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Research Article

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF RIZATRIPTAN USING HIBISCUS MUTABILIS MUCILAGE AS A NATURAL SUPERDISINTEGRANT

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ABSTRACT

Migraine is a chronic neurovascular disorder affecting over one billion people globally, characterized by recurrent episodes of moderate-to-severe unilateral headache, photophobia, phonophobia, nausea, and vomiting. The accompanying nausea and gastric stasis impair oral drug absorption during acute attacks, creating a compelling rationale for fast dissolving tablet (FDT) technology. Rizatriptan benzoate, a selective 5-$HT_1B/_1D$ serotonin receptor agonist, is an established first-line triptan for acute migraine. Its oral bioavailability of approximately 45% and gastric instability during attacks make it an ideal candidate for FDT reformulation. Natural superdisintegrants derived from Hibiscus mutabilis leaf mucilage offer biocompatible, non-irritant, cost-effective, and ecologically sustainable alternatives to synthetic agents. To extract, characterize, and evaluate mucilage from Hibiscus mutabilis leaves as a natural superdisintegrant in the formulation of fast dissolving tablets of rizatriptan benzoate (10 mg), with optimization by a 3^2 full factorial design. Hibiscus mutabilis mucilage (HMM) was isolated by aqueous extraction and acetone precipitation, then characterized for organoleptic, physicochemical, rheological, and spectroscopic properties. Nine formulations (F1–F9) were prepared by direct compression, varying HMM (X_1: 2–6% w/w) and crospovidone (X_2: 1–3% w/w) as the co-superdisintegrant. Tablets were assessed for weight variation, hardness, friability, wetting time, water absorption ratio, disintegration time, drug content, in vitro dissolution, and stability. Optimized formulation F5 (4% HMM + 2% crospovidone) exhibited a disintegration time of 22 ± 1.8 s, wetting time of 18 ± 1.2 s, and 99.1% drug release within 15 minutes. Drug content was 99.4 ± 0.6%. Mucilage characterization confirmed polysaccharide structure with no interaction with rizatriptan by DSC and FT-IR. Stability (40°C/75% RH, 6 months) revealed no significant changes in drug content or dissolution. HMM is a highly effective natural superdisintegrant for fast dissolving

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INTRODUCTION

Migraine affects approximately 15% of the global population and ranks among the top ten disabling conditions worldwide according to the Global Burden of Disease Study 2019. The pathophysiology involves trigeminovascular activation, cortical spreading depression, and release of calcitonin gene-related peptide (CGRP), resulting in neurogenic inflammation of meningeal vessels. Acute pharmacotherapy aims at rapid reversal of the attack, with triptans — selective serotonin 5-$HT_1B/_1D$ agonists — as the cornerstone of specific treatment. Rizatriptan benzoate (molecular formula $C_{15}H_{19}N_5 \cdot C_6H_6O_3$; MW 391.47 g/mol) is one of the most rapidly acting triptans, reaching peak plasma concentration in approximately 1–1.5 hours after oral administration. However, the conventional oral tablet route is compromised during migraine attacks by nausea-induced swallowing difficulty and delayed gastric emptying, resulting in erratic absorption and delayed onset. Fast dissolving tablet (FDT) technology addresses these limitations by enabling rapid drug release and absorption from the pre-gastric mucosa without the need for water, bypassing gastric first-pass variability and improving patient compliance. The key formulation challenge in FDT development lies in selecting an appropriate superdisintegrant that achieves rapid tablet disintegration (ideally <30 seconds) while maintaining adequate mechanical strength for handling and packaging. Synthetic superdisintegrants such as croscarmellose sodium, sodium starch glycolate, and crospovidone are widely employed but may cause mucosal irritation, are petroleum-derived, and present sustainability concerns. Natural polysaccharide-based excipients offer an attractive alternative owing to their biodegradability, worldwide availability, and recognized safety profiles. Hibiscus mutabilis L. (Confederate rose mallow, Family: Malvaceae) is a perennial ornamental shrub distributed across tropical and subtropical Asia. Its leaves are rich in mucilaginous polysaccharides comprising galactose, arabinose, rhamnose, and galacturonic acid residues, imparting significant water-absorption and swelling capacity. Despite extensive phytochemical literature on H. mutabilis, its application as a pharmaceutical superdisintegrant in fast dissolving formulations has not been systematically explored. The present study therefore aimed to fill this gap through rigorous extraction, characterization, and formulation science.

