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Formulation and Evaluation of Sustained-Release Matrix Tablets of Diltiazem Hydrochloride Utilizing Novel Natural Biopolymer Blends

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Abstract

Background: The oral approach to medication administration remains highly preferred due to its convenience and improved patient compliance compared to parenteral methods. Oral controlled-delivery systems maintain consistent therapeutic drug levels, thereby maximizing safety and reducing side effects. Among these, matrix sustained-release tablets are highly favored for their manufacturing simplicity, cost-effectiveness, and resistance to dose dumping. ***Objective:*** This research aimed to develop and optimize sustained-release matrix tablets of Diltiazem Hydrochloride—a calcium channel blocker for hypertension and angina characterized by a short elimination half-life (3.5 hours) and low bioavailability (30–40%) due to extensive first-pass metabolism—using the natural biopolymers Tamarind gum and *Cassia roxburghii* gum as release modifiers. ***Methods:*** Preformulation Fourier Transform Infrared (FTIR) spectroscopy was performed to evaluate drug-polymer compatibility. Powder blends were characterized for flow properties prior to compression. The formulated tablets were evaluated for physical parameters per official Indian Pharmacopoeia (IP) standards, alongside *in-vitro* dissolution testing. ***Results:*** FTIR spectra revealed no chemical interactions between the drug and the natural gums. The powder blends exhibited favorable flow properties, with an angle of repose between 25° and 33° and a Carr's Index ranging from 9.0 to 19.0. All compressed tablets met IP specifications for hardness, thickness, friability, weight variation, and content uniformity. *In-vitro* drug release studies demonstrated that the optimized formulation, DH13, successfully prolonged drug release, achieving a maximum dissolution of 99.94% at 12 hours. Kinetic modeling indicated that the release mechanism strictly adhered to the Higuchi model, exhibiting a high correlation coefficient ($R^2 = 0.980$). Furthermore, accelerated stability testing (40 °C±2°C 75 ± 5%) of the optimized DH13 batch over 30 days showed no significant changes in physical appearance, chemical content, or dissolution profiles. ***Conclusion:*** The study demonstrates that the optimized natural polymer-based matrix tablet (DH13) provides a robust, stable, and highly reproducible 12-hour sustained-release profile suitable for the effective oral administration of Diltiazem Hydrochloride.

Keywords: Diltiazem Hydrochloride; Matrix Tablet; *Tamarindus indica*; *Cassia roxburghii*; Natural Biopolymers; Higuchi Kinetics; In-Vitro Dissolution; Accelerated Stability.

1. INTRODUCTION

The oral route remains the undisputed gold standard for medication administration in modern therapeutics, offering unmatched advantages such as non-invasive dosing, ease of ingestion, and high patient compliance compared to parenteral methods. However, conventional immediate-release oral delivery systems frequently yield dramatic peaks and troughs in systemic blood plasma concentrations. These systemic oscillations can lead to transient toxicity when blood levels spike or sub-therapeutic failure when concentrations fall below the minimum effective threshold, necessitating frequent daily dosing frequencies.

To overcome these clinical drawbacks, pharmaceutical engineers have prioritized oral controlled and sustained-release (SR) drug delivery networks. These advanced architectures are designed to release the active pharmaceutical ingredient (API) at a carefully predetermined rate, establishing and maintaining static therapeutic plasma levels for prolonged durations while mitigating toxic side effects.

Among the diverse processing methods utilized to fabricate oral sustained-release systems, matrix tablet technology stands out for its high process efficiency, structural robustness, and ease of industrial scalability. In a matrix configuration, the drug is uniformly

distributed throughout a structured polymeric network. The rate of drug liberation is governed by the hydration, swelling, diffusion, and erosion kinetics of the selected polymer matrix formers.

While synthetic hydrophilic polymers like Hydroxypropyl Methylcellulose (HPMC) are widely used, modern pharmaceutical research is focusing heavily on natural plant-derived biopolymers. Natural gums and mucilages are highly advantageous matrix modifiers due to their excellent biocompatibility, non-toxic nature, low cost, environmental sustainability, and favorable regulatory status. Upon contact with gastrointestinal fluid, these polysaccharides hydrate rapidly to form an intricate, viscous gel barrier that successfully retards drug dissolution and controls diffusion pathways.

