FORMULATION AND EVALUATION OF GASTRORETENTIVE FLOATING TABLETS OF LOSARTAN POTASSIUM

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Abstract

The present research work aimed to formulate and evaluate gastroretentive floating tablets of Losartan Potassium for prolonged gastric retention and sustained drug release. Losartan potassium is an antihypertensive drug with short biological half-life and moderate bioavailability, making it suitable for gastroretentive floating drug delivery systems (FDDS). Floating tablets were prepared using hydrophilic polymers such as HPMC and Carbopol along with sodium bicarbonate and citric acid as gas-generating agents by direct compression technique. The prepared formulations were evaluated for pre-compression and post-compression parameters including angle of repose, bulk density, tapped density, Carr's index, Hausner ratio, hardness, friability, floating lag time, total floating duration, swelling index, and in-vitro drug release studies. The optimized formulation F9 exhibited excellent buoyancy, prolonged floating duration exceeding 24 hours, and sustained drug release following Higuchi diffusion kinetics. Stability studies confirmed that the formulation remained stable under accelerated conditions. The study concluded that gastroretentive floating tablets of Losartan potassium can effectively improve bioavailability, sustain drug release, and enhance patient compliance in hypertension therapy.

Keywords: Gastroretentive Drug Delivery System (GRDDS), Floating Tablets, Losartan Potassium, Sustained Release, Hypertension, Floating Lag Time, Gastric Retention,

1. Introduction

Hypertension is one of the most prevalent chronic cardiovascular disorders worldwide and represents a major public health concern due to its association with increased morbidity and mortality. Persistent elevation of blood pressure significantly contributes to life-threatening complications such as stroke, myocardial infarction, congestive heart failure, renal impairment, and coronary artery disease. According to the World Health Organization, hypertension affects millions of people globally and remains one of the leading causes of premature death. Effective management of hypertension requires maintenance of optimum plasma drug concentration for prolonged duration in order to achieve sustained therapeutic response and minimize fluctuations in blood pressure.

Losartan Potassium is a selective angiotensin II receptor blocker (ARB) extensively used for the treatment of hypertension, diabetic nephropathy, heart failure, and cardiovascular complications. The drug acts by selectively blocking AT1 receptors, thereby inhibiting vasoconstriction and aldosterone secretion mediated by angiotensin II. Although Losartan potassium exhibits significant antihypertensive efficacy, it possesses several pharmacokinetic limitations such as low and variable oral bioavailability (approximately 33%), short biological half-life of about 1.5–2 hours, and incomplete gastrointestinal absorption. Due to these limitations, frequent administration is required to maintain effective plasma concentration, which may reduce patient compliance and therapeutic effectiveness. Conventional oral dosage forms such as tablets and capsules often fail to maintain prolonged therapeutic levels because of rapid gastric emptying and limited gastric residence time. Drugs that are primarily absorbed from the stomach or upper part of the small intestine exhibit reduced bioavailability when they pass rapidly through the gastrointestinal tract. Therefore, development of gastroretentive drug delivery systems has gained considerable attention in recent years.

Gastroretentive Floating Drug Delivery Systems (GRDDS) are designed to prolong gastric residence time by remaining buoyant on gastric fluids for extended periods without affecting gastric emptying rate. These systems possess a bulk density lower than gastric fluid and therefore float in the stomach while continuously releasing the drug in a controlled manner. Floating tablets improve gastric retention, enhance drug absorption, minimize plasma concentration fluctuations, and reduce dosing frequency. Such systems are particularly beneficial for drugs like Losartan potassium that exhibit better absorption in the upper gastrointestinal tract.

Floating drug delivery systems generally contain hydrophilic polymers such as Hydroxypropyl Methylcellulose (HPMC), Carbopol, and sodium alginate, which swell in contact with gastric fluid and form a gel barrier around the tablet. Gas-generating agents such as sodium bicarbonate and citric acid produce carbon dioxide upon contact with acidic gastric medium, resulting in buoyancy of the dosage form. The combination of swelling polymers and gas-generating agents helps maintain prolonged floating behavior and sustained drug release profile.

