



DEVELOPMENT AND OPTIMIZATION OF KETOPROFEN FAST DISSOLVING TABLETS USING PLANTAGO OVATA HUSK MUCILAGE AS A NATURAL SUPERDISINTEGRANT EMPLOYING BOX-BEHNKEN DESIGN

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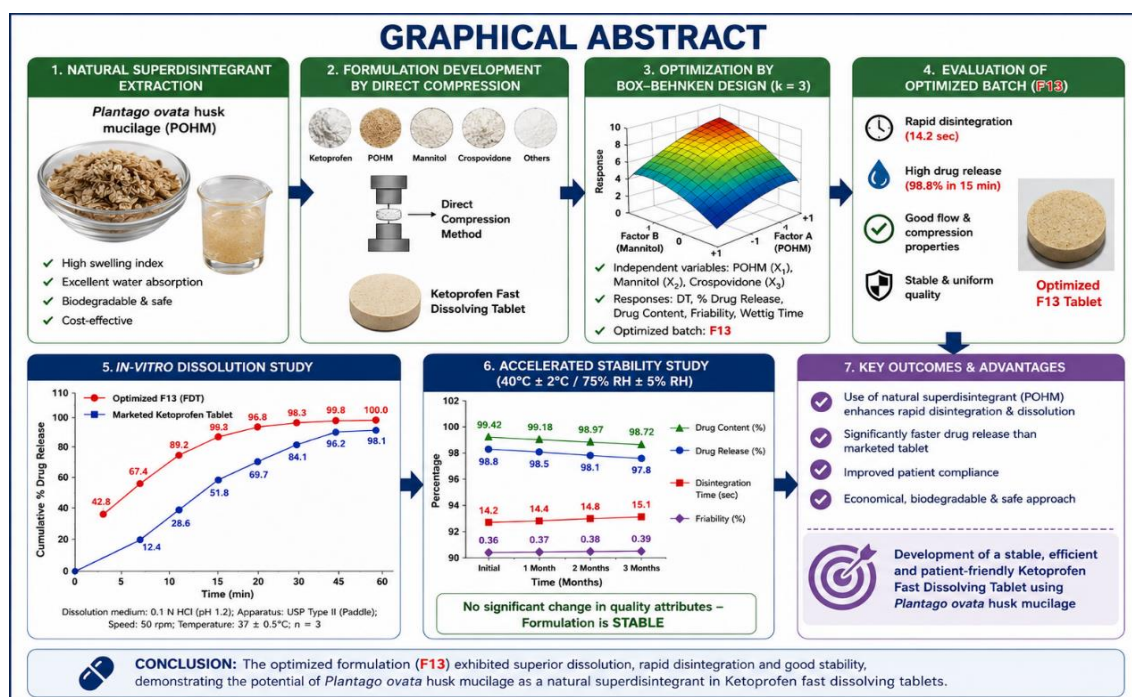
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ABSTRACT

Fast dissolving tablets (FDTs) have emerged as an effective oral drug delivery system designed to improve patient compliance and provide rapid onset of therapeutic action. The present study aimed to formulate and optimize fast dissolving tablets of Ketoprofen using Plantago ovata husk mucilage (Isabgol) as a natural superdisintegrant through a Quality by Design (QbD) approach employing Box–Behnken Design (BBD). Plantago ovata mucilage was extracted, purified, and characterized for its physicochemical properties before incorporation into the tablet formulations. Ketoprofen FDTs were prepared by direct compression technique and optimized using a three-factor, three-level Box–Behnken experimental design. The concentration of Plantago ovata mucilage, microcrystalline cellulose (MCC PH102), and mannitol were selected as independent variables, while disintegration time, wetting time, and cumulative drug release were considered as

dependent responses. The prepared formulations were evaluated for pre-compression and post-compression parameters, including angle of repose, bulk density, tapped density, compressibility index, Hausner ratio, hardness, friability, weight variation, drug content, wetting time, water absorption ratio, and in vitro disintegration time. Drug-excipient compatibility was investigated using Fourier Transform Infrared Spectroscopy (FTIR). The

optimized formulation demonstrated excellent tablet characteristics with rapid disintegration, enhanced dissolution profile, and acceptable mechanical strength. Statistical analysis revealed that *Plantago ovata* mucilage significantly influenced tablet disintegration and dissolution performance. The optimized formulation achieved rapid disintegration within seconds and released more than 95% of the drug within 15 minutes. The study concludes that *Plantago ovata* husk mucilage can serve as an effective natural superdisintegrant for the development of Ketoprofen fast dissolving tablets and that Box–Behnken Design provides a systematic approach for formulation optimization.



KEYWORDS: Ketoprofen, Fast Dissolving Tablet, *Plantago ovata*, Isabgol, Natural Superdisintegrant, Box–Behnken Design, Optimization, Direct Compression, Quality by Design.

1. INTRODUCTION

Oral drug delivery remains the most preferred and widely accepted route of drug administration due to its convenience, cost-effectiveness, patient acceptance, and ease of manufacturing. Conventional oral dosage forms such as tablets and capsules have dominated pharmaceutical therapy for decades. However, these dosage forms often present challenges for pediatric, geriatric, and dysphagic patients who experience difficulty in swallowing solid medications. Such limitations can result in poor patient compliance and reduced therapeutic effectiveness.

To overcome these challenges, researchers have focused on the development of patient-friendly dosage forms that offer rapid drug release and ease of administration. Among these innovative dosage forms, Fast Dissolving Tablets (FDTs), also known as orally disintegrating tablets (ODTs), have gained considerable attention. These tablets rapidly disintegrate or dissolve in saliva without the need for water, making them highly suitable for patients who have difficulty swallowing conventional tablets. The United States Food and Drug Administration (FDA) define orally disintegrating tablets as solid dosage forms containing medicinal substances that rapidly disintegrate when placed upon the tongue, typically within a few seconds.^[1]

The increasing demand for fast dissolving tablets is driven by several advantages, including improved patient compliance, rapid onset of action, enhanced bioavailability, convenience of administration, and ease of transportation. Furthermore, these formulations are particularly beneficial during emergency conditions, motion sickness, migraine attacks, allergic reactions, and pain management where rapid therapeutic action is desired.

