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Review Article

# Formulation and Evaluation of Stomach-Specific Bioadhesive Drug Delivery System of Diltiazem Hydrochloride

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## A B S T R A C T

The present study aimed to develop a stomach-specific bioadhesive tablet of Diltiazem Hydrochloride to achieve controlled and sustained drug release for enhanced bioavailability. The formulation strategy focused on gastroretentive and bioadhesive mechanisms to prolong gastric residence time and improve therapeutic efficacy. Nine formulations (F1–F9) were prepared using varying concentrations of bioadhesive polymers such as chitosan and HPMC K15M, along with excipients like MCC, talc, magnesium stearate, and aerosil.The optimized formulation, F9, exhibited excellent pre-compression and post-compression parameters, with notable bioadhesive strength and a sustained in vitro drug release over 12 hours. It showed a bioadhesive retention time of 12 hours and followed zero-order drug release kinetics, ensuring a steady release independent of drug concentration. This prolonged gastric retention enhances drug absorption at its preferred site, addressing limitations of conventional formulations such as low bioavailability and frequent dosing.The study concludes that the bioadhesive tablet system of Diltiazem Hydrochloride is a promising approach for improving patient compliance and achieving consistent therapeutic effects. The formulation offers potential for scale-up and application to other drugs with similar absorption characteristics.

**Keywords: -** Bioadhesive tablets, Gastric retention, Bioadhesive polymers, Drug absorption, Therapeutic efficacy, Formulation strategies, Mucoadhesion

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## INTRODUCTION

Inrecentyears, significant research has focused on the potential for sustained and site-specific drug delivery to the gastrointestinal tract (GIT) by controlling the transit of orally administered dosage forms. Stomach specific drug delivery system is designed to retain the drug in the GIT, particularly in the stomach, for extended periods.

The concept of gastro retention arises from the need to localize drug delivery to specific regions of the GIT, such as the stomach. Often, drug absorption is limited bythe time the drug remains at the absorption site. Gastrointestinal transit time, from the oral cavity to the rectum, varies among individuals and depends on both the physical properties of the ingested substance and the physiological conditions of the digestive tract.

Gastroretentive systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste and improves solubility for drugs that are less soluble in a high pH environment. It has applications also for local drug delivery to the stomach and proximal small intestines. Gastro retention helps to providebetteravailability ofnew products with new therapeutic possibilities and substantial benefits for patients.

The controlled gastric retention of solid dosage forms may be achieved by the mechanisms of mucoadhesion, flotation, sedimentation, expansion modified shape systems or by the simultaneous administration of pharmacological agent that delay gastric emptying.This review focuses on the principal mechanism of bioadhesion to achieve gastric retention.

The relatively short gastric emptying time in humans, typically averaging 2-3 hours through the primary absorption zones (stomach or upper small intestine), can lead to incomplete drug release from the delivery system, reducing the effectiveness of the administered dose. Close contact between the dosage form and the absorbing membrane can

maximize drug absorption and may also influence the absorption rate. These factors have driven the development of oral sustained release dosage forms with gastric retention capabilities. The key challenge in developing oral sustained release dosage forms is not only to extend the release of the drug but also to ensure that the dosage form remains in the stomach or upper small intestine for a prolonged period. Stomachspecific dosage forms can be highly beneficial for drugs with narrow absorption windows, as these drugs are absorbed only from specific sites in the GIT, primarily the stomach and proximal small intestine.

## MATERIALS AND METHOD

## MATERIALS

Diltiazem Hydrochloride was purchased from Yarrow chem products, Mumbai, Maharashtra. HPMC K100 M and HPMC K 15M was obtained as a gift sample from Colorcon Asia Pvt. Ltd., Goa. Talc, Aerocil, magnesium stearate, micro crystalline cellulose were purchased from S.D. Fine Chemicals Ltd. Mumbai.

## METHOD

Stomach-specific bioadhesive tablets were formulated using the direct compression technique. The drug diltiazem hydrochloride, bioadhesive polymers (such as Chitosan, HPMC K15M), diluent (Microcrystalline cellulose) and glidant (Talc) were all passed through a 60-mesh sieve. Accurately weighed ingredients were blended for 10 minutes. In the final stage, lubricant (Magnesium Stearate, Aerosil) was added and mixed for an additional 5 minutes. The prepared blend was compressed into tablets using a Rotary Tablet Press (CPM030-10 Chamunda Pharma Machinery) fitted with a flat bevelled punch. Tablets with a hardness of 5–7 Kg/cm² were evaluated for pre-compression and post-compression parameters to assess their suitability for gastric retention and bioadhesion.

