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DEVELOPMENT AND EVALUATION OF OSMOTICALLY CONTROLLED LOSARTAN POTASSIUM TABLETS FOR SUSTAINED RELEASE

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ABSTRACT

The present study aimed to develop an osmotically controlled drug delivery system for Losartan potassium, a BCS Class I antihypertensive agent with a short half-life (1.5–2 hours), to achieve zero-order release and enhance therapeutic efficacy. Five formulations (LP1–LP5) were prepared by direct compression using HPMC K100M as the rate-controlling polymer and mannitol as the osmotic agent. Formulation development included core tablet compression followed by coating with a semi-permeable membrane and orifice drilling. Pre-compression parameters (bulk density, tapped density, Carr's index, Hausner ratio) and post-compression characteristics (weight variation, hardness, friability, thickness, drug content, and in vitro release) were within acceptable limits. FTIR studies confirmed drug-excipient compatibility. In vitro dissolution studies in phosphate buffer (pH 6.8) demonstrated sustained drug release, with formulation LP3 showing the most promising profile—achieving 99.99% release over 12 hours and exhibiting near-zero-order kinetics. A 3-month stability study of LP3 confirmed its physical and chemical stability. Overall, a stable and effective osmotic drug delivery system for Losartan potassium was successfully developed, offering sustained release, reduced dosing frequency, and potential for improved patient compliance.

INTRODUCTION

Osmotic drug delivery systems (ODDS) are advanced oral controlled-release systems that offer precise and prolonged drug release independent of gastrointestinal pH and motility. (1) These systems typically consist of a core tablet containing a drug and osmogens, coated with a semipermeable membrane. Upon ingestion, water enters the core through the membrane, generating osmotic pressure that drives the drug solution through a delivery orifice, ensuring zero-order release kinetics. (2) Losartan potassium, an angiotensin II receptor antagonist, is used in the management of hypertension. (3) It is a BCS Class I drug with good solubility and permeability but undergoes extensive first-pass metabolism, resulting in only 33% oral bioavailability. Its short half-life (1.5–2 hours) necessitates frequent dosing, which may reduce patient compliance. (4)

To address these limitations, this study aimed to develop an osmotically controlled oral delivery system of Losartan potassium to achieve sustained drug release over 12 hours. The formulation was designed using HPMC K100M as the swellable polymer and mannitol as the osmotic agent. The core tablets were coated with ethyl cellulose and PEG-4000 to form a semipermeable membrane, followed by orifice drilling to facilitate controlled drug release.

The developed system is expected to improve therapeutic efficacy by maintaining steady plasma drug concentrations, minimizing dosing frequency, and enhancing patient compliance. Key formulation variables such as polymer concentration, osmogen levels, and coating composition were optimized to achieve desired release kinetics.

2. MATERIAL AND METHODS

Losartan potassium was received as a gift sample from M/s Aurobindo Pharma Ltd., Hyderabad. Hydroxypropyl methylcellulose (HPMC K100M) was obtained from M/s Colorcon Asia Pvt. Ltd., Mumbai. Mannitol and microcrystalline cellulose were procured from M/s Matrix Pharma, Hyderabad. Talc and magnesium stearate were purchased from Loba Chemie Pvt. Ltd., Mumbai.

Compatibility Studies – FTIR (5)

Fourier Transform Infrared (FTIR) spectroscopy was employed to assess potential chemical interactions between Losartan potassium and the selected formulation excipients. FTIR spectra were recorded for the pure drug and physical mixtures containing Losartan potassium and excipients in a 1:1 ratio.

Samples were prepared by triturating the drug or drug-excipient mixtures with spectroscopic-grade potassium bromide (KBr) in a mortar and pestle. The resulting powders were compressed into transparent pellets using a hydraulic press under a pressure of approximately 5–6 tons for 5 minutes.

The pellets were then analyzed using an FTIR spectrophotometer (Shimadzu) over a scanning range of 4000–400 cm^{-1}, at a resolution of 4 cm^{-1}. The spectra were recorded and compared to identify any potential shifts, disappearance, or appearance of new peaks, which may indicate chemical incompatibility between the drug and excipients.