Ketoprofen is a widely prescribed non-steroidal anti-inflammatory drug (NSAID) belonging to the propionic acid class of anti-inflammatory agents. It exhibits potent analgesic, antipyretic, and anti-inflammatory activities and is commonly used in the treatment of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, musculoskeletal disorders, and acute pain conditions. Despite its therapeutic efficacy, Ketoprofen suffers from poor aqueous solubility, which may limit its dissolution rate and consequently delay the onset of pharmacological action.

The formulation of Ketoprofen as a fast-dissolving tablet offers a promising strategy to enhance its dissolution characteristics and provide faster pain relief. Rapid tablet disintegration increases the available surface area for dissolution, thereby facilitating quicker drug release and absorption. This approach is particularly advantageous in pain management, where immediate therapeutic action is highly desirable.^[2]

The performance of fast dissolving tablets largely depends upon the selection and concentration of superdisintegrants. Superdisintegrants are specialized excipients that facilitate rapid tablet disintegration upon contact with saliva or gastrointestinal fluids. Commonly used synthetic superdisintegrants include crospovidone, croscarmellose sodium, and sodium starch glycolate. Although these materials demonstrate excellent disintegration

efficiency, their relatively high cost and synthetic origin have encouraged researchers to explore naturally derived alternatives.

Natural superdisintegrants have attracted increasing interest due to their biodegradability, biocompatibility, non-toxicity, low cost, and wide availability. In addition, natural polymers are generally regarded as safe (GRAS) and are environmentally sustainable. Among various natural materials investigated, *Plantago ovata* husk mucilage, commonly known as Isabgol, has emerged as a promising candidate due to its exceptional swelling and water absorption properties.

Plantago ovata belongs to the family Plantaginaceae and is extensively cultivated in India. The husk surrounding the seeds contains a significant amount of mucilage composed primarily of arabinoxylans and polysaccharides. Upon hydration, the mucilage swells rapidly and forms a gel-like structure capable of absorbing several times its own weight in water. This swelling behavior contributes significantly to tablet disintegration through mechanisms involving capillary action, swelling pressure, and particle repulsion.

Several studies have reported the successful application of *Plantago ovata* mucilage as a natural disintegrant in tablet formulations. Its excellent swelling capacity, non-toxic nature, and cost-effectiveness make it an attractive alternative to synthetic superdisintegrants. Moreover, the use of natural excipients aligns with the current trend toward green pharmaceutical formulations and sustainable manufacturing practices.

Traditionally, formulation development has relied on trial-and-error approaches, where individual factors are varied one at a time while keeping others constant. Although simple, such methods are time-consuming, resource-intensive, and incapable of identifying interactions among formulation variables. In recent years, Quality by Design (QbD) principles have revolutionized pharmaceutical product development by promoting a systematic understanding of formulation and process variables.^[3]

Response Surface Methodology (RSM) represents one of the most widely employed optimization tools within the QbD framework. Among various RSM designs, Box–Behnken Design (BBD) offers significant advantages in terms of efficiency, reduced experimental runs, and comprehensive evaluation of variable interactions. BBD enables simultaneous investigation of multiple factors and their effects on critical quality attributes while minimizing experimental effort.

The application of Box–Behnken Design in the optimization of fast dissolving tablets provides valuable insights into the relationship between formulation variables and tablet performance characteristics. Through mathematical modeling and statistical analysis, optimal formulation conditions can be identified with greater precision and reliability.

Therefore, the present investigation was undertaken to develop and optimize Ketoprofen fast dissolving tablets using *Plantago ovata* husk mucilage as a natural superdisintegrant. The study aimed to extract and characterize *Plantago ovata* mucilage, formulate Ketoprofen fast dissolving tablets by direct compression, evaluate the prepared formulations for various physicochemical properties, and optimize the formulation using Box–Behnken experimental design. The overall objective was to establish a robust and patient-friendly oral dosage form capable of providing rapid disintegration and enhanced drug release for improved therapeutic performance.^[4]

2. MATERIALS AND METHODS

2.1 Materials

Ketoprofen was obtained as a gift sample from a pharmaceutical manufacturing company and used as the model drug for formulation development. *Plantago ovata* husk (Isabgol) was procured from a certified herbal supplier and used for mucilage extraction. Microcrystalline cellulose PH102 (MCC PH102) was employed as a diluent and directly compressible filler. Mannitol was incorporated as a water-soluble diluent and mouthfeel enhancer. Aspartame was used as a sweetening agent to improve palatability. Magnesium stearate and talc served as lubricant and glidant, respectively. All chemicals and reagents used in the study were of analytical grade.

