RESEARCH ARTICLE

Formulation and Development of Sustained Release Tablets of Losartan Potassium using Chitosan as Rate Retarding Polymer

Chaitali Kulkarni[1*], Saurabh Mundada[2], Pawan Meshram[3], Madhuri Desai[4]

[1]*Dept of Pharmaceutical Chemistry, Shree Santkrupa College of Pharmacy Ghogaon, Karad, MH,India*
[2]*Department Quality assurance, Raosaheb Patil Danve College of Pharmacy, Badnapur, Jalna, Maharashtra, 431202, India*
[3]*University Institute of Chemical Technology, Kavayitri Bahinabai Chaudhari North Maharashtra University, Jalgaon, 425001, India*
[4]*Department of Pharmaceutics, KVV, Krishna Institute of Pharmacy, Karad, MH, India*

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ABSTRACT
This study aims to develop and evaluate the SR tablets of Losartan Potassium (LP) using chitosan as rate retarding polymer. The tablets were developed by direct compression technique with varying concentration of chitosan at constat HPMC K100M concentration. The granules were characterised for various micromeritics characteristics followed by compression of tablets. The compressed tablets were characterised for physico chemical properties. The CI values for the lubricated blend ranged from 7.35% (F3) to 14.97% (F5). These values suggest that all formulations exhibit good to fair flow properties, with F3 showing the best flow characteristics (CI = 7.35%). The HR values of the lubricated blends varied between 1.079 (F3) and 1.176 (F5), indicating acceptable to good flowability across all formulations. All tablet batches showed acceptable physical properties. Content uniformity was well maintained across batches, with values ranging from 97.25% to 100.29%. The lowest friability was observed in F3 (0.35%), suggesting superior tablet robustness. The pure LP was found to be released 100% within 1 hour time period. F1 exhibited the highest dissolution, with 100% drug release at 24 hours, while F5 shows the slowest release, reaching only 52% at the same time point. The stability study of losartan potassium (LP) sustained-release (SR) tablets under accelerated conditions over six months indicates minimal variations in critical quality attributes, demonstrating good stability. This study underscores the potential of chitosan-based SR formulations for enhancing therapeutic efficacy in hypertension management.
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INTRODUCTION

Hypertension, is a common cardiovascular condition that raises the risk of renal disease, heart failure, and stroke considerably[1]. Angiotensin II receptor antagonists like Losartan Potassium (LP) are frequently provided to people with type 2 diabetes to manage their hypertension and nephropathy[2]. LP is effective, but because of its short elimination half-life (about two hours), it must be administered often to maintain therapeutic plasma concentrations. Variations in medication plasma levels, poor patient compliance, and less than ideal therapeutic results might result from this frequent dose schedule. It is essential to create a prolonged release formulation in order to get around these restrictions. By extending the medication's release over a longer time span, sustained release drug delivery systems minimize adverse effects linked to peak plasma drug concentrations, guarantee steady therapeutic levels, and cut down on the frequency of dosage[3]. The necessity to create a sustained release tablet with chitosan as a rate-retarding polymer in order to enhance the pharmacokinetic profile of losartan potassium is the driving force behind this investigation. Because of its superior drug-retarding qualities, chitosan—a biocompatible, biodegradable, and mucoadhesive polymer derived from chitin—has drawn a lot of interest in pharmaceutical research. In aqueous conditions, the polymer swells to produce a gel layer that prolongs the release profile and regulates drug diffusion[4]. Furthermore, chitosan has benefits including increased mucosal permeability, better bioavailability, and the capacity to control drug release via ionic interactions[5]. The current study intends to improve patient adherence, sustain stable plasma concentrations, and offer long-lasting antihypertensive benefits by including chitosan into the formulation of sustained release LP tablets. Due to its short half-life and quick elimination, LP requires several daily dosages, which might be difficult for patients, especially those with persistent hypertension who need long-term treatment. By releasing the medication gradually, sustained release formulations solve this problem by lowering the frequency of doses and preserving more stable plasma drug levels[6]. By minimizing variations between peak and trough

*Author for Correspondence: ckulkarni355@gmail.com

Table 1: Batches of LP tablets

Sr. No	Ingredients	F1	F2	F3	F4	F5
1	Losartan Potassium (LP)	50	50	50	50	50
2	Di-basic calcium phosphate	122	112	102	92	82
3	Chitosan	60	70	80	90	100
4	HPMC K100M	10	10	10	10	10
	Talc	5	5	5	5	5
5	Magnesium stearate	3	3	3	3	3
6	Total (mg)	250	250	250	250	250

