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Formulation And Evaluation Of Losartan Potassium Microspheres Using Sodium Alginate

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ABSTRACT

Hypertension affects millions of patients worldwide, yet conventional oral medications deliver fluctuating drug levels that often lead to inconsistent therapeutic effects and unwanted side effects. This research addresses a fundamental challenge in pharmaceutical delivery: creating a formulation that maintains steady drug concentrations in the bloodstream while reducing dosing frequency. The study focuses on losartan potassium, an antihypertensive agent commonly used to manage high blood pressure and diabetic kidney disease. To extend its duration of action, microspheres—tiny spherical polymer-based carriers—were developed using sodium alginate, a naturally derived, biodegradable polymer. Microspheres were prepared using a solvent evaporation technique with varying polymer-to-drug ratios (1:1 through 6:1). Six formulations were systematically evaluated using multiple analytical methods. The average particle size ranged from approximately 48 micrometers to 150 micrometers, with size increasing proportionally as polymer concentration increased. Drug entrapment efficiency—a critical measure of formulation success—ranged from 53.78% to 89.60%, with higher polymer concentrations yielding superior encapsulation. *In vitro* drug release studies demonstrated sustained, controlled release over 12 hours, with formulations releasing the drug gradually rather than in sudden bursts. Release kinetics followed zero-order kinetics, indicating predictable and consistent drug availability. Formulation F5 showed the best results because of highest entrapment with optimal drug content. The results indicate that sodium alginate-based microspheres represent a promising vehicle for sustained delivery of losartan potassium, potentially improving patient compliance through less frequent dosing.

Keywords: Losartan potassium, sodium alginate, microspheres, sustained drug delivery, controlled release.

I. INTRODUCTION

Hypertension remains one of the most significant health challenges affecting millions of people worldwide, Carey et al. [1]. Over the past two decades, mortality rates from hypertension-related cardiovascular diseases have shown an alarming upward trend, emphasizing the persistent difficulty in achieving effective blood pressure control despite having multiple therapeutic options available, Kario et al. [2]. Current evidence suggests that with comprehensive hypertension prevention and proper management strategies, a substantial portion of cardiovascular deaths could potentially be prevented, highlighting the critical importance of developing better therapeutic approaches, Burnier and Damianaki [3].

Among the various pharmacological strategies for managing hypertension, angiotensin II receptor blockers have emerged as a major therapeutic class. Losartan potassium, representing the first non-peptide angiotensin II receptor antagonist approved for clinical use, works by selectively blocking angiotensin II type 1 receptors, Kumari et al. [4]. This mechanism prevents the vasoconstrictive and aldosterone-secreting effects of angiotensin II, Fu [5].

Following oral administration, losartan undergoes hepatic metabolism to form its active metabolite E-3174, which is significantly more potent than the parent compound, Maharani et al [6]. These favorable pharmacological characteristics have made losartan one of the widely prescribed antihypertensive medications globally, Messerli et al. [7]. However, despite these advantages, conventional oral losartan formulations encounter inherent limitations that compromise therapeutic outcomes in clinical practice.

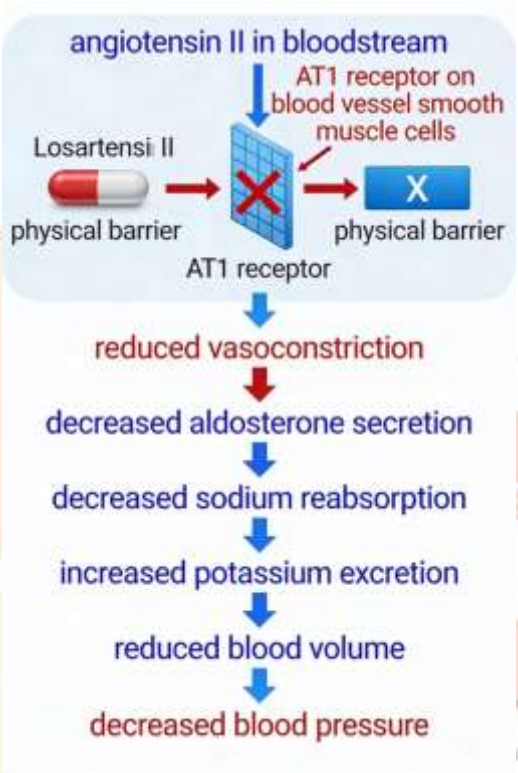


Fig 1. Mechanism of action of losartan potassium

II. Materials and methods

Losartan potassium was obtained as a gift sample from Dr. Reddy's Laboratories. Sodium alginate, HPMC, liquid paraffin, ethanol, acetone, and Carbopol were procured from SD fine chemical Ltd Mumbai. All reagents used were of pharma grade. All experiments were conducted using double distilled water.

