demonstrated excellent disintegrant properties in tablet formulations, with tablets disintegrating in as little as 25 sec (Dhingra *et al*., 2021). The seeds yield a high mucilage content of 12.5% w/w, making them an attractive source for pharmaceutical applications (Dhingra *et al*., 2021). Beyond its excipient properties, L. sativum seeds possess various pharmacological activities, including anticarcinogenic, antidiabetic, and antidiarrheal effects, attributed to their rich nutritional profile and bioactive compounds (Mali *et al*., 2022).

Various seed mucilages have been studied for their binding properties. For instance, M. Kamble investigated the binding potential of *Ocimum tenuiflorum* mucilage (Waghmare *et al*., 2012), A. Waghmare examined flaxseed mucilage (Patel *et al*., 2011), and N. Patel explored *Cydonia vulgaris* mucilage (Ghule *et al*., 2006), Additionally, the binding properties of *Eulophia campestris* (Selvi *et al*., 2010), *Prosopis juliflora* (Selvi *et al*., 2010), and other plant-based polymers have also been estimated. However, there remains a need for plant-derived polymers that are safer, more stable, cost-effective to produce, and capable of providing superior binding properties at lower concentrations (Panda and Suryawanshi, 2023; Gupta *et al*., 2023; Rajkule *et al*., 2020). Notably, no substantial research has been conducted on mucilage used as a binder for tablet preparation. Therefore, this investigation aims in the direction of analyzing the binding properties of *Lepidium sativum* seed mucilage (LSM) by formulating tablets utilizing the wet granulation and direct compression methods.

MATERIALS AND METHODS

Materials

Lepidium sativum seeds were sourced locally in Nagpur, Maharashtra, and authenticated by Dr. N. M. Dongarwar, Department of Botany, RTMNU, Maharashtra (specimen no. 9890). A voucher specimen was deposited in the department. Risperidone was gifted by ZIM Laboratories, Nagpur, and all other materials were of analytical grade.

Methods

Extraction of Mucilage from seeds

10 g of seeds were soaked in 80 mL of distilled water for 24 hr and then blended at about 2000 rpm. The mixture was filtered utilizing muslin cloth, after which 20 mL of water was added to the residue, re-blended, and filtered again to maximize yield. To precipitate the mucilage, 80 mL of acetone was added to the filtrate. The resulting white coagulant mass was separated and filtered through muslin cloth. The precipitated mucilage was dried in a tray dryer at temperatures below 60°C, ground into powder utilizing size reduction, and sieved through an 80# sieve. The percentage yield was estimated, FTIR analysis was performed (Panda and Suryawanshi, 2023).

Tablet formulation

Risperidone tablets using *Lepidium sativum* seeds extract was developed by direct compression method. All ingredients were

weighed accurately. Risperidone, LSM mucilage, MCC, and lactose were co-sifted through #40 and blended together for 15 min for uniform mixing. Talc was sifted through #40 sieve and added to previous mixture and blended for 5 min. Finally, magnesium stearate was passed through #60 sieve and added to pre lubricated blend and blended for 3 min to get lubricated blend. The tablets were compressed at 250 mg weight and used for further analysis.

Experimental design: Central Composite Design (CCD)

Design Expert® (Version 13.0) was used to implement a CCD with three independent variables: LSM mucilage (mg) (A), Lactose (mg) (B), and Magnesium stearate (%) (C). The dependent variables were Hardness, Thickness, and Drug release. The CCD, comprising factorial, center, and axial points, included 9 runs. Details are in Table 1.

Estimation of Tablets

Pre-compression Parameters

Before compressing the powder into tablet form, pre-compression studies were conducted to assess the quality of the granules.

Angle of repose

The angle of repose (θ) was evaluated to measure the frictional forces in the loose granules. For this, a funnel was placed 2-4 cm above a graph sheet, and the granules were permitted to flow freely under gravity, forming a cone. The height (h) and radius (r) of the cone were estimated, and the θ was estimated utilizing the formula:

$$\text{Tan } \theta = h/r;\ \theta = \tan^{-1}(h/r) \text{ ----- (1)}$$

Bulk Density

The Bulk Density (BD) of the granules was determined by transferring 25 g of granules, earlier passed through a 22# sieve, into a 100 mL graduated cylinder. The granules were leveled without compaction, and the apparent volume (V_0) was recorded. BD was estimated utilizing the formula:

$$BD = M/V_0 \text{ ----- (2)}$$

M = Mass of the granules; V_0 = Bulk volume.