concentrations, this lowers the possibility of dose-related side effects such hyperkalemia, hypotension, and vertigo. Additionally, by preserving steady medication levels, prolonged release formulations improve therapeutic efficacy and lower the risk of cardiovascular problems and blood pressure problems[7]. Because of its many uses, chitosan's function in sustained release medication administration is particularly intriguing. Through diffusion and erosion processes, chitosan's capacity to produce hydrogels in aquatic conditions enables controlled drug release. Additionally, chitosan's pH-dependent solubility allows for preferential medication release under particular gastrointestinal circumstances, which enhances absorption. It is also known to interact with molecules that are negatively charged, creating ionic complexes that further alter the kinetics of drug release. Chitosan is a perfect option for the formulation of sustained release tablets because of these qualities, which provide a balance between biocompatibility and drug release regulation[8]. The main goal of this study is to create and assess sustained release Losartan Potassium tablets employing chitosan as a rate-retarding polymer. To sum up, the development of a sustained release formulation for LP utilizing chitosan as a polymeric matrix is a viable tactic to increase patient adherence, decrease dosage frequency, and improve

Table 2: Flow properties of granules

Sr. No	Batch	BD (g/ml)	TD	CI	HR
1	F1	0.462	0.517	10.64	1.119
2	F2	0.521	0.610	14.59	1.171
3	F3	0.479	0.517	7.35	1.079
4	F4	0.467	0.515	9.32	1.103
5	F5	0.517	0.608	14.97	1.176

therapeutic results. This formulation seeks to improve the management of hypertension and related cardiovascular illnesses by reducing side effects and providing prolonged antihypertensive benefits by modulation of medication release.

MATERIALS AND METHODS

Materials

Losartan Potassium (LP) was obtained from Cipla Ltd Mumbai, India. Chitosan was obtained from Marshall Marine Products, Kerala. HPMC K100M was obtained from Himedia Laboratories Pvt. Ltd, Mumbai, India. Di-basic calcium phosphate, Talc and Magnesium stearate were obtained from S.D. Fine Chem. Ltd, Mumbai, India

Methods

Development of LP sustained release tablets

LP sustained release tablets were developed by DC technique[9]. Excipients were weighed accurately as per formula composition given in Table 1. LP, Di-basic calcium phosphate, Chitosan and HPMC K100M were co-sifted through #40 sieve and blended in polybag for 15 minutes to ensure proper mixing of the ingredients. Talc was sifted through #40 sieve and added to previous material and blended for 5 minutes in polybag. Finally magnesium stearate was passed through #60 sieve and added to previous material and blended for 3 minutes to complete the lubrication. This lubricated blend was used for further compression to get flat-faced tablets.[10-11]