## FORMULATION DESIGN

**Table 1:** Formulation Design of All Formulation Batches

| Nameof Ingredients | Formulation Code with Their Quantity (Mg) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| **Diltiazem Hcl** | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| **Chitosan Hcl** | 50 | 75 | 100 | 50 | 75 | 100 | 50 | 75 | 100 |
| **HPMC K15 M** | 50 | 50 | 50 | 75 | 75 | 75 | 100 | 100 | 100 |
| **MCC** | 230 | 205 | 180 | 180 | 155 | 130 | 205 | 180 | 130 |
| **Magnesium Stearate** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Talc** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Aerosil** | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| **Total** | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 | 500 |

## Characterization Bioadhesive Tablets

**Compatibility Study of Drug with Polymers:**

**a. Fourier Transform Infra-Red S pectroscopy[4]**

The FTIR spectrum of the drug was recorded on as Infrared spectrophotometer (Shimadzu Asia Pacific-840050). IR spectrum of drug was recorded in the frequency range 400– 4000 $cm^{-1}$. The significant peaks were recorded and were matched with standard FTIR.

**b. Differential Scanning Calorimetry[5]**

Thermal analysis was performed using system with differentials canning calorimeter equipped with a computerized data station. All samples were weighed and heated at a scanning rate of 10°C /min between 30 and 300° C and 40 ml/min of nitrogen flow. The differential scanning calorimetric analysis gives an idea about the interaction of various materials at different temperature. It also allows us to study the possible degradation pathways of the materials.

## Precompression Study[6,7]

**Bulk Density**

Bulk density is determined by measuring the volume of a known mass of a powder sample that has been passed through a screen into a graduated cylinder. The bulk volume of blend was determined. The bulk density calculated by using following formula,

$$\rho_b = m / V_b$$

Where,

$\rho_b$= Bulk density

m =mass of powder

Vb = initial/bulk volume

**Tapped Density**

Tapped Density is the volume of powder determine by tapping by using a measuring cylinder containing weight amount of sample. The measuring cylinder containing known mass of microsphere were tapped for fixed time, and minimum volume occupied in cylinder was determined. Tapped density was calculated by using following formula,

$$\rho_t = m/V_t$$

Where,

$\rho_t$= Tapped density

m= Mass of the powder

$V_t$=Final tapped Volume

**Angle of Repose**

Angle of Repose is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel Method and is the measure of the flowability of powder/granules.

**$q=\tan^{-1}(h/r)$**

Where,

h=Height

r=radius

q=Angle of repose

**Compressibility Index**

The compressibility index is measures of the propensity of a powder to be compressed.

**% Compressibility = $\frac{\text{Tapped density- Bulk density}}{\text{Tapped density}} \times 100$**

**Hausner Ratio**

Flow property is very important parameter to be measured since it affects the mass of uniformity of the dose. It is usually predicted from Hausner Ratio and Angle of Repose Measurement.

**Hausner Ratio = Tapped Density/Bulk Density**

## Post Compression Study[8]

**Bioadhesive Strength**

The bio adhesive strength of the formulated tablets was evaluated using a modified physical balance method. A fresh mucosal membrane (porcine gastric mucosa or egg membrane) was fixed onto a support, and the tablet was attached to a glass slide. After a fixed contact period, weights were gradually added to the opposite pan until the tablet detached. The force required to detach the tablet from the membrane was recorded and expressed in Newtons (N). This test determines the tablet's ability to adhere to the gastric mucosa and ensures gastric retention.

**Bioadhesive Time**

Place a 3×3 cm piece of fresh gastric mucosa (mucosal side in) inside a disintegration basket and secure it flat. Fill the apparatus with 0.1 N HCl (pH 1.2) at 37 °C and set the standard stroke rate (≈30 strokes/min). Lightly moisten one face of the tablet, press it against the mucosa, close the basket, and lower it into the medium. Start timing immediately, and stop when the tablet detaches. Repeat three times and report the average detachment time.

**Swelling Index[9]**

The swelling index of the tablets was determined in 0.1N HCl (pH 1.2) at room temperature. The swollen weight of thetablets was determined at predefined time intervals and weight till it come to constantweight

Tablets composed of bioadhesive polymers that swell when it comes in contact with water. This swelling governs the drug release. The kinetic of swelling is important because the bioadhesive polymers swell when it absorbs the water. Swelling is also vital to ensure Bioadhesion.