Tapped Density

Tapped Density (TD) was measured by placing 25 g of granules into a graduated cylinder fitted to a tap density tester. The tester was operated until the granule volume stabilized, and the TD was estimated utilizing the formula:

$$TD = M/V_t \text{ ----- (3)}$$

M = Mass of the granules; V_t = Tapped volume.

Carr's Index

Carr's Index (CI) was used to evaluate the compressibility of the granules by comparing bulk and tapped densities. It was estimated utilizing formula:

$$CI = [(TD - BD)/TD] \times 100 \text{ ------ (4)}$$

This index helps categorize the flow character of the granules, with lower values indicating better flowability.

Hausner's ratio

Hausner's ratio, an indirect measure of powder flow ease, was determined utilizing the formula (Panda and Suryawanshi, 2023).

$$\text{Hausner's Ratio} = TD/BD \text{ ---- (5)}$$

Table 1: Experimental and DOE Suggested batches.

Formulation code	Risperidone (mg)	A: LSM mucilage's (mg)	B: Lactose (mg)	C: Magnesium stearate (%)	MCC (mg)	Talc (mg)
F1	4	20	150	1	69.5	4
F2	4	20	150	2.5	64.75	4
F3	4	20	175	2.5	36.75	4
F4	4	130	100	2.5	5.75	4
F5	4	20	175	1	44.5	4
F6	4	120	110	1	9.5	4
F7	4	110	101	2.5	24.75	4
F8	4	70	162.5	1.75	5.5	4
F9	4	90	100	1	49.5	4
F10 Tablet without Mucilage	4	70 (HPMC 750)	162.5	1.75	5.5	4

Post-compression Parameters

General appearance

The formulated tablets were evaluated for general appearance, including shape, color, and texture.

Weight Variation test

20 tablets were weighed collectively and individually to determine the average weight. Individual weights were compared to the average, ensuring no more than two deviated by over 5% for tablets above 324 mg (Panda and Suryawanshi, 2023).

Thickness

Thickness of the tablets (n=3) was determined utilizing a Vernier Calliper.

Hardness test

Tablet hardness was tested utilizing a Monsanto hardness tester (n=3). The lower plunger contacted the tablet, and the force needed to break it was measured on a gauge as the spring compressed (Gupta *et al*., 2023).

Friability test

The friability test assesses a tablet's resistance to abrasion during handling. Twenty tablets are weighed, placed in a Friabilator rotating at 25 rpm for 4 min, and the weight loss is measured as a percentage. Acceptable loss is typically amongst 0.5% and 1.0%.

$$\%\text{Friability} = [(W1-W2)/W1] \times 100 \text{ --- (6)}$$

Where, W1= weight of tablets before test, W2 = weight of tablets after test.

Table 2: Responses on Suggested batches.

Formulation code	Y1: Hardness	Y2: Thickness	Y3: %CDR
F1	2.82±0.67	5.7±0.04	91.00±1.5
F2	2.78±0.73	5.3±0.05	93.25±1.6
F3	2.68±0.79	4.9±0.07	92.45±1.4
F4	2.69±0.89	5.2±0.03	79.13±2.1
F5	2.53±0.90	5.5±0.05	78.34±1.7
F6	3.2±0.77	4.8±0.03	83.14±1.9
F7	2.72±0.78	5.1±0.05	83.14±1.6
F8	2.35±0.80	4.2±0.03	95.46±1.8
F9	3.55±0.82	5.8±0.03	93.14±1.4
F10	3.64±0.83	5.7±0.02	81.56±1.7