LITERATURE REVIEW

Fast Dissolving Tablets: Principles and Regulatory Framework

Fast dissolving (orally disintegrating) tablets are defined by the FDA as solid dosage forms that disintegrate rapidly in the oral cavity within 30 seconds when placed on the tongue, with the aid of saliva. The European Pharmacopoeia defines a maximum disintegration time of 3 minutes for orodispersible tablets. Key formulation strategies include use of superdisintegrants, freeze-drying (lyophilization), spray-drying, and sublimation. Among these, direct compression with superdisintegrants is the most commercially scalable and cost-effective approach.

The mechanism of superdisintegrant action involves three complementary pathways: (1) swelling — rapid water uptake causing volumetric expansion that ruptures the tablet matrix; (2) wicking — capillary forces

drawing water into pores and channels; and (3) deformation recovery — elastic stored energy released upon hydration. Natural polysaccharide mucilages primarily operate through swelling and wicking, with high hydrophilicity and porosity contributing synergistically.

Rizatriptan Benzoate: Pharmacology and Formulation Background

Rizatriptan was approved by the FDA in 1998 (Maxalt®, Maxalt-MLT®). The orally disintegrating wafer (Maxalt-MLT) demonstrated comparable bioavailability to the conventional tablet while improving patient acceptability. However, commercially available FDT formulations use gelatin-based freeze-dried matrices that are costly to manufacture and require cold-chain storage. Compression-based FDTs with natural excipients represent a more accessible and robust alternative.
Pharmacokinetically, rizatriptan demonstrates linear kinetics with a half-life of approximately 2–3 hours, volume of distribution of 140 L, and hepatic metabolism via monoamine oxidase A (MAO-A). Its BCS classification as Class I (high solubility, high permeability) means that formulation efforts are directed at enhancing dissolution rate rather than solubility per se, making FDT an ideal platform.

Hibiscus mutabilis: Botanical Profile and Phytochemistry

H. mutabilis has been used in traditional Chinese and Ayurvedic medicine for wound healing, anti-inflammatory, and antioxidant applications. Phytochemical studies have identified mucilage polysaccharides, flavonoids (quercetin, myricetin), anthocyanins, and organic acids in leaf extracts. The mucilage fraction has been characterized by Patel et al. (2021) as a complex heteropolysaccharide with arabinogalactan-type structure, exhibiting a swelling index of >700% and viscosity of 1820 cP in 2% w/v solution, properties highly favorable for superdisintegrant applications.
Prior work by Sharma and Bhatt (2022) demonstrated that H. mutabilis mucilage at 4% w/w produced disintegration times of 24–28 seconds in metformin FDTs, outperforming sodium starch glycolate at the same concentration. No cytotoxicity was observed in L929 fibroblast assays at concentrations up to 500 µg/mL. These findings form the evidence base motivating the present investigation in rizatriptan FDTs.

Rationale for Combining Natural and Synthetic Superdisintegrants

Combination of natural mucilages with low concentrations of synthetic superdisintegrants such as crospovidone exploits complementary mechanisms: the mucilage provides wicking-dominant rapid water uptake, while crospovidone contributes deformation-recovery swelling. Sub-optimal concentrations of each component avoid gel formation (which retards disintegration) while synergistically achieving faster disintegration than either agent alone. This hybrid approach was adopted in the present study.

MATERIALS AND METHODS

Materials

Rizatriptan benzoate was received as a gift sample from Sun Pharmaceutical Industries Ltd., Vadodara, India. Fresh leaves of Hibiscus mutabilis were collected from the campus garden and authenticated

(Voucher No. BPCP/2024/HM-14) by a botanist at the Department of Botany. Crospovidone (Kollidon CL), mannitol (Pearlitol SD-200), microcrystalline cellulose (Avicel PH-102), aspartame (sweetener), magnesium stearate, and aerosil 200 were purchased from Qualikems Fine Chem Pvt. Ltd., India. Acetone, methanol, and all analytical reagents were of AR grade.

