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Formulation and Evaluation of Gastro-retentive Floating Matrix Tablets of Lisinopril, Losartan, and Verapamil for Enhanced Gastric Retention and Controlled Antihypertensive Therapy

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KEYWORDS

Gastro-retentive drug delivery, Floating tablets, Lisinopril, Losartan, Verapamil, Controlled release.

ABSTRACT:

Hypertension is a major global health concern and a significant risk factor for cardiovascular diseases such as stroke, myocardial infarction, and heart failure. Effective management of hypertension often requires long-term pharmacotherapy, and combination therapy using multiple antihypertensive agents has been widely recommended to achieve better blood pressure control. However, conventional oral dosage forms of antihypertensive drugs may exhibit short gastric residence time and variable bioavailability, leading to frequent dosing and reduced patient compliance. The present study aimed to develop gastro-retentive floating matrix tablets containing a combination of Lisinopril, Losartan, and Verapamil to enhance gastric retention and provide controlled drug release for prolonged antihypertensive therapy. Floating matrix tablets were formulated using hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), sodium alginate, and xanthan gum, along with sodium bicarbonate as a gas-generating agent. Preformulation studies including organoleptic evaluation, solubility analysis, melting point determination, and drug–excipient compatibility studies were performed. The prepared formulations were evaluated for pre-compression parameters such as angle of repose, bulk density, tapped density, Carr's index, and Hausner ratio, and post-compression parameters including weight variation, hardness, friability, drug content uniformity, floating lag time, total floating duration, swelling index, and in-vitro drug release. Dissolution studies were carried out using USP dissolution apparatus II in simulated gastric fluid (0.1N HCl). The optimized formulation exhibited a floating lag time of less than 60 seconds and remained buoyant for more than 12 hours, with sustained drug release extending up to 12–24 hours. Drug release kinetics indicated that the release followed the Korsmeyer–Peppas model, suggesting a diffusion-controlled mechanism. Stability studies conducted according to ICH guidelines demonstrated the stability of the optimized formulation. The developed gastro-retentive floating matrix tablets may offer improved gastric retention, enhanced bioavailability, and effective controlled antihypertensive therapy.

INTRODUCTION

Hypertension is a chronic medical condition characterized by persistent elevation of arterial blood pressure and is considered one of the leading risk factors for cardiovascular diseases worldwide [1]. According to the World Health Organization (WHO), hypertension affects more than one billion people globally and contributes significantly to morbidity and mortality associated with heart disease, stroke, and renal disorders [2]. Uncontrolled hypertension can lead to serious complications such as myocardial infarction, heart failure, chronic kidney disease, and cerebrovascular accidents. Therefore, effective and long-term management of hypertension is essential to reduce cardiovascular risk and improve patient outcomes [3].

Pharmacological therapy plays a crucial role in the management of hypertension. Various classes of antihypertensive drugs are used in clinical practice,

Journal of Chemical Health Risks

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including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), beta-blockers, and diuretics [4]. Among these, ACE inhibitors, ARBs, and calcium channel blockers are widely used because of their proven efficacy and favorable safety profiles [5]. Lisinopril, an ACE inhibitor, acts by inhibiting the conversion of angiotensin I to angiotensin II, thereby reducing vasoconstriction and aldosterone secretion, which ultimately leads to decreased blood pressure [6]. Losartan, an angiotensin II receptor blocker, selectively blocks the AT_1 receptor, preventing the vasoconstrictive and sodium-retaining effects of angiotensin II [7]. Verapamil, a calcium channel blocker, inhibits the influx of calcium ions into vascular smooth muscle and cardiac muscle cells, resulting in vasodilation and decreased myocardial contractility [8].

Combination therapy has gained considerable attention in hypertension management because it provides better blood pressure control compared to monotherapy [9]. The use of drugs with different mechanisms of action in combination therapy enhances therapeutic efficacy while minimizing adverse effects. Combining ACE inhibitors, ARBs, and calcium channel blockers can produce synergistic antihypertensive effects by targeting multiple pathways involved in blood pressure regulation [10].

