

Development of a Natural Psyllium Husk Enabled Orodispersible Tablet of Mebeverine Hydrochloride: Formulation Optimization, *In Vitro* Performance, and Analytical Characterization

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ABSTRACT

Background: Irritable bowel syndrome (IBS) is characterized by recurrent abdominal pain and altered bowel habits and can impair daily functioning and quality of life. Conventional mebeverine hydrochloride tablets may be inconvenient for patients with swallowing difficulties. This study developed an orodispersible tablet using natural psyllium husk as a superdisintegrant. Its high water uptake and swelling capacity, together with biodegradability and low cost, support its use as a natural excipient. The formulation was optimized using Response Surface Methodology.

Methods: Nine formulations were prepared by direct compression using a 3×3 response surface design with psyllium husk and microcrystalline cellulose concentrations as independent variables. Powder blends and tablets were evaluated for flow properties, hardness, friability, weight variation, drug content, disintegration time, dissolution, and stability. Statistical analysis included ANOVA, regression modelling, response surface analysis, and optimization.

Results: Both formulation variables significantly influenced disintegration time and hardness ($p < 0.0001$). Increasing psyllium husk shortened disintegration, whereas higher binder levels improved hardness. The optimized formulation (F3) showed rapid disintegration in 24.3 s, hardness of 21 N, friability of 0.63%, drug content of 100.12%, and 99.49% drug release within 30 min. Powder blends showed good flow after glidant addition, and accelerated stability testing showed preservation of tablet quality and dissolution performance for six months.

Conclusion: Psyllium husk functioned as an effective natural superdisintegrant, producing rapidly disintegrating tablets with satisfactory mechanical strength, high drug release, and acceptable stability. The optimized formulation provides a promising patient friendly dosage form for patients who have difficulty swallowing conventional tablets.

Keywords: Orodispersible tablet, Mebeverine hydrochloride, Psyllium husk, Natural disintegrant, Response Surface Methodology

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GRAPHICAL ABSTRACT

INTRODUCTION

Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder characterized by recurrent abdominal pain, bloating, and altered bowel habits without an identifiable structural abnormality. Recent meta analytic evidence indicates that global IBS prevalence varies substantially with diagnostic criteria, with estimates of approximately 13–17% across Rome III and Rome IV definitions [29]. Based on clinical presentation, IBS is classified into constipation-predominant, diarrhea-predominant, mixed, and unclassified subtypes. Although IBS is not life-threatening, it can substantially affect quality of life, daily activities, and psychological well-being [2]. The development of IBS is complex and involves multiple factors, including abnormal gastrointestinal motility, visceral hypersensitivity, altered gut microbiota, intestinal inflammation, dysregulation of the gut–brain axis, and psychological stress [3]. Since intestinal smooth muscle spasm is a major contributor to abdominal pain, antispasmodic drugs remain an important therapeutic option. Mebeverine hydrochloride is one of the most widely prescribed antispasmodic agents because it selectively relaxes gastrointestinal smooth muscles without producing the undesirable anticholinergic effects commonly associated with conventional antispasmodics [4]. The drug acts by regulating sodium and calcium ion movement across smooth muscle cell membranes, thereby reducing abnormal contractions while preserving normal intestinal motility [5]. However, its rapid metabolism and relatively short biological half-life often necessitate repeated dosing or modified-release formulations to maintain therapeutic efficacy [6].

Conventional tablets and sustained-release capsules of mebeverine hydrochloride have practical limitations. They generally require swallowing with water and may be difficult to administer to pediatric, geriatric, dysphagic, or bedridden patients. These limitations can reduce adherence and delay convenient symptom management [7].

Orodispersible tablets (ODTs) have emerged as an attractive alternative because they rapidly disintegrate in the oral cavity without the need for water, improving convenience and ease of administration [8]. Their rapid disintegration enhances drug dissolution and may provide a faster onset of therapeutic action. ODTs are particularly beneficial for patients with swallowing difficulties and those requiring prompt relief of abdominal spasms associated with IBS [9]. The success of ODTs largely depends on the efficiency of the disintegrating agent used in the formulation. However, ODTs can also present formulation challenges, including mechanical weakness, moisture sensitivity, and a narrow balance

between rapid disintegration and sufficient tablet strength. These limitations can be addressed through appropriate excipient selection and systematic optimization.

Synthetic superdisintegrants such as croscopovidone, sodium starch glycolate, and croscarmellose sodium are widely used; however, sustainable pharmaceutical development has increased interest in natural alternatives. Natural excipients may offer biodegradability, low toxicity, affordability, and improved environmental compatibility [10]. Psyllium husk (*Plantago ovata*) is a polysaccharide rich material with high water absorption and swelling capacity. Hydration produces swelling pressure that can promote tablet break-up and drug release [11–13]. These properties, together with its low cost and biodegradability, support its investigation as a natural superdisintegrant.

Optimizing the concentration of natural excipients is essential because excessive or insufficient amounts can adversely influence tablet hardness, friability, and disintegration performance. Conventional trial-and-error methods are often laborious and inefficient for such optimization. Therefore, modern Quality by Design (QbD) principles, combined with Response Surface Methodology (RSM), provide a systematic and statistically robust approach for evaluating formulation variables, understanding their interactions, and establishing an optimized design space with fewer experimental trials [14–15].