The present research work focuses on the formulation and evaluation of gastroretentive floating tablets of Losartan Potassium using direct compression technique. The study aims to improve gastric retention time, sustain drug release, enhance bioavailability, and improve patient compliance by developing an optimized floating tablet formulation.

2. Objectives

- To prolong gastric residence time of the drug.
- To reduce fluctuations in plasma drug concentration.
- To provide controlled and sustained drug release.
- To reduce dosing frequency and improve patient compliance.
- To enhance oral bioavailability of Losartan potassium.
- To evaluate buoyancy and drug release characteristics of floating tablets.

3. Drug Profile

Drug: Losartan Potassium

Chemical Information

Parameter	Description
Generic Name	Losartan Potassium
Category	Antihypertensive Agent
Pharmacological Class	Angiotensin II Receptor Blocker
Molecular Formula	$C_{22}H_{22}ClKN_6O$
Molecular Weight	461.01 g/mol
Appearance	White to off-white crystalline powder
Solubility	Freely soluble in water
Biological Half-life	1.5–2 hours
Bioavailability	Approximately 33%

Mechanism of Action

Losartan potassium selectively blocks angiotensin II type-1 (AT1) receptors, leading to vasodilation, reduced aldosterone secretion, decreased sodium retention, and reduction in peripheral vascular resistance.

Therapeutic Uses

- Hypertension
- Heart failure
- Diabetic nephropathy
- Stroke prevention in hypertensive patients

4. Materials and Methods

Materials Used

Material	Function
Losartan Potassium	Active pharmaceutical ingredient
HPMC K4M/K15M	Hydrophilic polymer
Carbopol 934P	Swelling polymer
Sodium Bicarbonate	Gas-generating agent
Citric Acid	Acidifying agent
Lactose Monohydrate	Diluent
MCC PH102	Binder/Diluent
Magnesium Stearate	Lubricant
Talc	Glidant

Method of Preparation

Floating tablets were prepared by direct compression technique. Hydrophilic polymers such as HPMC and Carbopol were used to form a gel matrix system, while sodium bicarbonate and citric acid were incorporated as gas-generating agents to impart buoyancy.

Steps Involved

1. Weighing of ingredients
2. Sieving of powder blend
3. Mixing of drug and excipients
4. Lubrication using magnesium stearate and talc
5. Compression using rotary tablet punching machine

5. Preformulation Studies

Preformulation studies were performed to evaluate physicochemical properties of Losartan potassium and powder blend characteristics.

Parameters Evaluated

- Organoleptic properties
- Solubility analysis
- Melting point determination
- λmax determination
- FTIR compatibility studies
- Bulk density
- Tapped density
- Carr's index
- Hausner ratio

Solubility Analysis

Losartan potassium showed high solubility in acidic medium (0.1N HCl), indicating suitability for gastroretentive drug delivery systems.

6. Evaluation Parameters

Pre-compression Parameters

The powder blend showed good flow properties suitable for direct compression.

Formulation	Angle of Repose	Carr's Index	Hausner Ratio
F1	27.45°	14.28%	1.16
F5	27.63°	12.24%	1.14
F9	25.76°	11.32%	1.12

The angle of repose values below 30° indicated excellent flowability of powder blends. Carr's index and Hausner ratio confirmed acceptable compressibility characteristics.

Post-compression Parameters

Prepared tablets were evaluated for:

- Hardness
- Friability
- Weight variation
- Thickness
- Floating lag time
- Total floating time

- Swelling index
- Drug content
- In-vitro drug release

7. Results and Discussion

The optimized formulation F9 exhibited excellent gastroretentive floating behavior along with sustained and controlled drug release characteristics. The formulation showed a very short floating lag time of approximately 18 seconds, indicating rapid generation of carbon dioxide and immediate buoyancy upon contact with gastric fluid. In addition, the total floating duration exceeded 24 hours, confirming the ability of the formulation to remain buoyant in the gastric environment for prolonged periods without disintegration. Prolonged gastric retention is highly beneficial for drugs like Losartan Potassium, which are preferentially absorbed in the upper gastrointestinal tract.