Preparation of an osmotic tablet of Losartan Potassium: (6)

The core tablets of Losartan potassium were prepared using the direct compression technique. Initially, Losartan potassium was uniformly blended with HPMC K100M in a double cone blender for 10 minutes to ensure homogeneous distribution of the polymer. The blend was then passed through a #30 mesh sieve to achieve uniform particle size. Microcrystalline cellulose (MCC), serving as the diluent and osmotic agent, was incorporated into the blend using geometric dilution, followed by an additional 10 minutes of mixing. Lubricants—talc and magnesium stearate—previously sieved through a #60 mesh, were added and mixed for 5 minutes to ensure uniform lubrication of the blend. The final powder blend was compressed into tablets using a Clit 10-station rotary compression machine. Five different formulations (LP1–LP5) were prepared by varying the concentration of mannitol while keeping the quantities of other excipients and processing parameters constant to ensure batch-to-batch consistency.

Coating procedure: (7)

The core tablets of Losartan potassium were coated using a conventional stainless-steel coating pan with an outer diameter of 10 cm, equipped with three baffles positioned at 120° intervals to ensure uniform tablet movement. The coating solution was prepared by sequentially dissolving ethyl cellulose and PEG-4000 in a solvent mixture of dichloromethane, ensuring complete dissolution of each component before the addition of the next. The coating process was carried out at a controlled pan temperature between 38°C and 42°C. The coating solution was applied using a spray gun at a rate of 4–5 mL/min under continuous rotation of the pan to ensure uniform coating. The desired coat weight and film thickness were achieved by adjusting the total volume of coating solution, monitored by regular weight gain measurements. After completion of the coating process, the tablets were dried at 50°C for 6 hours in a hot air oven to ensure complete solvent evaporation and proper film formation. Following drying, a single delivery orifice was created on one face of each coated tablet using a stainless steel microdrill with a diameter of approximately 0.5 mm (500 µm). To maintain consistency in orifice size and position, all drilling was performed manually under magnification using a micrometre-guided needle punch. The orifice diameter was periodically verified using an optical microscope fitted with a calibrated eyepiece reticle. Only tablets with a uniform orifice size and centrally located openings were selected for further evaluation to ensure reproducible osmotic drug release.

Table 1: Composition of Core Osmotic Tablets of Losartan Potassium (per tablet)

Excipients (mg/tablet)	LP1	LP2	LP3	LP4	LP5
Losartan potassium	90	90	90	90	90
HPMC K100M	50	50	50	50	50
Mannitol	30	40	50	60	70
Microcrystalline cellulose	175	165	155	145	135
Talc	3	3	3	3	3
Magnesium stearate	2	2	2	2	2

Table 2: Coating Composition of Losartan Potassium Osmotic Tablets

Excipient	LP1	LP2	LP3	LP4	LP5
Ethyl cellulose (gm)	1.0	1.1	1.2	1.3	1.4
PEG-4000 (% w/w)	0.6	0.7	0.8	0.9	1.0
Dichloromethane (mL)	20	20	20	20	20

Evaluation Parameters of Losartan Potassium Osmotic Tablets

The pre-compression flow properties of the Losartan potassium osmotic tablet blend were evaluated to ensure uniform die filling and consistent tablet weight. These properties depend on particle size, shape, porosity, and density of the powder blend.

a. Bulk Density (g/mL) (8)

Bulk density refers to the mass of powder occupying a unit volume without tapping and is an indicator of powder packing characteristics. An accurately weighed quantity of the powder blend (m) was transferred into a 100 mL graduated cylinder without tapping. The bulk volume (V_1) was recorded, and bulk density was calculated using:

$$\text{Bulk Density} = \frac{m}{V_1}$$

Where, m = mass of the powder (g) and V_1 = bulk (untapped) volume (mL)

b. Tapped Density (g/mL) (8)

