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Research Paper

Formulation and Evaluation of Bilayer Floating Tablets for Gastro-Retentive Drug Delivery

Nilesh Ghuge*¹, Aditya Patil², Sudesh Sanap², Swati Zade², Dr. Sanjay Toshniwal⁴,
Dr. Vishal R. Rasve⁵

¹Associate Professor, Vidarbha Institute of Pharmacy, Gut no. 114, Anjankhed, Borala Phata, Washim

²Assistant Professor, Vidarbha Institute of Pharmacy, Gut no. 114, Anjankhed, Borala Phata, Washim

³Director, Vidarbha Institute of Pharmacy, Gut no. 114, Anjankhed, Borala Phata, Washim

⁴Associate Professor, SAJVPMS, College of Pharmaceutical Sciences and Research Center, Kada, Beed, Maharashtra-414202

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ABSTRACT

The objective of the present study was to formulate and evaluate bilayer floating tablets of Lisinopril to enhance its gastric residence time and provide sustained drug release, thereby improving its bioavailability and therapeutic efficacy. Nine formulations (FE1–FE9) were developed and subjected to comprehensive post-compression evaluations including thickness, hardness, friability, weight variation, and drug content uniformity. All formulations complied with pharmacopeial standards, exhibiting acceptable physical properties. In vitro floating studies demonstrated that all tablets had a floating lag time of less than 3.5 minutes and a floating duration exceeding 12 hours. In vitro drug release studies, performed in 0.1N HCl, revealed a controlled release pattern with cumulative drug release ranging from 86.70% to 94.12% over a 12-hour period. Among all formulations, FE8 was identified as the optimized batch, showing excellent floating behavior, mechanical integrity, and sustained drug release (89.02% at 12 hours). These results confirm the potential of bilayer floating tablets as a promising gastro-retentive delivery system for Lisinopril, ensuring prolonged drug availability and enhanced patient compliance in the management of hypertension.

INTRODUCTION

The development of bilayer floating tablets for gastro-retentive drug delivery represents a novel and effective strategy to address the limitations

*Corresponding Author: Nilesh Ghuge

Address: Associate Professor, Vidarbha Institute of Pharmacy, Gut no. 114, Anjankhed, Borala Phata, Washim

Email ✉: vishalrasve@gmail.com

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associated with conventional oral dosage forms, particularly for drugs that have a narrow absorption window or require controlled release in the upper gastrointestinal tract. This system combines the advantages of both floating drug delivery and bilayer tablet technology to improve drug bioavailability and prolong therapeutic action.¹ Floating tablets are designed to remain buoyant on gastric fluids due to the presence of gas-generating agents and low-density polymers, thus prolonging gastric residence time and enhancing drug absorption in the stomach or upper small intestine. By formulating the drug in a bilayer tablet, the dosage form can offer two distinct release profiles an immediate release for rapid onset of action and a sustained release layer for prolonged drug delivery, providing a controlled and consistent therapeutic effect over time.² Lisinopril, an angiotensin-converting

enzyme (ACE) inhibitor, is a prime candidate for this delivery approach due to its pharmacokinetic and pharmacodynamic properties. It is commonly used for the management of hypertension, congestive heart failure, and post-myocardial infarction therapy. Lisinopril exerts its action by inhibiting the enzyme responsible for the conversion of angiotensin I to angiotensin II, a substance that causes blood vessels to constrict. By preventing this conversion, lisinopril promotes vasodilation, reduces blood pressure, and decreases the workload on the heart. However, one of the major limitations of lisinopril is its relatively short half-life and narrow absorption window in the proximal regions of the gastrointestinal tract. Additionally, its absorption can be inconsistent due to variations in gastric emptying and pH, which may reduce its therapeutic efficiency when administered in conventional dosage forms.³

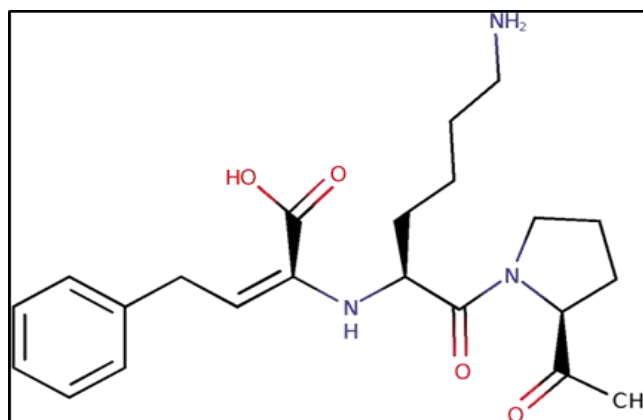


Figure 1: Structure of Lisinopril

To overcome these challenges, a bilayer floating tablet system provides an ideal platform for improving the performance of lisinopril. The immediate release layer ensures a rapid increase in plasma drug concentration, offering quick symptom relief, especially in hypertensive emergencies. Meanwhile, the sustained release floating layer maintains therapeutic drug levels by continuously releasing lisinopril over an extended period while floating in the stomach.⁴ This not only enhances the overall bioavailability of the

drug but also reduces dosing frequency and improves patient compliance. The floating mechanism is typically achieved by incorporating effervescent agents like sodium bicarbonate and citric acid, which react with gastric acid to produce carbon dioxide, enabling the tablet to float. Polymers such as hydroxypropyl methylcellulose (HPMC), carbopol, and ethyl cellulose are commonly used to modulate the drug release rate and maintain matrix integrity.⁵