Drug identification/Pre formulation studies

2.1 Melting point

A digital melting point apparatus was used to determine the melting point of losartan potassium, Abrar et al.[8] . Glass capillary tubes were filled with losartan potassium powder by gently pressing the open end into the powder and tapping the closed end to compact it (approximately 3-4 mm height).

2.2 Solubility

Solubility studies of losartan potassium were performed in different solvents to assess its dissolution characteristics. Approximately 100 mg of losartan potassium powder was added to 10 mL of distilled water in a beaker and stirred continuously for 24 hours at room temperature, Sun et al. [9]. The mixture was then filtered through filter paper to separate undissolved particles.

2.3 UV spectrophotometric determination

UV-visible spectrophotometry was used to determine the wavelength of maximum absorption (λmax) of losartan potassium and to prepare a standard calibration curve for quantification in subsequent experiments, Pooresmaeil and Namazi [10]. A stock solution of losartan potassium was prepared by dissolving 10 mg in 100 mL of distilled water to obtain a concentration of 100 µg/mL. This was further diluted to 10 µg/mL and scanned from 200-400 nm wavelength range.

2.4 Compatibility study using FTIR

Fourier transform infrared spectroscopy was performed to assess the compatibility between losartan potassium and sodium alginate polymer, Su et al. [11]. FTIR spectra were recorded for pure losartan potassium powder, pure sodium alginate polymer, a physical mixture of losartan potassium and sodium alginate in a 1:1 ratio, and the prepared losartan-sodium alginate microspheres. All samples were analyzed using an ATR (Attenuated Total Reflectance) attachment with a scanning range of 4000-400 cm^{-1}.

2.5 Preparation of microspheres

Microspheres were produced using a solvent evaporation technique. A 1% w/v sodium alginate solution was first prepared in purified water, into which losartan potassium was dispersed uniformly. This drug–polymer dispersion was then transferred into a 250 mL beaker containing 0.5 mL of liquid paraffin and stirred at 1000 rpm for 30 minutes to form microspheres. The formed particles were separated and washed successively with n-hexane, ether, and finally acetone to remove residual oil and impurities. The cleaned microspheres were then dried in a hot air oven at 50°C and stored for further evaluation.

Evaluation parameters

2.6 Organoleptic properties

The prepared losartan potassium microspheres were visually examined for colour, odour, texture, and appearance.

2.7 Frequency distribution analysis

Average particle size and size distribution were determined by optical microscopy using a calibrated stage micrometer. For each batch, around 300 microspheres were measured, grouped into size ranges, and the data were plotted as a histogram to obtain the particle size frequency distribution and mean particle diameter, Patel et al. [12].

2.8 Percentage drug entrapment efficiency

Accurately weighed microspheres containing theoretical drug quantity were crushed and extracted overnight in appropriate solvent. After filtration and dilution, losartan content was quantified at 206 nm by UV spectrophotometry, and entrapment efficiency was calculated as (actual drug/theoretical drug) × 100.

2.9 In-vitro dissolution studies

Dissolution testing employed USP basket apparatus in 0.1 N HCl then pH 7.4 phosphate buffer at 37°C and 50 rpm. Microspheres equivalent to 100 mg losartan were tested; samples collected at fixed intervals up to 12 hours were analyzed at 206 nm to plot cumulative release profiles and kinetic models, Chen et al. [13].

2.10 Stability studies

Optimized microspheres were stored in sealed containers under room temperature and accelerated conditions. Periodic evaluation checked physical appearance, drug assay, and dissolution profiles to confirm formulation stability over time, Yuan et al. [14].

III. Results

Results of preformulation studies

3.1 Solubility

Losartan potassium exhibited good solubility in ethanol and methanol (10 mg/10 mL), while showing practical insolubility in acetone, confirming its suitability for the aqueous-based solvent evaporation process.

3.2 Melting point

The melting point of losartan potassium was determined to be 183°C, which aligns closely with literature values and indicates thermal stability suitable for microsphere processing.

3.3 UV spectrophotometric determination

It was discovered that the maximum wavelength (λ max) is 234 nm.