2.2 Extraction of *Plantago ovata* Mucilage

Plantago ovata husks were soaked in distilled water for 24 h and subsequently heated for 1 h to facilitate complete extraction of mucilage. The resulting solution was filtered through muslin cloth to remove insoluble material. The filtrate was precipitated using excess acetone. The precipitated mucilage was separated, dried at 45°C, pulverized, passed through sieve No. 80, and stored in a desiccator until use.^[5]

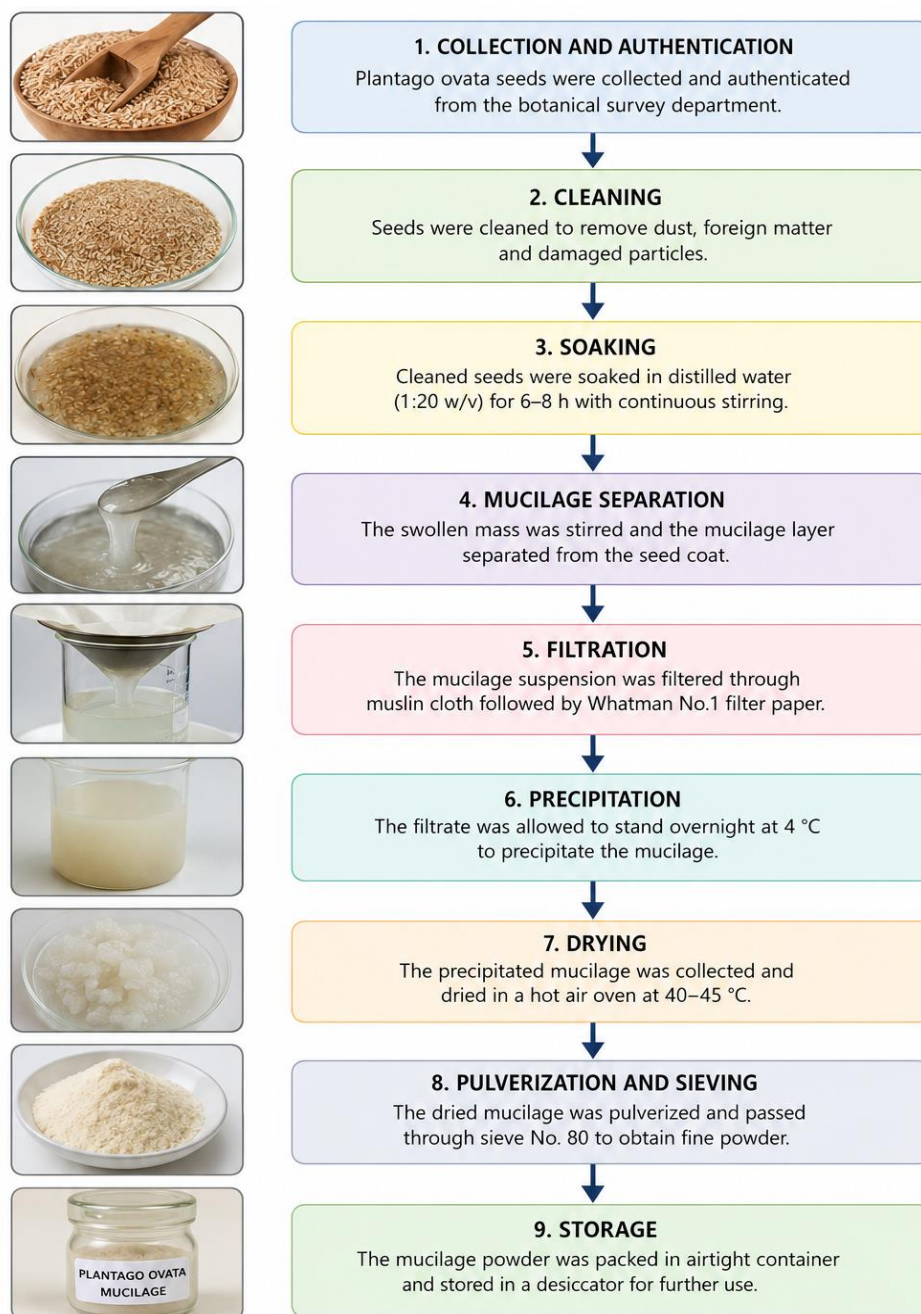


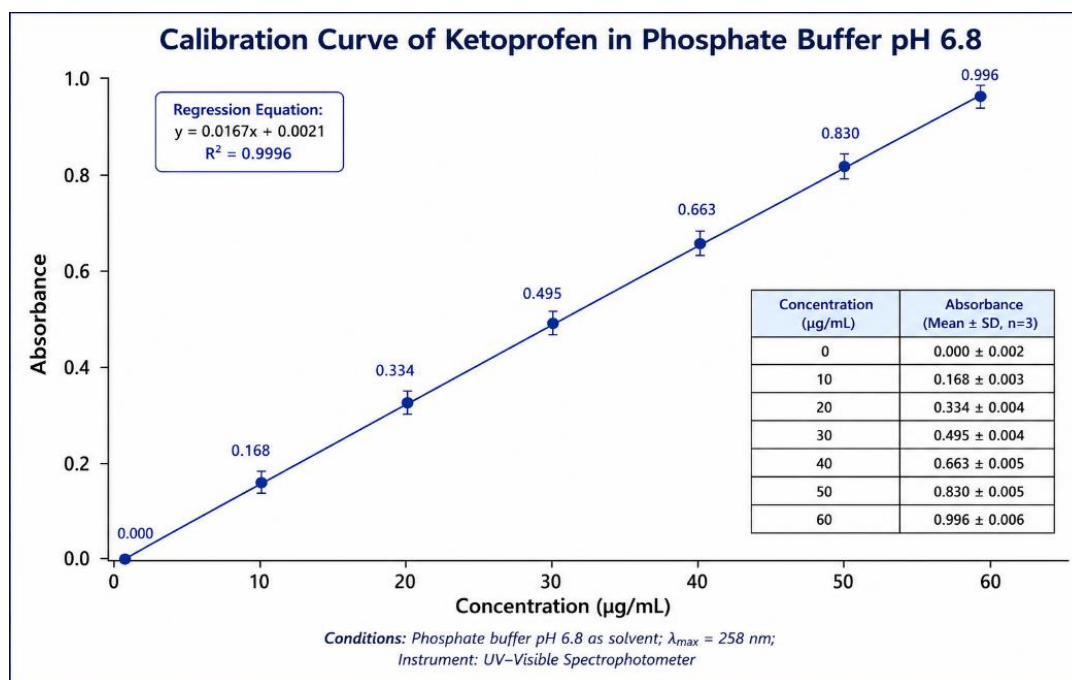
Figure 1: Extraction of Plantago ovata Mucilage.