The primary objective of this study was to develop and optimize mebeverine hydrochloride orodispersible tablets using psyllium husk as a natural superdisintegrant. The secondary objectives were to characterize the powder blends and tablets, evaluate *in vitro* disintegration and dissolution, assess drug excipient compatibility, and determine the accelerated stability of the optimized formulation.

2. Materials and Methods

2.1 Materials

Mebeverine hydrochloride was obtained as a gift sample from Cohance Lifesciences Ltd., Hyderabad. Psyllium husk powder (*Plantago ovata*) was procured from Yarrow Chem Products, Mumbai. Lactose monohydrate, mannitol, croscopovidone, magnesium stearate, talc, sodium saccharin, and peppermint flavour were purchased from Loba Chemie Pvt. Ltd., Mumbai. All chemicals and reagents used in the study were of pharmaceutical or analytical grade.

2.2 Experimental Design

The formulation of mebeverine hydrochloride orodispersible tablets (ODTs) was optimized using Response Surface Methodology (RSM) implemented in Design Expert® software (Version 13.0.5). Based on the nine experimental combinations reported in the manuscript, a 3 × 3 factorial response surface design

was used to evaluate the effects of psyllium husk and binder concentration on tablet performance.

Two formulation variables were selected as independent factors. Factor A was the concentration of psyllium husk powder, investigated at 30, 40, and 50 mg. Factor B was the concentration of microcrystalline cellulose, investigated at 8, 16, and 24 mg. These variables were selected because they directly influence disintegration and mechanical strength of ODTs [16–18].

The primary response was disintegration time (Y1),

because rapid disintegration is a key performance attribute of ODTs. Tablet hardness (Y2) was selected as the secondary response to ensure adequate mechanical strength for handling, packaging, and transportation without compromising rapid disintegration.

Nine experimental formulations were evaluated across the three levels of each factor. The resulting data were analyzed using Design Expert® software to obtain regression models, ANOVA, response plots, and the optimized formulation composition [16–18].

Table 1. Experimental Design for Optimization of Mebeverine Hydrochloride Orodispersible Tablets

Run	Psyllium Husk (mg)	Binder (mg)	Disintegration Time (s)	Hardness (N)
1	40	24	36.6	39
2	50	24	30.8	31
3	50	8	24.3	21
4	50	16	27.5	27
5	40	8	31.5	25
6	30	8	38.4	32
7	30	24	43.1	45
8	40	16	33.5	33
9	30	16	41.5	37

Table 1 presents the nine experimental combinations in a systematic 3×3 matrix for clarity; the corresponding batch identities and measured responses are retained.

2.3 Drug–Excipient Compatibility

Drug excipient compatibility was evaluated to assess the chemical stability of mebeverine hydrochloride in the presence of the selected formulation ingredients. Physical mixtures of mebeverine hydrochloride were prepared separately with each excipient in the intended formulation ratio. Initial drug content (% assay) was determined at T0, and the mixtures were stored at 50 °C for 30 days. The samples were then reanalyzed by the RP HPLC assay method used in the study. No significant change in assay was observed, indicating no detectable degradation under the study conditions (Table 4).

2.4 Formulation of Orodispersible Tablets

ODTs of mebeverine hydrochloride were prepared by direct compression. Each tablet contained 146.5 mg of mebeverine hydrochloride, equivalent to 135 mg of mebeverine. Psyllium husk (30–50 mg) and microcrystalline cellulose (8–24 mg) were varied according to the experimental design. Lactose monohydrate was used as diluent, magnesium stearate as lubricant/glidant, sodium saccharin as sweetener,

and peppermint oil as flavouring agent.

All ingredients were accurately weighed and passed individually through a #40 sieve. Mebeverine hydrochloride, psyllium husk, microcrystalline cellulose, and lactose monohydrate were blended for 10 min. Sodium saccharin and peppermint oil were then incorporated and mixed uniformly. Magnesium stearate was added last and mixed gently for 2–3 min to minimize over lubrication.

The final powder blend was compressed using a rotary tablet compression machine fitted with 10 mm standard round concave punches. The compression force was adjusted to obtain adequate mechanical strength while maintaining rapid disintegration. A target tablet weight of 400 mg was retained because this was the experimentally evaluated composition; reducing the tablet weight to 300 mg would require rebalancing the diluent and reoptimizing compression, flow, disintegration, and dissolution performance. The prepared tablets were stored in airtight containers at room temperature until evaluation.