Tapped density is the volume occupied after mechanical tapping of the measuring cylinder, indicating powder consolidation. The same sample was subjected to tapping using a tap density

apparatus (Electro Lab USP II). Tapping was performed in stages (initial 500 taps, then an additional 750 taps). Tapped volume (Vt) was recorded, and tapped density calculated as:

$$\text{Tapped Density} = \frac{M}{V_t}$$

Where, M = mass of the powder (g) and V_t = tapped volume (mL)

c. Carr's Compressibility Index (%) (9)

Carr's Index measures the flowability and compressibility of the powder blend. It is calculated using:

$$\text{Carr's Compressibility Index } (\%) = \left(\frac{\rho_t - \rho_b}{\rho_t}\right) \times 100$$

A lower value indicates better flowability (ideal: <15%).

d. Hausner Ratio

Hausner Ratio also indicates powder flow properties and is calculated by:

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Values <1.25 indicate good flow, whereas >1.25 suggest poor flowability.

e. Angle of Repose (θ)

The angle of repose represents the maximum angle between the surface of the powder heap and the horizontal plane, reflecting flow behaviour. The powder blend was allowed to flow freely through a funnel fixed at a height of 2 cm to form a cone-shaped heap. The height (h) and radius (r) of the heap were measured, and the angle was calculated as:

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Where, θ = angle of repose, h = height of heap (cm), r = radius of base (cm)

Post-Compression Evaluation Parameters:

The prepared osmotic tablets of Losartan potassium were evaluated for the following post-compression quality control parameters to ensure mechanical strength, uniformity, and resistance to physical stress.

a. Thickness (mm)

Tablet thickness was measured using a vernier calliper. Five tablets from each batch were randomly selected, and the average thickness was calculated. The results were expressed in millimetres (mm) to assess uniformity across the formulation.

b. Hardness (kg/cm²)

Tablet hardness, indicating mechanical strength, was determined using a Monsanto hardness tester. The force required to break each tablet was measured in kilograms. Adequate hardness ensures the tablet can withstand handling without breaking or crumbling.

c. Weight Variation Test (10)

The uniformity of tablet weight was evaluated as per USP guidelines. Twenty tablets were individually weighed, and the average weight was calculated. Each tablet's weight was compared against the average, and the percentage deviation was determined. Tablets were considered to comply if no more than two tablets deviated by more than the allowed limits, and none deviated excessively.

d. Friability (%) (11)

Friability assesses the tablet's ability to resist abrasion during handling and transportation. Ten tablets were accurately weighed (initial weight W_1) and placed in a Roche friabilator, which was operated at 25 rpm for 100 revolutions. Tablets were then removed, dusted, and reweighed (final weight W_2). Friability was calculated using the formula:

$$\text{Friability } (\%) = \frac{W_1 - W_2}{W_1} \times 100$$

A friability value of less than 1% is generally considered acceptable.

e. Drug Content Uniformity (12)

Drug content uniformity was evaluated to ensure a consistent dosage of Losartan potassium in each tablet. Six tablets (N=6) were randomly selected from each batch and subjected to analysis. Each selected tablet was crushed to a fine powder. An accurately weighed amount of the powder, equivalent to one tablet, was transferred into a 100 mL volumetric flask. About 70 mL of distilled water was added, and the flask was shaken occasionally for 30 minutes to ensure complete drug dissolution. The volume was then made up to 100 mL with distilled water. From this solution, 10 mL was withdrawn and centrifuged. The clear supernatant was carefully collected and filtered through a 0.45 µm Millipore filter. The filtrate was appropriately diluted, and the absorbance was measured at 250 nm using a UV-Visible spectrophotometer. The concentration of Losartan potassium was determined using a previously constructed calibration curve. The test was performed in triplicate for each batch (n=6), and the average drug content was calculated. The formulation was considered to pass the content uniformity test if the drug content ranged between 90–110% of the labelled claim, as per pharmacopeial standards.