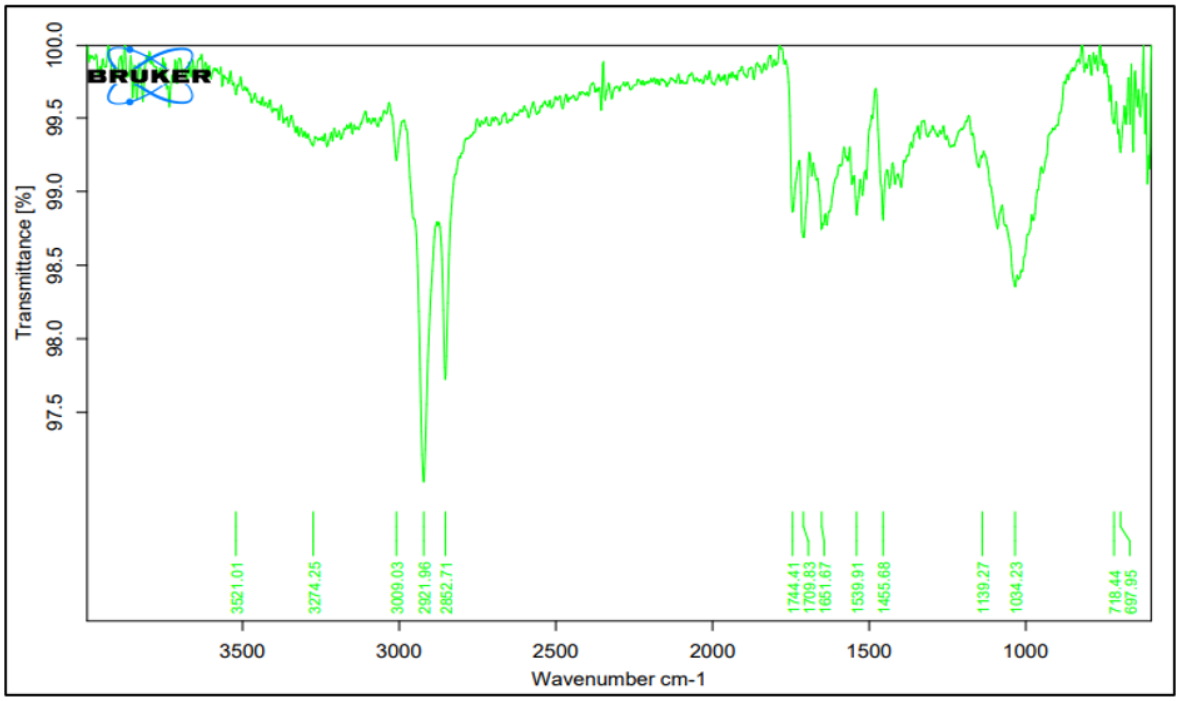

Figure 1: FTIR spectrum of Mucilage from *Lepidium sativum* seeds.

Disintegration test

The disintegration time of tablets was measured utilizing a disintegration apparatus. 3 tablets were placed, and the time for complete disintegration at 37°C was recorded (Rajkule *et al*., 2020).

Drug content of tablet

Two tablets were weighed, crushed, and a 250 mg risperidone equivalent was dissolved in 100 mL phosphate buffer (pH 6.8). The absorbance was measured at 280 nm utilizing a UV spectrophotometer (Panda and Suryawanshi, 2023).

In vitro Dissolution and Kinetics Study

Dissolution studies for batches F1-F9 followed USP guidelines, utilizing 900 mL of phosphate buffer (pH 6.8) at 50 rpm. Samples were collected at 1, 2, 6, 8, and 12 hr, and drug release was measured by absorbance at 280 nm utilizing UV spectrophotometry (Rajkule *et al*., 2020).