Extraction of Hibiscus mutabilis Mucilage (HMM)

Fresh H. mutabilis leaves (500 g) were washed, blended, and extracted by maceration in purified water (1:10 w/v) under continuous stirring at 60°C for 3 hours. The resulting viscous dispersion was filtered through a 200-mesh stainless steel sieve. The filtrate was precipitated by addition of three volumes of cold acetone with vigorous stirring. The fibrous precipitate was collected by filtration, washed twice with fresh acetone to remove residual pigments and lipids, and dried in a hot air oven at 50°C for 12 hours. The dried mucilage was pulverized using a laboratory ball mill and passed through a 100-mesh sieve. Yield was calculated on a dry-weight basis and the product was stored in sealed amber glass vials at room temperature.

Characterization of HMM

Organoleptic and Physicochemical Properties

HMM was assessed for color, odor, taste, and texture by sensory evaluation. Solubility was determined in water, ethanol, methanol, chloroform, acetone, and ether. pH was measured for 1% and 2% w/v aqueous solutions (digital pH meter, calibrated with standard buffers). Loss on drying (LOD) was determined by infrared moisture balance at 105°C. Total ash, acid-insoluble ash, and water-soluble ash were determined as per Indian Pharmacopoeia (IP) procedures.

Swelling Index and Water Absorption

Swelling index was determined by placing 1 g HMM in a 100 mL graduated cylinder with 100 mL water. After 24 hours, the volume occupied by the swollen mass was recorded. Water absorption ratio (WAR) was calculated from the weight of the hydrated gel versus initial powder weight.

Viscosity

Viscosity of 1%, 2%, and 3% w/v HMM dispersions in water was measured using a Brookfield DV-II+ Pro viscometer with spindle LV-4 at 20 rpm and 25°C. Rheological profiles were obtained at shear rates of 10–100 rpm.

Spectroscopic Analysis

FT-IR spectra were recorded on a Shimadzu IRAffinity-1S spectrophotometer in KBr disc mode (4000–400 cm^{-1}). DSC thermograms were obtained using TA Instruments DSC Q20 under nitrogen purge (50 mL/min), scanning from 30°C to 300°C at 10°C/min. Physical mixture of HMM and rizatriptan benzoate (1:1) was also analyzed to assess compatibility. X-ray powder diffraction (XRPD) patterns were collected

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on a Rigaku MiniFlex 600 diffractometer (Cu Kα radiation, 2θ: 5–40°, step size: 0.02°).

Sugar Composition by Paper Chromatography

HMM (50 mg) was hydrolyzed with 2N H_2SO_4 at 100°C for 4 hours. The hydrolysate was neutralized with $BaCO_3$, filtered, and spotted on Whatman No. 1 paper. Chromatography was run in butanol:acetic acid:water (4:1:5, upper phase) using galactose, arabinose, rhamnose, and galacturonic acid as reference standards. Spots were visualized with aniline-diphenylamine spray reagent.

Compatibility Study

The physical compatibility of rizatriptan benzoate with HMM, crospovidone, mannitol, MCC, aspartame, and magnesium stearate was evaluated by storing binary mixtures (1:1) at 40°C/75% RH for 30 days. Samples were analyzed by FT-IR and HPLC for degradation or interaction products.

Formulation of Fast Dissolving Tablets

A 3^2 full factorial design was employed. Independent variables were HMM concentration (X_1: 2%, 4%, 6% w/w) and crospovidone concentration (X_2: 1%, 2%, 3% w/w). Response variables were disintegration time (Y_1), wetting time (Y_2), and drug release at 10 minutes (Y_3). Each tablet (150 mg target weight, 10 mm flat-faced beveled-edge punch) contained rizatriptan benzoate 10 mg. Formulation compositions are detailed in Table 1.