Diltiazem Hydrochloride is a widely prescribed benzothiazepine calcium channel blocker used to treat essential hypertension, angina pectoris, and certain cardiac arrhythmias. Structurally, it is a highly water-soluble crystalline powder that undergoes rapid and extensive hepatic first-pass metabolism upon conventional oral ingestion. Consequently, its systemic bioavailability is limited to a mere 30–40%. Coupled with a brief elimination half-life of approximately 3.5 hours, immediate-release diltiazem requires multiple daily doses (typically three to four times a day) to maintain therapeutic control. This intensive dosing schedule often reduces patient compliance and compromises therapy.

Therefore, developing an optimized 12-hour sustained-release matrix tablet using natural plant polysaccharides is a highly desirable strategy. This study explores the isolation, preformulation, and post-compression optimization of a dual-action natural polymer matrix composed of Tamarind seed gum (*Tamarindus indica*) and *Cassia roxburghii* seed gum to achieve a stable, diffusion-controlled release profile for Diltiazem Hydrochloride.

2. MATERIALS AND METHODS

2.1. Materials

Diltiazem Hydrochloride (Analytical Reagent [AR] Grade) was generously provided as a gift sample by Teva Pharmaceutical Industries Pvt. Ltd., India. Hydroxypropyl Methylcellulose (HPMC K100) was procured from Modimudi Pharmaceuticals. Standard pharmaceutical-grade excipients, including Microcrystalline Cellulose (MCC 101), Lactose, Magnesium Stearate, and Aerosil 200, were sourced from Aurobindo Pharma Ltd., Hyderabad, India. The natural biopolymers evaluated as modified-release modifiers were locally isolated and identified as detailed below:

Table 1: Phytochemical Screening of Isolated Seed Gums of *Tamarindus indica* and *Cassia roxburghii*

Material No.	Isolated Natural Polymer	Botanical Source Isolation	Family Classification
1	Tamarind Gum	Endosperm Seeds of *Tamarindus indica*	Leguminosae
2	*Cassia roxburghii* Gum	Endosperm Seeds of *Cassia roxburghii*	Caesalpiniaceae

2.2. Equipment and Instrumentation

The analytical and mechanical instrumentation used throughout this research includes:

- **Digital Analytical Balance:** Sartorius Balance – BT124S (High-precision mass tracking)
- **UV-Visible Spectrophotometer:** Shimadzu Model UV-1800, Japan (Quantitative drug analysis)
- **FTIR Spectrophotometer:** Shimadzu Model FTIR-8700 (Functional group and compatibility tracking)
- **Dissolution Test Apparatus:** LabIndia Ltd. USP Type II Paddle Station
- **Digital pH Meter:** LabIndia Digital pH Calibration Desk
- **Tablet Hardness Tester:** Monsanto Mechanical Crushing Force Indicator
- **Tablet Friability Apparatus:** Roche Friabilator Station
- **Tablet Compression System:** Cadmach Single-Punch Rotary Mechanical Press, Ahmedabad

2.3. Phytochemical Screening and Qualitative Chemical Characterization

To confirm the purity, extraction efficiency, and biochemical profile of the isolated natural gums, the extracts were subjected to qualitative chemical tests for various phytoconstituents.

2.3.1. Test for Alkaloids

A 0.5 g portion of each isolated plant extract was separately stirred with a few milliliters of dilute hydrochloric acid (HCl) and filtered. The resulting filtrate was systematically tested with specific alkaloidal reagents:

- **Dragendorff's Test:** A 2 mL aliquot of filtrate was treated with 1 mL of Dragendorff's reagent (Potassium bismuth iodide solution). The presence of alkaloids is marked by a reddish-brown precipitate.
- **Mayer's Test:** A 2 mL sample of filtrate was treated with 1 mL of Mayer's reagent (Potassium mercuric iodide solution). The formation of a creamy white precipitate indicates alkaloidal entities.
- **Hager's Test:** A 2 mL portion of filtrate was treated with 2 mL of Hager's reagent (Saturated

aqueous picric acid solution). A distinct yellow precipitate confirms the presence of alkaloids.