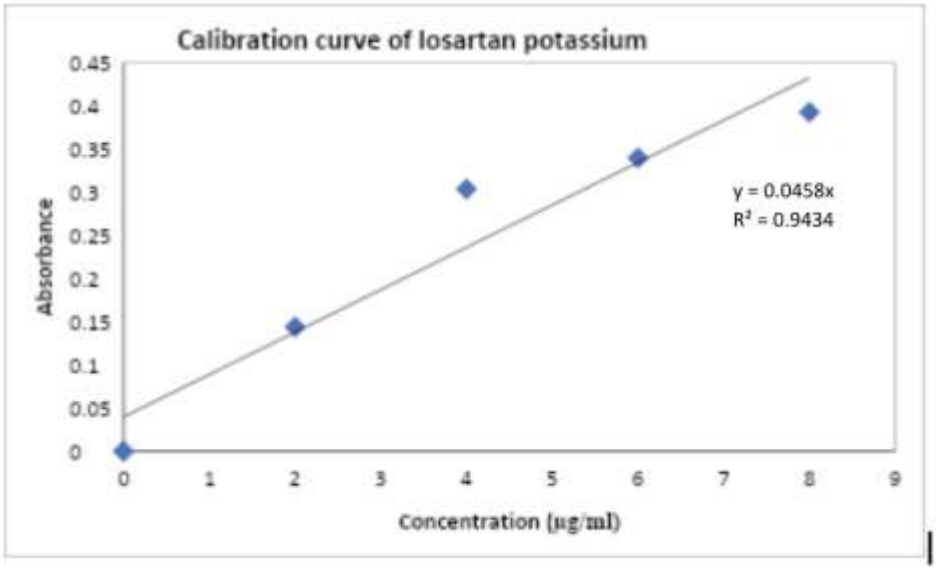


Fig. 3.1 Calibration curve of losartan potassium in phosphate buffer pH 6.8

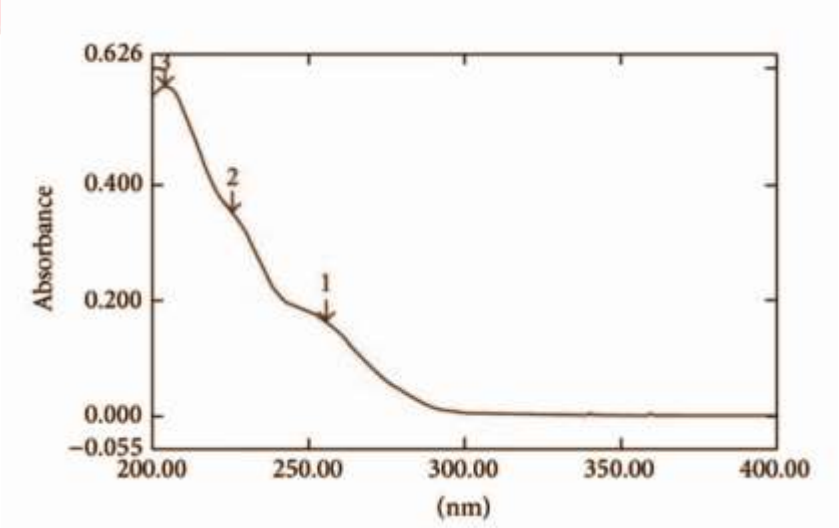


Fig. 3.2 UV spectrum of losartan potassium in phosphate buffer pH 6.8

Table 3.1 Absorbance of losartan potassium at various concentrations

Concentration (µg/ml)	Absorbance
0	0
2	0.114
4	0.309
6	0.342
8	0.395
10	0.485

Table 3.2 Statistical parameters for calibration curve of losartan potassium in phosphate buffer pH 6.8

Parameter	Value
λ max(nm)	234
Linearity Range	0-10
Correlation coefficient (R^2)	0.9985
Slope	0.0485

3.4 Compatibility study using FTIR

FTIR spectra of losartan potassium, sodium alginate, their physical mixture, and formulated microspheres revealed retention of all characteristic peaks without significant shifts or new peak formation, confirming no drug-polymer interaction and complete compatibility.