f. In-vitro dissolution studies

Dissolution studies for core and coated Losartan potassium osmotic tablets were conducted using a USP paddle-type dissolution apparatus (LabIndia, 8-station). The test was performed in 900 mL of phosphate buffer (pH 6.8) at 37 ± 0.5°C, with paddle rotation maintained at 100 rpm for 12 hours. Samples were withdrawn at regular intervals, replaced with fresh buffer to maintain sink conditions, and analyzed at 234 nm using a double-beam UV-Visible spectrophotometer (Shimadzu 1800). Each formulation was tested in six replicates (n=6), and the average cumulative drug release was calculated. This study was used to assess the release behavior of both uncoated and coated osmotic tablets and to evaluate the impact of formulation variables on sustained drug release, as per IP acceptance criteria.

g. Evaluation of drug release kinetics:

To investigate the mechanism and rate of drug release from the osmotic tablets, in vitro dissolution data were analyzed using various mathematical models, including Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models. These kinetic models provide insight into the release behavior by characterizing whether the drug is released at a constant rate (zero-order), concentration-dependent rate (first-order), diffusion-controlled (Higuchi), or through a combination of diffusion and erosion mechanisms (Korsmeyer–Peppas). The correlation coefficients (R^2) obtained from each model were used to determine the best-fit release kinetics, while the release exponent (n) from the Korsmeyer–Peppas model further elucidated the underlying drug release mechanism.

3.RESULT AND DISCUSSION

IR Spectra of Losartan Potassium of Pure Drug:

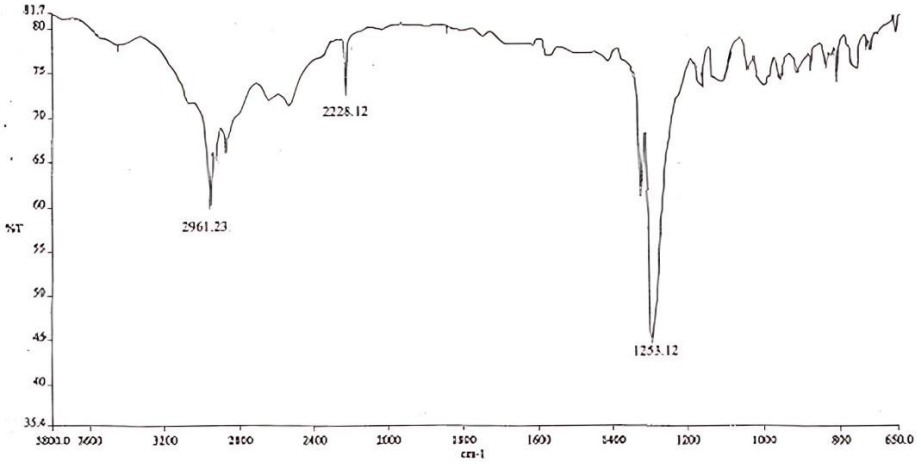

Fig 1: IR Spectra of Losartan potassium

The FTIR spectrum of Losartan potassium exhibited characteristic peaks corresponding to its functional groups, confirming the structural integrity of the drug. The C–H stretching vibration was observed at 2961.23 cm^{-1}. The N–H bending vibration appeared at 1620 cm^{-1}, matching the typical range of 1640–1430 cm^{-1}. A broad peak at 2228.12 cm^{-1} was attributed to O–H stretching, corresponding to its expected range of 2400–2000 cm^{-1}. Additionally, the C–Cl stretching was observed at 994.63 cm^{-1}, consistent with its characteristic range of 500–1000 cm^{-1}. These observed peaks align well with standard values, indicating the absence of chemical modification and confirming the identity and purity of Losartan potassium.