**In Vitro Dissolution Study[10]**

The in vitro drug release study was performed using a disintegration test apparatus as a modified method for evaluating the drug release profile of the prepared tablet formulation. 900 mL of 0.1 N HCl was used as the dissolution medium and was maintained at a temperature of 37 ± 0.5°C throughout the study using a thermostatic water bath. One tablet was placed in each tube of the disintegration basket, and the mesh at the bottom of the tubes was removed to allow the drug to release freely into the medium. The basket assembly was then placed in the beakers containing the medium and operated at 50RPM. At regular time intervals (such as1,2,3, upto12 hours),5mLof the sample was withdrawn from the medium and replaced with an equal volume of fresh pre-warmed dissolution medium to maintain sink conditions.

Each withdrawn sample was filtered using Whatman filter paper or a syringe filter, and the absorbance was measured using a UV-Visible spectrophotometer at the λmax of the drug (237 nm forDiltiazemHydrochloride).

**Kinetics of drug release[11]**

The invitro dissolution profile of all batches were fitted to Zero order, first order, Higuchi model, Korsemeyer Peppas model and Hixson Crowel Model to ascertain the kinetic modelling of drug release. Correlation coefficient (R2) values were calculated for linear curves obtained by the regression analysis of the above plot.

Zero-order kinetic model: Cumulative % drug released vs. time

First order kinetic model: log cumulative % drug remaining vs. time

Korsemeyer-Peppas model: Log cumulative % drug released vs. Log time

**Stability Study[12,13]**

Stability studies were carried out at 40°C±2°C/75%RH±5% for a specific period of up to 28 days for the optimized formulation.