Table 2: Composition of Mebeverine Hydrochloride Orodispersible Tablet Formulations

Ingredients (mg/tablet)	Function	F1	F2	F3	F4	F5	F6	F7	F8	F9
Mebeverine HCl (equivalent to 135 mg Mebeverine)	Active ingredient	146.5	146.5	146.5	146.5	146.5	146.5	146.5	146.5	146.5

Psyllium husk	Natural disintegrant	40	50	50	50	40	30	30	40	30
Microcrystalline cellulose	Binder	24	24	8	16	8	8	24	16	16
Lactose monohydrate	Diluent	182.5	172.5	188.5	180.5	198.5	208.5	192.5	190.5	200.5
Magnesium stearate	Glidant/Lubricant	4	4	4	4	4	4	4	4	4
Sodium saccharin	Sweetener	1	1	1	1	1	1	1	1	1
Peppermint oil	Flavouring agent	2	2	2	2	2	2	2	2	2
Total weight (mg)		400	400	400	400	400	400	400	400	400

2.5 Evaluation Parameters

2.5.1 Bulk Density

Bulk density was determined by gently transferring a known quantity of the powder blend into a graduated measuring cylinder without applying any external force. The initial volume occupied by the powder was recorded, and the bulk density was calculated as the ratio of the powder mass to its untapped volume. This parameter was used to assess the packing characteristics of the blend before compression and its suitability for direct compression processes [22].

2.5.2 Tapped Density

Tapped density was measured by subjecting the graduated cylinder containing the powder blend to 100 mechanical taps using a tapped density tester. After tapping, the final volume of the powder bed was noted, and tapped density was calculated by dividing the powder mass by the tapped volume. The obtained value provided information regarding the compressibility and packing behavior of the formulation blend [22].

2.5.3 Carr's Compressibility Index

Carr's Compressibility Index was calculated using the values of bulk density and tapped density to evaluate the compressibility of the powder blend. Lower Carr's Index values indicate better flowability, whereas higher values suggest poor flow characteristics. The obtained results were interpreted according to the United States Pharmacopeia (USP) criteria [23].

2.5.4 Hausner Ratio

Hausner Ratio was calculated as the ratio of tapped density to bulk density. It serves as an indicator of powder flow properties, where values close to 1.0 represent excellent flow, while higher values indicate increased cohesiveness and poor flow behavior. The results were interpreted based on USP recommendations [23].

2.5.5 Angle of Repose

The angle of repose was determined using the fixed funnel method. The powder blend was allowed to flow through a funnel to form a conical heap on a flat surface. The height and radius of the powder pile were measured, and the angle of repose was calculated. This test provided an indication of the flowability of the

powder blend, with smaller angles representing better flow characteristics [24].

2.5.6 Weight Variation

The weight variation test was performed by randomly selecting twenty tablets and weighing each tablet individually. The average weight and percentage deviation from the average were calculated. Results were interpreted according to the applicable Indian Pharmacopoeia and USP requirements [25].

2.5.7 Thickness

Tablet thickness was measured using a calibrated Vernier caliper by randomly selecting ten tablets from each batch. The average thickness was calculated to assess dimensional uniformity.

2.5.8 Hardness

Tablet hardness was evaluated using a Monsanto hardness tester. Ten tablets from each batch were tested individually, and the force required to break each tablet was recorded. Adequate hardness is essential to withstand handling, packaging, and transportation while ensuring rapid disintegration of the orodispersible tablets [26].

2.5.9 Friability

Friability testing was carried out using a Roche friabilator. Twenty pre-weighed tablets were rotated at the prescribed speed for 100 revolutions, after which the tablets were dedusted and reweighed. The percentage weight loss was calculated to assess the mechanical strength of the tablets. A friability value of less than 1% was considered acceptable according to pharmacopoeial specifications [26].

2.5.10 Drug Content Uniformity

Drug content was estimated using the RP HPLC assay method used in the study. Tablets were finely powdered, and an accurately weighed quantity equivalent to the required amount of mebeverine hydrochloride was dissolved, suitably diluted, and analyzed under the established chromatographic conditions. Mebeverine hydrochloride was treated as the active pharmaceutical ingredient (API), and the assay was used to assess content uniformity.

2.5.11 *in vitro* Disintegration Time

Disintegration time was determined using the standard

pharmacopoeial disintegration apparatus. A modified test using 6–8 mL of phosphate buffer at pH 5.4 was also used as a study specific oral cavity challenge medium. Normal resting salivary pH is generally reported around 6.2–7.6; therefore, the pH 5.4 medium was retained as the experimental condition and is not claimed to reproduce physiological saliva exactly [30]. Complete disintegration was recorded when no visible firm residue remained.

2.5.12 *in vitro* Dissolution Study

The dissolution profile was evaluated using a USP Type II paddle apparatus containing 900 mL of 0.1 N hydrochloric acid at 37 ± 0.5 °C and 50 rpm. Samples were withdrawn at 2, 5, 10, 15, and 30 min, filtered, and analyzed at 219 nm using the spectrophotometric procedure employed in the study. The withdrawn volume was replaced with fresh medium to maintain sink conditions [28]. The analytical wavelength should be cross checked against the laboratory validated method before submission.

2.5.13 Stability Study

The optimized formulation was subjected to accelerated stability testing at 40 ± 2 °C/ $75 \pm 5\%$ RH for six months in accordance with ICH stability guidance. Samples were evaluated at T0, T3, and T6 for appearance, hardness, friability, disintegration time, drug content, and dissolution.

3. RESULTS

3.1 Design Summary

The optimization study evaluated nine formulations covering three levels of psyllium husk and three levels of microcrystalline cellulose. The selected responses were disintegration time (Y1) and tablet hardness (Y2). The design allowed systematic evaluation of the formulation space and identification of the best performing batch.