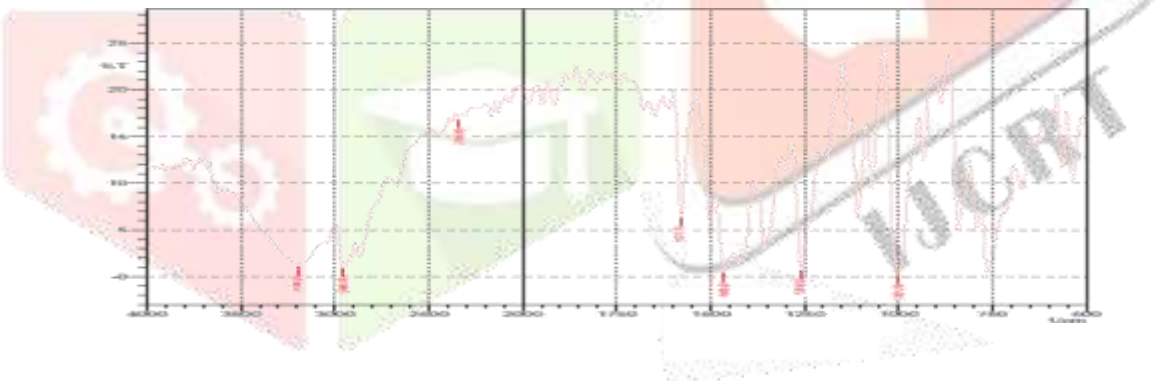


Fig 3.3 IR spectrum of losartan potassium

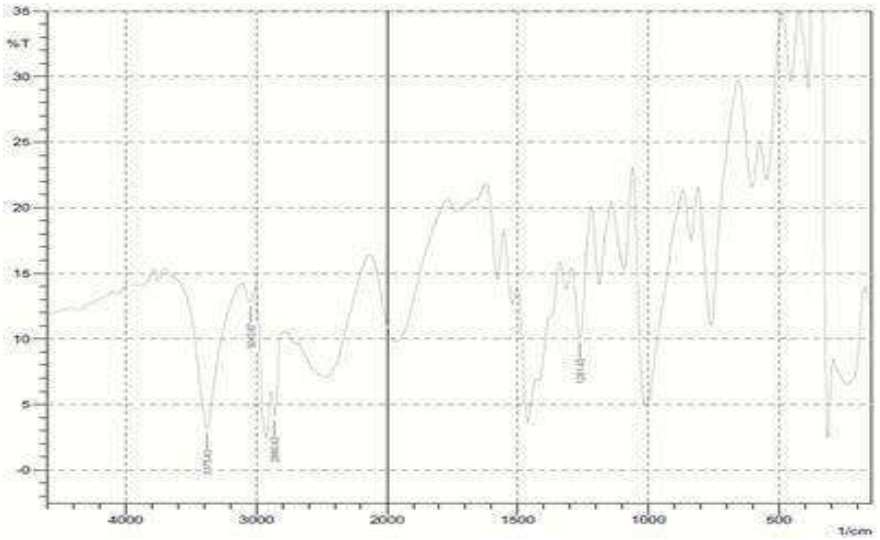


Fig 3.4 IR spectrum of sodium alginate

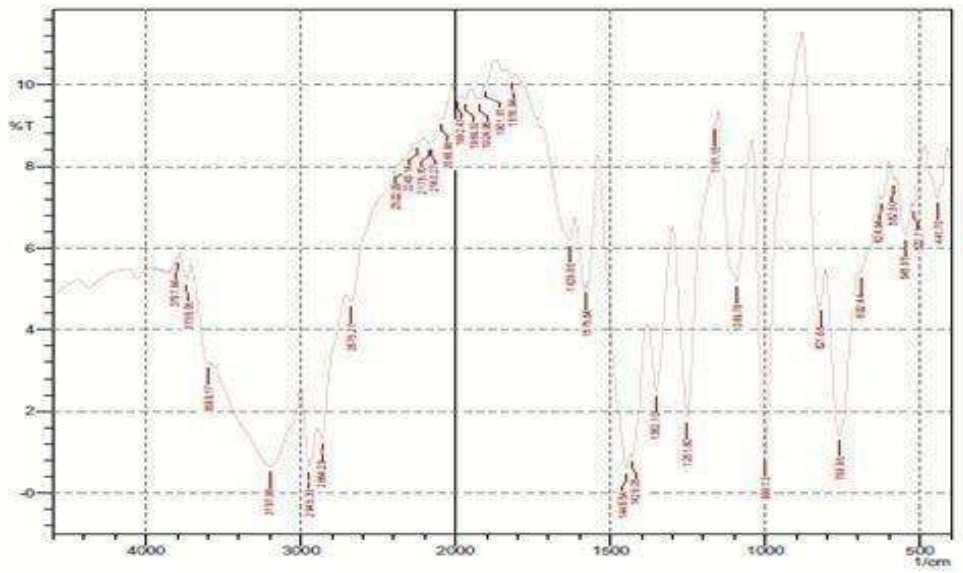


Fig 3.5 IR spectrum of physical mixture

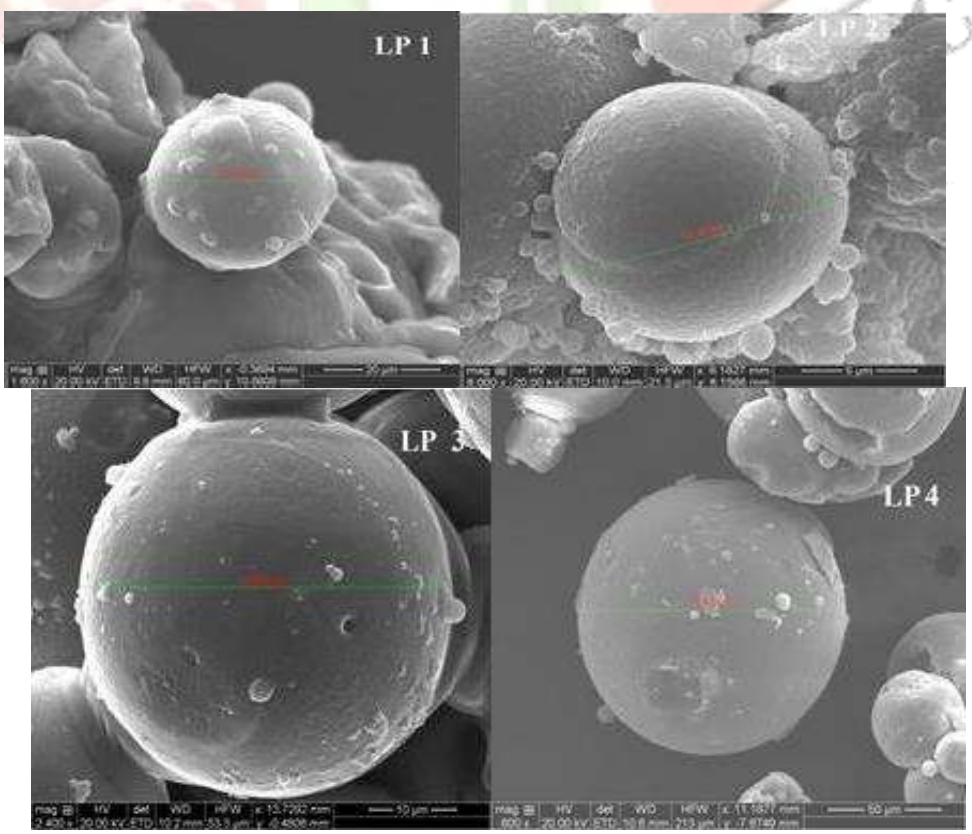
Results of evaluation parameters

3.5 Organoleptic properties

All microsphere formulations (LP1-LP6) appeared as uniform off-white to pale yellow, free-flowing powders with discrete spherical particles and no aggregation or discoloration observed.