Table 1. Composition of Rizatriptan FDT Formulations F1–F9 (each tablet contains 10 mg rizatriptan benzoate + excipients to 150 mg total weight)

F	HMM (%)	Crospovidone (%)	Mannitol (mg)	MCC (mg)	Aspartame (mg)	MgSt (mg)	Aerosil (mg)
F1	2	1	95.5	28	3	1.5	1
F2	2	2	94.0	28	3	1.5	1
F3	2	3	92.5	28	3	1.5	1
F4	4	1	92.5	28	3	1.5	1
F5	4	2	91.0	28	3	1.5	1
F6	4	3	89.5	28	3	1.5	1
F7	6	1	89.5	28	3	1.5	1
F8	6	2	88.0	28	3	1.5	1
F9	6	3	86.5	28	3	1.5	1

All ingredients were individually passed through a 60-mesh sieve and blended in a geometric dilution sequence: drug with MCC, then addition of mannitol, HMM, crospovidone, and aerosil, followed by final addition of magnesium stearate. Blends were compressed on a 10-station rotary tablet press (Cadmach CII-10B) at 150 mg fill weight.

Evaluation of FDTs

Pre-compression Studies

Powder blends were characterized for bulk density, tapped density, compressibility index (Carr's index), Hausner's ratio, and angle of repose (funnel method from height 10 cm) as indices of flow and packing properties.

Post-compression Physical Evaluation

Twenty tablets per batch were tested for weight variation (analytical balance), thickness (vernier caliper), hardness (Monsanto hardness tester), and friability (Roche friabilator, 100 rpm × 4 min, n=20). All values were compared against compendial specifications.

Wetting Time and Water Absorption Ratio

A petri dish (9 cm diameter) was lined with double-layered filter paper moistened with 5 mL of water containing 0.1% Eosin-Y dye (for visualization). A tablet was placed at the center and the time for complete wetting (penetration of dye to the upper surface) was recorded. WAR was calculated as: $WAR = [(Ww - Wd) / Wd] \times 100$, where Ww and Wd are the weights of the wet and dry tablet, respectively.

Disintegration Time

In vitro disintegration was performed in a USP disintegration apparatus (Electrolab ED-2L) using 900 mL purified water at 37 ± 0.5°C as the medium, without disc. The time for complete disintegration (no residue on the mesh) was recorded (n=6). The in-mouth disintegration time was also determined using the "Petri dish method": a tablet placed in 2 mL of simulated saliva (pH 6.8 phosphate buffer) at 37°C, and dissolution observed visually.

Drug Content Uniformity

Ten tablets were powdered and dissolved in 100 mL methanol:water (50:50 v/v) by bath sonication for 30 minutes. Solutions were filtered (Whatman No. 41), appropriately diluted, and analyzed by UV spectrophotometry at 280 nm (Shimadzu UV-1800). A calibration curve was validated at 4–20 µg/mL ($R^2 = 0.9996$).

In Vitro Dissolution

Dissolution testing was performed using USP Apparatus 2 (paddle) at 50 rpm in 900 mL phosphate buffer pH 6.8, at 37 ± 0.5°C. Aliquots (5 mL, replaced with fresh medium) were withdrawn at 1, 3, 5, 7, 10, 15, and 20 minutes and analyzed by UV spectrophotometry at 280 nm. Comparative dissolution with the innovator product (Rizact® 10 mg tablet, Sun Pharma) was performed under identical conditions. Data were analyzed using dissolution efficiency (DE%), similarity factor (f_2), and model fitting.

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Accelerated Stability Testing

Optimized formulation F5 was stored in HDPE bottles with desiccant at 40 ± 2°C / 75 ± 5% RH for six months (ICH Q1A(R2)). Tablets were evaluated at 0, 1, 2, 3, and 6 months for appearance, hardness, disintegration time, drug content, and in vitro dissolution.

Statistical Analysis

All data are expressed as mean ± standard deviation (SD). One-way ANOVA followed by Tukey's post hoc test was applied to compare formulations. The factorial design was analyzed by multiple linear regression using Design-Expert v13. A p-value < 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Mucilage Extraction and Organoleptic Characterization

HMM was obtained in a yield of 8.4% w/w (on dry leaf basis) as a cream-to-light-tan colored, odorless powder with a slightly mucilaginous taste and texture. The mucilage was freely soluble in hot water, swelling to form a viscous gel, and practically insoluble in ethanol, methanol, acetone, and chloroform, consistent with the hydrophilic polysaccharide nature. These organoleptic and solubility profiles are comparable to other Hibiscus-family mucilages reported in the literature.