## RESULTS AND DISCUSSION:

**Compatibility Study of Drug with Polymers:**

**Fourier-Transform Infrared Spectroscopy Study (FTIR):**

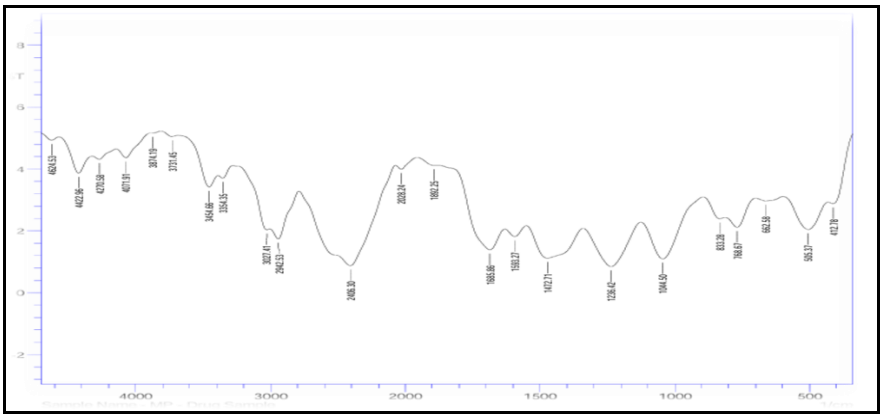


**Figure 01:** FTIR of Diltiazem Hydrochloride

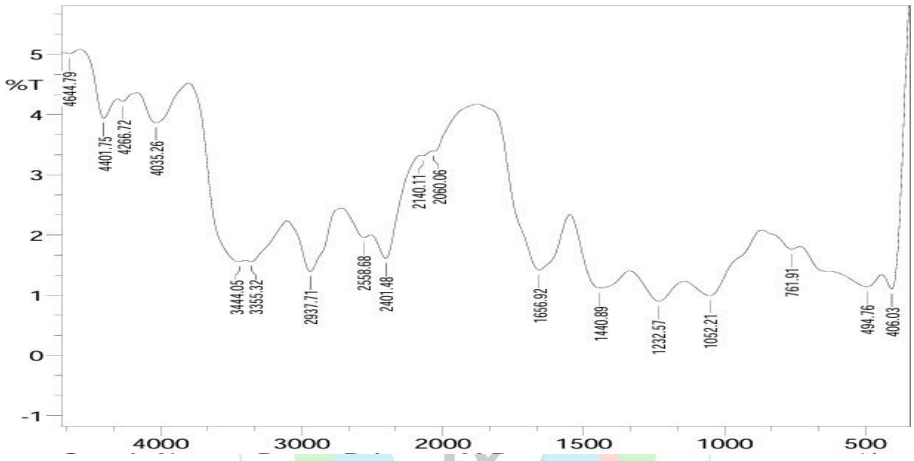



**Figure 02:** FTIR of Drug-Polymer mixture

The FTIR spectra of Diltiazem HCl and the FTIR spectra of drug and polymer physical mixture shown in Figure No. 01 and 02 respectively. The thermogram of Diltiazem hydrochloride shows an endothermic peak at 1682cm$^{-1}$, 1512cm$^{-1}$, 1252 cm$^{-1}$, and 1033 cm$^{-1}$. The principal peak of Diltiazem hydrochloride was found in the FTIR of procured Diltiazem hydrochloride. The broad peak at **3444–3355 cm$^{-1}$** indicates **O–H/N–H stretching**, suggesting hydrogen bonding within the polymer. The **2937 cm$^{-1}$** peak corresponds to **C–H stretching**, confirming intact aliphatic chains of drug and polymer. Peaks at **2140–2060 cm$^{-1}$** may relate to triple bonds but show no drug-polymer interaction. A strong peak at **1656 cm$^{-1}$** represents **C=O/C=C stretching** of the drug, indicating structural stability. Peaks between **1223–1052 cm$^{-1}$** are due to **C–O stretching** from the polymer, and the **761 cm$^{-1}$** peak confirms the drug's aromatic structure. Overall, no significant peak shifts were observed, confirming **no chemical interaction** between drug and polymer.

**Differential Scanning Calorimeter Analysis (DSC)**

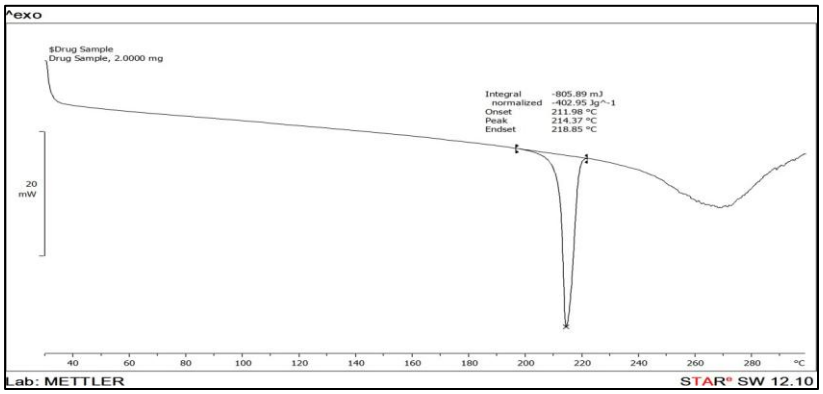



**Figure 03:** DSC of Diltiazem Hydrochloride

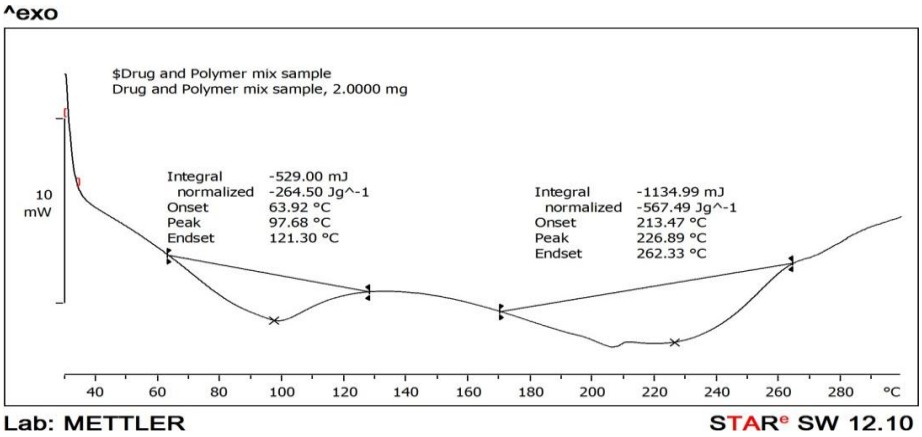



**Figure 04:** DSC of Diltiazem Hydrochloride-Polymer mixture

DSC spectra of procure drug Diltiazem hydrochloride was shown in graph No. 3. It was observed that primarily endothermic corresponding to melting was observed with a peak onset temperature of ~210°C to 212°C and peak of temperature ~215°C to 218°C. Decomposition was become apparent about 230°C. As per literature survey DSC behaviour diltiazem hydrochloride also have peak onset temperature 210°C to 212°C and peak of temperature 215°C to 218°C. Show similar decomposition behaviour above 230°C. Drug polymer study was carried out by Differential Scanning Calorimeter (DSC). Thermogram of a drug Diltiazem Hydrochloride and DSC thermogram of drug and polymer are shown in Graph No.4 It was observed that peak and the temperature and peak of temperature were prominent in DSC spectra of physical mixture of drug and polymer as compared with the DSC spectra behaviour as noted in DSC spectra of pure polymer. This there was no physical and chemical interaction between drug and polymer.