3.6 Frequency distribution analysis

Mean particle sizes increased progressively with polymer concentration: LP1 (47.6 ± 2.72 µm), LP2 (76 ± 6.19 µm), LP3 (99.8 ± 8.23 µm), LP4 (107.2 ± 9.18 µm), LP5 (113.1 ± 7.13 µm), and LP6 (150.3 ± 5.39 µm), with normal distribution patterns across all batches.



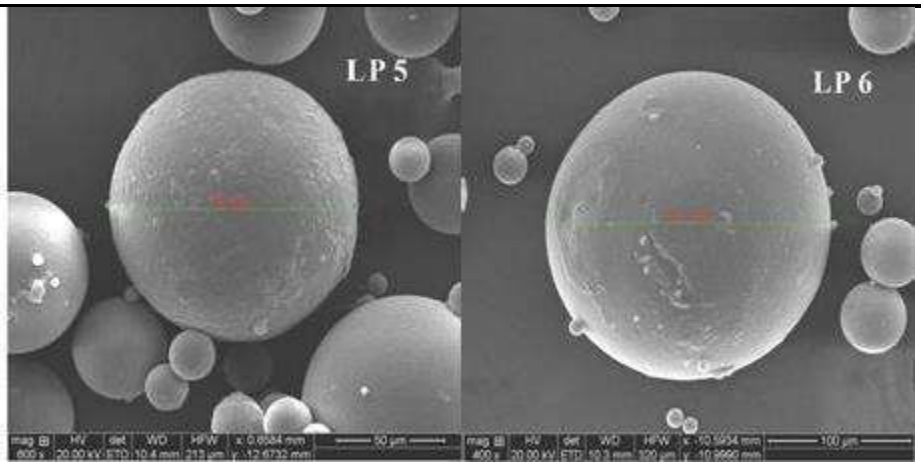


Fig 3.6 Surface morphology of prepared microspheres

Table 3.3 Average particle size

S.No	Formulation code	Average size (µm)±SEM
1.	LP1	47.6±2.72
2.	LP2	76±6.19
3.	LP3	99.8±8.23
4.	LP4	107.2±9.18
5.	LP5	113.1±7.13
6.	LP6	150.3±5.39