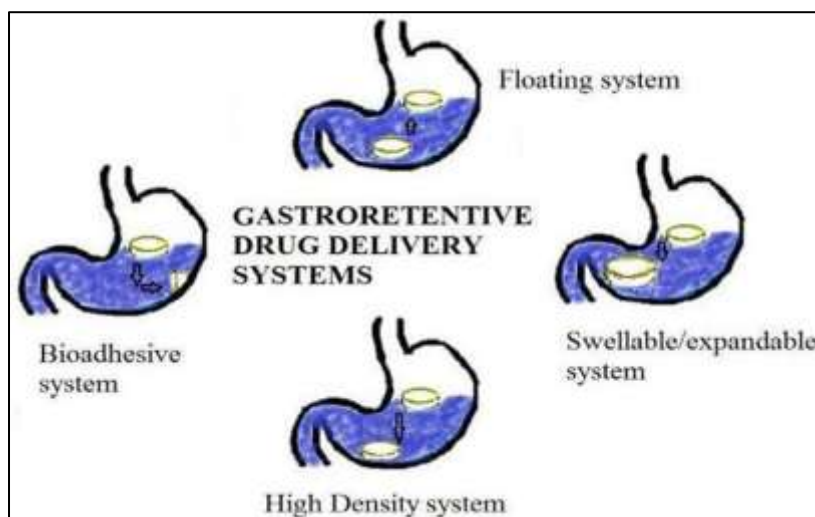


Figure 2: Gastro Retentive Drug Delivery Systems

The formulation process requires careful optimization of various formulation and processing parameters to achieve desired characteristics such as tablet hardness, friability, swelling index, drug content uniformity, floating lag time, total floating duration, and in vitro drug release profile.⁶ Furthermore, evaluation of the drug release kinetics using models like zero-order, first-order, Higuchi, and Korsmeyer-Peppas helps in understanding the mechanism of drug release and ensuring consistency in therapeutic outcomes. Stability studies are also essential to confirm the physical and chemical stability of the formulation under different storage conditions.⁷ The formulation and evaluation of bilayer floating tablets of lisinopril hold significant promise in improving the drug's pharmacokinetic profile, enhancing bioavailability, and offering better patient compliance. This advanced gastro-retentive drug delivery system not only ensures sustained therapeutic efficacy but also addresses the limitations of traditional oral dosage forms, making it a valuable strategy for chronic disease management such as hypertension and heart failure.⁸⁻¹⁰

MATERIALS AND METHODS:

MATERIALS:

The active pharmaceutical ingredient, lisinopril, was sourced from Lupin Pharmaceuticals Pvt. Ltd. (Chhatrapati Sambhajinagar). Polymers used for tablet formulation, Hydroxypropyl Methylcellulose (HPMC) K100M and HPMC K4M, were obtained from Research-Lab Fine Chem Industries, Mumbai. Other excipients included Carboxymethyl Cellulose Sodium, Lactose, Talc, Magnesium Stearate, Sodium Starch Glycolate, and Crosscarmellose Sodium, purchased from Thomas Baker Chemicals Pvt. Ltd., S. Kanth Health Care Ltd., N.B. Enterprises, and FMC-Ireland. Sodium Bicarbonate, used for buoyancy, was acquired from Research-Lab Bombay, and Methyl Orange pH Indicator from Thomas Baker Chemicals Pvt. Ltd. For tablet formulation and evaluation, several instruments were utilized: dissolution testing was conducted using a dissolution apparatus from Electrochemical Lab, Mumbai, while a Citizen electronic balance was used for weighing. Drug analysis was carried out with an Agilent Cary 60 UV-Visible Spectrophotometer, and pH measurements were taken using a Hanna Instruments pH meter. A Fill-Well distillation apparatus, Shital Scientific Industries' hot air oven, and a Vernier caliper from ICI Checking Instruments were used for water purification,

drying, and dimension measurements, respectively. Tablet compression was done using a Cadmach single-punch tablet machine, while mechanical strength was assessed with a Roche friability tester and a Monsanto hardness tester. Particle size analysis was performed using laboratory sieves from Unique, and disintegration testing was conducted with a Veego disintegration apparatus. FTIR analysis for drug-excipient compatibility was done using an Agilent Cary 630 ATR FTIR Spectrophotometer.