Evaluation of Lubricated blend

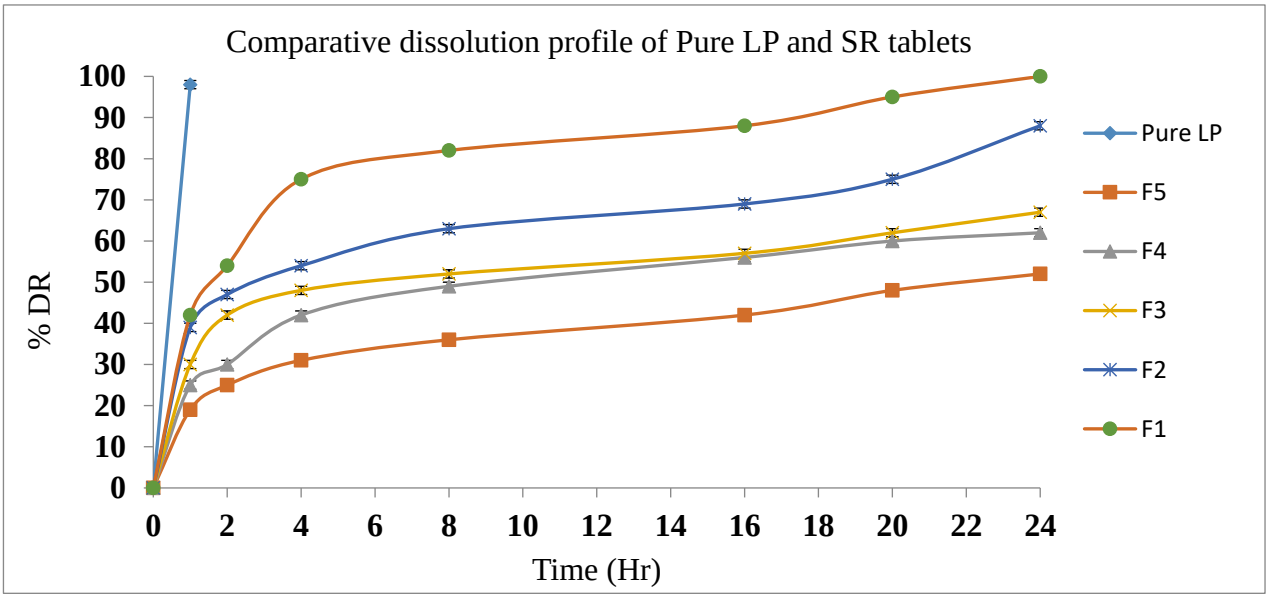

Figure 1: Comparative dissolution profile of LP

Table 3: Post-compression parameters

Formulation	Diameter (mm)	Thickness (mm)	Hardness (kg/cm^2)	Weight variation (%)	Content uniformity (%)	Friability (%)
F1	8.03	5.3	6.55	0.251	99.58	0.7
F2	7.99	5.6	6.87	0.249	97.25	0.65
F3	8.07	5.5	6.60	0.253	100.29	0.35
F4	8.05	5.6	6.90	0.253	99.71	0.63
F5	8.04	5.4	6.78	0.251	98.52	0.72

Table 3: Comparative dissolution profile of LP in pH 6.8 phosphate buffer

Time (Hr)	Formulation					
	Pure LP	F1	F2	F3	F4	F5
0	0	0	0	0	0	0
1	98	41	40	32	23	20
2		53	48	41	33	27
4		74	56	44	44	32
8		79	65	51	47	39
16		87	68	55	56	44
20		97	75	61	58	47
24		100	88	67	62	52

The lubricated blend was evaluated for various flow properties

Bulk density (BD)

The granules were weighed and added to 50 ml measuring cylinder and volume was noted down and BD was calculated using following formula.

$$\text{BD} = \frac{\text{Granule weight (g)}}{\text{volume (ml)}}$$

Tapped density (TD)

The granules were weighed and added to 50 ml measuring cylinder and initial volume was noted down and followed by tapping till no volume was changed. The tapped volume was noted down and TD was calculated.

$$\text{TD} = \frac{\text{Granule weight (g)}}{\text{tapped volume (ml)}}$$

Compressibility Index (CI)

CI was calculated using this formula

$$\text{CI} = \frac{\text{TD} - \text{BD}}{\text{TD}} \text{X } 100$$

Hausner's Ratio (HR)

HR was calculated using this formula

$$\text{HR} = \frac{\text{TD}}{\text{BD}}$$

Evaluation of compressed tablets

Thickness and diameter

It was determined by vernier caliper for 10 tablets and avg was noted down.

Hardness

It was determined using Stokes Monsanto hardness tester on 10 tablets and average was noted down.

Friability

Randomly selected 20 tablets were placed in friabilator and 100 rotations were performed. The weight of tablets was noted down. Considering initial weight and final weight, weight loss was determined.

Content uniformity

Table 4: Stability study results of LP SR tablets at accelerated condition

Sr. No	Parameters	Initial	1M	3M	6M
1	Weight variation (%)	0.251	0.253	0.255	0.258
2	Content uniformity (%)	98.52	98.67	98.89	98.78
3	Friability (%)	0.72	0.77	0.77	0.79
4	Dissolution @24 hrs (%)	52	55	54	53

Randomly selected 10 tablets were crushed and placed in pH 6.8 phosphate buffer for period of 24 hours. Solution was filtered and LP content was determined at 205 nm.

Weight Variation

20 tablets were weighed to check the variations.

In-vitro release studies

Drug release was performed in pH 6.8 phosphate buffer (900 ml, 37°C ± 0.5°C) in USP type II apparatus. The test was performed at 50 rpm for 24 hours. The samples were withdrawn at each time point and fresh buffer was added. The solutions were filtered and analysed at 205 nm.

Stability study

Accelerated stability was performed on optimised tablets at 40°C ± 2°C/75% RH ± 5% RH for 6 months. Tablets were packed in HDPE bottles and loaded for stability testing. The samples were taken out at 1, 3, and 6 months to check the drug content, dissolution, and physical characteristics.

Result and Discussion

Chitosan was used as a rate retarding polymer in combination with HPMC K100M. Chitosan plays a crucial role in sustained drug delivery due to its unique physicochemical properties, including biodegradability, biocompatibility, mucoadhesiveness, and pH-dependent solubility. As a rate-retarding polymer, chitosan forms a gel-like matrix upon hydration, which modulates drug release by controlling diffusion and erosion mechanisms[12].