2.3.2. Test for Fixed Oils and Fats

- **Oily Spot Test:** A small drop of each concentrated liquid extract was spotted onto a quantitative filter paper. After solvent evaporation, the presence of fixed oils or lipid fractions is identified by a persistent translucent oily stain.

2.3.3. Test for Phenolics and Tannins

A 100 mg portion of individual dry gum extract was boiled with 1 mL of distilled water and filtered. The clear filtrate was divided and evaluated using two distinct methods:

- **Ferric Chloride Test:** The filtrate was treated with 2 mL of a 1% ferric chloride solution. The development of a deep bluish-black color indicates a phenolic nucleus.
- **Lead Acetate Test:** The filtrate was treated dropwise with a lead acetate solution. The formation of a bulky yellow precipitate confirms tannin structures.

2.3.4. Test for Flavonoids

- **Alkaline Reagent Assay:** A 100 mg sample of the plant polymer extract was treated with a few drops of sodium hydroxide (NaOH) solution, generating an intense yellow color. The subsequent addition of dilute hydrochloric acid causes the solution to turn colorless, confirming the presence of flavonoids.

2.4. Formulating Diltiazem Hydrochloride SR Matrix Tablets

Sustained-release matrix tablet batches were prepared using the direct compression technique. The formulations incorporated varying weight ratios of individual and combined biopolymer combinations (Tamarind Gum, *Cassia roxburghii* gum, and Xanthan gum) acting as rate-controlling matrices, alongside a fixed dose of Diltiazem Hydrochloride (100 mg). The formulations were finalized into sequential batches labeled DH1 through DH13.

2.5. Analytical Evaluation of Pre-Compression Powder Blends

Prior to compression, the physical attributes and flowability parameters of the micro-heterogeneous powder matrices were systematically characterized.

2.5.1. Angle of Repose

The friction forces within the loose powder blend were measured using the fixed-funnel method. The blend was poured through a funnel onto a horizontal surface until a stable conical heap formed. The height (h) and radius (r) of the cone were measured, and the angle of repose (θ) was calculated using the following equation:

Formula:

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

2.5.2. Bulk Density and Tapped Density

An accurately weighed mass of the powder blend was introduced into a clean, graduated measuring cylinder to record the initial unsettled bulk volume. The cylinder was then mechanically tapped 500 to 1250 times until a constant, minimum volume was reached. The bulk density and tapped were calculated using the following formulas:

Formula For Bulk Density:

$$\rho_b = \frac{M}{V_0}$$

Where:
ρb = bulk density (g/cm³)
M = weight of powder (g)
V_0 = initial volume (cm³)

Formula For Tapped Formula:

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

Where:
ρt = tapped density (g/cm³)
M = weight of powder (g)
Vt = tapped volume (cm³)

2.5.3. Carr's Compressibility Index

The percentage compressibility of the powder matrix, which indicates its relative structural flowability, was determined using Carr's Index ([1]Carr):

$$(\rho_{tapped} - \rho_{bulk})/\rho_{tapped} \times 100,$$

2.5.4. Hausner's Ratio

Hausner's Ratio (H_R) provides an index of inter particulate friction and was calculated as follows:

H = ρ_tapped / ρ_bulk

Where:

- **ρ_tapped** = tapped density of the powder (density after tapping or vibration to reduce air gaps)
- **ρ_bulk** = bulk density of the powder (freely settled, without tapping) A higher Hausner ratio indicates poorer flowability, while a lower ratio suggests better flowability and easier handling of the powder

2.6. Characterization of Post-Compression Physical Parameters

2.6.1. Thickness and Diameter

Dimensional uniformity ensures consistent tablet production and consumer acceptance. Ten tablets were randomly sampled from each batch, and their thickness and diameter were measured individually using a calibrated digital Vernier caliper.