METHODS:

Preformulation Studies of Drug

Preformulation involves investigating the physical and chemical properties of the drug, both independently and in combination with excipients. This step helps gather crucial information about the drug to guide the formulation process. The study aims to establish the physicochemical characteristics, release profile, and excipient compatibility of Lisinopril.¹¹⁻¹⁴

Description and Physical Characteristics

Lisinopril was analyzed for its color, odor, and taste to assess its sensory properties.

Melting Point

The melting point of Lisinopril was determined using the open capillary method, which is essential for confirming its purity.¹⁵

Solubility Characteristics

Solubility was determined by gradually adding Lisinopril to various solvents (distilled water, phosphate buffer pH 6.8, buffer pH 1.2, methanol, alcohol, and isopropyl alcohol), observing for undissolved particles to assess its solubility profile.¹⁶⁻¹⁸

Drug-Polymer Interaction Studies

Compatibility studies were conducted by mixing Lisinopril with excipients (HPMC, Ethyl Cellulose) in a 100:1 ratio with IR grade KBr. The infrared spectra were analyzed for any potential interactions between the drug and the polymers, which could affect the formulation's stability.¹⁹⁻²²

Formulation and Optimization of Bilayer Tablets Containing a Release Layer of Lisinopril²³⁻³⁴

Development of Immediate Release Layer by Dry Granulation Method

The formulation of bilayer gastro-retentive floating tablets involves two key layers: the immediate release layer and the floating sustained release layer. The immediate release layer contains Lisinopril, sodium starch glycolate, and croscarmellose sodium (super disintegrants) along with small amounts of lubricants and binders. The floating sustained release layer consists of Lisinopril, sodium bicarbonate (a gas-generating agent), and polymers such as Hydroxypropyl methylcellulose (HPMC) and sodium carboxymethylcellulose, along with additional excipients. The preparation of the bilayer tablets was carried out via the direct compression method. All ingredients, including the drug and excipients, were sifted through mesh #40. The components were accurately weighed and mixed for 5 minutes in a plastic bag. Magnesium stearate was added as a lubricant, and the mixture was further blended. The granules were then compressed into tablets using 6mm round flat punches, ensuring low hardness to facilitate floating.

Formulation of Immediate Release Layer

The formulation of the immediate release layer varies across different batches (F1-F9), with Lisinopril concentration kept constant at 4 mg. The amount of sodium starch glycolate and croscarmellose sodium was adjusted across



different formulations to optimize the disintegration and release properties. Other excipients, including lactose, talc, and magnesium stearate, were added to improve the flow and lubrication properties. The sodium bicarbonate content (20 mg) was consistent across all formulations, serving as the gas-generating agent to aid the floating mechanism. Methyl Orange was included as a pH indicator for monitoring the dissolution profile.

Table 1: Formulation of Immediate Release Layer (Lisinopril).

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Lisinopril (mg)	4	4	4	4	4	4	4	4	4
Sodium Starch Glycolate (mg)	5	7.5	10	5	-	10	5	7.5	10
Cross Carmilose Sodium (mg)	5	5	5	7.5	7.5	7.5	10	10	-
Lactose (mg)	16	13.5	11	13.5	18.5	8.5	11	8.5	16
Talc (mg)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium Stearate (mg)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Sodium bicarbonate (mg)	20	20	20	20	20	20	20	20	20
Methyl Orange pH Indicator	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total	51	51	51	51	51	51	51	51	51

Formulation of Sustained Release Layer

The sustained release layer formulations (E1-E9) were designed with Lisinopril at 16 mg per tablet. The polymers used for the sustained release layer include HPMC K100M, HPMC K4M, and sodium carboxymethylcellulose, with varying concentrations to achieve optimal release characteristics. Lactose, talc, and magnesium stearate were incorporated to improve the tablet's

flow, compressibility, and lubrication. The total weight of the sustained release layer in all formulations was maintained at 129 mg, ensuring consistency in tablet weight and release properties. Both layers were designed to work synergistically, with the immediate release layer providing rapid drug release, while the sustained release layer ensures prolonged drug delivery, contributing to the overall gastro-retentive floating property of the tablet.

Table 2: Formulation of Sustained Release Layer (Lisinopril)

Ingredients	E1	E2	E3	E4	E5	E6	E7	E8	E9
Lisinopril (mg)	16	16	16	16	16	16	16	16	16
HPMC K100M (mg)	13	13	13	19.5	19.5	19.5	26	26	26
HPMC K4M (mg)	13	19.5	26	13	19.5	26	13	19.5	26
Sodium Carboxy Methyl Cellulose (mg)	14	14	14	14	14	14	14	14	14
Lactose (mg)	70	63.5	57	63.5	57	50.5	57	50.5	44
Talc (mg)	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Magnesium Stearate (mg)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total	129	129	129	129	129	129	129	129	129

Pre-formulation Study³⁵⁻³⁷

Bulk Density (Db):

The loose bulk density was determined by measuring the mass of the powder and dividing it by the volume it occupies. A 10g sample was



introduced into a 25ml graduated cylinder, and the volume was recorded to calculate the bulk density.