Disintegration time varied from 24.3 to 43.1 s, while hardness ranged from 21 to 45 N, demonstrating clear formulation dependent changes in tablet performance.

3.2 Statistical Analysis of Disintegration Time

The statistical analysis identified the linear model as the most suitable mathematical model for describing

the effect of formulation variables on tablet disintegration time. The model was found to be highly significant with a Model F-value of 529.63 ($p < 0.0001$), indicating that the observed changes in disintegration time were primarily due to the selected formulation variables rather than random experimental error (Figure 1).

The model exhibited excellent predictive capability with an R^2 value of 0.9944, indicating that approximately 99.44% of the variability in disintegration time was explained by the selected variables. Similarly, the Adjusted R^2 (0.9925) and Predicted R^2 (0.9862) were in close agreement, confirming the reliability and robustness of the developed model. Furthermore, the Adequate Precision value of 59.91, which is well above the acceptable limit of 4, demonstrated an excellent signal-to-noise ratio and confirmed the suitability of the model for navigating the design space (Table 3, Figure 2).

The ANOVA results revealed that both psyllium husk concentration (Factor A) and binder concentration (Factor B) significantly influenced tablet disintegration time ($p < 0.0001$). Among the two variables, the concentration of psyllium husk exerted the greatest influence, as indicated by its higher F-value. Increasing the concentration of psyllium husk progressively reduced the disintegration time because of its excellent swelling and water uptake capacity (Figure 3). In contrast, increasing the binder concentration delayed tablet disintegration by producing a stronger and more cohesive tablet matrix. The relationship between formulation variables and disintegration time was represented by the following regression equation (actual factors):

$$\text{Disintegration Time (s)} = 55.6333 - 0.673333(A) + 0.339583(B)$$

This equation indicates that an increase in psyllium husk concentration decreases disintegration time (negative coefficient), whereas increasing binder concentration increases disintegration time (positive coefficient) (Figure 4).

Table 3: Combined statistical summary of the response models

Response	Model	F-value	p-value	R^2	Adjusted R^2	Predicted R^2	Adequate Precision	Significant factors
Disintegration time	Linear	529.63	<0.0001	0.9944	0.9925	0.9862	59.91	A and B
Tablet hardness	Linear	179.58	<0.0001	0.9836	0.9781	0.9584	37.89	A and B

3.3 Statistical Analysis of Tablet Hardness

Tablet hardness was also successfully modelled using a linear regression equation. The developed model was highly significant with a Model F-value of 179.58 (p

< 0.0001), confirming that the formulation variables had a statistically significant effect on tablet hardness (Table 3, Figure 5).

The model demonstrated excellent goodness-of-fit

with an R^2 value of 0.9836, indicating that more than 98% of the variability in hardness could be explained by the selected formulation variables. The Adjusted R^2 (0.9781) and Predicted R^2 (0.9584) showed good agreement, suggesting reliable predictive performance. The Adequate Precision value of 37.89 further confirmed that the model possessed sufficient signal strength for optimization and prediction (Figure 6).

Both independent variables significantly affected tablet hardness. Increasing the binder concentration resulted in a progressive increase in hardness due to improved particle binding and stronger interparticulate bonding during compression (Figure 7). On the other

hand, increasing the concentration of psyllium husk slightly reduced hardness because of its fibrous and highly swellable nature, which produced tablets with comparatively lower mechanical strength while still remaining suitable for handling and packaging.

The final regression equation obtained for tablet hardness in terms of actual factors was:

$$\text{Hardness (N)} = 43.2222 - 0.583333(A) + 0.770833(B)$$

The negative coefficient for Factor A indicates that higher psyllium husk levels reduce hardness, whereas the positive coefficient for Factor B confirms that binder concentration enhances tablet hardness (Figure 8).

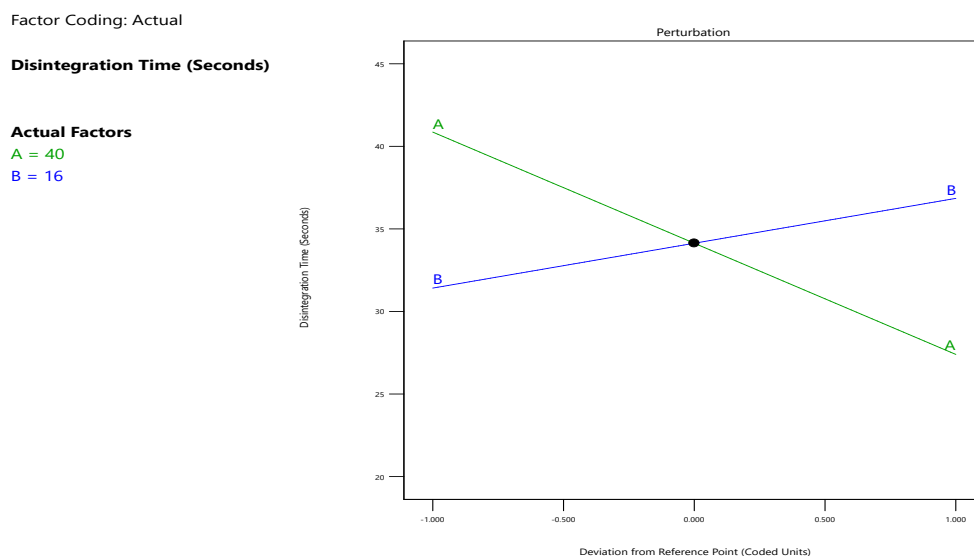


Figure 1: Perturbation plot showing the influence of psyllium husk concentration and binder concentration on disintegration time