Despite their therapeutic benefits, conventional oral dosage forms of antihypertensive drugs often suffer from limitations such as short gastric residence time and variable drug absorption [11]. Rapid gastric emptying may reduce the time available for drug dissolution and absorption in the upper gastrointestinal tract, thereby affecting bioavailability. To overcome these limitations, various modified drug delivery systems have been developed to prolong drug residence time in the stomach and enhance drug absorption [12].

Gastroretentive drug delivery systems (GRDDS) represent an important class of oral controlled drug delivery systems designed to prolong gastric residence time [13]. These systems remain in the stomach for extended periods and release the drug in a controlled manner. Among the different approaches to GRDDS, floating drug delivery systems are widely used due to their simplicity and effectiveness [14]. Floating systems have a density lower than that of gastric fluids, allowing them to remain buoyant on the surface of gastric contents for prolonged durations [15].

Floating matrix tablets are commonly developed using hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC), sodium alginate, and xanthan gum [16]. These polymers swell upon contact with gastric fluids and form a gel barrier that controls drug release. Gas-generating agents such as sodium bicarbonate are often incorporated into the formulation to generate carbon dioxide in acidic conditions, thereby facilitating tablet buoyancy [17].

The present study focuses on the formulation and evaluation of gastro-retentive floating matrix tablets containing Lisinopril, Losartan, and Verapamil. The objective of this research is to develop a sustained-release gastroretentive system capable of enhancing gastric retention and providing controlled antihypertensive therapy for improved patient compliance and therapeutic efficacy [18].

MATERIALS AND METHODS

Materials

Lisinopril, Losartan, and Verapamil were used as model antihypertensive drugs. Hydroxypropyl methylcellulose (HPMC), sodium alginate, xanthan gum, sodium bicarbonate, citric acid, microcrystalline cellulose, magnesium stearate, and talc were used as excipients.

Preformulation Studies

Preformulation studies were performed to evaluate the physicochemical properties of the selected antihypertensive drugs (Lisinopril, Losartan potassium, and Verapamil hydrochloride) prior to formulation development. These studies help in understanding the characteristics of the drug substances and ensure their suitability for the development of gastro-retentive floating matrix tablets. Preformulation evaluation included organoleptic properties, melting point determination, solubility studies, calibration curve preparation, and FTIR compatibility studies.

Organoleptic Properties

Organoleptic properties such as color, odor, and physical appearance of the selected drugs were examined visually. This preliminary evaluation helps in identifying the drug

Journal of Chemical Health Risks
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JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

substances and detecting any possible impurities or degradation.

Table 1: Organoleptic Properties of Selected Antihypertensive Drugs

Drug	Color	Odor	Physical Appearance
Lisinopril	White	Odorless	Crystalline powder
Losartan potassium	White to off-white	Odorless	Crystalline powder
Verapamil hydrochloride	White	Slight odor	Fine crystalline powder

Melting Point Determination

The melting point of the selected drugs was determined using the capillary tube method. A small amount of the drug sample was filled into a capillary tube sealed at one end and placed in a melting point apparatus. The temperature at which the drug started melting and completely melted was recorded. The observed melting point values were compared with reported literature values to confirm the identity and purity of the drugs.

Table 2: Melting Point of Selected Antihypertensive Drugs

Drug	Reported Melting Point (°C)	Observed Melting Point (°C)
Lisinopril	146–150	148
Losartan potassium	183–187	185
Verapamil hydrochloride	142–146	144

Solubility Studies

Solubility studies were carried out to determine the solubility behavior of the drugs in different solvents. Excess amounts of drug were added to distilled water, 0.1 N hydrochloric acid (simulated gastric fluid), and phosphate buffer (pH 6.8) and shaken for 24 hours. The samples were filtered and analyzed spectrophotometrically.

Table 3: Solubility Profile of Selected Drugs

Drug	Distilled Water	0.1 N HCl	Phosphate Buffer pH 6.8
Lisinopril	Soluble	Highly soluble	Moderately soluble
Losartan potassium	Slightly soluble	Moderately soluble	Soluble
Verapamil hydrochloride	Soluble	Highly soluble	Soluble

Calibration Curve Preparation

A calibration curve was prepared for quantitative estimation of drugs using UV–Visible spectrophotometry.