Tapped Density (Dt):

Tapped density was measured by filling a 25ml graduated cylinder with 10g of powder and then subjecting the cylinder to 100 taps from a height of 1 inch. The final tapped volume was recorded, and the tapped density was calculated.

Compressibility Index:

The compressibility index, an indicator of powder flowability, was calculated from both bulk and tapped densities. It provides insight into the material's size, shape, moisture content, and cohesiveness. A higher compressibility index generally indicates poorer flow properties.

Hausner Ratio:

The Hausner ratio was calculated by dividing the tapped density by the bulk density. It is another parameter used to predict powder flow, with higher values indicating poorer flowability.

Angle of Repose:

The angle of repose was determined by allowing the powder to flow from a funnel onto a horizontal surface and measuring the height and radius of the resulting pile. The angle of repose provides information on the powder's flowability and resistance to movement. Lower angles suggest better flow properties.

Post Compression Parameters of Bilayer Floating Tablet³⁸⁻⁴⁰

Hardness Test:

The hardness of tablets was assessed using a Monsanto hardness tester, which measures the force required to fracture a tablet. The mean

hardness of three tablets from each batch was recorded, expressed in kg/cm².

Friability Test:

The friability test evaluates the ability of tablets to withstand mechanical stress during handling. Tablets were subjected to abrasion and shock in a Roche friabilator. After 100 revolutions, the tablets were weighed again, and the percentage weight loss (friability) was calculated. Tablets should not lose more than 1% of their weight.

Weight Variation Test:

Twenty tablets were individually weighed, and the average weight was compared to individual tablet weights. The test checks for uniformity in tablet weight, with specified tolerances based on tablet weight.

Thickness:

Tablet thickness was measured using a Vernier caliper. Three tablets from each batch were measured, and the average thickness was recorded.

Swelling Characteristics of Tablet:

Swelling behavior was assessed by measuring the percent weight gain of tablets placed in pH 1.2 buffer. Tablets were withdrawn hourly, blotted dry, weighed, and the swelling index was calculated.

Drug Content Uniformity:

For drug content uniformity, ten tablets were powdered, and an amount equivalent to 100 mg of the drug was dissolved in a buffer solution. The solution was filtered and analyzed using UV spectrophotometry at 205 nm to determine the drug content.

Disintegration Test:

The disintegration test evaluated how quickly the tablet breaks down into smaller particles. Tablets were placed in a disintegration apparatus at $37\pm 2^\circ\text{C}$, and the time taken for the tablets to disintegrate was recorded.

In-Vitro Dissolution Studies:

Dissolution testing was performed using USP Dissolution Apparatus type II in pH 1.2 medium. Samples were withdrawn at specified intervals and analyzed using UV spectrophotometry to determine the drug release profile. The percentage of drug release was calculated based on the label claim.

Stability Studies of Bilayer Floating Tablets:

Stability studies are essential in evaluating the long-term viability of dosage forms, as they assess the active drug's integrity and performance. The main concerns for stability include the potential chemical degradation of the active ingredient, which could reduce therapeutic effectiveness or even produce harmful by-products. Additionally, drug instability may lower bioavailability, compromising the drug's therapeutic efficacy. In the present study, the optimized bilayer floating tablets were subjected to accelerated stability testing by storing them at 40°C and 75% relative humidity for 90 days. After this period, physical

parameters such as thickness, hardness, drug content, and in-vitro drug release were evaluated to determine the stability of the formulation.

RESULT AND DISCUSSION:

Characterization of Lisinopril

The physicochemical and organoleptic properties of Lisinopril were evaluated to confirm its identity and purity before formulation. Organoleptic evaluation showed that the drug is a white to off-white crystalline powder with a pungent odour and a persistent taste characterized by sweet, sour, salty, bitter, or metallic notes. The melting point was determined to be in the range of 146°C to 148°C , which is consistent with the Indian Pharmacopoeia (I.P.) standards, indicating the purity of the drug substance. The pH range of the aqueous solution was found to be 6.5–7.4, which aligns with expected values, further supporting the drug's quality and suitability for formulation development. The solubility profile of Lisinopril was studied in various solvents to assess its compatibility with different formulation media. The drug was found to be highly soluble in water and 0.1 N HCl, sparingly soluble in methanol, and insoluble in ethanol. This solubility behavior supports its use in oral dosage forms, particularly for gastric-release applications due to its good solubility in acidic media.