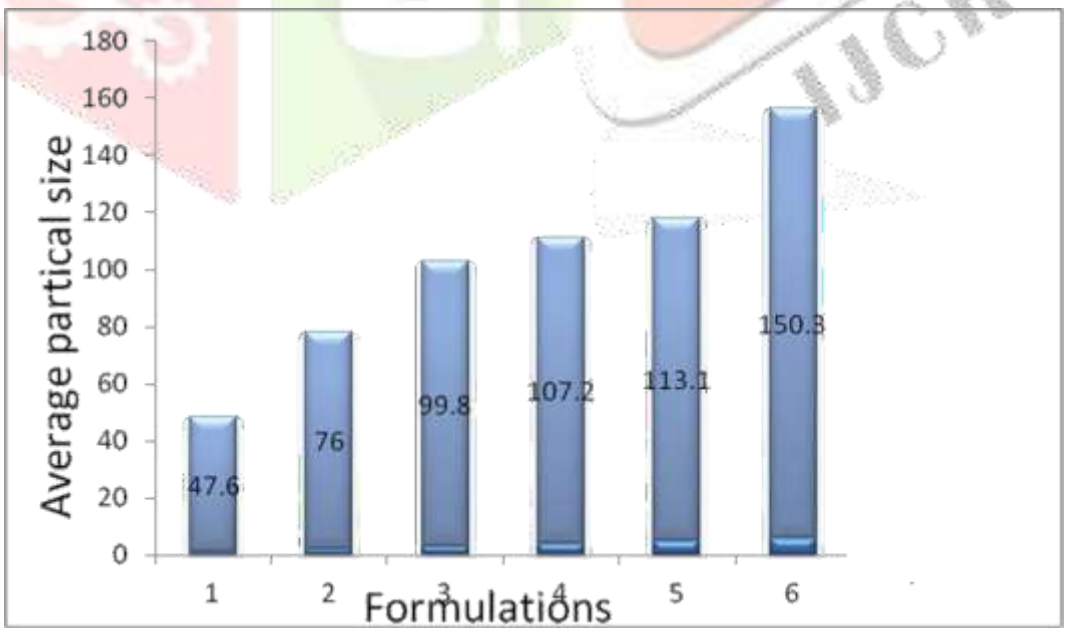


Fig. 3.7 Average particle size

3.7 Percentage drug entrapment efficiency

Drug entrapment efficiency improved with increasing polymer ratio: LP1 (53.78%), LP2 (59.71%), LP3 (62.35%), LP4 (70.80%), LP5 (78.88%), and LP6 (89.60%), while drug content decreased from 26.45 mg (LP1) to 13.57 mg (LP6); percentage yields ranged from 60.22% (LP1) to 93.88% (LP6).

Table 3.4 Percentage drug entrapment efficiency, percentage yield and drug content of prepared microspheres

Sl.no	Formulation code	Percentage yield	Drug content(%)	Entrapment efficiency(%)
1.	LP1	59.22	26.45	53.78 ± 1.02
2.	LP2	65.23	25.56	59.71 ± 1.11
3.	LP3	78.35	23.69	62.35 ± 2.25
4.	LP4	85.20	18.65	70.80 ± 1.10
5.	LP5	88.76	15.96	78.88 ± 0.98
6.	LP6	92.88	13.57	89.60 ± 1.12

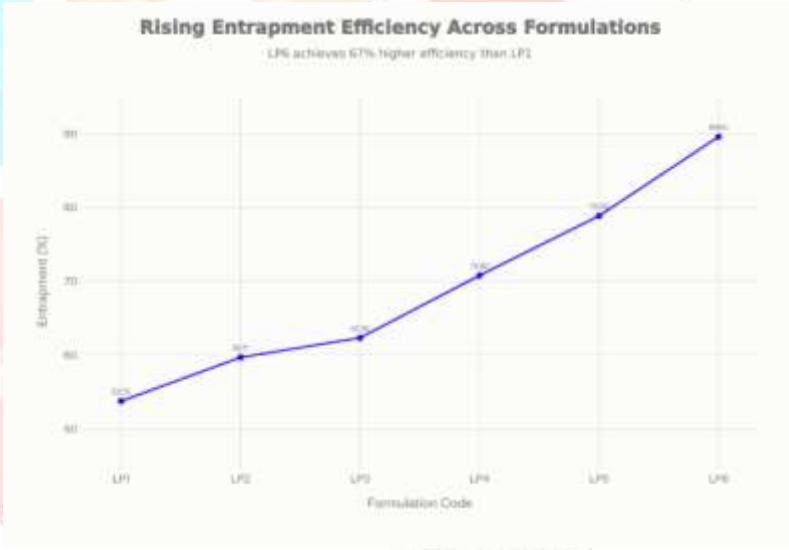


Fig. 3.8 Entrapment efficiency

3.8 In-vitro dissolution studies

Cumulative drug release at 12 hours decreased with higher polymer content: LP1 (94.64%), LP2 (87.43%), LP3 (78.47%), LP4 (72.53%), LP5 (59.50%), and LP6 (64.35%), demonstrating sustained release characteristics; all formulations best fitted zero-order kinetics ($r^2 > 0.99$)