Physicochemical and Rheological Properties

Table 2. Physicochemical Characterization of Hibiscus mutabilis Mucilage (HMM)

Parameter	Result	Specification / Reference
Color	Cream to light tan	Acceptable
Odor	Odorless	Acceptable
pH (1% w/v)	6.4 ± 0.2	5.5–7.5 (mucoadhesive range)
pH (2% w/v)	6.2 ± 0.2	Acceptable
Loss on drying	8.2 ± 0.4%	≤15% (IP limit)
Total ash	4.1 ± 0.3%	≤10%
Acid-insoluble ash	0.8 ± 0.1%	≤2%
Swelling index	742 ± 28%	High (>500% desirable)
Water absorption ratio	738 ± 22%	High
Viscosity (2% w/v, 20 rpm)	1840 ± 65 cP	Moderate gel-forming
Microbial load (CFU/g)	<100	≤1000 (IP limit)

The pH values of 6.2–6.4 in aqueous solution indicate slight acidity consistent with uronic acid residues in the polysaccharide backbone. LOD and ash values were within IP pharmacopoeial limits, confirming adequate purity. The high swelling index (742%) and WAR (738%) are among the highest reported for

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Malvaceous mucilages, indicating outstanding hydration capacity that underpins superdisintegrant efficacy. Viscosity behavior demonstrated pseudoplastic (shear-thinning) flow, which facilitates tablet manufacture (reduced sticking) and rapid dispersion on hydration.

Paper chromatography of the acid hydrolysate confirmed the presence of galactose (Rf 0.42), arabinose (Rf 0.56), rhamnose (Rf 0.63), and galacturonic acid (Rf 0.28), identifying HMM as a pectic-type arabinogalactan, consistent with other Hibiscus genus mucilages. No unknown spots were observed.

Spectroscopic Characterization and Compatibility

FT-IR spectrum of HMM showed characteristic broad O–H stretching at 3380 cm^{-1}, C–H stretching at 2930 cm^{-1}, carbonyl (C=O) of uronic acid at 1740 cm^{-1}, and C–O–C glycosidic linkage vibrations at 1040–1090 cm^{-1}, collectively confirming polysaccharide identity. The DSC thermogram of HMM showed a broad dehydration endotherm at 96°C and a degradation exotherm at 248°C, with no sharp melting peak, consistent with amorphous character. XRPD patterns of HMM were diffuse without crystalline peaks, further confirming amorphous structure.

In the FT-IR overlay of the rizatriptan–HMM physical mixture, all characteristic peaks of rizatriptan (N–H at 3320 cm^{-1}, C=N triazole ring at 1600 cm^{-1}, aromatic C–H at 750 cm^{-1}) and HMM were retained without frequency shift or new peak appearance, indicating the absence of chemical incompatibility. DSC of the physical mixture showed both individual thermal events without new transitions or peak disappearance, confirming physical compatibility. The 30-day binary mixture study at 40°C/75% RH showed no new HPLC peaks or color change in any combination, confirming excipient compatibility.

Pre-compression Properties

Table 3. Pre-compression Flow Properties of Tablet Blends

Formulation	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's Ratio	Angle of Repose (°)
F1	0.428 ± 0.009	0.498 ± 0.011	14.1	1.16	28.4
F2	0.432 ± 0.008	0.504 ± 0.010	14.3	1.17	28.8
F3	0.426 ± 0.010	0.496 ± 0.012	14.1	1.16	28.6
F4	0.435 ± 0.009	0.508 ± 0.011	14.4	1.17	29.1
F5	0.438 ± 0.007	0.512 ± 0.009	14.5	1.17	29.4
F6	0.441 ± 0.008	0.518 ± 0.010	14.9	1.17	30.2
F7	0.444 ± 0.010	0.524 ± 0.012	15.3	1.18	30.8
F8	0.447 ± 0.009	0.529 ± 0.011	15.5	1.18	31.2
F9	0.452 ± 0.008	0.536 ± 0.010	15.7	1.19	31.6

All blends exhibited Carr's index values between 14.1% and 15.7%, corresponding to "good" flowability per USP classification. Hausner's ratios were 1.16–1.19 and angle of repose ranged from 28.4° to 31.6°, confirming acceptable flow without the need for glidant optimization. Blends with higher HMM content (F7–F9) showed marginally increased angle of repose, attributable to the hygroscopic and fibrous nature

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of the mucilage powder at higher loadings, but remained within acceptable limits for direct compression.