The enhanced floating properties of formulation F9 may be attributed to the synergistic effect of hydrophilic polymers and gas-generating agents. The incorporation of Hydroxypropyl Methylcellulose (HPMC) and Carbopol formed a strong gel barrier around the tablet upon hydration. This gel matrix effectively entrapped the carbon dioxide generated by sodium bicarbonate and citric acid in acidic medium, thereby reducing tablet density and maintaining buoyancy for an extended duration. In-vitro drug release studies demonstrated that formulation F9 provided sustained drug release over a period of 24 hours with controlled release kinetics. The drug release profile showed an initial moderate release followed by prolonged and gradual drug diffusion from the hydrated polymeric matrix. The sustained release behavior is advantageous in maintaining constant plasma drug concentration, minimizing dosing frequency, and improving patient compliance in antihypertensive therapy.

Kinetic analysis of dissolution data revealed that the drug release followed the Higuchi diffusion model, indicating diffusion-controlled release mechanism from the polymeric matrix system. Furthermore, the Korsmeyer–Peppas kinetic model suggested a non-Fickian or anomalous transport mechanism involving a combination of drug diffusion and polymer relaxation/erosion processes. This indicates that both swelling of hydrophilic polymers and diffusion of drug molecules contributed significantly to the overall release pattern. The superior performance of formulation F9 may therefore be attributed to the optimized concentration of release-retarding polymers, efficient swelling behavior, and effective gas generation system using sodium bicarbonate and citric acid. The formulation successfully achieved prolonged gastric retention, sustained drug release, and improved floating characteristics, making it a promising gastroretentive drug delivery system for effective management of hypertension.

8. Stability Studies

Stability studies were conducted according to ICH guidelines under long-term and accelerated conditions.

Condition	Temperature	Relative Humidity
Long-term	25°C ± 2°C	60% RH ± 5%
Accelerated	40°C ± 2°C	75% RH ± 5%

The optimized formulation remained stable without significant changes in appearance, hardness, friability, drug content, or floating behavior after 3 months of storage.

9. Conclusion

The present research work successfully formulated and evaluated gastroretentive floating tablets of Losartan Potassium using direct compression technique with suitable hydrophilic polymers and gas-generating agents.

The developed floating tablets demonstrated satisfactory pre-compression and post-compression characteristics including acceptable hardness, low friability, uniform weight variation, adequate swelling behavior, and excellent floating properties. Among all formulations, the optimized formulation F9 exhibited superior performance with a very short floating lag time and prolonged total floating duration exceeding 24 hours, indicating efficient gastroretentive behavior. The formulation also showed sustained and controlled drug release over an extended period, which is highly advantageous for maintaining consistent plasma drug concentration and reducing fluctuations associated with conventional dosage forms.

The incorporation of polymers such as Hydroxypropyl Methylcellulose (HPMC) and Carbopol successfully formed a stable gel matrix system that controlled drug release and maintained tablet buoyancy. The combination of sodium bicarbonate and citric acid effectively generated carbon dioxide, which contributed to prolonged floating capability of the dosage form. Drug release kinetic studies indicated that the optimized formulation followed Higuchi diffusion kinetics with non-Fickian diffusion mechanism, suggesting combined effects of drug diffusion and polymer relaxation.

Stability studies performed under accelerated conditions confirmed that the optimized formulation remained stable without significant changes in physical appearance, floating characteristics, drug content, or dissolution profile. The study demonstrated that gastroretentive floating drug delivery systems can effectively enhance gastric residence time, improve oral bioavailability, prolong drug release, and improve therapeutic efficacy of Losartan Potassium.

Therefore, the developed floating tablet formulation may serve as a promising and effective sustained-release gastroretentive drug delivery system for long-term management of hypertension and associated cardiovascular disorders.

10. **References**

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