## Precompression Study:

**Table 2:** Pre compression Study of All Formulation Batches

| Batch | Bulk Density (g/cm³)±SD | Tapped Density (g/cm³)±SD | Carr's Index (%)±SD | Hausner Ratio± SD | Angle of Repose (°)±SD |
|---|---|---|---|---|---|
| **F1** | 0.42±0.037 | 0.56±0.0026 | 25.00±0.052 | 1.14±0.5168 | 29.5±0.2656 |
| **F2** | 0.45±0.0056 | 0.58±0.0058 | 22.41±0.058 | 1.03±0.2579 | 26.8±0.1548 |
| **F3** | 0.47±0.0013 | 0.60±0.0064 | 21.67±0.059 | 1.15±0.1596 | 25.7±0.4853 |
| **F4** | 0.44±0.0058 | 0.56±0.0051 | 21.43±0.049 | 1.10±0.1596 | 24.9±0.1486 |
| **F5** | 0.46±0.0069 | 0.59±0.0076 | 22.03±0.049 | 1.13±0.3596 | 26.2±0.2694 |
| **F6** | 0.43±0.0045 | 0.55±0.0035 | 21.82±0.051 | 1.11±0.4586 | 25.4±0.1576 |
| **F7** | 0.45±0.0063 | 0.57±0.0044 | 21.05±0.062 | 1.15±0.5296 | 24.8±0.1586 |
| **F8** | 0.46±0.0052 | 0.58±0.0043 | 20.69±0.050 | 1.13±0.6596 | 26.5±0.2357 |
| **F9** | 0.48±0.0042 | 0.58±0.0076 | 17.24±0.057 | 1.12±0.5963 | 22.3±0.3149 |

All values are expressed as Mean ± Standard Deviation, n=3

All the formulations (F1–F9) were evaluated for bulk density, tapped density, Carr's Index, Hausner Ratio, and angle of repose to assess their flow and compressibility characteristics.

**Bulk Density and Tapped Density:** These values ranged from 0.42to0.48g/cm³ (bulk) and 0.55 to 0.60g/cm³ (tapped), indicating moderate to good packing ability.

**Carr's Index:** All batches had Carr's Index values between 17.24% (F8) and 25.00% (F1). F1 had the highest index, indicating relatively poor flow, while F8 had the lowest, suggesting good flow.

**Hausner Ratio:** The values were in the range of 1.03 to1.15. A ratio close to 1.00 indicates excellent flow. F2 showed the best flow (1.03), while F7 had the highest value (1.15), indicating fair flow.

**Angle of Repose:** Values ranged between 24.8°and 29.5°. All batches had angles below30°, indicating good flow properties overall. F7 and F9had the lowest angles, indicating the best flow.

## Post Compression Study

**Table 3:** Post compression Study of All Formulation Batches

| Batch | Bioadhesive Strength (g) ± SD | Bioadhesive Time (hrs) ± SD |
|---|---|---|
| F1 | 32 ± 0.5963 | 8.6 ± 0.0259 |
| F2 | 34 ± 0.5876 | 9.0 ± 0.0452 |
| F3 | 37 ± 0.5165 | 9.4 ± 0.0274 |
| F4 | 35 ± 0.5986 | 9.1 ± 0.0364 |
| F5 | 38 ± 0.5486 | 9.7 ± 0.248 |
| F6 | 41 ± 0.5419 | 10.5 ± 0.296 |
| F7 | 39 ± 0.5285 | 9.7 ± 0.254 |
| F8 | 42 ± 0.4963 | 10.9 ± 0.296 |
| F9 | 45 ± 0.4856 | 11.6 ± 0.429 |

All values are expressed as Mean ± Standard Deviation,n=3

Bioadhesive strength across the batches ranged from **32 ± 0.5963 g (F1)** to **45 ± 0.4856 g (F9)**, showing a gradual increase in adhesive capacity. This increase suggests improved polymer interaction and formulation optimization, with F9 demonstrating the strongest mucoadhesion potentially leading to prolonged residence time at the site of application.

Bioadhesive time extended from **8.6 ± 0.0259 hours (F1)** to **11.6 ± 0.429 hours (F9)**, indicating consistent improvement in mucosal retention. Batches F6 through F9 displayed significantly prolonged bioadhesion, suggesting enhanced formulation stability and stronger mucosal interactions beneficial for sustained drug delivery.