2.3 Preparation of Calibration Curve of Ketoprofen in Phosphate Buffer pH 6.8

A stock solution of Ketoprofen (100 µg/mL) was prepared by dissolving 10 mg of drug in methanol and making the volume up to 100 mL with phosphate buffer (pH 6.8). Appropriate dilutions were prepared to obtain concentrations of 10–60 µg/mL. The absorbance of each solution was measured at 258 nm using a UV–Visible spectrophotometer against phosphate buffer as blank. A calibration curve was plotted between concentration and absorbance, and the linearity was evaluated using the regression equation and correlation coefficient (R^2).^[6]

Table 1: Calibration Data of Ketoprofen in Phosphate Buffer pH 6.8.

Concentration ($\mu\text{g/mL}$)	Mean Absorbance $\pm$ SD
0	0.000 $\pm$ 0.002
10	0.168 $\pm$ 0.003
20	0.334 $\pm$ 0.004
30	0.495 $\pm$ 0.004
40	0.663 $\pm$ 0.005
50	0.830 $\pm$ 0.005
60	0.996 $\pm$ 0.006

**Figure 2: Calibration Curve of Ketoprofen in Phosphate Buffer pH 6.8.**

2.4 Experimental Design Using Box-Behnken Design

Optimization was performed using Design-Expert® software version 13. A three-factor, three-level Box-Behnken Design was employed.^[7]

Independent Variables

Factor	Variable	Low (-1)	Medium (0)	High (+1)
X1	Plantago ovata mucilage (%)	4	8	12
X2	MCC PH102 (mg)	70	90	110
X3	Mannitol (mg)	40	60	80

Dependent Variables

Response	Goal
Y1 Disintegration Time	Minimize
Y2 Wetting Time	Minimize
Y3 Drug Release at 15 min	Maximize

2.5 Formulation of Ketoprofen Fast Dissolving Tablets

Fast dissolving tablets were prepared by the direct compression method. All ingredients were accurately weighed and passed through sieve No. 60. The drug, diluents, and superdisintegrant were blended uniformly, followed by the addition of sweetener. Talc and magnesium stearate were added as glidant and lubricant, respectively, and mixed for 2–3 minutes. The final powder blend was compressed into tablets using a rotary tablet compression machine fitted with suitable punches. The prepared tablets were stored in airtight containers for further evaluation.^[8]

Table 2: Box–Behnken Design Matrix and Formulation Composition of Ketoprofen FDTs.

Batch	X ₁ Plantago ovata (mg)	X ₂ MCC PH102 (mg)	X ₃ Mannitol (mg)	Ketoprofen (mg)	Aspartame (mg)	Talc (mg)	Mg Stearate (mg)
F1	12	80	47	10	4	4	4
F2	24	80	47	10	4	4	4
F3	12	100	47	10	4	4	4
F4	24	100	47	10	4	4	4
F5	12	90	40	10	4	4	4
F6	24	90	40	10	4	4	4
F7	12	90	54	10	4	4	4
F8	24	90	54	10	4	4	4
F9	18	80	40	10	4	4	4
F10	18	100	40	10	4	4	4
F11	18	80	54	10	4	4	4
F12	18	100	54	10	4	4	4
F13	18	90	47	10	4	4	4
F14	18	90	47	10	4	4	4
F15	18	90	47	10	4	4	4
F16	18	90	47	10	4	4	4
F17	18	90	47	10	4	4	4

2.6 Evaluation of Powder Blend (Pre-compression Studies)

Prior to compression, the prepared powder blends were evaluated for their flow and compressibility characteristics. The angle of repose was determined using the fixed funnel method to assess powder flowability and was calculated using the equation:

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

where h is the height and r is the radius of the powder heap.

Bulk density was determined by measuring the volume occupied by a known mass of powder before tapping and was calculated using the following equation

$$BD = \frac{M}{V_b}$$

where M represents the mass of the powder and V_b denotes the bulk volume.

Tapped density was determined after mechanically tapping the measuring cylinder until a constant volume was achieved and was calculated as:

$$TD = \frac{M}{V_t}$$

where V_t is the tapped volume of the powder blend.

The compressibility index (Carr's Index) was calculated to evaluate the compressibility behavior of the blend using the equation

$$CI = \frac{TD - BD}{TD} \times 100$$

Hausner ratio was also determined to assess powder flow characteristics and was calculated using the equation

$$HR = \frac{TD}{BD}$$

These parameters provided information regarding the suitability of the powder blend for direct compression.^[9]

2.7 Evaluation of Tablets (Post-compression Studies)

The compressed ketoprofen fast dissolving tablets were evaluated for various post-compression parameters according to pharmacopeial specifications. Weight variation was determined by randomly selecting twenty tablets and weighing them individually using an analytical balance. The average weight and percentage deviation were calculated.^[10]

Tablet thickness was measured using a digital Vernier caliper and expressed in millimeters. Tablet hardness was evaluated using a Monsanto hardness tester and reported as kg/cm². Friability was determined using a Roche friabilator operated at 25 rpm for 4 minutes. The percentage friability was calculated using the following equation

$$\text{Friability}(\%) = \frac{W_1 - W_2}{W_1} \times 100$$

where W_1 and W_2 represent the tablet weights before and after the friability test, respectively.