IR Spectrum of Losartan Potassium + Excipients:

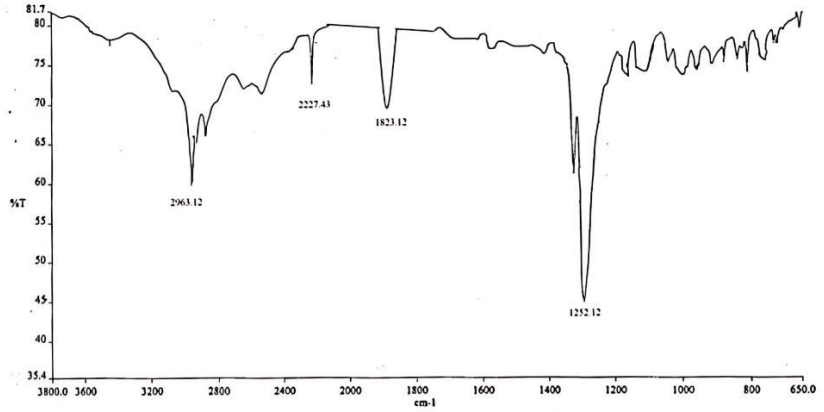

Fig. 2: IR Spectra of Losartan potassium + excipients

The FTIR spectrum of the physical mixture of Losartan potassium with excipients demonstrated the presence of all major functional group peaks, confirming compatibility and absence of interaction. The C–H stretching vibration was observed at 2963.12 cm^{-1}, which falls within the expected range of 3200–2800 cm^{-1}. The O–H stretching band appeared at 2227.12 cm^{-1}, consistent with its characteristic range of 2400–2000 cm^{-1}. A distinct peak at 1251.21 cm^{-1} was attributed to C–N amine stretching, aligning with the standard range of 1400–1200 cm^{-1}. Additionally, the C–Cl stretching was identified at 920.21 cm^{-1}, which lies within the expected range of 1000–800 cm^{-1}. These results suggest that no significant shifts or disappearance of peaks occurred, indicating no chemical interaction between the drug and excipients.

Table 3: Evaluation parameters of pre-compression studies.

Formulation	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner Ratio	Angle of Repose (°)
LP1	0.49 ± 0.02	0.59 ± 0.02	16.44	1.20 ± 0.03	30.96 ± 0.96
LP2	0.48 ± 0.02	0.58 ± 0.02	16.03	1.21 ± 0.02	30.14 ± 0.87
LP3	0.49 ± 0.02	0.58 ± 0.03	15.51	1.18 ± 0.02	29.33 ± 0.70
LP4	0.45 ± 0.03	0.57 ± 0.03	21.03	1.27 ± 0.02	30.37 ± 0.66
LP5	0.48 ± 0.02	0.56 ± 0.03	14.28	1.17 ± 0.02	29.88 ± 0.78

Pre-compression parameters of Losartan potassium osmotic tablet blends (LP1–LP5) were evaluated to assess their flow and compressibility characteristics, which are crucial for ensuring uniform die filling and consistent tablet weight during manufacturing. The bulk density of the formulations ranged from 0.45 ± 0.03 to 0.49 ± 0.02 g/mL, and tapped density ranged from 0.56 ± 0.03 to 0.59 ± 0.02 g/mL, indicating good packing ability of the powder blends. The Carr's index, which indicates compressibility, ranged from 14.28% (LP5) to 21.03% (LP4). LP5 showed the best compressibility, while LP4 exceeded the ideal

range (<15%), suggesting slightly poor flow. The Hausner ratio values were within 1.17 ± 0.02 to 1.27 ± 0.02, where values below 1.25 indicate good flow. LP4 again showed the highest value (1.27), supporting its relatively poor flow properties. In contrast, LP5 and LP3 had the most favourable ratios. The angle of repose for all formulations was below 31°, indicating acceptable flowability. LP3 exhibited the lowest angle (29.33 ± 0.70°), implying superior flow behaviour, while LP1 showed the highest (30.96 ± 0.96°). In summary, all formulations demonstrated satisfactory pre-compression characteristics, suitable for direct compression. Among them, LP3 and LP5 were found to possess optimal flow and compressibility properties, making them the most promising formulations for further processing. LP4 may require formulation adjustments to enhance its flow properties.