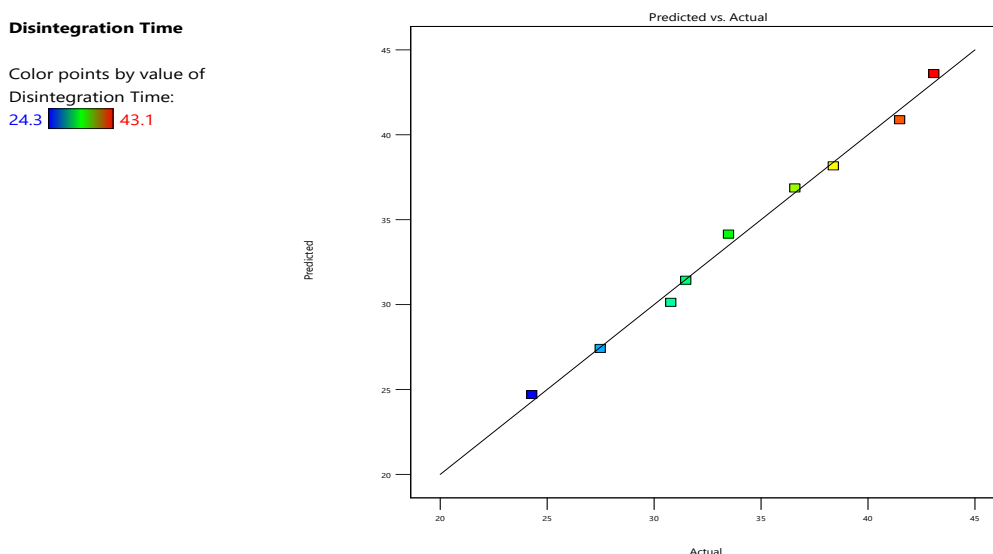


Figure 2: Predicted versus actual plot for disintegration time showing excellent agreement between experimental and predicted values

Factor Coding: Actual

Disintegration Time (Seconds)

● Design Points

24.3 43.1

X1 = A

X2 = B

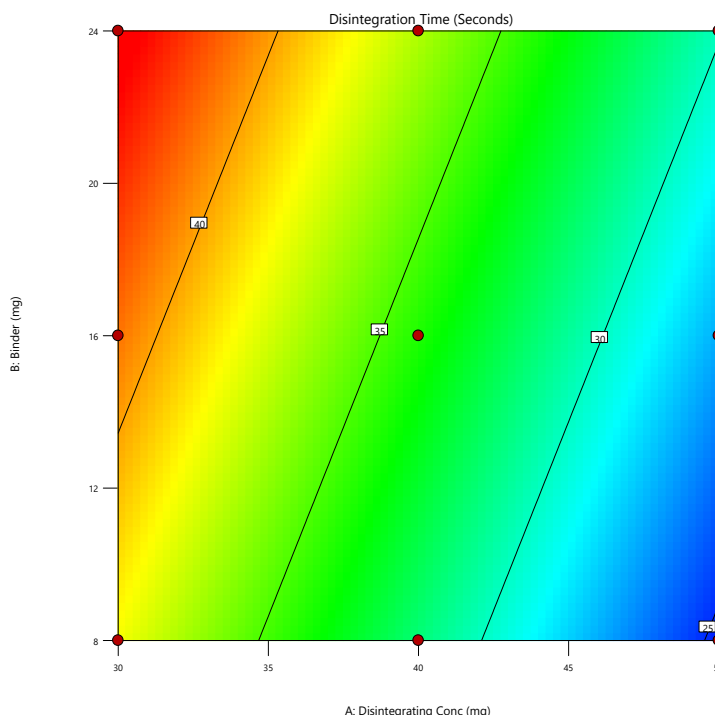


Figure 3: Contour plot illustrating the combined effect of disintegrant and binder concentrations on tablet disintegration time

Factor Coding: Actual

Disintegration Time (Seconds)

Design Points:

● Above Surface

○ Below Surface

24.3 43.1

X1 = A

X2 = B

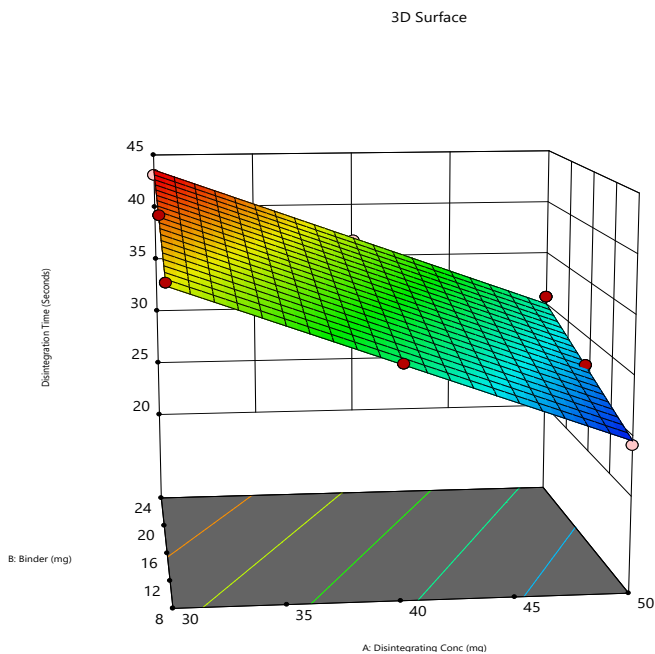


Figure 4: Three-dimensional response surface plot for disintegration time

3.4 Response Surface Analysis

The combined response analysis showed that increasing psyllium husk from 30 to 50 mg reduced disintegration time, whereas increasing binder from 8

to 24 mg increased tablet hardness and prolonged disintegration. The predicted versus actual plots showed close agreement between experimental and model predicted values, supporting the suitability of

the fitted linear models within the studied formulation space.

In contrast, increasing the binder concentration from 8 mg to 24 mg produced tablets with greater mechanical strength but simultaneously prolonged the disintegration process. Higher binder levels created a denser and more cohesive tablet structure that resisted rapid penetration of the dissolution medium, thereby increasing the disintegration time. The response surface plots also showed that tablet hardness increased consistently with increasing binder concentration, confirming the strengthening effect of the binder on tablet integrity.

The predicted versus actual relationships were close to the reference line, with high coefficients of determination for both responses. The results support the use of the fitted models for interpretation within

the studied design space.

3.5 Drug–Excipient Compatibility Study

The drug excipient compatibility study demonstrated that mebeverine hydrochloride remained chemically stable in the presence of all selected excipients after storage at 50 °C for 30 days. The % assay values at the initial time point (T_0) and after storage (T_1) showed only negligible variations, with all samples remaining within the acceptable assay range (99–101%). No visible degradation or significant loss of drug content was observed, indicating the absence of any drug excipient interaction (Table 4). These results confirmed the compatibility of mebeverine hydrochloride with the selected excipients, supporting their suitability for the formulation of orodispersible tablets.

Table 4: Drug Excipient Compatibility Study of Mebeverine Hydrochloride

Sample	Description	% Assay (T_0)	% Assay (T_1)
EC-01	Mebeverine + Isabghol husk	99.28	99.35
EC-02	Mebeverine + Microcrystalline cellulose	99.37	99.14
EC-03	Mebeverine + Lactose monohydrate	99.85	99.56
EC-04	Mebeverine + Magnesium stearate	100.42	100.23
EC-05	Mebeverine + Sodium saccharin	99.81	99.24
EC-06	Mebeverine + Peppermint oil	99.54	99.35

3.6 Formulation of Mebeverine Hydrochloride Orodispersible Tablets

Nine ODT formulations (F1–F9) were prepared by direct compression with a fixed tablet weight of 400 mg. Each formulation contained 146.5 mg of mebeverine hydrochloride, equivalent to 135 mg of mebeverine. Psyllium husk (30–50 mg) and microcrystalline cellulose (8–24 mg) were varied according to the design, while lactose monohydrate was adjusted to maintain tablet weight. Magnesium stearate (4 mg), sodium saccharin (1 mg), and peppermint oil (2 mg) were constant.

3.7 Pre-compression Evaluation of Powder Blend

Pre compression characteristics were evaluated using

bulk density, tapped density, Carr's compressibility index, Hausner ratio, and angle of repose before and after glidant addition. Unless a test method specifies a larger sample size, numerical results are reported as mean $\pm$ SD from replicate determinations. Before magnesium stearate addition, the blends showed moderate flowability, with Carr's index of 22.97–30.84%, Hausner ratio of 1.30–1.45, and angle of repose of 29.28°–37.12%. After glidant addition, Carr's index decreased to 11.42–15.03%, Hausner ratio to 1.13–1.18, and angle of repose to 25.37°–29.45%, indicating improved flow. F5 showed the best flow characteristics.