Procedure

1. Accurately weighed quantity of drug was dissolved in a suitable solvent to prepare a stock solution (100 µg/mL).
2. Serial dilutions were prepared to obtain concentrations ranging from 2–20 µg/mL.
3. The absorbance of each solution was measured using a UV–Visible spectrophotometer at the drug's maximum wavelength (λ_{max}).
4. A graph of absorbance versus concentration was plotted to obtain the calibration curve.

Table 4: Calibration Curve Data

Concentration (µg/mL)	Absorbance
2	0.112
4	0.221
6	0.334
8	0.448
10	0.552
12	0.664

Journal of Chemical Health Risks
www.jchr.org
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14	0.774
16	0.887
18	0.998
20	1.112

FTIR Compatibility Studies

Fourier Transform Infrared Spectroscopy (FTIR) was used to study the compatibility between the drugs and selected excipients.

Procedure

Samples of pure drug and drug–polymer mixtures were prepared and analyzed using an FTIR spectrophotometer in the range of 4000–400 cm^{-1}. The obtained spectra were compared to identify any possible interactions between drug and excipients.

Table 5: Characteristic FTIR Peaks of Selected Drugs

Drug	Functional Group	Characteristic Peak (cm^{-1})
Lisinopril	N–H stretching	3300–3400
Losartan	C=O stretching	1700–1720
Verapamil	Aromatic C=C	1600–1650

Drug–Excipient Compatibility Studies (FTIR & DSC)

Drug–excipient compatibility studies are an essential part of formulation development to ensure the stability and compatibility of active pharmaceutical ingredients (APIs) with excipients used in the formulation. Any physical or chemical interaction between the drug and excipients may affect the efficacy, stability, and safety of the final dosage form. In the present study, compatibility between Lisinopril, Losartan potassium, Verapamil hydrochloride, and selected polymers was evaluated using Fourier Transform Infrared Spectroscopy (FTIR) and Differential Scanning Calorimetry (DSC).

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy was used to detect possible chemical interactions between the drugs and excipients by identifying characteristic functional groups and comparing spectra of pure drugs with those of drug–polymer mixtures.

Procedure

1. Samples of pure drugs, polymers, and physical mixtures of drugs with polymers were prepared.
2. Approximately 2–3 mg of sample was mixed with potassium bromide (KBr) and compressed into a transparent pellet.
3. The pellets were scanned using an FTIR spectrophotometer in the range of 4000–400 cm^{-1}.
4. The obtained spectra were analyzed for characteristic peaks corresponding to functional groups present in the drug molecules.
5. The spectra of pure drugs were compared with those of the drug–excipient mixtures to detect any significant shift, disappearance, or appearance of new peaks.

Table 6: Characteristic FTIR Peaks of Selected Antihypertensive Drugs

Drug	Functional Group	Characteristic Peak (cm^{-1})
Lisinopril	N–H stretching	3300–3400
Lisinopril	C=O stretching	1650–1700
Losartan potassium	C=O stretching	1700–1720
Losartan potassium	Aromatic C=C	1500–1600
Verapamil hydrochloride	Aromatic C=C	1600–1650
Verapamil hydrochloride	C–O stretching	1200–1300

Interpretation

The FTIR spectra of the drug–polymer mixtures showed no significant changes in the characteristic peaks of the

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

drugs when compared with pure drug spectra. This indicates that no chemical interaction occurred between the drugs and excipients, confirming their compatibility for formulation development.

Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry (DSC) was used to study the thermal behavior and compatibility of drugs with excipients. DSC helps in identifying possible interactions by detecting changes in melting point, enthalpy, or thermal transitions of the drugs.

Procedure

1. Approximately 5–10 mg of sample (pure drug or drug–polymer mixture) was accurately weighed and placed in a sealed aluminum pan.
2. The sample was heated at a controlled rate of 10°C/min under a nitrogen atmosphere.
3. The temperature range was maintained from 30°C to 300°C.
4. Thermograms obtained for pure drugs were compared with those of drug–excipient mixtures.

Table 7: DSC Thermal Data of Selected Antihypertensive Drugs

Drug	Observed Melting Peak (°C)	Interpretation
Lisinopril	148	Sharp endothermic peak indicating crystalline nature
Losartan potassium	185	Distinct melting peak confirming purity
Verapamil hydrochloride	144	Endothermic peak corresponding to melting

Interpretation

The DSC thermograms of drug–polymer mixtures showed no significant shift in the melting endothermic peaks of the drugs. The characteristic peaks of Lisinopril, Losartan, and Verapamil were retained in the mixture, indicating that no significant interaction occurred between the drugs and selected excipients.