Table 4: Evaluation parameters of post compression studies

Code	Weight Uniformity (mg)	Hardness (kg/cm²)	Thickness (mm)	Diameter (mm)	Final Weight (mg)	% Weight Gain	Friability (%)	Drug Content (mg/tablet)
LP1	348 ± 5.0	5.8 ± 0.2	2.00 ± 0.38	10.00 ± 0.28	375	8.22	0.17	88.8 ± 0.4
LP2	350 ± 2.0	5.4 ± 0.4	2.00 ± 0.40	10.00 ± 0.18	388	8.42	0.14	90.2 ± 0.3
LP3	349 ± 2.0	6.2 ± 0.2	2.00 ± 0.24	10.00 ± 0.34	389	8.62	0.14	89.42 ± 0.4
LP4	347 ± 2.0	5.6 ± 0.2	2.00 ± 0.12	10.00 ± 0.15	391	9.13	0.16	89.5 ± 0.2
LP5	350 ± 5.0	5.5 ± 0.2	2.00 ± 0.23	10.00 ± 0.24	390	8.92	0.12	90.4 ± 0.2

Post-compression and coating evaluation of Losartan potassium osmotic tablet formulations (LP1–LP5) was conducted to assess uniformity, mechanical integrity, coating efficiency, and drug content consistency. All formulations demonstrated acceptable weight uniformity, ranging from 347 ± 2.0 mg to 350 ± 5.0 mg, indicating consistent powder flow and die fill during compression. After coating, the final weights increased to 375–391 mg, with percentage weight gain between 8.22% and 9.13%, confirming uniform and controlled coating application. LP4 exhibited the highest weight gain (9.13%), suggesting a slightly thicker coating layer. Tablet hardness was within the optimal range (5.4 ± 0.4 to 6.2 ± 0.2 kg/cm²), ensuring sufficient mechanical strength to withstand handling and coating procedures. Thickness and diameter remained consistent across batches, with values around 2.00 mm and 10.00 mm, respectively, indicating uniform compaction and equipment settings. Friability values for all batches were well below the pharmacopeial limit of 1%, ranging from 0.12% to 0.17%, suggesting good mechanical resistance and tablet integrity. The lowest friability (0.12%) was observed in LP5, indicating superior robustness. Drug content analysis showed values between 88.8 ± 0.4 mg and 90.4 ± 0.2 mg per tablet, falling within the acceptable range of 85–115% of the label claim. LP5 showed the highest drug content (90.4 mg), while LP1 had slightly lower content (88.8 mg), yet still within acceptable limits. Overall, all five formulations complied with the pharmacopeial standards for physical and chemical parameters. Among them, LP3 and LP5 demonstrated the most favourable profile, combining mechanical strength, low friability, appropriate coating weight, and uniform drug content—making them ideal candidates for further dissolution and stability studies.

Table 5: Dissolution profile of various batches of osmotic tablet in 6.8 pH (phosphate buffer)

Time (hrs)	% Drug Release				
	LP1	LP2	LP3	LP4	LP5
0	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
1	10.93 ± 0.35	12.88 ± 0.41	13.47 ± 0.32	13.40 ± 0.30	12.80 ± 0.38
2	29.00 ± 0.42	20.76 ± 0.36	21.35 ± 0.33	21.10 ± 0.40	21.51 ± 0.34
3	30.72 ± 0.46	23.46 ± 0.38	26.90 ± 0.29	26.76 ± 0.31	26.41 ± 0.35
4	34.63 ± 0.48	28.85 ± 0.45	30.90 ± 0.42	30.82 ± 0.40	30.92 ± 0.39
5	35.62 ± 0.51	40.53 ± 0.46	43.05 ± 0.38	45.03 ± 0.41	45.13 ± 0.40
6	36.70 ± 0.53	44.58 ± 0.49	52.25 ± 0.35	52.20 ± 0.36	52.35 ± 0.33
7	38.45 ± 0.55	54.02 ± 0.52	57.95 ± 0.31	57.97 ± 0.30	58.05 ± 0.28
8	57.93 ± 0.58	57.25 ± 0.50	62.28 ± 0.27	65.00 ± 0.29	65.15 ± 0.25
9	75.35 ± 0.61	68.15 ± 0.53	76.74 ± 0.22	76.56 ± 0.24	75.36 ± 0.26
10	83.68 ± 0.64	79.97 ± 0.56	82.13 ± 0.20	84.20 ± 0.23	79.86 ± 0.21
11	87.54 ± 0.66	86.34 ± 0.59	91.82 ± 0.18	91.34 ± 0.21	90.25 ± 0.19
12	93.21 ± 0.68	94.37 ± 0.61	99.99 ± 0.00	96.42 ± 0.20	97.21 ± 0.17