Table 5: Pre-compression Evaluation of Powder Blend without Glidant

Batch	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio	Angle of Repose (°)
F1	0.571 $\pm$ 0.08	0.795 $\pm$ 0.03	28.18 $\pm$ 0.43	1.39 $\pm$ 0.05	34.22 $\pm$ 1.28
F2	0.624 $\pm$ 0.06	0.827 $\pm$ 0.07	24.55 $\pm$ 0.28	1.33 $\pm$ 0.07	37.12 $\pm$ 1.37
F3	0.592 $\pm$ 0.11	0.856 $\pm$ 0.09	30.84 $\pm$ 0.24	1.45 $\pm$ 0.02	31.65 $\pm$ 1.65
F4	0.677 $\pm$ 0.06	0.917 $\pm$ 0.05	26.17 $\pm$ 0.46	1.35 $\pm$ 0.08	33.57 $\pm$ 2.13
F5	0.597 $\pm$ 0.05	0.775 $\pm$ 0.08	22.97 $\pm$ 0.37	1.30 $\pm$ 0.04	32.65 $\pm$ 1.19
F6	0.575 $\pm$ 0.02	0.796 $\pm$ 0.03	27.76 $\pm$ 0.29	1.38 $\pm$ 0.03	36.95 $\pm$ 0.94
F7	0.519 $\pm$ 0.07	0.726 $\pm$ 0.04	28.51 $\pm$ 0.37	1.40 $\pm$ 0.01	35.41 $\pm$ 1.15
F8	0.599 $\pm$ 0.03	0.834 $\pm$ 0.07	28.51 $\pm$ 0.49	1.39 $\pm$ 0.04	34.97 $\pm$ 0.85
F9	0.541 $\pm$ 0.04	0.726 $\pm$ 0.09	25.48 $\pm$ 0.57	1.34 $\pm$ 0.06	29.28 $\pm$ 1.46

Table 6: Pre-compression Evaluation of Powder Blend with Glidant

Batch	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio	Angle of Repose (°)
F1	0.593 ± 0.13	0.694 ± 0.05	14.55 ± 0.77	1.17 ± 0.07	27.65 ± 1.22
F2	0.633 ± 0.08	0.745 ± 0.01	15.03 ± 0.14	1.18 ± 0.04	28.38 ± 1.19
F3	0.584 ± 0.04	0.684 ± 0.03	14.62 ± 0.37	1.17 ± 0.05	27.25 ± 1.37
F4	0.671 ± 0.09	0.771 ± 0.03	12.97 ± 0.31	1.15 ± 0.01	26.49 ± 1.08
F5	0.582 ± 0.07	0.657 ± 0.05	11.42 ± 0.42	1.13 ± 0.03	25.37 ± 0.72
F6	0.593 ± 0.09	0.687 ± 0.09	13.68 ± 0.22	1.16 ± 0.01	26.97 ± 1.25
F7	0.505 ± 0.05	0.589 ± 0.02	14.26 ± 0.17	1.17 ± 0.04	29.45 ± 0.64
F8	0.583 ± 0.07	0.671 ± 0.05	13.11 ± 0.29	1.15 ± 0.04	27.95 ± 1.18
F9	0.549 ± 0.08	0.635 ± 0.04	13.54 ± 0.37	1.16 ± 0.07	26.33 ± 1.12

3.8 Post-compression Evaluation

The prepared tablets showed acceptable post compression quality. Thickness ranged from 4.3–4.7 mm, average tablet weight from 386.2–411.7 mg, hardness from 21–45 N, and friability from 0.43–0.89%. Drug content ranged from 98.61–100.38%.

Values slightly above 100% can arise from normal analytical and sampling variability and should be interpreted with the corresponding method precision and assay acceptance criteria. F3 exhibited the fastest disintegration (24.3 s) with a hardness of 21 N.

Table 7: Post-compression Evaluation of Orodispersible Tablets

Batch	Disintegration Time (s)	Thickness (mm)	Weight Variation (mg)	Hardness (N)	Friability (%)	Drug Content (%)
F1	36.6 ± 2.1	4.5 ± 0.09	391.4 ± 4.5	39 ± 3	0.89 ± 0.07	98.61 ± 1.12
F2	30.8 ± 3.7	4.4 ± 0.11	398.2 ± 3.4	31 ± 5	0.71 ± 0.04	99.28 ± 0.29
F3	24.3 ± 2.5	4.6 ± 0.08	411.7 ± 7.1	21 ± 3	0.63 ± 0.13	100.12 ± 0.37
F4	27.5 ± 3.3	4.4 ± 0.06	403.9 ± 5.7	27 ± 1	0.44 ± 0.11	99.76 ± 0.21
F5	31.5 ± 1.1	4.5 ± 0.07	389.5 ± 6.3	25 ± 2	0.51 ± 0.19	98.84 ± 0.64
F6	38.4 ± 0.5	4.6 ± 0.11	394.5 ± 4.4	32 ± 4	0.43 ± 0.09	99.31 ± 1.32
F7	43.1 ± 2.4	4.7 ± 0.13	409.8 ± 5.5	45 ± 2	0.65 ± 0.07	98.73 ± 0.41
F8	33.5 ± 3.0	4.6 ± 0.08	386.2 ± 3.1	33 ± 5	0.52 ± 0.21	100.38 ± 0.29
F9	41.5 ± 2.4	4.3 ± 0.07	405.2 ± 5.7	37 ± 3	0.61 ± 0.09	99.42 ± 0.58

3.9 *in vitro* Dissolution Study

All formulations showed rapid drug release, with more than 75% released within 10 min and more than 87% within 15 min. F3 produced the highest release,

reaching 38.49%, 63.21%, 87.25%, 98.54%, and 99.49% at 2, 5, 10, 15, and 30 min, respectively. F3 was therefore selected as the optimized formulation.