Table 3: Physicochemical Characteristics of Lisinopril

Sr. No.	Test	Observation
1	Colour	White to off-white, crystalline powder
2	Odour	Pungent
3	Taste	Persistent sweet, sour, salty, bitter or metallic
4	Melting Point	$146^\circ\text{--}148^\circ\text{C}$
5	pH	6.5–7.4

Table 4: Solubility Profile of Lisinopril

Sr. No.	Solvent	Solubility
1	Water	Soluble
2	0.1 N HCl	Soluble
3	Methanol	Sparingly soluble
4	Ethanol	Insoluble



These results confirm that the drug complies with pharmacopeial standards and is appropriate for use in the bilayer floating tablet formulation.

Drug Excipient Interaction:

There was no alteration and no interaction observed between polymer and drug in combination. All the characteristic peaks of Lisinopril were present in combination, thus indicating compatibility between drug and polymers and finally confirm that there was no chemical change of drug taken place.

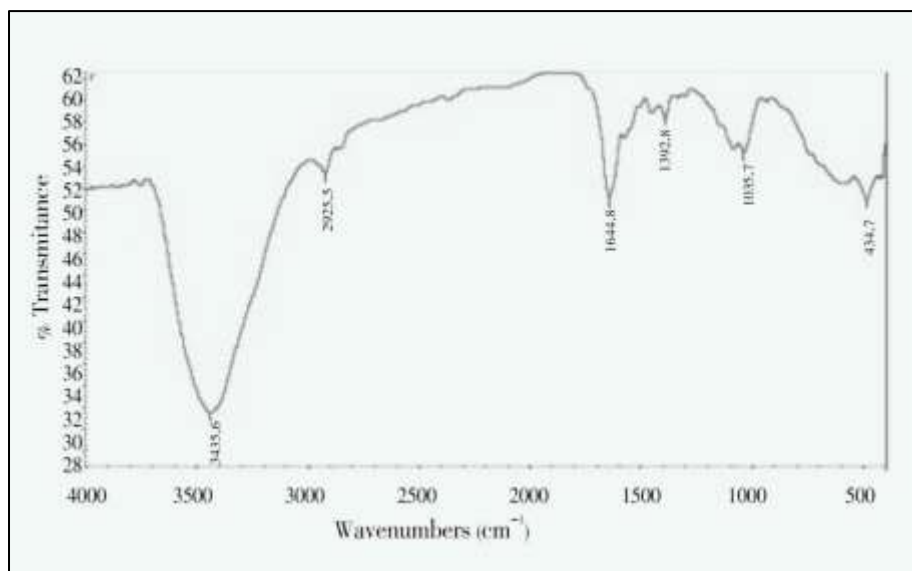


Figure 3: FTIR study of Lisinopril with excipients

Formulation and Development of Bilayer Tablets of Lisinopril

Preparation of Bilayer Tablets (Immediate Release and Sustained Release Layers)

Immediate Release Layer:

A series of nine formulations (F1–F9) of the immediate release (IR) layer of lisinopril were developed using lactose as the diluent. Sodium starch glycolate and croscarmellose sodium were employed as superdisintegrants at concentrations of 10%, 15%, and 20% across the formulations. To enhance disintegration and effervescence, sodium bicarbonate was incorporated. Orange lake was used as a colorant to differentiate this layer, and magnesium stearate and talc were added as lubricant and glidant, respectively. These excipients collectively aimed to achieve rapid

disintegration and immediate drug release upon administration.

Sustained Release Layer:

The sustained release (SR) layer was formulated using varying proportions of hydrophilic polymers HPMC K100M and HPMC K4M, intended to provide extended drug release over time. Lactose served as the diluent, while magnesium stearate and talc were added to improve compressibility and flow properties. The polymer ratios were optimized to modulate drug release kinetics effectively.

Bilayer Tablet Compression:

Bilayer tablets were compressed in a sequential manner. The weighed quantity of the sustained release blend was first filled into the die cavity and lightly compressed to form a compact base layer.

The immediate release blend was then added on top and final compression was performed to form a cohesive bilayer structure. The orange-colored IR layer facilitated visual identification and uniformity of compression.

Evaluation of Powder Blends for Immediate Release Layer

The pre-compression parameters for the powder blends of the IR formulations were assessed to evaluate flow and packing properties. Parameters such as bulk density, tapped density, angle of repose, Carr's index, and Hausner ratio were analyzed (Table 1). The angle of repose for all formulations was less than 33°, and Carr's index was under 20%, indicating good flowability of the granules, which is essential for uniform die filling and consistent tablet weight during compression.