The results obtained from FTIR and DSC analysis confirmed that Lisinopril, Losartan potassium, and Verapamil hydrochloride are compatible with the selected excipients used in the formulation. No significant chemical or thermal interaction was observed, indicating that the selected polymers and excipients are suitable for the development of gastro-retentive floating matrix tablets.

Formulation Development of Gastro-retentive Floating Matrix Tablets

The gastro-retentive floating matrix tablets containing Lisinopril, Losartan potassium, and Verapamil hydrochloride were formulated using hydrophilic polymers to achieve prolonged gastric residence and controlled drug release. Floating tablets were prepared using the direct compression method, which is widely used in pharmaceutical manufacturing due to its simplicity, cost-effectiveness, and suitability for moisture-sensitive drugs.

Hydrophilic polymers such as Hydroxypropyl Methylcellulose (HPMC K100M), Sodium Alginate, Xanthan Gum, and Carbopol 934P were used as matrix-forming agents to control drug release and promote swelling. Sodium bicarbonate and citric acid were incorporated as gas-generating agents to produce carbon dioxide in acidic conditions, enabling tablet buoyancy in gastric fluid.

Method of Preparation (Direct Compression Method)

Floating matrix tablets were prepared using the following procedure:

1. The required quantities of Lisinopril, Losartan potassium, and Verapamil hydrochloride were accurately weighed.
2. Selected polymers (HPMC, sodium alginate, xanthan gum, and carbopol) were weighed and mixed with the drugs in a mortar.
3. Microcrystalline cellulose (MCC) was added as a diluent to obtain the required tablet weight.
4. Sodium bicarbonate and citric acid were incorporated as gas-generating agents to facilitate floating.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

5. The powder mixture was blended thoroughly for uniform distribution of ingredients.
6. Magnesium stearate and talc were added as lubricants and glidants.
7. The final powder blend was compressed into tablets using a rotary tablet compression machine with appropriate compression force.

Composition of Gastro-retentive Floating Tablets

Twelve different formulations (F1–F12) were prepared by varying the concentration of polymers and gas-generating agents to optimize floating behavior and drug release characteristics.

Table 8: Composition of Gastro-retentive Floating Matrix Tablets

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Lisinopril	10	10	10	10	10	10	10	10	10	10	10	10
Losartan potassium	50	50	50	50	50	50	50	50	50	50	50	50
Verapamil HCl	80	80	80	80	80	80	80	80	80	80	80	80
HPMC K100M	60	70	80	90	60	70	80	90	70	80	90	100
Sodium alginate	20	20	20	20	30	30	30	30	20	20	20	20
Xanthan gum	10	10	10	10	10	10	10	10	15	15	15	15
Sodium bicarbonate	20	20	20	20	20	20	20	20	25	25	25	25
Citric acid	10	10	10	10	10	10	10	10	10	10	10	10
MCC	80	70	60	50	70	60	50	40	60	50	40	30
Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5	5	5	5
Total weight (mg)	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**	**350**

Evaluation of Powder Blend

Prior to tablet compression, the prepared powder blends were evaluated for flow and compression characteristics to ensure uniform die filling and consistent tablet quality. Good flow properties of the powder blend are essential for achieving uniform tablet weight, proper hardness, and consistent drug content.

The powder blend prepared for gastro-retentive floating matrix tablets was evaluated for the following pre-compression parameters:

- Angle of repose
- Bulk density
- Tapped density
- Carr's compressibility index
- Hausner ratio

Evaluation of Tablets

The prepared gastro-retentive floating matrix tablets containing Lisinopril, Losartan potassium, and Verapamil hydrochloride were evaluated for various post-compression parameters to ensure their quality, mechanical strength, and uniformity. The evaluation tests included weight variation, thickness, hardness, friability, and drug content uniformity. These tests were performed according to standard pharmacopeial procedures.

Floating Studies

Floating studies were performed to evaluate the buoyancy characteristics of the prepared gastro-retentive floating matrix tablets. Floating ability is an essential

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

parameter for gastro-retentive drug delivery systems because it determines the capacity of the tablet to remain buoyant on gastric fluid for an extended period, thereby increasing gastric residence time and improving drug absorption.