Table 8: *in vitro* Dissolution Profile of Orodispersible Tablets (% Drug Release)

Time (min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	28.75	32.37	38.49	33.45	31.99	27.55	24.02	29.24	26.49
5	52.97	57.58	63.21	59.25	55.75	51.47	47.05	53.11	50.45
10	80.36	83.42	87.25	85.54	82.19	78.05	75.11	81.72	77.12
15	93.27	98.12	98.54	98.41	96.04	91.45	87.01	94.46	90.43
30	94.05	98.74	99.49	99.19	96.37	92.85	89.25	95.25	91.46

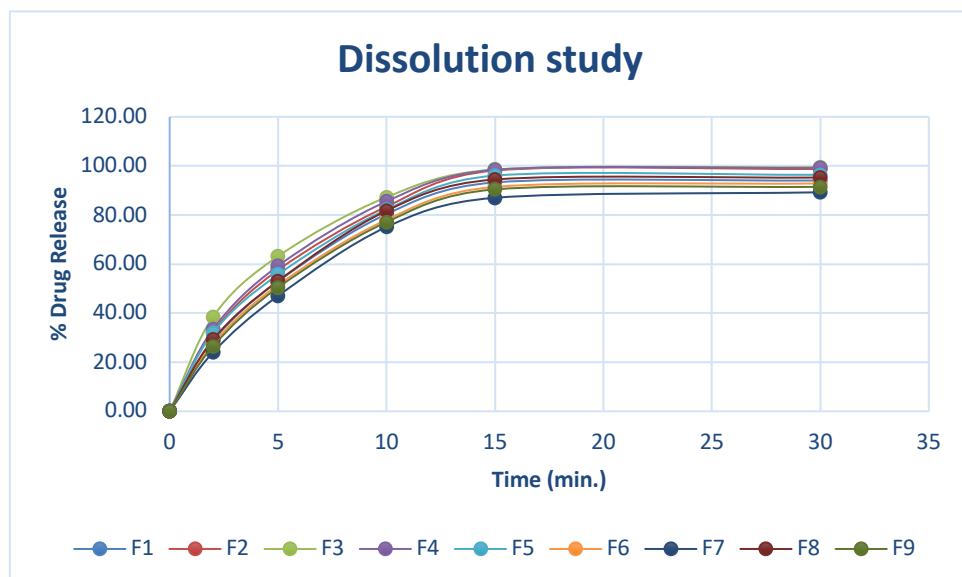


Figure 9: *in vitro* dissolution profiles of formulations F1–F9

3.10 Accelerated Stability Study of Optimized Formulation (F3)

The optimized formulation (F3) was subjected to accelerated stability testing for six months. No appreciable changes were observed in appearance, thickness, hardness, friability, disintegration time,

drug content, or dissolution profile. Drug content remained within 99.78–100.12%, and drug release at 30 min remained above 99% at T0, T3, and T6. The detailed stability dissolution data are provided as Supplementary Table S1, while the comparative profiles are retained in Figure 10.

Table 9: Accelerated Stability Study of Optimized Formulation (F3)

Time (min)	T0	T3	T6
0	0.00	0.00	0.00
2	38.49	38.54	38.37
5	63.21	63.19	63.05
10	87.25	87.51	84.36
15	98.54	98.44	98.39
30	99.49	99.21	99.37

4. Discussion

The main limitations of the present work are that the study was limited to *in vitro* evaluation and accelerated stability, and the experimental matrix did not include *in vivo* performance or patient acceptability testing. Further studies should evaluate pharmacokinetic performance, clinical usability, and scale up robustness before clinical translation.

The drug excipient compatibility study showed only negligible changes in assay after storage at 50 °C for 30 days. The optimized formulation also maintained its physical quality and dissolution performance during six months of accelerated stability testing. These findings support formulation stability under the tested conditions.

Powder evaluation showed that magnesium stearate improved flow properties, supporting direct compression. Post compression tests showed

acceptable thickness, weight variation, friability, and drug content across all batches. The few assay values slightly above 100% are most appropriately interpreted in relation to analytical variability and method precision.

The optimized formulation, F3, contained 50 mg psyllium husk and 8 mg microcrystalline cellulose and showed the shortest disintegration time (24.3 s) with acceptable hardness (21 N). Its superior dissolution profile is consistent with rapid disintegration and increased wetting of the tablet matrix. The finding supports the use of psyllium husk as a natural, sustainable disintegrant for ODT development.

The formulation study showed that psyllium husk concentration was the principal factor governing rapid disintegration, whereas microcrystalline cellulose primarily contributed to tablet hardness. Increasing psyllium husk from 30 to 50 mg reduced disintegration

time, consistent with its high water uptake and swelling behaviour. Increasing binder concentration strengthened the compact but slowed water penetration and tablet break up.

5. Conclusion

The study developed a mebeverine hydrochloride ODT using psyllium husk as a natural superdisintegrant and optimized the formulation through systematic response analysis. F3, containing 50 mg psyllium husk and 8 mg microcrystalline cellulose, provided rapid disintegration (24.3 s), acceptable mechanical strength, low friability, near target drug content, high drug release, and satisfactory six month accelerated stability. The findings support further development of psyllium husk based ODTs, while *in vivo*, patient acceptability, and scale up studies remain necessary.

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