Table 5: Pre-Compression Evaluation of Lisinopril Immediate Release Powder Blend

Formulation	Bulk Density (g/cm ³)	Tapped Density (g/cm ³)	Angle of Repose (°)	Carr's Index (%)	Hausner Ratio
F1	0.536 ± 0.02	0.525 ± 0.01	29.1 ± 0.02	10.0	1.11
F2	0.520 ± 0.02	0.552 ± 0.02	29.8 ± 0.01	12.2	1.14
F3	0.510 ± 0.04	0.567 ± 0.04	30.5 ± 0.01	12.1	1.14
F4	0.507 ± 0.04	0.559 ± 0.03	31.6 ± 0.03	12.4	1.13
F5	0.518 ± 0.03	0.579 ± 0.05	31.2 ± 0.03	13.5	1.14
F6	0.520 ± 0.01	0.590 ± 0.02	33.5 ± 0.02	12.5	1.14
F7	0.504 ± 0.04	0.560 ± 0.03	31.7 ± 0.03	12.4	1.13
F8	0.519 ± 0.03	0.580 ± 0.05	31.3 ± 0.03	13.5	1.14
F9	0.521 ± 0.01	0.591 ± 0.02	33.6 ± 0.02	12.5	1.14

(n = 3; values expressed as mean ± SD)

Evaluation of Immediate Release Tablets

The IR tablets were evaluated for disintegration time and drug content uniformity (Table 2). Disintegration time ranged between 5.03 to 10.5

minutes. Formulations F6, F8, and F9 exhibited the fastest disintegration times, supporting the efficacy of sodium starch glycolate and croscarmellose sodium at higher concentrations. Drug content ranged from 93.30% to 99.90%, confirming uniform drug distribution in the IR layer.

Table 6: Evaluation of Lisinopril Immediate Release Tablets

Formulation	Disintegration Time (min)	Drug Content (%)
F1	6.5	93.30 ± 0.55
F2	10.5	97.80 ± 0.54
F3	10.3	95.80 ± 0.40
F4	7.12	98.80 ± 0.65
F5	9.13	97.80 ± 0.43
F6	5.03	99.90 ± 0.45
F7	8.41	96.90 ± 0.43
F8	5.59	94.56 ± 0.54
F9	6.92	94.20 ± 0.55



Evaluation and Optimization of Sustained Release Layer

Pre-Compression Parameters of Sustained Release Blends

The flow properties of the sustained release powder blends (E1–E9) were assessed (Table 3). Most formulations exhibited acceptable flow

characteristics, with angles of repose $<35^\circ$, Carr's index $<20\%$, and Hausner ratios below 1.25, indicating suitability for compression. However, formulations E5 and E8 showed comparatively poor flow, as indicated by higher Carr's index ($>25\%$) and Hausner ratios (>1.35), possibly due to higher polymer concentration and particle cohesiveness.

Table 7: Pre-Compression Evaluation of Lisinopril Sustained Release Powder Blend

Formulation	Bulk Density (g/cm ³)	Tapped Density (g/cm ³)	Angle of Repose (°)	Carr's Index (%)	Hausner Ratio
E1	0.379 ± 0.01	0.422 ± 0.02	33.4 ± 0.01	10.2	1.12
E2	0.408 ± 0.01	0.472 ± 0.01	31.5 ± 0.02	13.5	1.16
E3	0.399 ± 0.02	0.462 ± 0.02	34.7 ± 0.01	13.6	1.16
E4	0.389 ± 0.03	0.457 ± 0.03	32.6 ± 0.02	14.8	1.17
E5	0.346 ± 0.02	0.476 ± 0.02	48.4 ± 0.03	27.3	1.38
E6	0.405 ± 0.01	0.468 ± 0.01	31.0 ± 0.01	13.4	1.16
E7	0.396 ± 0.03	0.458 ± 0.03	34.6 ± 0.02	15.8	1.19
E8	0.358 ± 0.02	0.478 ± 0.02	47.4 ± 0.03	28.3	1.42
E9	0.421 ± 0.01	0.470 ± 0.01	34.0 ± 0.01	14.4	1.18

(n = 3; values expressed as mean ± SD)

The formulation of bilayer tablets comprising an immediate release and a sustained release layer of Lisinopril was successfully achieved. The pre-compression characteristics of both layers demonstrated adequate flow properties, which facilitated uniform die filling and robust tablet formation. Optimization of superdisintegrant concentration in the IR layer effectively modulated disintegration time, while variations in HPMC ratios in the SR layer influenced blend properties. These findings confirm the suitability of selected excipients and process parameters for the development of bilayer tablets with desired release characteristics.

Post-Compression Evaluation of Lisinopril Bilayer Floating Tablets

All nine formulations (FE1–FE9) of Lisinopril bilayer floating tablets underwent comprehensive post-compression evaluations to assess critical

quality parameters including thickness, hardness, friability, weight variation, and drug content uniformity. These tests ensure consistency, mechanical strength, and pharmaceutical acceptability of the tablets.