Zero order release kinetics

Sl.no.	Time(h)	LP1±SD	LP2±SD	LP3±SD	LP4±SD	LP5±SD	LP6±SD
1.	0	0	0	0	0	0	0
2.	1	24.815 ± 0.62	20.97 ± 0.10	12.23 ± 0.60	17.47 ± 0.09	7.68 ± 0.50	7.33 ± 0.59
3.	2	31.64 ±	27.44 ±	18.35 ±	22.52 ±	13.98 ±	7.86 ±
4.	3	38.65 ±	32.53 ±	24.30 ±	27.45 ±	17.48 ±	10.66 ±
5.	4	44.44 ±	38.49 ±	31.48 ±	33.24 ±	23.61 ±	15.39 ±
6.	5	56.17 ±	44.62 ±	36.74 ±	36.75 ±	28.34 ±	17.49 ±
7.	6	64.59 ±	52.51 ±	42.01 ±	42.01 ±	34.30 ±	21.00 ±
8.	7	71.96 ±	59.18 ±	49.02 ±	47.28 ±	38.16 ±	26.25 ±
9.	8	78.65 ±	66.38 ±	54.29 ±	52.55 ±	44.12 ±	28.02 ±
10.	9	83.76 ±	74.63 ±	61.31 ±	57.82 ±	49.04 ±	31.53 ±
11.	10	86.42 ±	79.39 ±	66.41 ±	63.09 ±	54.84 ±	45.52 ±
12.	11	91.08 ±	83.41 ±	72.35 ±	67.46 ±	59.56 ±	52.51 ±
13.	12	94.64 ±	87.43 ±	78.47 ±	72.53 ±	64.35 ±	59.50 ±

Table 3.6 First order release kinetics

Sl.no.	Time(h)	LP1±SD	LP2±SD	LP3±SD	LP4±SD	LP5±SD	LP6±SD
1.	0	2 ± 0.000	2 ± 0.000	2 ± 0.000	2 ± 0.000	2 ± 0.000	2 ± 0.000
2.	1	1.876 ± 0.003	1.898 ± 0.003	1.943 ± 0.002	1.952 ± 0.003	1.965 ± 0.002	1.967 ± 0.002
3.	2	1.835 ± 0.002	1.861 ± 0.003	1.912 ± 0.003	1.916 ± 0.002	1.935 ± 0.002	1.964 ± 0.002

4.	3	1.788 ±0.004	1.829 ± 0.003	1.879 ± 0.003	1.861 ± 0.003	1.917 ± 0.003	1.951 ± 0.003
5.	4	1.745 ± 0.004	1.789 ± 0.003	1.836 ± 0.003	1.825 ± 0.003	1.883 ± 0.003	1.927 ± 0.002
6.	5	1.642 ± 0.005	1.743 ± 0.004	1.801 ± 0.003	1.801 ± 0.003	1.855 ± 0.003	1.917 ± 0.003
7.	6	1.549 ± 0.005	1.677 ± 0.004	1.763 ± 0.004	1.763 ± 0.003	1.818 ± 0.003	1.898 ± 0.003
8.	7	1.329 ± 0.006	1.611 ± 0.004	1.707 ± 0.004	1.718 ± 0.004	1.791 ± 0.004	1.868 ± 0.003
9.	8	1.211 ± 0.010	1.527 ± 0.005	1.660 ± 0.005	1.676 ± 0.004	1.747 ± 0.005	1.857 ± 0.004
10.	9	1.133 ± 0.010	1.404 ± 0.006	1.588 ± 0.006	1.625 ± 0.006	1.707 ± 0.006	1.836 ± 0.003
11.	10	0.950 ± 0.016	1.314 ± 0.010	1.526 ± 0.008	1.567 ± 0.005	1.655 ± 0.006	1.736 ± 0.005