2.6.2. Crushing Strength (Hardness)

The mechanical resistance of the tablets to chipping or breakage during handling was evaluated

using a Monsanto hardness tester. A tablet was aligned between the fixed and movable jaws of the tester, and the load was gradually increased until structural fracture occurred. Hardness values were recorded in kg/cm^2.

2.6.3. Friability

Surface robustness and resistance to mechanical abrasion were assessed using a Roche friabilator. A pre-weighed sample of twenty tablets ($W_{initial}$) was placed in the drum and rotated at 25 rpm for 4 minutes (100 revolutions). The tablets were then removed, gently dedusted, and reweighed (W_{final}). The percentage friability (F) was calculated using the following formula, with a target limit of less than 1.0%:

Friability (%) = $((W_1 - W_2) / W_1) \times 100$,

Where;

W_1 is the initial weight of the tablets and W_2 is the final weight after testing.

2.6.4. Weight Variation and Mass Uniformity

Twenty tablets were randomly selected from each formulation batch and weighed both individually and collectively using an analytical balance. The average tablet weight was calculated, and individual deviations were evaluated against standard Indian Pharmacopoeia (IP) limits:

Weight Variation (%) = [(Individual Unit Weight − Average Weight) / Average Weight] × 100

Where:

- **Individual Unit Weight** is the weight of a single tablet or capsule
- **Average Weight** is the mean weight of all units in the sample batch

Table 2: Average Mass classification

Standard Group	Average Mass Classification (IP)	Maximum Permissible Deviation (%)
1	≤ 80mg	10.0%
2	> 80 mg to < 250 mg	7.5%
3	> 250 mg	5.0%

2.6.5. Uniformity of Drug Content

To ensure uniform distribution of the active pharmaceutical ingredient, a quantity of tablet powder equivalent to 100 mg of Diltiazem Hydrochloride was dissolved in 50 mL of pH 6.8 phosphate buffer inside a 100 mL volumetric flask. The mixture was sonicated using high-frequency ultrasound for 10 minutes to ensure complete dissolution, and the volume was adjusted to 100 mL with additional buffer.

The solution was filtered through a 0.45µm membrane filter disc. A 5 mL aliquot of the clear filtrate was diluted to 100 mL with the same buffer and analyzed using a UV spectrophotometer at λmax of 237 nm against a blank standard.

2.7. Standardization and Calibration Curves

Standard stock solutions of Diltiazem Hydrochloride were prepared in both 0.1 N HCl and pH 6.8 phosphate buffer. Serial dilutions were prepared to yield precise target concentrations ranging from 4 to 20 µg/mL. The solutions were analyzed at an absorption maximum λmax of 237 nm using a UV spectrophotometer. Linear regression analysis was applied to generate standard calibration curves.

2.8. FTIR Spectroscopic Compatibility Profiling

To investigate any potential solid-state chemical interactions or structural changes between Diltiazem Hydrochloride and the isolated plant polymers during compression, Fourier Transform Infrared (FTIR) spectroscopy was performed. Spectra of the pure API, individual polymers, and the optimized formulation blend (DH13) were acquired using the potassium bromide (KBr) pellet technique on a Shimadzu FTIR-8400S spectrometer over a scan range of 4000 to 400 cm-1.

2.9. In-Vitro Drug Dissolution Profiling

In-vitro dissolution studies were performed over a 12-hour period using a USP Type II (paddle) dissolution apparatus. The experimental conditions were maintained as follows:

- **Dissolution Media Fluid:** Phosphate Buffer (pH 6.8)
- **Total Fluid Volume:** 900 mL
- **Hydrodynamic Agitation Speed:** 50 rpm
- **Thermal Equilibrium State:** \$37^\circ\text{C} \pm 0.5^\circ\text{C}\$
- **Sampling Protocol:** 5 mL samples were withdrawn at 1-hour intervals and immediately replaced with an equal volume of fresh, pre-warmed buffer to maintain sink conditions.
- **Spectrophotometric Quantitation:** Samples were filtered and analyzed at 237 nm using a UV spectrophotometer. Cumulative drug release percentages were plotted over time.