Tablet Thickness

The thickness of the formulations ranged between 5.2 ± 0.001 mm to 5.4 ± 0.011 mm, indicating uniformity in tablet size and appropriate die fill during compression. Slight variations were observed due to differences in excipient bulk and polymer swelling behavior. All tablets maintained dimensional stability suitable for further coating or packaging processes.

Tablet Hardness

Hardness values for all formulations were within the range of 5.35 ± 0.210 to 6.30 ± 0.100 kg/cm², demonstrating sufficient mechanical strength to withstand handling during manufacturing,



packaging, and transportation. The highest hardness was observed in formulation FE5, whereas FE7 exhibited the lowest, yet all batches met the standard requirement for robustness.

Friability Test

All formulations showed friability values of less than 1%, with the range being 0.18% to 0.40%, suggesting excellent mechanical resistance and durability. This conforms to pharmacopeial limits, indicating that none of the tablets were prone to crumbling or breaking under stress conditions.

Weight Variation

The average tablet weights varied from 175 ± 4.01 mg to 180 ± 3.30 mg, with all formulations falling

well within the acceptable pharmacopeial limits for tablets weighing between 80 mg and 250 mg ($\pm 7.5\%$). This confirms uniform die filling and mass production feasibility without compromising dosage accuracy.

Drug Content Uniformity

Drug content across all formulations ranged from $98.12 \pm 1.36\%$ to $99.77 \pm 0.32\%$, indicating uniform distribution of Lisinopril within the tablet matrix. This uniformity confirms that the drug was blended and incorporated consistently, satisfying the criteria for content uniformity in solid dosage forms.

Table 8: Post-Compression Evaluation of Lisinopril Bilayer Floating Tablets

Formulation	Thickness (mm) \pm S. D	Hardness (kg/cm ²) \pm S. D	Friability (%)	Weight Variation (mg) \pm S. D	Drug Content (% w/w) \pm S. D
FE1	5.20 ± 0.006	5.72 ± 0.360	0.40	178 ± 3.79	98.78 ± 0.54
FE2	5.20 ± 0.010	5.70 ± 0.288	0.18	180 ± 3.54	99.77 ± 0.32
FE3	5.20 ± 0.009	6.01 ± 0.154	0.25	175 ± 4.01	98.46 ± 1.22
FE4	5.20 ± 0.001	6.25 ± 0.152	0.27	180 ± 3.58	98.71 ± 0.95
FE5	5.40 ± 0.010	6.30 ± 0.100	0.34	177 ± 3.91	99.02 ± 0.82
FE6	5.40 ± 0.011	5.49 ± 0.058	0.26	176 ± 3.97	98.65 ± 0.96
FE7	5.30 ± 0.010	5.35 ± 0.210	0.20	180 ± 3.30	99.52 ± 0.57
FE8	5.30 ± 0.006	6.05 ± 0.156	0.21	176 ± 3.98	98.73 ± 0.83
FE9	5.30 ± 0.008	5.91 ± 0.018	0.22	178 ± 3.76	98.12 ± 1.36

In Vitro Floating Behavior

The buoyancy of the bilayer tablets was assessed through floating lag time and total floating duration, and results are presented in Table 22. All formulations exhibited a floating lag time (FLT) of less than 4 minutes, ranging from 2 min 07 sec (FE9) to 3 min 24 sec (FE6). Importantly, every formulation demonstrated a floating duration of more than 12 hours, confirming prolonged gastric retention potential, which is critical for enhancing bioavailability in gastro-retentive delivery systems.

In-vitro Drug Release Profile

The dissolution behavior of the Lisinopril bilayer tablets was evaluated over a 12-hour period using USP Type II (paddle) apparatus in 0.1N HCl. The cumulative drug release profiles for all formulations are detailed in Table 23. Initial release rates varied significantly, with formulations FE6, FE7, and FE8 showing faster drug release in the early time points (e.g., FE6 showed $\sim 39\%$ release at 5 min), attributed to variations in matrix composition and polymer swelling characteristics.

Over the 12-hour period, formulation FE2 exhibited the highest cumulative release (94.12%),



followed closely by FE5 (91.74%) and FE6 (91.84%), indicating their suitability for sustained-release delivery. Conversely, FE3 demonstrated the slowest release (71.25%), likely due to higher polymer concentration or less soluble excipients retarding drug diffusion. All formulations showed a biphasic release profile with an initial burst

followed by a sustained phase, appropriate for bilayer systems where immediate and controlled drug release is desired. The results highlight the potential of the selected polymer combinations to modulate Lisinopril release effectively over a prolonged period, improving therapeutic efficacy and patient compliance.