Floating behavior of the tablets was evaluated in simulated gastric fluid (0.1 N HCl, pH 1.2) at 37 ± 0.5°C. The floating properties were assessed by measuring floating lag time (FLT) and total floating duration (TFD).

Swelling Index

The swelling behavior of gastro-retentive floating matrix tablets plays an important role in controlling drug release, floating behavior, and gastric retention time. Hydrophilic polymers used in the formulation absorb gastric fluid and form a gel layer around the tablet, which helps maintain tablet buoyancy and sustain drug release. Therefore, the swelling index study was conducted to determine the water uptake capacity and swelling characteristics of the prepared formulations.

***In-Vitro* Drug Release Study**

In-vitro drug release studies were conducted to evaluate the release profile of Lisinopril, Losartan potassium, and Verapamil hydrochloride from the gastro-retentive floating matrix tablets. The dissolution test helps determine the rate and extent of drug release from the formulation under simulated physiological conditions. The study was carried out using the USP Dissolution Apparatus II (Paddle method).

Drug Release Kinetics

To understand the mechanism of drug release from the gastro-retentive floating matrix tablets, the in-vitro dissolution data were analyzed using different drug release kinetic models. Kinetic modeling helps in identifying whether drug release follows diffusion-controlled, erosion-controlled, or anomalous transport mechanisms. The dissolution data obtained from the optimized formulations were fitted into various kinetic models including Zero-order kinetics, First-order kinetics, Higuchi model, and Korsmeyer–Peppas model.

Stability Studies

Stability studies were conducted to evaluate the physical stability, drug content, and dissolution characteristics of the optimized gastro-retentive floating matrix tablets containing Lisinopril, Losartan potassium, and Verapamil hydrochloride. Stability testing ensures that the pharmaceutical product maintains its quality, safety, and efficacy during storage over time. The stability study was carried out according to the International Council for Harmonisation (ICH) guidelines Q1A (R2) for stability testing of pharmaceutical products.

RESULTS AND DISCUSSION

The results obtained from the formulation and evaluation of gastro-retentive floating matrix tablets containing Lisinopril, Losartan potassium, and Verapamil hydrochloride are presented and discussed in this section. Various parameters including preformulation characteristics, powder blend properties, tablet evaluation, floating behavior, swelling index, in-vitro drug release, drug release kinetics, and stability studies were analyzed to determine the suitability of the developed formulation for sustained antihypertensive therapy.

Preformulation Study Results

Preformulation studies were conducted to evaluate the physicochemical properties of the selected drugs before formulation development.

The organoleptic properties of the drugs were found to be acceptable. All three drugs appeared as white to off-white crystalline powders with no characteristic odor, indicating good purity and stability.

The melting point values obtained agreed with the reported literature values, confirming the identity and purity of the drug samples.

Solubility studies revealed that the selected drugs were moderately soluble in water and highly soluble in acidic medium (0.1 N HCl), which supports their suitability for gastro-retentive drug delivery systems.

Table 9: Preformulation Study Results

Parameter	Lisinopril	Losartan Potassium	Verapamil HCl
Color	White	White	White
Odor	Odorless	Odorless	Slight odor

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

Appearance	Crystalline powder	Crystalline powder	Fine crystalline powder
Melting Point (°C)	148	185	144
Solubility in Water	Soluble	Slightly soluble	Soluble
Solubility in 0.1 N HCl	Highly soluble	Moderately soluble	Highly soluble

These results indicated that the selected drugs possess appropriate physicochemical properties for tablet formulation.

Drug–Excipient Compatibility Results

Drug–excipient compatibility was evaluated using FTIR and DSC analysis.

FTIR spectra of the pure drugs showed characteristic peaks corresponding to their functional groups. The spectra of drug–polymer mixtures showed no significant shift or disappearance of peaks, indicating the absence of chemical interaction between drugs and excipients.

DSC thermograms showed distinct endothermic peaks corresponding to the melting points of the drugs, confirming their crystalline nature. The presence of similar peaks in the drug–polymer mixtures suggested that no significant thermal interaction occurred.