## Swelling Index

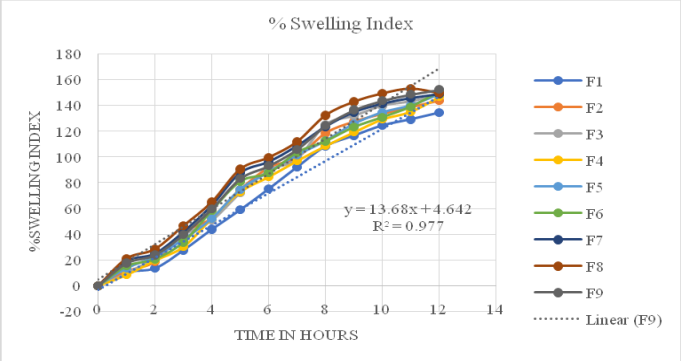
**Table 4:** Swelling Index of All Formulation Batches

| Time (hr) | Formulation Batches for the Swelling Index | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| **0** | 0±0 | 0±0 | 0±0 | 0±0 | 0±0 | 0±0 | 0±0 | 0±0 | 0±0 |
| **1** | 10.55 ± 0.65 | 11.25 ±0.72 | 9.71 ±0.84 | 8.47 ±0.73 | 13.71 ±0.81 | 15.39 ±0.91 | 19.31 ±0.88 | 21.25 ±0.76 | 17.55 ±0.79 |
| **2** | 13.70 ±0.78 | 18.92 ±0.87 | 22.06 ±0.88 | 19.68 ±0.77 | 22.72 ±0.89 | 20.83 ±0.85 | 25.04 ±0.93 | 28.66 ±0.81 | 23.87 ±0.84 |
| **3** | 27.70 ±0.76 | 41.26 ±0.88 | 39.25 ±0.91 | 30.22 ±0.85 | 36.12 ±0.92 | 33.94 ±0.83 | 41.86 ±0.94 | 46.73 ±0.78 | 39.58 ±0.86 |
| **4** | 43.92 ±0.82 | 52.60 ±0.77 | 50.83 ±0.85 | 52.46 ±0.90 | 52.35 ±0.78 | 58.69 ±0.92 | 62.43 ±0.89 | 65.22 ±0.80 | 59.61 ±0.87 |
| **5** | 59.09 ±0.80 | 74.71 ±0.76 | 72.11 ±0.87 | 73.03 ±0.91 | 74.90 ±0.86 | 81.23 ±0.91 | 87.65 ±0.93 | 90.78 ±0.79 | 83.12 ±0.85 |
| **6** | 75.35 ±0.82 | 91.69 ±0.89 | 89.54 ±0.91 | 84.57 ±0.86 | 88.36 ±0.85 | 87.78 ±0.93 | 96.25 ±0.96 | 99.84 ±0.82 | 93.10 ±0.89 |
| **7** | 92.37 ±0.91 | 99.61 ±0.94 | 98.54 ±0.96 | 97.03 ±0.92 | 101.55± 0.91 | 103.80± 0.95 | 108.56± 0.98 | 112.05± 0.84 | 105.82± 0.93 |
| **8** | 108.59± 0.93 | 118.57± 0.96 | 125.10± 0.94 | 108.65± 0.91 | 112.66± 0.95 | 112.55± 0.97 | 123.55± 0.99 | 132.53± 0.86 | 124.21± 0.94 |
| **9** | 116.80± 0.96 | 127.42± 0.98 | 132.04± 0.95 | 119.26± 0.94 | 125.82± 0.96 | 123.46± 0.98 | 134.75± 0.96 | 143.11± 0.89 | 136.42± 0.97 |
| **10** | 124.77± 0.97 | 133.54± 0.94 | 139.86± 0.97 | 129.33± 0.93 | 134.72± 0.98 | 131.15± 0.97 | 141.33± 0.94 | 149.62± 0.91 | 143.78± 0.95 |

All values are expressed as Mean ± Standard Deviation, n=3

Swelling index is crucial for evaluating hydration and gel formation, which affect drug release and mucoadhesion in hydrophilic matrix tablets. At the 1st hour, F8 and F7 showed the highest swelling (up to 21.25%), indicating rapid water uptake due to higher hydrophilic polymer content.

By the 12th hour, maximum swelling was seen in F9 (152.27%), F8 (149.94%), F6 (150.90%), and F5 (148.82%), confirming high water absorption and matrix expansion. Gradual swelling in F3, F6, F8, and F9 correlated well with their sustained drug release profiles, supporting their use in controlled-release systems.