In-vitro dissolution studies were conducted for all formulations (LP1–LP5) over a 12-hour period in phosphate buffer (pH 6.8) to evaluate the drug release behaviour of the osmotic tablets. The cumulative percentage drug release at each time point is shown in the table below. All formulations exhibited zero initial release (0%) at 0 hours, confirming the integrity of the coating. Gradual and sustained release was observed across all batches, demonstrating controlled drug release characteristics. Among the

formulations, LP3 showed the most consistent and extended release, achieving 99.99% drug release at 12 hours, which closely approximates ideal zero-order kinetics. The release profile of LP3 was linear and controlled, with minimal initial burst and a steady increase over time, indicating effective osmotic behavior and optimal formulation design. LP5 and LP4 also showed high cumulative release values at 12 hours (97.21% and 96.42%, respectively), reflecting successful modulation of release rate by coating and osmotic agents. However, both exhibited a slightly faster release between the 5th and 9th hours compared to LP3. LP2 released 94.37%, whereas LP1 exhibited the lowest release at 93.21%, indicating relatively slower drug diffusion, possibly due to differences in osmogen concentration or polymer content affecting osmotic pressure. Overall, LP3 demonstrated the most desirable release profile, achieving near-complete release at 12 hours with sustained and controlled kinetics. This supports the conclusion that LP3 is the optimized formulation for osmotic-controlled delivery of Losartan potassium.

Table 6: drug release kinetic parameters of losartan potassium osmotic tablet formulations

Formulation	Zero-order (R^2)	First-order (R^2)	Higuchi Model (R^2)	Korsmeyer-Peppas (R^2)	n (Release Exponent)
LP1	0.958	0.9917	0.9281	0.9477	0.7757
LP2	0.990	0.9922	0.9691	0.9863	0.8207
LP3	0.996	0.9910	0.9801	0.9912	0.8440
LP4	0.996	0.9871	0.9835	0.9650	0.8235
LP5	0.997	0.9026	0.9846	0.9933	0.8352

The drug release kinetics data of Losartan potassium osmotic tablet formulations (LP1–LP5) were analyzed using various mathematical models to understand the mechanism of drug release. Among all models, the zero-order kinetics showed the best fit for formulations LP3 (R^2 = 0.996), LP4 (R^2 = 0.996), and LP5 (R^2 = 0.997), indicating a constant drug release rate independent of concentration—a desirable characteristic for controlled-release formulations. The Higuchi model also exhibited high correlation coefficients for all formulations (R^2 > 0.92), suggesting that diffusion plays a significant role in the release mechanism. The Korsmeyer–Peppas model further supported this, with R^2 values above 0.94 for most formulations. The release exponent (n) for all formulations ranged between 0.77 and 0.84, indicating an anomalous (non-Fickian) transport, which involves a combination of diffusion and polymer relaxation (swelling/erosion) mechanisms. Among all, LP3 demonstrated the most ideal release behavior, with high R^2 values across all models and an n value of 0.8440, confirming its suitability as an optimized osmotic formulation. In summary, the kinetic data confirm that drug release from the developed formulations is predominantly governed by zero-order kinetics and non-Fickian diffusion, validating the effectiveness of the osmotic system in delivering Losartan potassium in a sustained and controlled manner.

