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Development and Optimization of a Triple-Drug Gastroretentive Drug Delivery System Containing Lisinopril, Losartan, And Verapamil Using Hydrophilic Polymer Matrix Technology

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KEYWORDS

Gastroretentive drug delivery, Floating matrix tablets, Lisinopril, Losartan, Verapamil, Controlled release.

ABSTRACT:

Hypertension is a major global health concern that often requires combination therapy for effective blood pressure control. Conventional oral dosage forms of antihypertensive drugs frequently exhibit short gastric residence time and variable bioavailability, which may reduce therapeutic efficacy and patient compliance. The present study aimed to develop and optimize a gastroretentive floating matrix tablet containing a combination of Lisinopril, Losartan potassium, and Verapamil hydrochloride using hydrophilic polymer matrix technology. Floating tablets were formulated using hydroxypropyl methylcellulose (HPMC K100M), sodium alginate, and xanthan gum as matrix-forming polymers, while sodium bicarbonate and citric acid were used as gas-generating agents. Preformulation studies including organoleptic evaluation, melting point determination, solubility studies, and drug–excipient compatibility (FTIR and DSC) 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. Post-compression evaluation included 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 (0.1 N HCl). The optimized formulation showed floating lag time below 60 seconds and remained buoyant for more than 16 hours. In-vitro dissolution studies demonstrated sustained drug release up to 12 hours. Drug release kinetics followed the Korsmeyer–Peppas model, indicating diffusion-controlled drug release from the polymer matrix. Stability studies conducted according to ICH guidelines confirmed that the optimized formulation remained stable under accelerated storage conditions. The developed gastroretentive system demonstrated potential for improving gastric retention, enhancing drug bioavailability, and providing controlled antihypertensive therapy.

INTRODUCTION

Hypertension is one of the most prevalent cardiovascular disorders worldwide and represents a major risk factor for heart disease, stroke, and kidney failure [1-2]. According to the World Health Organization, hypertension affects over one billion individuals globally and remains a leading cause of morbidity and mortality [3-4].

Pharmacological treatment of hypertension commonly involves the use of antihypertensive agents such as ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, diuretics, and beta-blockers [5-6]. Combination therapy has gained considerable attention because it provides improved blood pressure control and reduces the risk of cardiovascular complications [7-8].

Lisinopril is an angiotensin-converting enzyme inhibitor that reduces the production of angiotensin II and aldosterone, leading to vasodilation and decreased blood pressure [9-10]. Losartan is an angiotensin II receptor blocker that selectively blocks the AT_1 receptor

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and prevents angiotensin II mediated vasoconstriction [11]. Verapamil is a calcium channel blocker that inhibits calcium influx into vascular smooth muscle cells, resulting in vasodilation and decreased cardiac workload [12].

Despite their therapeutic advantages, conventional oral formulations of antihypertensive drugs often suffer from limitations such as short gastric residence time and incomplete drug absorption [13]. Gastroretentive drug delivery systems have been developed to overcome these limitations by prolonging the residence time of dosage forms in the stomach [14].

Floating drug delivery systems are one of the most promising approaches to gastroretention. These systems have a density lower than gastric fluid and remain buoyant in the stomach for extended periods, allowing sustained drug release [15].

Hydrophilic polymer matrices such as hydroxypropyl methylcellulose, sodium alginate, and xanthan gum are widely used to develop floating tablets because they swell in gastric fluid and form a gel barrier that controls drug diffusion [16].

The present study focuses on the development and optimization of a triple-drug gastroretentive floating matrix tablet containing Lisinopril, Losartan, and Verapamil to improve therapeutic outcomes in hypertension management [17].

MATERIALS AND METHODS

Materials

Lisinopril, Losartan potassium, and Verapamil hydrochloride were used as active pharmaceutical ingredients. Hydroxypropyl methylcellulose (HPMC K100M), sodium alginate, xanthan gum, carbopol, 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 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

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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
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

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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 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

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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.
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

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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 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.

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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
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

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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.

Evaluation 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%

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.

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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 development and optimization of a gastroretentive floating matrix tablet containing the triple antihypertensive drug combination of Lisinopril, Losartan potassium, and Verapamil hydrochloride using hydrophilic polymer matrix technology. The objective of the research was to enhance gastric retention time and achieve sustained drug release, thereby improving therapeutic efficacy and patient compliance in hypertension management.

Preformulation studies confirmed that the selected drugs possessed suitable physicochemical characteristics, including acceptable melting point, solubility, and stability. Drug–excipient compatibility studies performed using FTIR and DSC analysis demonstrated that there were no significant interactions between the drugs and the selected excipients, confirming the suitability of polymers for formulation development.

The gastroretentive floating tablets prepared by the direct compression method exhibited satisfactory pre-compression and post-compression parameters. Powder blends showed good flow properties, as indicated by acceptable values of angle of repose, Carr's index, and Hausner ratio. The compressed tablets complied with pharmacopeial limits for weight variation, hardness, friability, thickness, and drug content

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uniformity, indicating uniformity and adequate mechanical strength.

Floating studies revealed that the developed tablets showed short floating lag time and prolonged floating duration, confirming their ability to remain buoyant in gastric fluid for extended periods. Swelling index studies demonstrated that the hydrophilic polymers formed a gel barrier matrix, which contributed to sustained drug release and improved tablet integrity.

In-vitro dissolution studies confirmed that the optimized formulation provided controlled drug release for up to 12 hours, which may help maintain consistent plasma drug concentrations. Drug release kinetics analysis showed that the release mechanism followed the Korsmeyer–Peppas model, indicating diffusion-controlled drug release from the polymer matrix.

Stability studies conducted according to ICH guidelines demonstrated that the optimized formulation remained stable under accelerated storage conditions, with no significant changes in physical properties, drug content, or dissolution profile.

Overall, the developed triple-drug gastroretentive floating matrix tablet represents a promising drug delivery system for the long-term management of hypertension. The formulation offers potential advantages such as improved gastric retention, enhanced bioavailability, reduced dosing frequency, and better patient compliance.

Further investigations including in-vivo pharmacokinetic studies, bioavailability evaluation, and clinical trials are recommended to confirm the therapeutic benefits and facilitate potential industrial scale-up and commercialization of the developed gastroretentive antihypertensive formulation.

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