**Graph 1:**Plot oftimeVS SwellingindexofAll Formulation batches

## In Vitro Dissolution Study:

**Table 5:** % Cumulative Drug Release of All Formulation Batches

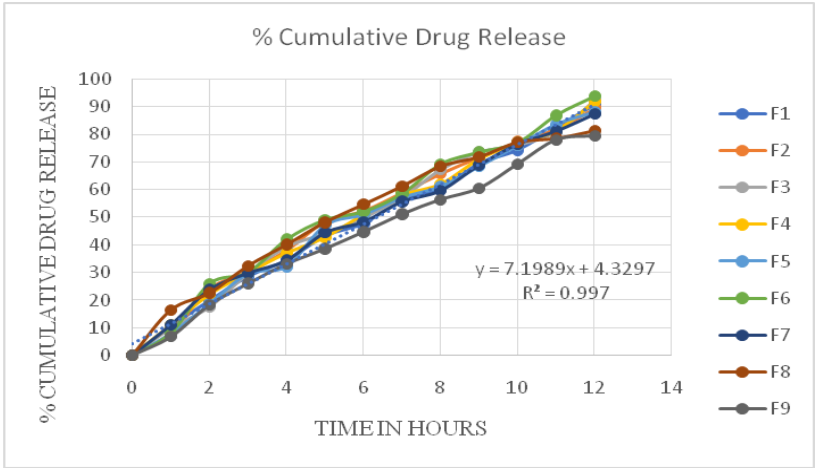
| Time (hrs) | F1 (±SD) | F2 (±SD) | F3 (±SD) | F4 (±SD) | F5 (±SD) | F6 (±SD) | F7 (±SD) | F8 (±SD) | F9 (±SD) |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 | 0 ± 0 |
| 1 | 10.5 ± 0.46 | 8.2 ± 0.59 | 9.8 ± 0.26 | 11.0 ± 0.46 | 7.9 ± 0.48 | 8.1 ± 0.96 | 11.0 ± 0.25 | 16.4 ± 0.55 | 6.7 ± 0.58 |
| 2 | 19.8 ± 0.36 | 24.0 ± 1.59 | 17.5 ± 0.66 | 22.0 ± 0.98 | 18.6 ± 0.36 | 25.9 ± 0.25 | 23.7 ± 0.43 | 22.6 ± 0.60 | 18.2 ± 0.48 |
| 3 | 28.5 ± 0.16 | 30.3 ± 0.37 | 29.6 ± 0.15 | 29.8 ± 0.46 | 29.5 ± 0.65 | 30.0 ± 0.36 | 29.7 ± 0.56 | 32.4 ± 0.49 | 25.9 ± 0.35 |
| 4 | 34.4 ± 0.26 | 38.0 ± 1.59 | 39.2 ± 0.26 | 37.0 ± 0.26 | 32.1 ± 0.46 | 41.9 ± 0.46 | 34.3 ± 0.42 | 40.1 ± 0.49 | 33.0 ± 0.26 |
| 5 | 43.2 ± 0.57 | 48.5 ± 0.37 | 44.1 ± 0.15 | 42.7 ± 0.75 | 47.0 ± 0.46 | 49.0 ± 4.60 | 44.3 ± 0.75 | 48.2 ± 0.60 | 38.5 ± 0.85 |
| 6 | 47.7 ± 0.55 | 52.3 ± 0.15 | 49.8 ± 0.15 | 51.0 ± 0.35 | 50.9 ± 0.15 | 52.0 ± 0.26 | 48.2 ± 0.42 | 54.7 ± 0.49 | 44.6 ± 0.43 |
| 7 | 56.3 ± 0.46 | 58.9 ± 0.26 | 57.1 ± 0.59 | 58.0 ± 0.32 | 57.0 ± 0.25 | 58.5 ± 0.15 | 55.5 ± 0.25 | 61.3 ± 0.98 | 51.0 ± 0.63 |
| 8 | 60.5 ± 0.26 | 65.8 ± 0.59 | 67.2 ± 0.63 | 62.0 ± 0.26 | 61.0 ± 0.36 | 69.2 ± 0.26 | 59.5 ± 0.42 | 68.5 ± 0.24 | 56.3 ± 0.76 |
| 9 | 69.4 ± 0.46 | 71.7 ± 0.97 | 73.5 ± 0.49 | 71.0 ± 0.59 | 68.3 ± 0.76 | 73.5 ± 0.31 | 68.8 ± 0.76 | 71.9 ± 0.56 | 60.4 ± 0.15 |
| 10 | 74.3 ± 0.49 | 77.2 ± 0.76 | 76.1 ± 0.89 | 76.8 ± 0.49 | 75.9 ± 0.56 | 77.0 ± 0.76 | 76.3 ± 0.96 | 77.2 ± 0.26 | 69.2 ± 0.68 |
| 11 | 82.5 ± 0.36 | 82.0 ± 0.76 | 80.9 ± 0.76 | 81.3 ± 0.76 | 83.5 ± 0.63 | 86.9 ± 0.85 | 81.0 ± 0.63 | 78.6 ± 0.53 | 77.9 ± 0.53 |
| 12 | 90.7 ± 0.48 | 89.4 ± 0.40 | 92.3 ± 0.24 | 91.9 ± 0.96 | 88.0 ± 0.25 | 93.8 ± 0.45 | 87.2 ± 0.43 | 81.4 ± 0.26 | 79.3 ± 0.63 |

All values are expressed as Mean ± Standard Deviation, n=3

The drug release profiles of batches F1–F9 showed sustained release over 12 hours, influenced by formulation composition and matrix integrity. Initial release ranged from 6.7% (F9) to 16.4% (F8), with F8 showing the highest burst release due to rapid swelling. By 4 hours, most batches released 32–42%, with F6 and F8 showing efficient release.