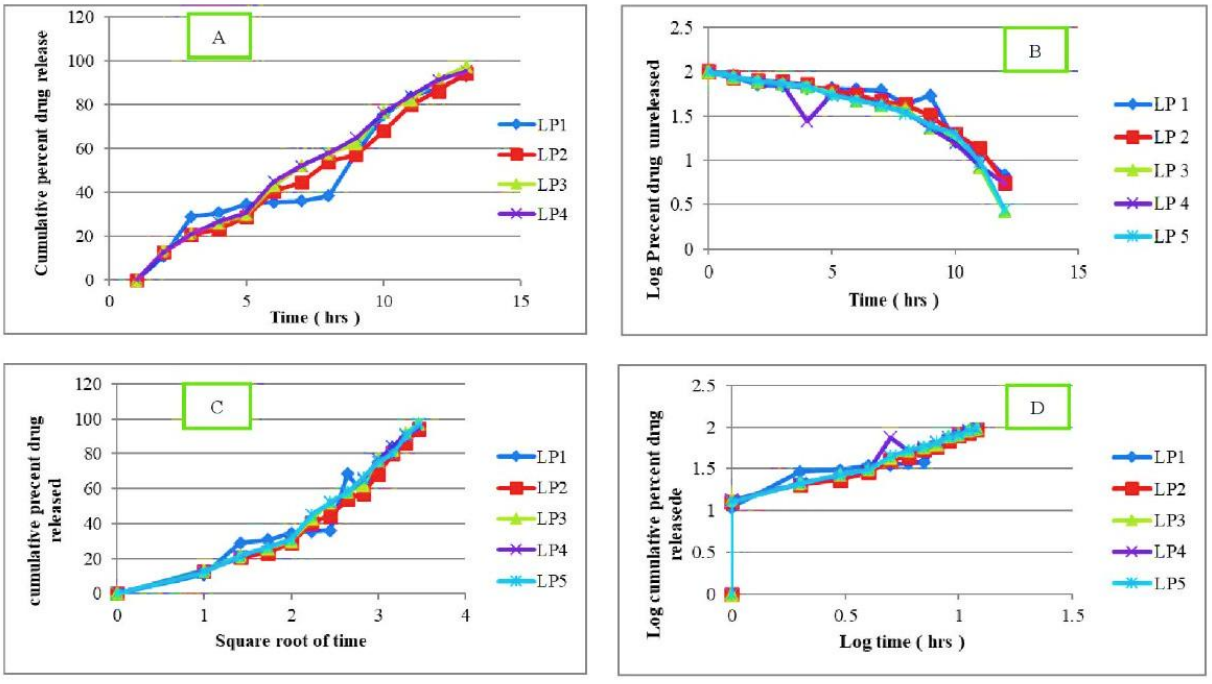

Figure 3: Drug release kinetics data, A: Zero order kinetics, B: First order kinetics, C: Higuchi plot, D: Korsmeyers & Peppas Plot

CONCLUSION

The present study successfully formulated and evaluated an osmotically controlled oral tablet of Losartan potassium to achieve sustained drug release over a 12-hour period. The optimized batch (LP3), formulated with 50 mg HPMC K100M and 50 mg mannitol, demonstrated a cumulative drug release of 99.99% following zero-order kinetics and anomalous (non-Fickian) release mechanism. Pre- and post-compression evaluation parameters confirmed good flowability, compressibility, mechanical integrity, and content uniformity across all formulations. Stability studies confirmed the physical and chemical stability of the optimized formulation over three months. These findings establish LP3 as a robust and effective once-daily formulation, offering improved patient compliance and therapeutic consistency in hypertension management through controlled drug delivery.

ETHICAL DECLARATIONS:

No human subjects were involved in this study.

FUNDING:

The authors received no specific funding for this research.

CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest regarding the publication of this article.

ETHICAL APPROVAL:

This article is based solely on literary analysis and does not involve any studies with human participants or animals. Hence, ethical approval was not required.

INFORMED CONSENT:

Not applicable.

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