Lubricated blend flow properties

The parameters provide insight into the blend's compressibility and flowability, which are critical for ensuring uniform tablet weight and content uniformity in the final formulation. Carr's Index, is used to assess the flowability of powder blends. A CI value below 15% indicates good flow properties, while values above 20% suggest poor flow characteristics. The CI values for the lubricated blend ranged from 7.35% (F3) to 14.97% (F5). These values suggest that all formulations exhibit good to fair flow properties, with F3 showing the best flow

characteristics (CI = 7.35%). The Hausner Ratio further supports the evaluation of flowability, where an HR value ≤1.25 indicates good flow, while values above 1.4 suggest poor flow properties. The HR values of the lubricated blends varied between 1.079 (F3) and 1.176 (F5), indicating acceptable to good flowability across all formulations. The formulation F3 demonstrated the most favorable flow properties (HR = 1.079), while F5 had relatively higher compressibility, though still within the acceptable range (HR = 1.176). All formulations exhibited good to moderate flowability, making them suitable for direct compression or granulation processes. Formulation F3 had the best flow properties, with the lowest CI (7.35%) and HR (1.079), suggesting minimal interparticle friction and better powder flow. The slightly higher CI and HR values in F5 (14.97% and 1.176, respectively) suggest that this batch may require additional flow enhancers or process modifications to improve flowability. Thus, based on the flow property analysis, the lubricated blend of Losartan Potassium is suitable for further processing, with minor adjustments required for formulations exhibiting slightly higher CI values (table 2).

Compressed tablets evaluation

The evaluation of compressed tablets for different formulations (F1–F5) was carried out by assessing their physical and mechanical properties. The diameter of all formulations remained consistent, ranging from 7.99 mm to 8.07 mm, indicating uniform compression and die fill during tablet manufacturing. The thickness varied slightly between 5.3 mm and 5.6 mm, which is within acceptable limits, suggesting uniform compaction across batches. Hardness values ranged from 6.55 to 6.90 kg/cm², demonstrating sufficient mechanical strength to withstand handling and packaging, with F4 showing the highest hardness (6.90 kg/cm²), ensuring better durability.

The weight variation for all formulations was minimal, ranging from 0.249% to 0.253%, indicating excellent weight consistency within pharmacopeial limits. Content uniformity was well maintained across batches, with values ranging from 97.25% to 100.29%, confirming uniform drug distribution in the tablet matrix. The highest content uniformity was observed in F3 (100.29%), while F2 showed slightly lower uniformity (97.25%), though still within the acceptable range.

Friability, which measures the tendency of tablets to break or crumble under mechanical stress, varied between 0.35% and 0.72%. The lowest friability was observed in F3 (0.35%), suggesting superior tablet robustness, whereas F5 exhibited the highest friability (0.72%), indicating a relatively higher tendency for mechanical attrition. Overall, the evaluation confirmed that all formulations met the required pharmacopeial standards, with F3 demonstrating optimal mechanical strength, minimal friability, and excellent content uniformity, making it the most robust formulation among the tested batches. The comparative tablet evaluation parameters are provided in Table 3.

In-vitro release studies

Dissolution study of losartan potassium (LP) sustained-release (SR) tablets in pH 6.8 phosphate buffer demonstrates the impact of chitosan concentration on drug release. As the chitosan content increases from F1 (60 mg) to F5 (100 mg), a significant retardation in drug release is observed. The pure LP was found to be released 100% within 1 hour time period. F1 exhibited the highest dissolution, with 100% drug release at 24 hours, while F5 shows the slowest release, reaching only 52% at the same time point. This trend suggests that chitosan, a hydrophilic polymer, contributes to the formation of a stronger gel barrier, limiting water penetration and drug diffusion. Consequently, higher chitosan concentrations lead to prolonged drug release, making it an effective excipient for controlling LP release in SR formulations[13]. The comparative dissolution profile is presented in Table 4 and Figure 1.

Stability study

The stability study of losartan potassium (LP) sustained-release (SR) tablets under accelerated conditions over six months indicates minimal variations in critical quality attributes, demonstrating good stability. The stability study results are presented in Table 4. The weight variation remains consistent, with only a slight increase from 0.251% to 0.258%, indicating uniformity. Content uniformity remains within acceptable limits, showing no significant degradation, with values ranging from 98.52% to 98.78%. Friability slightly increases from 0.72% to 0.79%, but remains below the standard limit, ensuring tablet integrity. The dissolution at 24 hours fluctuates between 52% and 55%, suggesting that the drug release profile remains largely unaffected. Overall, the tablets exhibit excellent stability with no significant degradation, maintaining their efficacy and physical properties over time.

CONCLUSION

The present research successfully formulated and evaluated losartan potassium (LP) sustained-release (SR) tablets using chitosan as a rate-controlling polymer. The optimized formulation demonstrated prolonged drug release, with only 52% LP release over 24 hours, indicating effective sustained-release behavior for this highly water-soluble drug. Stability studies confirmed that the tablets maintained physical integrity, drug content, and dissolution profile over six months under accelerated conditions. The findings highlight chitosan as a suitable polymer for LP, effectively modulating its release and reducing dosing frequency, thereby improving patient compliance. This study underscores the potential of chitosan-based SR formulations for enhancing therapeutic efficacy in hypertension management.

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