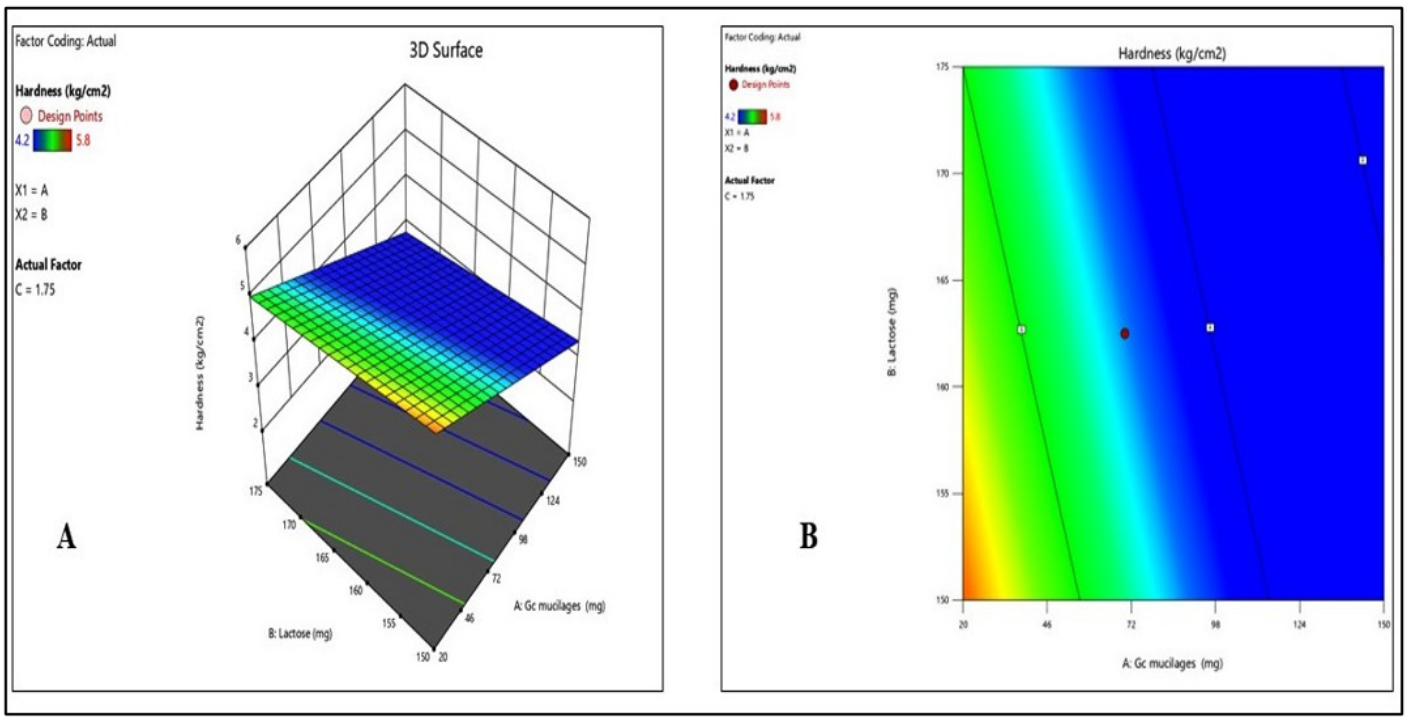

Figure 2: (A):3D surface of Hardness; B: Counter plot of Hardness.

Table 3: ANOVA of Hardness, Thickness and %CDR.

Source	Sum of Squares	d_f	Mean Square	F-value	*p*-value	
ANOVA of Hardness (Y1)						
Model: Linear	1.54	3	0.5125	6.06	0.0404	Significant
A-Gc mucilage	1.24	1	1.24	14.67	0.0122	
B-Lactose	1.24	1	1.24	14.73	0.0121	
C-Magnesium stearate	0.1258	1	0.1258	1.49	0.2768	
ANOVA of Thickness (Y2)						
Model: 2FI	1.02	6	0.1706	55.15	0.0179	Significant
A-Gc mucilage	0.1112	1	0.1112	35.95	0.0267	
B-Lactose	0.3575	1	0.3575	115.54	0.0085	
C-Magnesium stearate	0.0000	1	0.0000	0.0114	0.9246	
ANOVA of %CDR (Y3)						
Model: 2FI	337.42	6	56.24	24.99	0.0390	Significant
A-Gc mucilage	37.00	1	37.00	16.44	0.0558	
B-Lactose	17.45	1	17.45	7.75	0.1084	
C-Magnesium stearate	60.65	1	60.65	26.94	0.0352	

Stability Study

The stability of risperidone tablet was monitored up to 90 days at ambient temperature and relative humidity (40ºC/75%RH). Periodically samples were withdrawn and characterized by Thickness, Hardness and % Dissolution (Panda and Suryawanshi, 2023; Gupta *et al*., 2023; Rajkule *et al*., 2020).