2.10. Accelerated Stability Investigations

To evaluate the stability and structural integrity of the optimized formulation batch (DH13), tablets were subjected to accelerated aging conditions in compliance with ICH guidelines. The tablets were strip-packed and placed in an environmental stability chamber maintained at 40°C ±2°C and 75\% RH ±5\% for 30 days. At the end of the storage period, the samples were retrieved and analyzed for physical appearance, hardness, friability, drug content, and *in-vitro* dissolution characteristics.

3. RESULTS AND DISCUSSION

3.1. Phytochemical Profiles of Isolated Gums

Qualitative phytochemical assays performed on the isolated seed extracts of *Tamarindus indica* and *Cassia roxburghii* confirmed the absence of alkaloids and glycosides across all evaluated fractions (water, petroleum ether, and ethanol). The extracts tested strongly positive for carbohydrates and complex mucilaginous gums. These findings confirm the purity of the isolated biopolymers, verifying their suitability for use as non-reactive, safe excipients in oral drug delivery systems.

3.2. Fluorescence Trace Analysis of *Cassia roxburghii*

To establish standardization parameters and detect any fluorescent impurities, the seed powder of *Cassia roxburghii* was treated with various chemical reagents and examined under visible and ultraviolet (UV) light (254 nm and 365 nm).

Table 3: Fluorescence Trace Analysis and Chromatic Expressions of *Cassia roxburghii* Seed Powder under Visible and UV Light

Crude Matrix Sample	Reagent Treatment	Chromatic Expression (Visible)	Fluorescence Expression (UV)
Cassia roxburghii	1 N Sodium Hydroxide	Yellowish-White	Green
	50% Nitric Acid	Yellowish-White	Green
	1 N Hydrochloric Acid	Gray	Green
	1 N Sulfuric Acid	Pale Yellow	Green

3.3. Standard Calibration Profiles

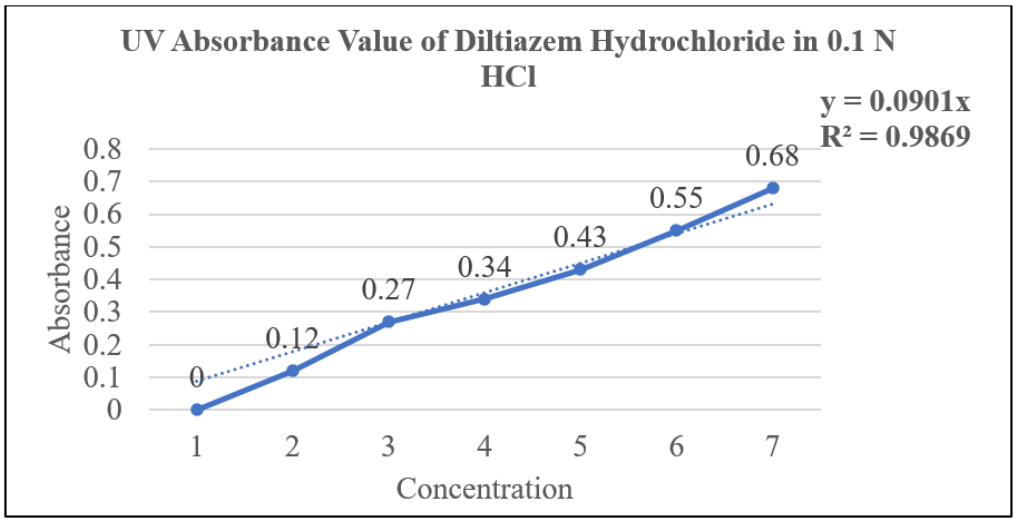
Linear regression analysis of Diltiazem Hydrochloride across the target concentration range showed excellent linearity (R2 value greater than 0.998) in both dissolution media, confirming compliance with Beer-Lambert's law.