At 6 hours, F8 again showed the fastest release (54.7%), while F9 remained the slowest (44.6%), indicating controlled delivery. After 12 hours, cumulative release ranged from 79.3% (F9) to 93.8% (F6). F6, F3, and F4 achieved near-complete release, while F8 and F9 sustained drug release longer.

Overall, F6, F3, and F4 are suited for faster, complete release, whereas F8 and F9 are ideal for extended-release applications.




**Graph 2:** Dissolution Profile of All Formulation Batches

**Kinetics of Drug Release:**

**Table 6:** Model Fitting Release of Formulation Batches

| Parameter | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|
| **Zero Order ($R^2$)** | 0.988 | 0.966 | 0.980 | 0.978 | 0.982 | 0.966 | 0.975 | 0.985 | 0.993 |
| **1st Order ($R^2$)** | 0.965 | 0.982 | 0.969 | 0.971 | 0.970 | 0.970 | 0.974 | 0.978 | 0.960 |
| **Higuchi ($R^2$) Model** | 0.909 | 0.934 | 0.913 | 0.925 | 0.909 | 0.928 | 0.926 | 0.908 | 0.931 |
| **Peppas ($R^2$) Model** | 0.998 | 0.996 | 0.995 | 0.998 | 0.994 | 0.993 | 0.997 | 0.996 | 0.991 |
| **n Value** | 0.961 | 0.953 | 0.938 | 0.944 | 0.936 | 0.922 | 0.947 | 0.928 | 0.842 |
| **k Value** | 35.16 | 33.47 | 31.23 | 32.21 | 30.56 | 30.22 | 28.88 | 29.45 | 28.87 |
| **Best fitted to** | Peppas | Peppas | Peppas | Peppas | Peppas | Peppas | Peppas | Peppas | Zero order |

It was observed that Stomach specific bioadhesive tablet (F1-F8) have best fitted to **Peppas model**. Among them, formulation batch F9 showed highest regression coefficient ($r^2$) value of **0.9807** and **n** value of **0.842**, indicating an anomalous (non-Fickian) diffusion mechanism.

Also, it was observed that Stomach specific bioadhesive tablet(F9) formulation has best fitted to **zero-order release** with an $r^2$ value of **0.9807**, which indicates a constant and concentration- independent drug release over time.

**Stability Study:**

**Table 07:** Stability Study at $40^0$C ± 2°C

| Time | Appearance | % Drug Content | % CDR | |
|---|---|---|---|---|
| | | | After 8 Hr | After 12 Hr |
| **0 days** | White | 99.83±0.0354 | 56.30±0.133 | 79.30±0.654 |
| **1 Weeks** | White | 99.81±0.0354 | 56.30±0.235 | 79.30±0.374 |
| **2 Weeks** | White | 99.77±0.0354 | 56.26±0.337 | 79.27±0.878 |
| **3 Weeks** | White | 99.75±0.0354 | 56.23±0.534 | 79.24±0.945 |
| **4 Weeks** | White | 99.72±0.0354 | 56.21±0.533 | 79.20±0.454 |

## CONCLUSION:

The present study has been a satisfactory attempt to formulate stomach-specific bioadhesive tablets of Diltiazem Hydrochloride with a view of achieving sustained drug release and prolonged gastric retention. From the experimental results, it can be concluded that, F9 is the best formulation batch and follows the zero-order kinetic model.

Formulation F9 contains 150 mg of Diltiazem Hydrochloride, with 400 mg of excipients including Chitosan, HPMC K15M, MCC, Talc, Magnesium Stearate, and Aerosil. The results of formulation F9 for Bulk Density, Tapped Density, Carr's Index, Hausner's Ratio, Angle of Repose, Bioadhesive Strength, Bioadhesive Time, and % Cumulative Drug Release were 0.48±0.0042, 0.58±0.0076, 17.24±0.057, 1.12±0.5963, 22.3±0.3149, 45 ± 0.4856, 12 hours, and 79.3 ± 0.63 respectively.

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## CONFLICT OF INTEREST:

All contributing authors declares no conflict of interest.

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