RESULTS AND DISCUSSION

Extraction of Mucilage from seeds

The % yield of Mucilage from seeds was found to be 5.25%.

Organoleptic studies

Powder of blend was found to be off-white.

FTIR Spectroscopy

The FTIR spectrum of mucilage indicates its polysaccharide composition through key functional groups. The broad band at 3200-3600 cm^{-1} reflects Hydroxyl (-OH) groups with hydrogen bonding, while peaks at 2900-2950 cm^{-1} match up to C-H stretching. The band at 1650-1750 cm^{-1} suggests C=O stretching of carboxyl or ester groups, indicating uronic acids. Peaks at

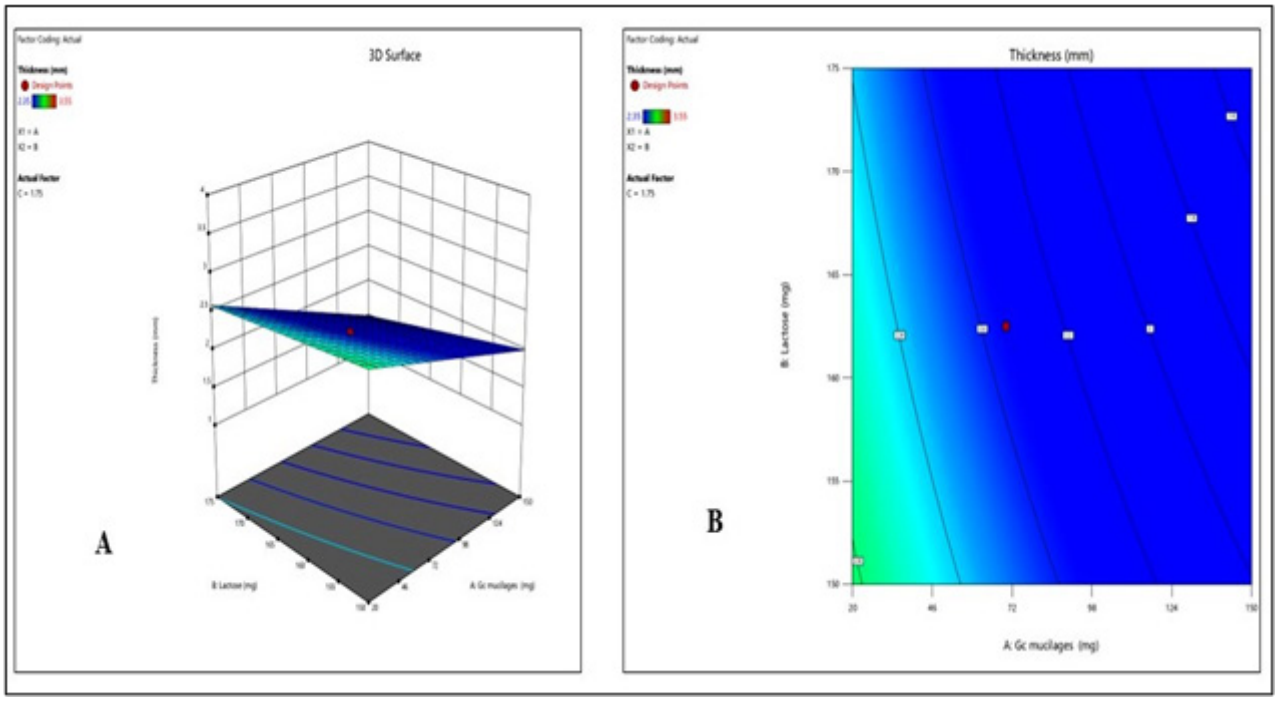

Figure 3: (A):3D surface of Thickness; B: Counter plot of Thickness.

Table 4: Cumulative drug release (F1-F9).