3.3.1. Calibration Data in 0.1 N HCl Media

Standard absorbances captured at a maximum wavelength (lambda max) of 237 nm are presented below:

Table 4: Standard Calibration Curve Data of Diltiazem Hydrochloride in 0.1 N HCl Media

Concentration (mcg/ml)	UV Absorbance Value (Mean +/- SD)
0.00	0.000 +/- 0.000
4.00	0.120 +/- 0.001
8.00	0.270 +/- 0.002
10.00	0.340 +/- 0.002
12.00	0.430 +/- 0.002
16.00	0.550 +/- 0.002
20.00	0.680 +/- 0.003



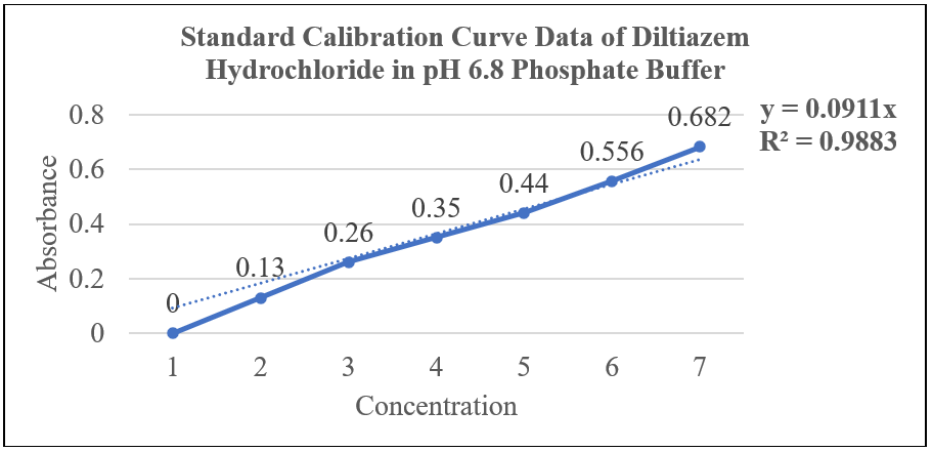
Graph: Standard Calibration Curve Data of Diltiazem Hydrochloride in 0.1 N HCl

3.3.2. Calibration Data in pH 6.8 Phosphate Buffer Media

Standard absorbances captured at a maximum wavelength (lambda max) of 237 nm are presented below.

Table 5: Standard Calibration Curve Data of Diltiazem Hydrochloride in pH 6.8 Phosphate Buffer Media at λmax 237 nm

Concentration (mcg/ml)	UV Absorbance Value (Mean +/- SD)
0.00	0.000 +/- 0.000
4.00	0.130 +/- 0.001
8.00	0.260 +/- 0.002
10.00	0.350 +/- 0.002
12.00	0.440 +/- 0.002
16.00	0.556 +/- 0.002
20.00	0.682 +/- 0.003



Graph: Standard Calibration Curve Data of Diltiazem Hydrochloride in pH 6.8 Phosphate Buffer

3.4. Drug-Polymer Compatibility Screening via FTIR Spectroscopy

FTIR spectroscopy was used to evaluate the chemical compatibility between the drug and the natural excipients. The baseline spectrum of pure Diltiazem Hydrochloride displayed its characteristic principal absorption peaks at 3219 cm-1 (C-H aromatic stretching), 2960 cm-1 (C-H stretching of aliphatic -CH3O groups), 2541.49 cm-1 (amine N-H stretching), 1722 cm-1 (carbonyl C=O stretching), 1502.52 cm-1 (alkane C-H bending), and 1247 cm-1 (ether C-O stretching).

The FTIR spectrum of the optimized binary formulation (DH13) preserved all major principal absorption peaks of the pure drug without significant shifts or attenuation. This confirms the lack of structural interactions or chemical incompatibility between Diltiazem Hydrochloride and the natural Tamarind and Cassia roxburghii polymer matrices during formulation processing.

3.5. Micromeritic Evaluation of Pre-Compression Powder Blends

The pre-compression powder blends for batches DH1 through DH13 were characterized to ensure acceptable flowability and compressibility.