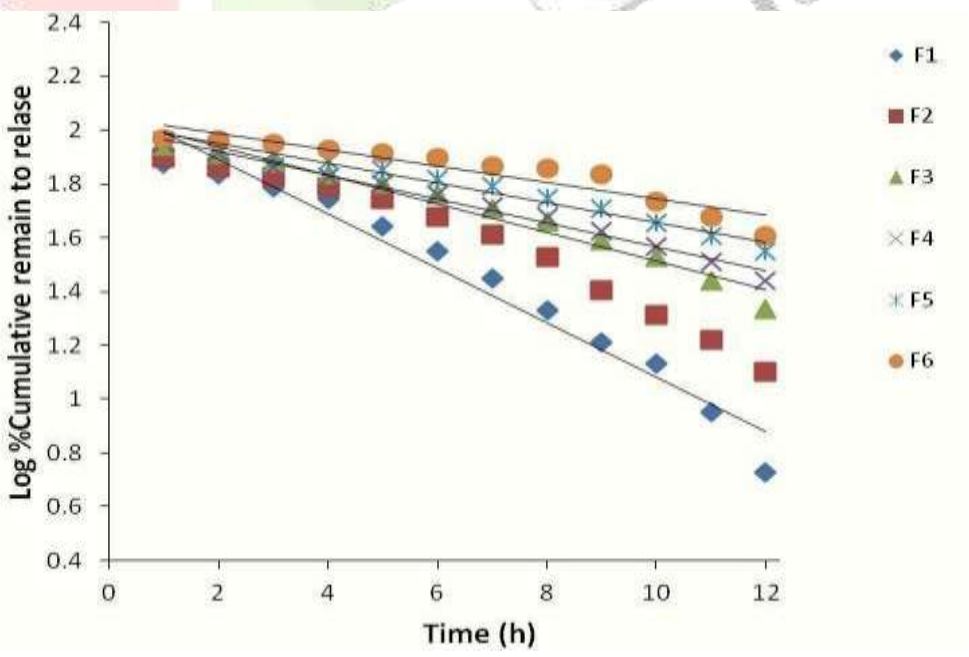


Fig 3.9 first order release kinetics of losartan potassium microspheres

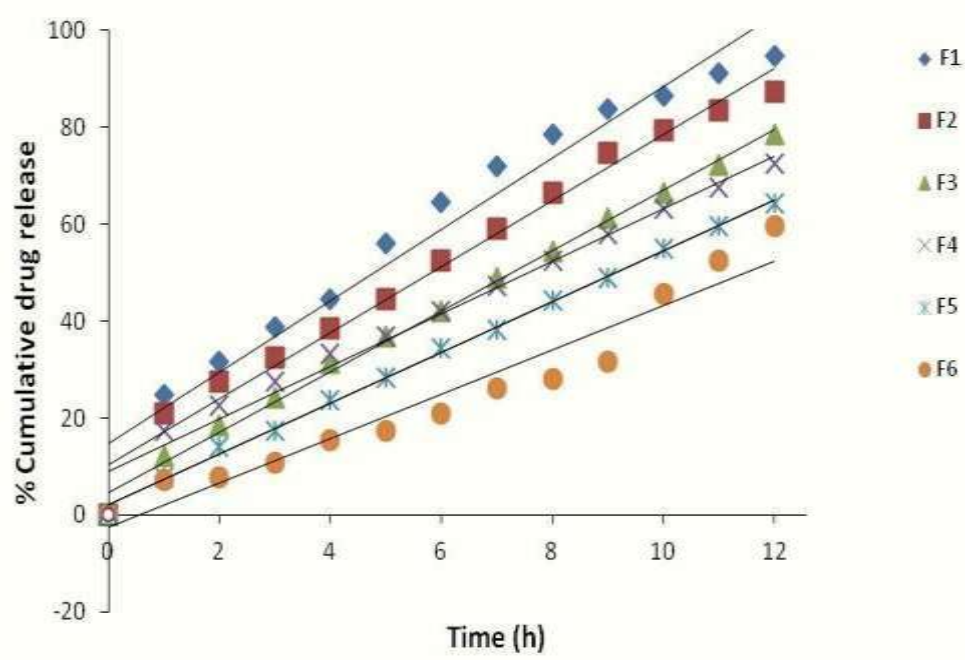


Fig 3.10 Zero order release kinetics of losartan potassium microspheres

3.9 Stability studies

Optimized LP5 microspheres stored at accelerated conditions (40°C/75% RH) for 3 months maintained physical appearance, drug content (98.2% of initial), and release profile (61.2% at 12h), confirming formulation stability.

IV. DISCUSSION

No change in colour or appearance; all microsphere batches remained physically stable.

FTIR spectra showed no new peaks or major shifts, confirming drug–polymer compatibility.

SEM images showed mostly spherical, discrete microspheres with smoother surfaces at higher polymer levels.

Mean particle size increased as the drug-to-polymer ratio increased.

Entrapment efficiency improved with higher sodium alginate concentration.

Lower polymer batches released drug faster; higher polymer batches showed slower, prolonged release.

LP5 showed the best overall performance: good entrapment, suitable size, high yield, and ideal sustained-release profile.

V. CONCLUSION

Preformulation studies confirmed that losartan potassium and sodium alginate were compatible and suitable for microsphere formulation. Increasing polymer concentration produced smoother, larger microspheres with higher entrapment efficiency and uniform drug distribution. In vitro studies showed that higher alginate levels slowed and prolonged drug release, and all formulations followed zero-order kinetics, indicating predictable, controlled release over more than 12 hours. Overall, sodium alginate–based sustained-release microspheres appear promising for reducing dosing frequency and improving compliance in hypertension, with formulation F5 showing the best overall performance.

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