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	7.15±0.01	6.15±0.02	5.96±0.03	5.52±0.03	6.03±0.31	6.96±0.2	6.96±0.03	15.15±0.01	10.4±0.02
2	16.58±0.02	12.37±0.01	12.5±0.41	11.27±0.05	11.19±0.03	15.88±0.03	15.88±0.14	28.01±0.02	26.65±0.01
3	28.84±0.02	24.12±0.0005	22.24±0.12	21.46±0.06	24.69±0.01	34.82±0.36	34.82±0.34	32.46±0.02	38.84±0.13
4	39.47±0.05	37.45±0.123	35.31±0.03	30.66±0.12	34.56±0.05	40.35±0.01	40.35±0.65	48.27±0.01	48.6±0.01
5	57.51±0.01	44.33±0.514	39.78±0.005	38.79±0.01	39.78±0.01	56.74±0.02	56.74±0.09	54.27±0.04	59.57±0.02
6	68.74±0.05	48.98±0.03	46.94±0.01	41.23±0.05	42.36±0.05	63.44±0.01	63.44±0.07	62.27±0.514	62.46±0.05
8	74.22±0.11	51.47±0.04	60.49±0.06	49.87±0.04	49.87±0.14	64.56±0.05	64.56±0.01	70.13±0..036	69.78±0.06
9	76.3±0.005	70.71±0.01	69.84±0.03	51.14±0.01	53.49±0.63	70.16±0.01	70.16±0.05	75.16±0.02	76.36±0.03
10	82.15±0.12	79.95±0.005	78.49±0.12	59.13±0.05	59.77±0.31	74.13±0.14	74.13±0.01	80.16±0.014	79.84±0.01
11	89.75±0.03	86.74±0.01	84.45±0.065	69.48±0.23	68.99±0.01	79.29±0.21	79.29±0.03	88.76±0.02	87.46±0.01
12	91±0.02	93.25±0.012	92.45±0.06	79.13±0.01	78.34±0.02	83.14±0.05	83.14±0.01	95.46±0.03	93.14±0.05

Value are expressed as mean±std.

Table 5: Stability study of parameters of the optimized formulation (F8).

Parameters	Initial Month	1st Month	2nd Month	3rd Month
Thickness (mm)	2.3±0.04	2.1±0.02	2.2±0.06	2.2±0.01
Hardness	4.2±0.03	4.0±0.01	4.2±0.04	4.3±0.08
Dissolution (%)	95.46±0.01	95.58±0.07	96.14±0.09	95.96±0.08