Table 6: Micromeritic Evaluation and Flow Properties of Pre-Compression Powder Blends (Batches DH1 to DH13)

Formulation Batch Code	Angle of Repose (Degrees)	Bulk Density (g/cm3)	Tapped Density (g/cm3)	Carr's Index (%)	Hausner's Ratio
DH1	32.61	0.619	0.825	24.69	1.30
DH2	33.04	0.621	0.838	26.06	1.34
DH3	32.15	0.617	0.810	25.16	1.33
DH4	33.61	0.625	0.839	21.10	1.26
DH5	33.02	0.664	0.885	24.29	1.32
DH6	33.09	0.621	0.840	26.07	1.35
DH7	32.19	0.602	0.808	25.06	1.33
DH8	33.71	0.625	0.839	21.12	1.26
DH9	33.02	0.667	0.885	24.29	1.32
DH10	35.18	0.635	0.810	21.60	1.27
DH11	34.07	0.622	0.826	24.69	1.32
DH12	35.16	0.607	0.806	25.06	1.33
DH13	33.09	0.620	0.841	26.07	1.34

The micromeritic analysis indicates that the bulk density ranged from 0.602 to 0.667 g/cm3, while the tapped density ranged from 0.806 to 0.885 g/cm3. The powder matrices exhibited angles of repose well below 40 degrees (spanning 25 to 33 degrees), and Carr's compressibility indexes remained within acceptable pharmaceutical limits, ensuring uniform die-filling and minimal weight variation during compression.

3.6. Evaluation of Post-Compression Physicochemical Parameters

The compressed matrix tablets were evaluated to verify compliance with official compendial standards.

Table 7: Post-Compression Physicochemical Parameters and Quality Control Evaluation of Matrix Tablets

Batch Code	Weight Variation (mg +/- SD)	Friability (%)	Mean Diameter (mm +/- SD)	Mean Thickness (mm +/- SD)	Crushing Hardness (kg/cm2 +/- SD)	Absolute Drug Content Uniformity (%)
DH1	402.01 +/- 05.2	0.20	7.72 +/- 0.05	3.55 +/- 0.245	5.60 +/- 0.26	99.16 +/- 4.74
DH2	397.95 +/- 05.6	0.18	7.82 +/- 0.03	3.51 +/- 0.114	5.80 +/- 0.78	98.51 +/- 4.68
DH3	399.69 +/- 09.6	0.16	7.70 +/- 0.08	3.55 +/- 0.212	6.00 +/- 0.68	99.35 +/- 5.36
DH4	401.32 +/- 03.6	0.21	7.78 +/- 0.09	3.59 +/- 0.124	5.20 +/- 0.68	101.15 +/- 3.36
DH5	403.36 +/- 05.8	0.24	7.70 +/- 0.10	3.58 +/- 0.089	5.40 +/- 0.25	103.11 +/- 3.25
DH6	402.31 +/- 17.5	0.20	7.58 +/- 0.05	3.53 +/- 0.014	5.60 +/- 0.48	98.80 +/- 2.01
DH7	402.01 +/- 05.2	0.20	7.72 +/- 0.05	3.55 +/- 0.245	5.00 +/- 0.26	97.16 +/- 4.74
DH8	397.95 +/- 05.6	0.18	7.82 +/- 0.03	3.51 +/- 0.114	5.20 +/- 0.78	97.51 +/- 4.68
DH9	396.69 +/- 09.6	0.17	7.70 +/- 0.08	3.55 +/- 0.212	6.00 +/- 0.68	99.35 +/- 5.36
DH10	399.26 +/- 06.4	0.15	7.71 +/- 0.08	3.65 +/- 0.168	6.40 +/- 0.35	97.43 +/- 3.85
DH11	401.40 +/- 05.6	0.18	7.70 +/- 0.05	3.66 +/- 0.212	6.20 +/- 0.26	95.90 +/- 2.74
DH12	398.93 +/- 07.4	0.18	7.72 +/- 0.07	3.57 +/- 0.078	6.40 +/- 0.56	97.20 +/- 4.45
DH13	404.01 +/- 05.2	0.20	7.72 +/- 0.05	3.55 +/- 0.245	6.60 +/- 0.26	98.10 +/- 4.74

All compressed tablet formulations fell well within the permissible mass variation thresholds (plus or minus 5.0% for weights greater than or equal to 250 mg), and friability losses remained far below the standard 1.0% limit, confirming suitable structural integrity during processing. Hardness readings spanned 5.0 to 6.6 kg/cm2, indicating good mechanical strength. Drug content uniformity values ranged from 95.90% to 103.11%, confirming an equitable distribution of the active pharmaceutical ingredient within the natural polymer matrices.