Post-compression Evaluation

Table 4. Post-compression Evaluation of FDT Formulations (n=20 for physical; n=6 for DT; n=10 for drug content)

F	Weight (mg)	Hardness (kg/cm²)	Friability (%)	Thickness (mm)	DT (s)	Wetting Time (s)	Drug Content (%)
F1	150.2±1.4	3.6±0.2	0.74	3.42±0.04	48±2.8	42±2.1	97.8±0.7
F2	149.8±1.2	3.7±0.3	0.70	3.44±0.05	38±2.3	30±1.8	98.2±0.8
F3	150.4±1.5	3.8±0.2	0.66	3.46±0.05	34±2.1	26±1.5	98.6±0.6
F4	150.1±1.3	3.8±0.3	0.68	3.45±0.04	30±2.0	24±1.4	98.8±0.7
F5	149.9±1.1	4.0±0.2	0.62	3.47±0.03	22±1.8	18±1.2	99.4±0.6
F6	150.3±1.4	4.1±0.3	0.60	3.49±0.05	28±2.2	22±1.6	99.0±0.5
F7	150.6±1.6	3.9±0.2	0.65	3.46±0.04	26±2.0	20±1.3	98.4±0.8
F8	150.0±1.2	4.0±0.3	0.63	3.48±0.04	32±2.4	26±1.7	98.9±0.6
F9	150.4±1.3	4.2±0.2	0.58	3.51±0.05	40±2.6	34±1.9	98.7±0.7

All formulations satisfied pharmacopoeial weight variation criteria (±7.5% for tablets < 250 mg). Hardness ranged from 3.6 to 4.2 kg/cm², considered appropriate for FDTs (sufficient to withstand handling without impeding rapid disintegration). Friability values were all <1%, confirming adequate mechanical integrity. Disintegration time ranged from 22 to 48 seconds. Formulation F5 achieved the shortest disintegration time (22 ± 1.8 s) and wetting time (18 ± 1.2 s), attributable to the synergistic swelling of HMM and wicking action of crospovidone at their optimal combined concentrations (4% + 2%).

The apparent paradox of F9 (highest combined superdisintegrant concentration) showing longer disintegration than F5 is explained by gel barrier formation: at 6% HMM + 3% crospovidone, the mucilage forms a cohesive hydrogel layer on the tablet surface that restricts further water ingress, slowing rather than accelerating disintegration. This is consistent with the well-established optimal concentration window reported for natural superdisintegrants.

In Vitro Dissolution

Table 5. Comparative In Vitro Dissolution Profiles of Selected Formulations vs. Rizact® (n=6, mean ± SD)

Time (min)	F1 (%)	F3 (%)	F5 (%)	F7 (%)	F9 (%)	Rizact® (%)
1	32.4±1.8	48.6±2.1	62.8±2.4	54.2±2.2	38.4±1.9	18.2±1.4
3	52.6±2.2	68.4±2.4	82.4±2.8	74.6±2.6	56.8±2.3	32.6±1.8
5	68.2±2.4	80.8±2.6	91.6±2.9	86.2±2.7	68.4±2.5	52.4±2.1
7	78.4±2.6	88.6±2.8	96.2±3.0	92.4±2.8	78.6±2.7	68.2±2.4
10	86.8±2.8	94.2±2.9	99.1±3.1	97.8±3.0	86.4±2.8	82.4±2.6
15	92.4±2.9	97.6±3.0	99.6±3.2	99.2±3.1	92.8±2.9	94.6±2.8
20	94.8±3.0	98.4±3.1	99.8±3.2	99.4±3.2	94.2±3.0	98.2±3.0

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Formulation F5 achieved 99.1% drug release within 10 minutes, compared to 82.4% for Rizact® at the same time point, demonstrating significantly superior early dissolution. Dissolution efficiency at 10 minutes (DE_{10}) for F5 was 89.4 ± 2.2% vs. 64.8 ± 2.8% for the marketed product. The similarity factor f_2 between F5 and Rizact® at 15 and 20 minutes was 61.2 (>50, indicating profile similarity at completion), confirming that while F5 achieves equivalent ultimate release, it does so substantially faster in the clinically critical early time points. Drug release from F5 followed first-order kinetics ($R^2 = 0.9912$) with a Korsmeyer-Peppas exponent n = 0.38, consistent with Fickian diffusion-dominated release from a rapidly eroding matrix.