Table 9: In-vitro Drug Release study

Time (h)	FE1	FE2	FE3	FE4	FE5	FE6	FE7	FE8	FE9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5 min	16.04	14.91	16.98	14.95	15.71	39.16	30.21	33.60	24.26
10 min	18.14	15.61	17.55	15.35	17.09	40.86	32.21	37.33	25.13
15 min	19.03	16.32	19.69	16.10	18.03	42.48	34.35	41.10	27.12
20 min	20.32	17.06	20.46	18.58	20.04	44.60	36.12	44.57	29.84
25 min	24.01	19.14	20.59	20.12	23.61	48.38	38.61	49.89	30.92
30 min	28.92	20.03	21.82	22.13	26.12	49.41	69.12	53.42	34.12
1 h	34.16	22.15	27.91	24.59	32.59	50.70	40.21	55.14	36.19
2 h	41.38	28.69	39.72	29.64	35.14	53.07	42.21	58.67	44.54
3 h	49.85	35.45	43.14	34.72	42.34	56.13	44.36	60.67	49.23
4 h	55.02	40.14	48.35	38.60	49.65	57.04	47.32	64.33	57.78
5 h	62.16	44.33	52.33	41.27	57.45	58.23	51.84	66.80	62.14
6 h	69.64	51.02	55.56	47.64	63.46	59.23	56.10	72.41	70.15
7 h	77.16	70.47	66.37	66.97	76.21	69.59	69.14	78.07	76.61
8 h	79.62	75.94	66.45	74.70	79.14	73.06	71.03	80.78	79.17
9 h	81.39	81.04	66.83	78.69	82.31	77.12	74.96	81.29	81.05
10 h	81.74	85.36	67.90	82.48	85.73	80.52	77.88	82.19	81.74
11 h	82.55	89.12	68.73	84.75	89.39	85.23	80.28	85.85	82.35
12 h	86.70	94.12	71.25	87.84	91.74	91.84	86.36	89.02	84.90

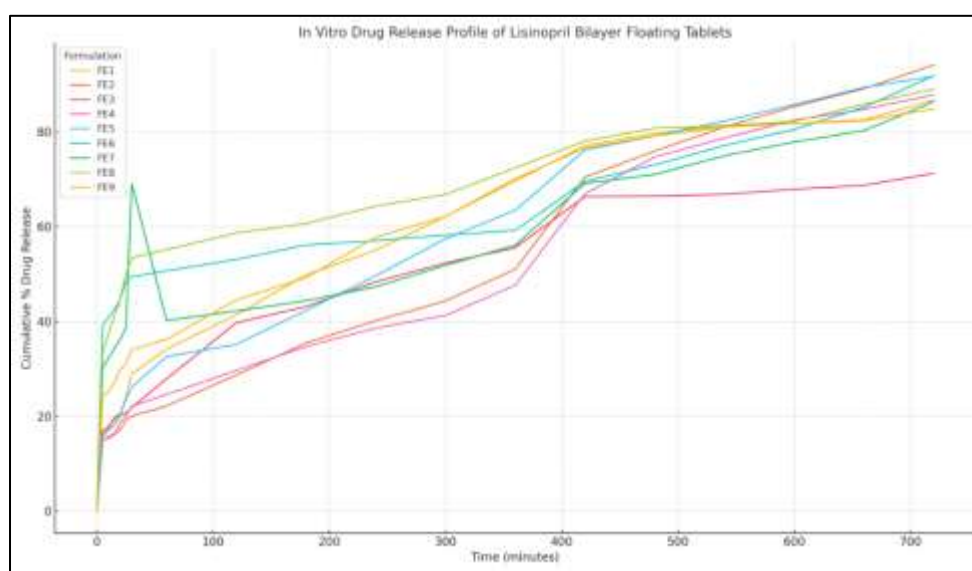


Figure 4: In-vitro Drug Release Profile of Lisinopril Bilayer Floating Tablets

CONCLUSION:

The present study successfully developed and evaluated bilayer floating tablets of Lisinopril with the aim of achieving sustained drug release and prolonged gastric retention. All nine formulations (FE1–FE9) were found to meet pharmacopeial criteria for post-compression parameters including thickness, hardness, friability, weight variation, and drug content uniformity. The hardness ranged from 5.35 to 6.30 kg/cm² and friability remained below 1% for all formulations, indicating acceptable mechanical integrity. The floating lag time for all batches was under 3.5 minutes, and all tablets floated for more than 12 hours, confirming the efficiency of the floating layer to retain tablets in the gastric environment for a prolonged period. Among the batches, formulation FE8 exhibited an optimal balance of mechanical strength, minimal lag time (3.03 min), prolonged floating ability (>12 hours), and sustained drug release, reaching 89.02% release at 12 hours. These results suggest that FE8 is the optimized formulation for delivering Lisinopril via a bilayer floating system, potentially improving its bioavailability by maintaining a longer gastric residence time and providing controlled drug release. This floating bilayer tablet approach holds promise for the effective management of hypertension with enhanced patient compliance.

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