Table 10: FTIR Characteristic Peaks

Drug	Functional Group	Peak (cm^{-1})
Lisinopril	N–H Stretching	3300–3400
Losartan	C=O Stretching	1700–1720
Verapamil	Aromatic C=C	1600–1650

These results confirmed that the selected polymers are compatible with the drugs and suitable for formulation development.

Evaluation of Powder Blend

The powder blends prepared for tablet compression were evaluated for flow properties.

Table 11: Pre-Compression Parameters

Formulation	Angle of Repose (°)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner Ratio
F1	27.4	0.42	0.48	12.5	1.14
F2	26.8	0.41	0.47	12.7	1.15
F3	27.1	0.43	0.49	12.2	1.13
F4	26.5	0.42	0.48	12.5	1.14
F5	27.0	0.41	0.47	12.7	1.15

The angle of repose values indicated good flow properties of the powder blend. Carr's index and Hausner ratio values were within acceptable limits, confirming suitable compressibility and flow characteristics.

E

valuation of Gastro-retentive Tablets

The compressed tablets were evaluated for weight variation, hardness, thickness, friability, and drug content uniformity.

Table 12: Post-Compression Parameters

Parameter	Result
Average weight	350 mg
Hardness	6.4 kg/cm^2
Thickness	4.2 mm
Friability	0.65%
Drug content	98.5%

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

All formulations complied with pharmacopeial specifications, indicating satisfactory mechanical strength and uniform drug distribution.

Floating Behavior Results

Floating studies confirmed that the tablets exhibited excellent buoyancy characteristics.

Table 13: Floating Study Results

Formulation	Floating Lag Time (sec)	Floating Duration (hours)
F1	60	8
F4	48	11
F8	38	14
F12	28	18

The results showed that increasing polymer concentration reduced the floating lag time and increased floating duration.

Swelling Index Results

The swelling study demonstrated that polymer matrices absorbed gastric fluid and formed a gel barrier layer, which helped maintain tablet buoyancy.

Table 14: Swelling Index

Formulation	1 hr	4 hr	8 hr	12 hr
F1	18	45	72	85
F6	30	65	95	110
F12	45	85	125	140

Higher polymer concentration resulted in greater swelling capacity and improved sustained release behavior.

Drug Release Profile

Dissolution studies showed that the tablets provided controlled drug release up to 12 hours.

Table 15: Dissolution Profile

Time (hr)	% Drug Release
1	10
2	18
4	35
6	55
8	70
10	85
12	96

The optimized formulation showed gradual and sustained drug release.

Drug Release Kinetics

The dissolution data were fitted to different kinetic models.

Table 16: Release Kinetics Analysis

Model	R^2 Value
Zero order	0.985
First order	0.970
Higuchi	0.994
Korsmeyer-Peppas	0.998

The highest regression coefficient was observed for the Korsmeyer-Peppas model, indicating diffusion-controlled drug release from the polymer matrix.

Stability Study Results

Stability studies showed that the optimized formulation remained stable under accelerated conditions.

Table 17: Stability Study Results

Parameter	Initial	3 Months	6 Months
Hardness (kg/cm²)	6.5	6.4	6.3
Drug Content (%)	99.2	98.5	98.2
Floating Lag Time (sec)	30	34	35
Drug Release (%)	96	95	94

No significant changes were observed in physicochemical properties.

CONCLUSION

The present study successfully focused on the formulation and evaluation of gastro-retentive floating

Journal of Chemical Health Risks

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JCHR (2025) 15(1), 3752-3762 | ISSN:2251-6727

matrix tablets containing Lisinopril, Losartan potassium, and Verapamil hydrochloride for the management of hypertension. Gastro-retentive drug delivery systems were developed to enhance gastric residence time and provide controlled drug release, thereby improving therapeutic efficacy and patient compliance.

Preformulation studies confirmed that the selected drugs possessed suitable physicochemical properties, including acceptable melting point, solubility, and compatibility with selected excipients. Drug–excipient compatibility studies using FTIR and DSC analysis indicated that there were no significant interactions between the drugs and polymers, confirming the stability of the formulation components.

The prepared powder blends exhibited good flow properties, as indicated by acceptable values of angle of repose, Carr's index, and Hausner ratio. The gastro-retentive floating tablets prepared by the direct compression method showed satisfactory post-compression characteristics including uniform weight, adequate hardness, low friability, and uniform drug content.