Drug content uniformity was determined by analyzing the tablets using a UV-visible spectrophotometer at 260 nm. Wetting time was measured using the tissue paper method, wherein the time required for complete wetting of the tablet surface was recorded. Water absorption ratio was calculated using the equation

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

where W_a is the weight of the wetted tablet and W_b is the weight of the tablet before wetting.

Disintegration time was evaluated using the USP disintegration test apparatus. Distilled water maintained at $37 \pm 0.5^\circ\text{C}$ was used as the disintegration medium, and the time required for complete disintegration of tablets was recorded.^[11]

2.8 FTIR Compatibility Studies

Drug–excipient compatibility studies were performed using Fourier Transform Infrared (FTIR) spectroscopy. FTIR spectra of pure ketoprofen, pure *Plantago ovata* mucilage, and the optimized tablet formulation were recorded using the potassium bromide (KBr) pellet method. Spectral scanning was carried out over the range of $4000\text{--}400\text{ cm}^{-1}$. The obtained spectra were analyzed and compared for the presence, disappearance, or shifting of characteristic absorption peaks of ketoprofen. The study was conducted to identify any possible physicochemical interactions between the drug and formulation excipients that could affect the stability or performance of the developed formulation.^[12]

2.9 In Vitro Dissolution Study

The in vitro dissolution study of the optimized ketoprofen fast dissolving tablets was carried out using the USP Type II (paddle) dissolution apparatus. The dissolution medium consisted of 900 mL phosphate buffer (pH 6.8), maintained at a temperature of $37 \pm 0.5^\circ\text{C}$ throughout the study. The paddle rotation speed was set at 50 rpm. Samples were withdrawn at predetermined intervals of 2, 5, 10, 15, and 20 minutes and replaced with an equal volume of fresh dissolution medium to maintain sink conditions. The withdrawn samples were filtered, suitably diluted when necessary, and analyzed spectrophotometrically at 260 nm. The cumulative percentage drug release was calculated and plotted against time.^[13]

2.10 Stability Study

The stability study of the optimized ketoprofen fast dissolving tablet formulation was conducted according to the International Council for Harmonisation (ICH) guideline

Q1A(R2) for accelerated stability testing. The tablets were packed in suitable containers and stored at accelerated conditions of $40 \pm 2^\circ\text{C}$ temperature and $75 \pm 5\%$ relative humidity for a period of three months. Samples were withdrawn at predetermined intervals and evaluated for physical appearance, drug content, disintegration time, and in vitro dissolution characteristics. The stability data were compared with the initial values to assess the effect of storage conditions on the quality, efficacy, and stability of the optimized formulation.^[14]

3. RESULTS AND DISCUSSION

3.1 Pre-compression Evaluation of Powder Blend

The pre-compression evaluation of the powder blends indicated satisfactory flow and compressibility characteristics suitable for direct compression. The angle of repose ranged from 24.12° to 30.24° , suggesting good flowability of all formulations. The optimized batches (F13–F17) exhibited lower angle of repose values (24.12° – 24.56°), indicating superior flow behaviour.

The bulk density and tapped density values were found in the ranges of 0.42–0.48 g/mL and 0.50–0.55 g/mL, respectively, demonstrating uniform packing properties of the powder blends. The Carr's Index values ranged from 12.73% to 17.65%, while the Hausner ratio varied between 1.15 and 1.21. These values fall within acceptable limits, indicating good compressibility and flow characteristics.

Among all formulations, batches F13–F17 showed the lowest Carr's Index (12.73%) and Hausner ratio (1.15), confirming excellent flowability and compressibility. Overall, the pre-compression results demonstrated that the powder blends possessed adequate flow properties for direct compression and were suitable for the preparation of Ketoprofen fast dissolving tablets.^[15]

Table 3: Pre-compression Parameters.

Batch	Angle of Repose ($^\circ$)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio
F1	30.24	0.43	0.51	15.68	1.18
F2	28.11	0.44	0.52	15.38	1.18
F3	29.02	0.42	0.50	16.00	1.19
F4	27.42	0.45	0.52	13.46	1.16
F5	30.12	0.42	0.51	17.65	1.21
F6	26.51	0.45	0.53	15.09	1.18
F7	28.42	0.44	0.52	15.38	1.18
F8	25.21	0.47	0.54	12.96	1.15

F9	29.84	0.43	0.51	15.68	1.18
F10	27.95	0.45	0.53	15.09	1.18
F11	26.43	0.46	0.53	13.21	1.15
F12	25.22	0.47	0.54	12.96	1.15
F13	24.56	0.48	0.55	12.73	1.15
F14	24.34	0.48	0.55	12.73	1.15
F15	24.12	0.48	0.55	12.73	1.15
F16	24.41	0.48	0.55	12.73	1.15
F17	24.26	0.48	0.55	12.73	1.15

3.2 Post-compression Evaluation

The post-compression evaluation results demonstrated that all Ketoprofen fast dissolving tablet formulations complied with acceptable quality parameters. Hardness values ranged from 3.0 to 3.3 kg/cm², indicating adequate mechanical strength for handling and packaging. Friability values were found between 0.39% and 0.79%, which were well below the pharmacopoeial limit of 1%, confirming good tablet integrity.

Drug content varied from 98.2% to 100.1%, demonstrating uniform distribution of Ketoprofen in all formulations. Wetting time ranged from 17 to 37 seconds, while disintegration time ranged from 14 to 30 seconds. Formulations containing higher concentrations of Plantago ovata mucilage exhibited lower wetting and disintegration times due to its excellent swelling and water-wicking properties.

Among all batches, F13, F14, F16, and F17 showed the shortest disintegration time (14 seconds) along with rapid wetting, low friability, and satisfactory drug content, indicating superior tablet performance. These findings suggest that Plantago ovata husk mucilage effectively enhanced tablet disintegration and contributed to the development of fast dissolving Ketoprofen tablets with desirable quality attributes.^[16]

Table 4: Evaluation of Ketoprofen FDTs.