3.7. In-Vitro Dissolution Kinetics and Modulation Performance

In-vitro dissolution studies performed in simulated intestinal fluid (pH 6.8 phosphate buffer) confirmed the sustained-release capacity of the biopolymer matrices over a 12-hour period. Formulation DH13, which utilized an optimized combination of Tamarind gum and Cassia roxburghii seed gum, achieved an ideal controlled release profile, reaching a maximum drug release of 99.94% at the 12th hour.

This sustained-release performance is attributed to the rapid hydration and synergistic swelling behavior of the combined natural polysaccharides. Upon exposure to the buffer medium, the biopolymers formed a cohesive, viscous hydrogel layer that successfully regulated water penetration and controlled the outward diffusion of the highly soluble diltiazem molecules. Formulations containing combinations of Tamarind gum and Cassia roxburghii exhibited superior swelling and drug-retarding profiles compared to batches prepared using Xanthan gum variations.

To define the underlying mass transport kinetics, the dissolution data were evaluated using various mathematical models. The optimized batch DH13 exhibited a linear correlation coefficient (R2) value of 0.980 when fitted to the Higuchi square-root-of-time model. This strong linearity confirms that the drug release mechanism is primarily governed by a classic Fickian diffusion process through the hydrated swelling matrix gel network.

3.8. Post-Chamber Accelerated Stability Profiling

The optimized formulation batch DH13 was subjected to an accelerated stability protocol (40 degrees C +/- 2 degrees C and 75% RH +/- 5%) for 30 days. The post-storage physicochemical parameters are compared with the baseline data below:

Table 8: Comparative Post-Chamber Accelerated Stability Profiling of Optimized Formulation DH13 (Initial vs. Day 30)

Critical Parameter Index	Initial State Baseline Value	Post-Aging Value (Day 30)
Average Mass Uniformity (mg)	404.01 +/- 5.2	402.15 +/- 2.9
Crushing Hardness Force (kg/cm2)	7.72 +/- 0.09	7.68 +/- 0.60
Mean Tablet Thickness (mm)	3.55 +/- 0.245	3.55 +/- 0.240
Surface Friability loss (%)	0.20 +/- 0.2	0.20 +/- 0.3

Critical Parameter Index	Initial State Baseline Value	Post-Aging Value (Day 30)
Absolute Drug Content (%)	98.15 +/- 5.36	98.10 +/- 4.74
Matrix Swelling Index (8 hours)	93.45 +/- 0.05	93.50 +/- 0.09

4. CONCLUSION

This study successfully designed and optimized an oral sustained-release matrix tablet of Diltiazem Hydrochloride utilizing a novel combination of natural plant polysaccharides isolated from *Tamarindus indica* and *Cassia roxburghii* seeds. Preformulation FTIR studies confirmed excellent chemical compatibility between the drug and excipients, preserving the structural integrity of the active molecule. The micro-heterogeneous powder blends displayed optimal flow properties, ensuring favorable processing during direct compression.

The finalized post-compression tablet batches complied fully with official Indian Pharmacopoeia directives for mass uniformity, dimensional tolerances, crushing strength, friability, and drug content. The optimized batch, DH13, successfully modulated drug release over a 12-hour window, achieving a maximum cumulative dissolution profile of 99.94% governed by a Higuchi diffusion-controlled mechanism ($R^2 = 0.980$). Furthermore, accelerated stability testing confirmed the physical and chemical robustness of the system over a 30-day period.

In conclusion, the synergistic use of Tamarind and *Cassia roxburghii* gums provides a highly stable, commercially scalable, and cost-effective biopolymer platform for the sustained oral delivery of Diltiazem Hydrochloride, offering an effective strategy to reduce dosing frequencies and enhance patient compliance.

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