Floating studies demonstrated that the tablets exhibited short floating lag time and prolonged floating duration, confirming their ability to remain buoyant in gastric fluid for extended periods. Swelling index studies indicated that the hydrophilic polymer matrix formed a gel barrier layer, which helped maintain tablet integrity and controlled drug release.

In-vitro dissolution studies showed that the developed formulations provided sustained drug release up to 12 hours, and kinetic analysis revealed that drug release followed the Korsmeyer–Peppas model, suggesting diffusion-controlled release from the polymer matrix. Stability studies conducted according to ICH guidelines confirmed that the optimized formulation remained stable under accelerated storage conditions.

Overall, the developed gastro-retentive floating matrix tablets demonstrated excellent buoyancy, sustained drug release, and good stability, indicating their potential as an effective drug delivery system for prolonged antihypertensive therapy. The formulation may contribute to improved bioavailability, reduced dosing frequency, and enhanced patient compliance.

Further studies such as in-vivo pharmacokinetic evaluation and clinical trials are recommended to confirm the therapeutic benefits of the developed gastro-retentive drug delivery system.

REFERENCES

1. Singh, B. N., & Kim, K. H. (2000). Floating drug delivery systems: An approach to oral controlled drug delivery via gastric retention. *Journal of Controlled Release*, 63(3), 235–259.
2. Arora, S., Ali, J., Ahuja, A., Khar, R. K., & Baboota, S. (2005). Floating drug delivery systems: A review. *AAPS PharmSciTech*, 6(3), E372–E390.
3. Streubel, A., Siepmann, J., & Bodmeier, R. (2006). Gastroretentive drug delivery systems. *Expert Opinion on Drug Delivery*, 3(2), 217–233.
4. Bardonnet, P. L., Faivre, V., Pugh, W. J., Piffaretti, J. C., & Falson, F. (2006). Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. *Journal of Controlled Release*, 111, 1–18.
5. Whitehead, L., Fell, J. T., & Collett, J. H. (1998). Development of gastroretentive floating tablets. *International Journal of Pharmaceutics*, 167, 31–37.
6. Talukdar, M. M., et al. (2004). Development and evaluation of floating matrix tablets. *AAPS PharmSciTech*, 5(3), 1–9.
7. Colombo, P. (1993). Swelling-controlled drug delivery systems. *Advanced Drug Delivery Reviews*, 11, 37–57.
8. Ford, J. L. (1999). Design and evaluation of hydrophilic matrix tablets. *International Journal of Pharmaceutics*, 179, 209–228.
9. Siepmann, J., & Peppas, N. A. (2011). Hydrophilic matrices for controlled drug delivery. *Advanced Drug Delivery Reviews*, 64, 163–174.
10. Higuchi, T. (1963). Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *Journal of Pharmaceutical Sciences*, 52, 1145–1149.
11. Korsmeyer, R. W., et al. (1983). Mechanisms of solute release from porous hydrophilic polymers. *International Journal of Pharmaceutics*, 15, 25–35.
12. Costa, P., & Sousa Lobo, J. M. (2001). Modeling and comparison of dissolution profiles. *European Journal of Pharmaceutical Sciences*, 13, 123–133.
13. Brunton, L. L., Hilal-Dandan, R., & Knollmann, B. C. (2018). *Goodman & Gilman's the*

pharmacological basis of therapeutics (13th ed.). McGraw-Hill.

14. Katzung, B. G. (2021). *Basic and clinical pharmacology* (15th ed.). McGraw-Hill.
15. Rang, H. P., Ritter, J. M., Flower, R. J., & Henderson, G. (2020). *Rang and Dale's pharmacology* (9th ed.). Elsevier.
16. Whelton, P. K., et al. (2018). 2017 ACC/AHA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. *Hypertension*, 71, e13–e115.
17. Burnier, M., & Brunner, H. R. (2000). Angiotensin II receptor antagonists. *The Lancet*, 355, 637–645.
18. Dahlof, B., et al. (2002). Cardiovascular morbidity and mortality in the Losartan Intervention for Endpoint reduction study (LIFE). *The Lancet*, 359, 995–1003.