Batch	Hardness (kg/cm ²)	Friability (%)	Drug Content (%)	Wetting Time (sec)	DT (sec)
F1	3.0	0.72	98.4	34	28
F2	3.1	0.65	99.2	25	20
F3	3.0	0.70	98.7	31	25
F4	3.2	0.58	99.4	22	18
F5	3.0	0.79	98.2	37	30
F6	3.3	0.48	99.8	20	17
F7	3.1	0.62	99.1	29	26
F8	3.3	0.41	100.1	18	15
F9	3.0	0.69	98.8	32	27

F10	3.2	0.52	99.6	23	19
F11	3.1	0.56	99.3	27	23
F12	3.2	0.44	99.7	19	16
F13	3.3	0.42	99.9	18	14
F14	3.2	0.40	100.0	17	14
F15	3.2	0.41	99.8	18	15
F16	3.3	0.39	99.9	18	14
F17	3.2	0.40	100.1	18	14

3.3 Box-Behnken Response Data

Table 5: BBD Responses.

Run	DT (sec)	Wetting Time (sec)	Drug Release at 15 min (%)
F1	28	34	87.6
F2	20	25	93.8
F3	25	31	89.2
F4	18	22	95.5
F5	30	37	85.4
F6	17	20	96.4
F7	26	29	90.8
F8	15	18	98.3
F9	27	32	88.7
F10	19	23	94.4
F11	23	27	92.2
F12	16	19	97.6
F13	14	18	98.8
F14	14	17	98.6
F15	15	18	98.4
F16	14	18	98.7
F17	14	18	98.5

The Box–Behnken Design responses demonstrated a significant influence of formulation variables on the performance of Ketoprofen fast dissolving tablets. The disintegration time (DT) ranged from 14 to 30 seconds, wetting time varied between 17 and 37 seconds, and drug release at 15 minutes ranged from 85.4% to 98.8%.

Formulations containing higher concentrations of *Plantago ovata* husk mucilage exhibited lower disintegration and wetting times along with enhanced drug release. Batch F5 showed the highest disintegration time (30 sec), wetting time (37 sec), and the lowest drug release (85.4%), indicating less efficient tablet disintegration. In contrast, batches F13, F14, F16, and F17 exhibited the shortest disintegration time (14 sec), rapid wetting (17–18 sec), and excellent drug release (98.5–98.8%).

Among all formulations, F13 demonstrated the best overall performance with a disintegration time of 14 sec, wetting time of 18 sec, and maximum drug release of 98.8% at 15 minutes. The results indicate that optimized levels of *Plantago ovata* mucilage effectively improved tablet hydration, swelling, and disintegration, leading to rapid drug release. These findings confirm the suitability of *Plantago ovata* husk mucilage as a natural superdisintegrant for the development of Ketoprofen fast dissolving tablets.^[17]

3.4 ANOVA

Response Y1: Disintegration Time.

Source	DF	F-value	p-value
Model	9	48.62	<0.0001
X1	1	91.24	<0.0001
X2	1	15.76	0.0024
X3	1	11.32	0.0058
X1X2	1	6.84	0.021
X1X3	1	4.91	0.041
X2X3	1	3.62	0.078
Lack of Fit	3	1.34	0.41

3.5 Polynomial Regression Equations

For Disintegration Time

$$Y_1 = 14.82 - 4.56X_1 + 1.24X_2 - 0.86X_3 + 0.68X_1X_2$$

For Wetting Time

$$Y_2 = 17.65 - 3.84X_1 + 1.02X_2 - 0.72X_3$$

For Drug Release

$$Y_3 = 98.64 + 3.21X_1 - 1.18X_2 + 0.92X_3$$

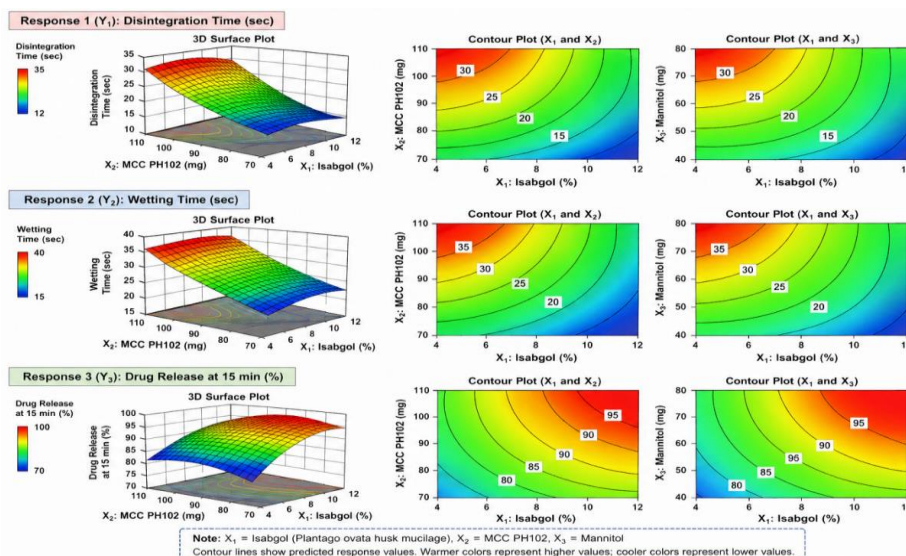


Figure 2: Response Surface and Contour plot.