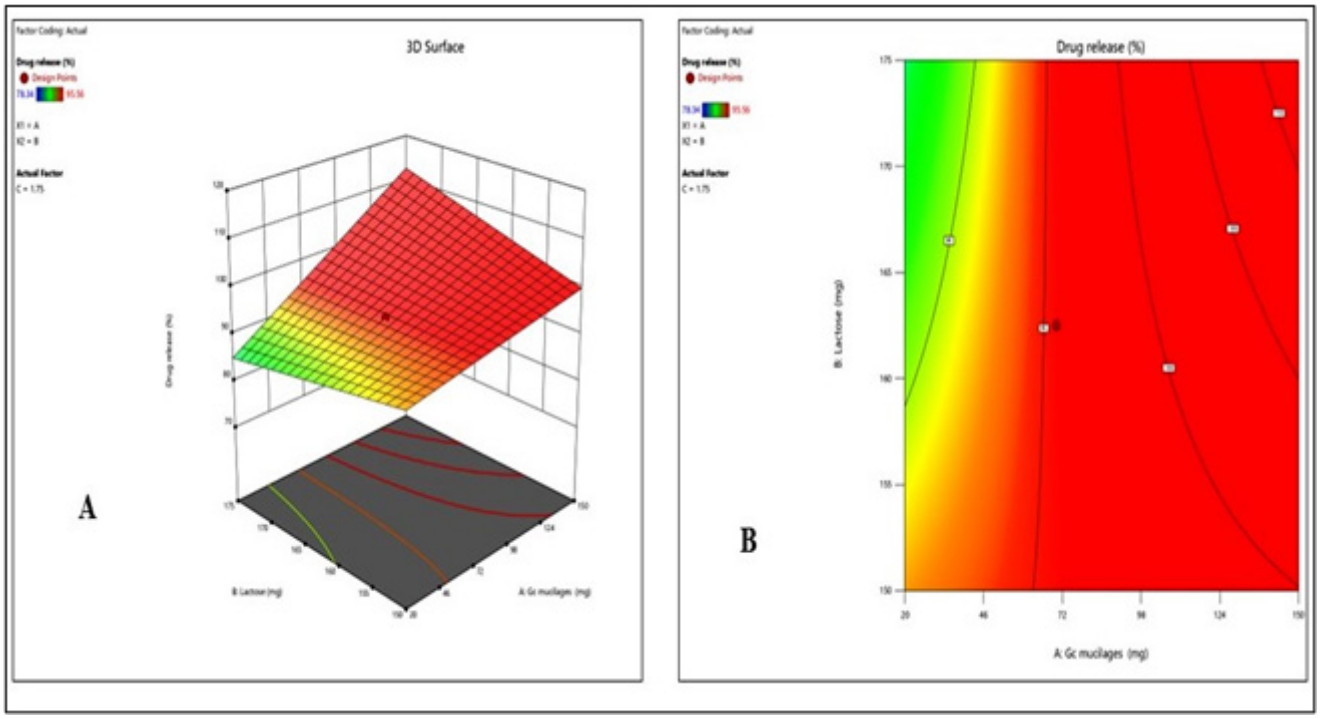

Figure 4: (A):3D surface of %CDR; B: Counter plot of %CDR.

1400-1450 cm^{-1} and 1200-1300 cm^{-1} denote C-H bending and C-O stretching, correspondingly, while intense signals at 1000-1200 cm^{-1} confirm glycosidic linkages. These features highlight its bioactive and physicochemical potential as presented in Figure 1.

Formulation Design

Table 2 exhibited responses on suggested batches by CCD design.

Statistical analysis of Hardness (Y1)

Table 3 and Figure 2 (A&B) showed effects of independent variables on response Y1.

The polynomial equation for tensile strength (Y1) can be presented below

$$Y1 = +4.20 - 1.11^{*}A - 0.3088^{*}B - 0.1261^{*}C \ldots\ldots\ldots\ldots (1)$$

Statistical analysis of Thickness (Y2)

Table 3 and Figure 3 (A&B) showed effects of independent variables on response Y2.

The polynomial equation for DR (Y2) can be presented below:

$$Y2 = +2.23 - 0.4776^{*}A - 0.1848^{*}B - 0.0079^{*}C - 0.0719^{*}AB - 0.0321^{*}AC + 0.0705^{*}BC \ldots\ldots\ldots\ldots (2)$$

Statistical analysis of %CDR (Y3)

Table 3 and Figure 4 (A&B) showed effects of independent variables on response Y3.

The polynomial equation for DR (Y3) can be presented below:

$$Y3 = +97.56 + 8.71^{*}A + 1.29^{*}B + 10.38^{*}C + 5.08^{*}AB + 6.24^{*}AC + 2.79^{*}BC \ldots\ldots (3)$$

Evaluation of Tablets

Pre-compression Parameters

Pre-compression studies assessed the granules' quality, including angle of repose, bulk density, tapped density, and compressibility index. F8 showed good flow properties, while other batches had fair flow. F8 formulation showed BD of 0.39±0.05 g/mL, TD of 0.43±0.04, CI of 9.30±0.04%, HR of 1.10±0.04 and angle of repose of 29.99±0.95 θ. In rest of the batches BD was varied from 0.39±0.02 to 0.40±0.05 g/mL, TD from 0.43±0.01 to 0.43±0.06 g/mL, CI from 0.04±0.07 to 9.30±0.05%, HR from 1.04±0.07 to 1.15±0.03 and angle of repose from 27.42±0.87 to 31.93±0.58 θ.