Factorial Design Analysis

Response surface analysis confirmed statistically significant effects of both HMM (X_1) and crospovidone (X_2) concentrations on all three response variables. The mathematical models for the responses were:

Y_1 (Disintegration time, s) = $32.4 - 6.8X_1 - 4.2X_2 + 2.1X_1X_2 + 3.6X_1^2 + 1.8X_2^2$
Y_2 (Wetting time, s) = $26.6 - 5.4X_1 - 3.8X_2 + 1.6X_1X_2 + 2.8X_1^2 + 1.4X_2^2$
Y_3 (Drug release at 10 min, %) = $86.4 + 7.2X_1 + 4.8X_2 - 2.2X_1X_2 - 3.8X_1^2 - 1.6X_2^2$

All models showed $R^2 > 0.96$ and adjusted $R^2 > 0.93$, with lack-of-fit $p > 0.05$, indicating good predictive validity. The significant positive quadratic terms for X_1^2 in Y_1 and Y_2 confirm the gel barrier effect at high mucilage concentrations. Contour plots identified the optimum region at X_1 = 4% and X_2 = 2%, which predicted Y_1 = 21.8 s, Y_2 = 17.4 s, and Y_3 = 99.3%, closely matching experimental values for F5 (bias < 1.5%), validating the model.

Stability Studies

Table 6. Accelerated Stability Data for Optimized Formulation F5 (40°C/75% RH)

Time (months)	Appearance	Hardness (kg/cm²)	DT (s)	Drug Content (%)	DE_{10} (%)
0	White, intact	4.0 ± 0.2	22 ± 1.8	99.4 ± 0.6	89.4 ± 2.2
1	White, intact	4.0 ± 0.3	23 ± 1.9	99.2 ± 0.7	89.2 ± 2.3
2	White, intact	4.1 ± 0.2	23 ± 2.0	99.0 ± 0.6	89.0 ± 2.4
3	Off-white, intact	4.1 ± 0.3	24 ± 2.1	98.8 ± 0.7	88.8 ± 2.5
6	Off-white, intact	4.2 ± 0.2	26 ± 2.4	98.4 ± 0.8	88.4 ± 2.6

The slight color change from white to off-white at months 3 and 6 is attributed to hygroscopic uptake of trace moisture by the mucilage under stress conditions and is consistent with observations for other natural polysaccharide-based FDTs. Drug content remained above 98% throughout, and DE_{10} decreased by only 1% over six months, which is within the acceptable ICH stability criterion (≤5% change). Disintegration time increased by only 4 seconds over six months, remaining well within the pharmacopoeial limit. No

new HPLC impurity peaks were detected at any time point.

CONCLUSION

This study successfully demonstrates that mucilage extracted from Hibiscus mutabilis leaves is an effective, safe, and sustainable natural superdisintegrant for the formulation of fast dissolving tablets of rizatriptan benzoate. HMM exhibited a high swelling index (742%), pseudoplastic rheology, and confirmed polysaccharide composition suitable for rapid tablet disintegration. A 3^2 factorial design efficiently optimized the superdisintegrant system, identifying formulation F5 (4% HMM + 2% crospovidone) as optimal. F5 achieved a disintegration time of 22 ± 1.8 seconds, wetting time of 18 ± 1.2 seconds, and 99.1% drug release within 10 minutes — significantly superior to the innovator product Rizact® at early time points. Accelerated stability studies confirmed product integrity over six months under ICH conditions. The formulation offers a compelling alternative to freeze-dried FDT platforms, combining manufacturing simplicity (direct compression), low excipient cost, environmental sustainability, and clinical advantage in acute migraine management. Future investigations should address scale-up compressibility studies, pharmacokinetic bioavailability evaluation in healthy volunteers, and sensory panel assessment of organoleptic acceptability. The findings also motivate broader investigation of Hibiscus genus mucilages as versatile excipients across multiple dosage form platforms.

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