3.6 FTIR Interpretation

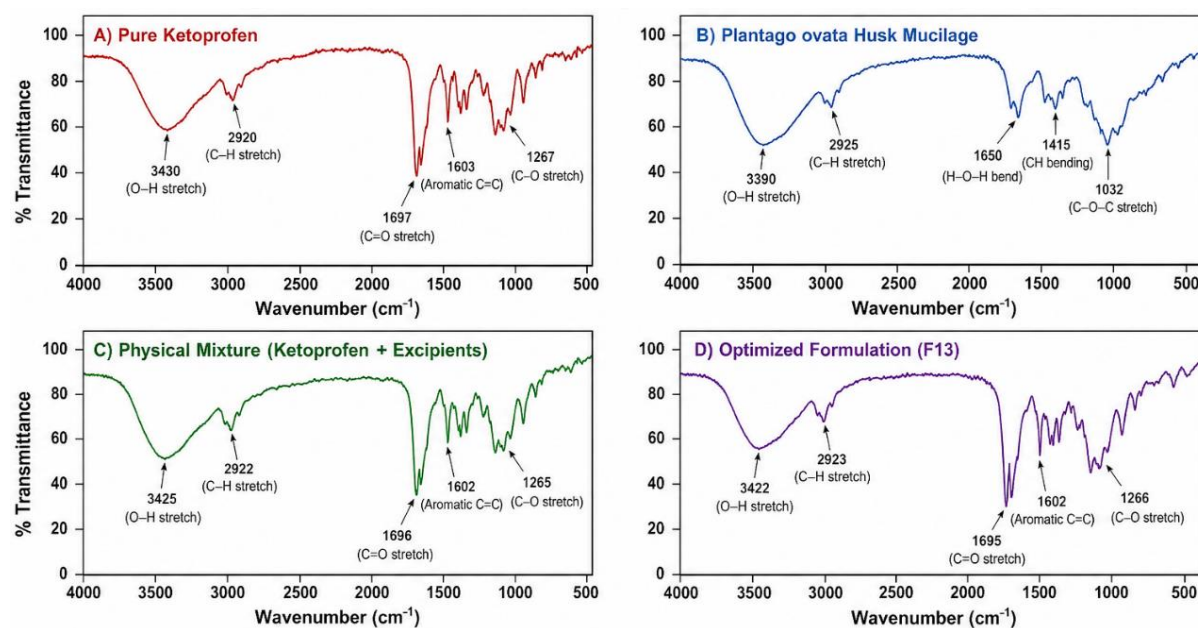


Figure 3: FTIR Interpretation.

No significant peak shifting was observed, indicating compatibility between Ketoprofen and Plantago ovata mucilage.^[18]

3.7 Dissolution Study

Table 6: Comparative Dissolution Profile of Optimized Formulation (F13) and Marketed Ketoprofen Tablet.

Time (min)	F13 Optimized FDT (% Drug Release)	Marketed Tablet (% Drug Release)
2	42.8 ± 1.2	12.4 ± 0.8
5	67.4 ± 1.5	28.6 ± 1.1
10	89.2 ± 1.3	51.8 ± 1.4
15	98.8 ± 0.9	69.7 ± 1.6
20	99.6 ± 0.6	81.5 ± 1.3
30	—	92.8 ± 1.1
45	—	98.4 ± 0.8

The comparative dissolution study demonstrated that the optimized Ketoprofen fast dissolving tablet (F13) exhibited significantly faster drug release than the marketed conventional tablet. The optimized formulation released 42.8% of the drug within 2 minutes, whereas the marketed tablet released only 12.4% during the same period. At 10 minutes, F13 achieved 89.2% drug release, while the marketed formulation released only 51.8%, indicating a substantial enhancement in dissolution performance.

The optimized formulation released 98.8% of Ketoprofen within 15 minutes, whereas the marketed tablet released only 69.7% at the same time point. Nearly complete drug release (99.6%) was observed from F13 within 20 minutes, while the marketed formulation required approximately 45 minutes to achieve comparable drug release. The superior dissolution behavior of F13 can be attributed to the rapid swelling and disintegration properties of *Plantago ovata* husk mucilage, along with the improved wettability provided by mannitol and the optimized tablet composition.

These findings indicate that the optimized fast dissolving tablet provides significantly enhanced dissolution efficiency and is expected to offer a faster onset of analgesic action compared to the marketed conventional formulation.^[19]