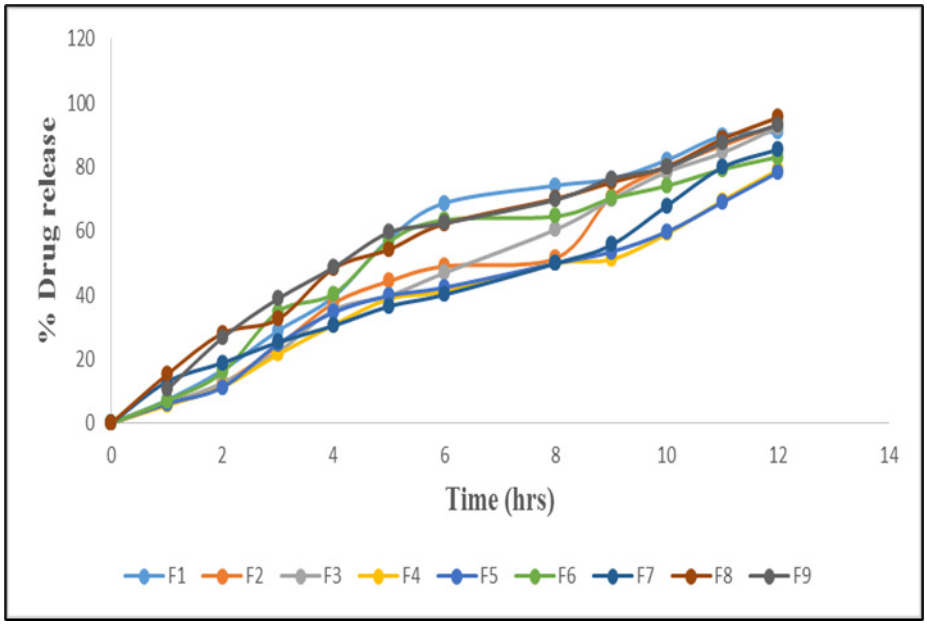

Figure 5: Cumulative drug release (F1-F9).

Post-compression Parameters

General appearance

The tablets were evaluated for appearance, showing a round shape, off-white color, and smooth texture. F8 optimised formulation showed weight variation of 0.43±0.15%, thickness of 2.35±0.44 mm, Hardness of 4.2±0.17 Kg/cm^2, friability of 0.21±0.19% and drug content of 98.77±0.15%. In rest of the batches Weight variation was found between 0.44±0.20 to 0.89±0.10%, thickness from 2.53±0.03 to 3.64±0.40 mm, Hardness from 4.8±0.12 to 5.8±0.16 Kg/cm^2, friability from 0.22±0.14 to 0.84±0.12% and drug content was varied from 90.08±0.11 to 94.44±0.19%.

In vitro Dissolution Study

The drug release profile of batch F8, reaching 95.56% within the 12-hr period, signifies its exceptional performance compared to the other batches tested. This achievement demonstrates batch F8's superior ability to release the drug compound within the specified timeframe, surpassing the drug release rates of the other batches. Consequently, batch F8 emerges as the leading candidate for pharmaceutical formulations, indicating its potential for efficient drug delivery as presented in Table 4 and Figure 5.

Kinetic Study

In vitro release data for optimized batch (F8) was analyzed utilizing zero-order, first-order, and Higuchi models. The Higuchi model provided the best fit, as shown by the highest R^2 value (0.9776).

Stability Study

The optimized tablets were subjected to stability studies and the results are given in Table 5. Based on these results it is revealed that, tablets (Formulation batch F8) were found to be stable formulation at the given temperature and humidity condition.

CONCLUSION

The successful extraction of mucilage from *Lepidium sativum* seeds yielded 5.25%, with FTIR analysis confirming its polysaccharide composition. Optimization studies using a Central Composite Design (CCD) identified batch F8 as the most effective formulation, demonstrating superior pre-compression and post-compression characteristics, including excellent flow properties, content uniformity, and high drug loading. *In vitro* dissolution testing revealed that batch F8 achieved 95.46% cumulative drug release over 12 hr, outperforming other formulations. Kinetic modeling indicated that drug release followed the Higuchi model, suggesting a diffusion-controlled mechanism. These findings highlight the potential of *Lepidium sativum* mucilage as a promising pharmaceutical excipient for controlled drug delivery applications.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

LSM: *Lepidium sativum* Mucilage; **BD:** Bulk Density; **TD:** Tapped Density; **CI:** Carr's Index; **CCD:** Central Composite Design; **(θ):** Angle of Repose.

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