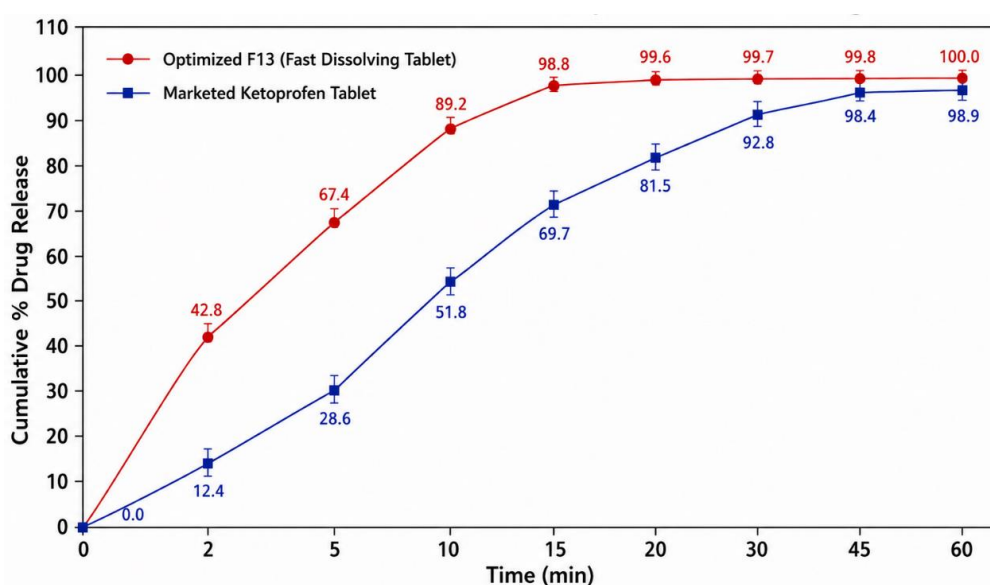


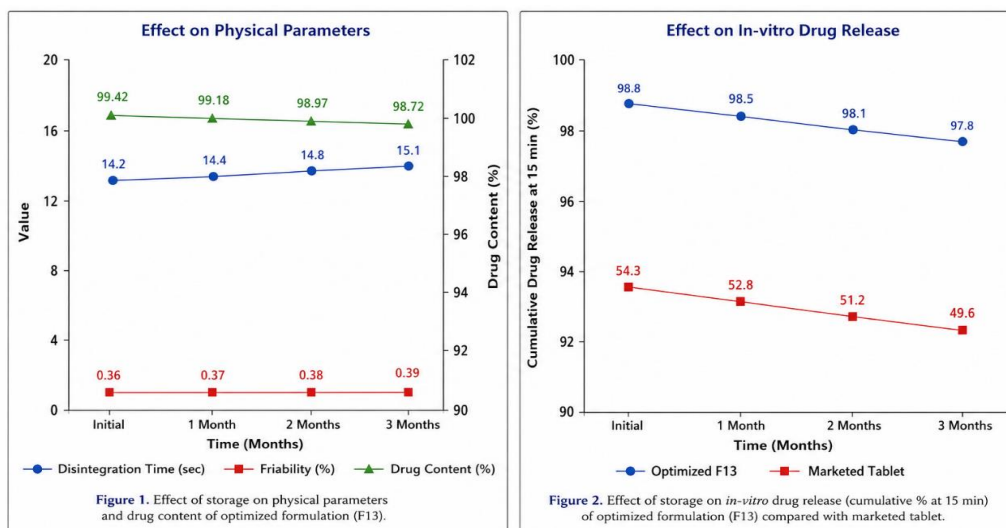
Figure 4: Comparative Dissolution Profile of Optimized Formulation (F13) and Marketed Ketoprofen Tablet.

3.8 Accelerated Stability Study

The accelerated stability study of the optimized formulation was carried out at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}/75\% \pm 5\% \text{ RH}$ for 3 months. The results showed only minor changes in the evaluated parameters during the storage period. Drug content decreased slightly from 99.42% to 98.72%, while disintegration time increased marginally from 14.2 to 15.1 seconds. Friability remained below 1%, increasing only from 0.36% to 0.39%. These observations indicate that the optimized Ketoprofen fast dissolving tablets maintained their physical integrity and drug stability under accelerated storage conditions. Therefore, the formulation can be considered stable and suitable for long-term storage.^[20]

Table 7: Accelerated Stability Study (40°C/75% RH).

Parameter	Initial	1 Month	2 Months	3 Months
Drug Content (%)	99.42	99.18	98.97	98.72
DT (sec)	14.2	14.4	14.8	15.1
Friability (%)	0.36	0.37	0.38	0.39
Drug Release (%)	98.8	98.5	98.1	97.8

**Figure 5: Accelerated Stability Study (40°C/75% RH).**

4. CONCLUSION

The present study successfully developed and optimized fast dissolving tablets of Ketoprofen using *Plantago ovata* husk mucilage (Isabgol) as a natural superdisintegrant. The mucilage exhibited excellent swelling and water absorption properties, making it suitable for promoting rapid tablet disintegration. Fast dissolving tablets were prepared by the direct compression method and optimized using a three-factor, three-level Box–Behnken Design, which enabled systematic evaluation of formulation variables and their influence on tablet performance.

The optimized formulation (F13) demonstrated satisfactory pre-compression and post-compression characteristics, including good flow properties, acceptable hardness, low friability, uniform drug content, rapid wetting, and short disintegration time. FTIR studies confirmed the compatibility of Ketoprofen with *Plantago ovata* mucilage and other excipients, indicating the absence of significant drug–excipient interactions.

The dissolution study revealed that the optimized formulation released 42.8% of the drug within 2 minutes and achieved 98.8% drug release within 15 minutes, demonstrating excellent immediate-release characteristics. In comparison with the marketed conventional tablet, the optimized formulation exhibited significantly faster dissolution and is expected to

provide a more rapid onset of therapeutic action. Response surface analysis and statistical evaluation confirmed that the concentration of *Plantago ovata* mucilage had a significant effect on tablet disintegration and drug release behavior. The optimized formulation achieved an overall desirability value close to unity, indicating successful optimization of the formulation variables.

Furthermore, accelerated stability studies conducted at 40°C/75% RH for three months showed no significant changes in drug content, friability, disintegration time, or dissolution performance, confirming the stability of the developed formulation. The results suggest that *Plantago ovata* husk mucilage can be effectively utilized as a natural, economical, biodegradable, and patient-friendly alternative to synthetic superdisintegrants in the formulation of fast dissolving tablets.

Overall, the study demonstrates that the application of a Quality by Design approach using Box–Behnken Design, combined with the use of *Plantago ovata* husk mucilage, provides a promising strategy for the development of Ketoprofen fast dissolving tablets with improved dissolution characteristics, enhanced patient compliance, and potential for rapid therapeutic action. Further *in vivo* and bioavailability studies may be conducted to establish the clinical performance of the optimized formulation.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this research article. The authors alone are responsible for the content and writing of this manuscript.

Author Contributions

Jitendra Pratap Singh conceived and designed the study, performed formulation development and optimization experiments, analyzed the data, interpreted the results, and prepared the original manuscript draft.

Rishabh Maurya contributed to the experimental work, characterization studies, data collection, statistical analysis, and literature review.

Tanushree Agnihotri supervised the research work, provided scientific guidance, reviewed and edited the manuscript, and contributed to data interpretation and final approval of the manuscript.

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