RESEARCH ARTICLE

Formulation and Evaluation of Bioadhesive Pulsatile Drug Delivery System of an Antihypertensive Drug

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ABSTRACT

The current research aimed to prepare and estimate bioadhesive pulsatile drug delivery system (BPDDS) of an antihypertensive drug, losartan potassium, containing the formulation of a fast-dissolving core tablet and a combination of core tablet to polymer coating to formulate (BPDDS) tablet through a direct compression procedure. The coating was completed by utilizing polymers ethyl cellulose and carbopol 934. Pre-compression and post-compression parameters, drug release, lag time and mucoadhesive examination was entirely assessed for the formulations. Altogether, estimation tests were found to be inside parameters. The expected lag time for hypertension is 8 hours; hence this lag time was achieved by using a bioadhesive pulsatile system. The optimized formulation showed 8 hours lag time with appropriate mucoadhesion for an equivalent period. Therefore, the BPDDS was greatest preventative substitute for drug which are the highest absorption in the stomach and for drugs which used to treat diseases with a circadian rhythm.

Keywords: BPDDS, Losartan potassium, Lag time, Circadian rhythm, Mucoadhesion, Drug release.

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INTRODUCTION

In the recent era, the demand of novel drug delivery system (NDDS) has been boomed as more need in the pharmaceutical industry. This happened because of the invention of the latest NDDS technologies in pharmaceuticals. One of the approaches of NDDS is the controlled drug delivery system (CDDS). The CDDS is more preferred because it achieves a constant drug concentration level in the body, leading to improved bioavailability of drug. However, variations in peak plasma levels and bioavailability are observed in oral dosage forms. This may be due to the gastric emptying rate of the stomach. As a result, the controlled release dosage forms (CRDF) approaches are not appropriate for a drug with a confined absorption range in the upper portion of the gastrointestinal tract. To conquer this drug, it should be developed in a suitable dosage form that helps to prolong gastro-retention time and enhance the absorption of the drug.[1-3]

The gastric residence time (GRT) of pharmaceutical dosage form is extended using gastroretentive dosage forms (GRDFs). The gastroretentive dosage forms can hold the drug inside the stomach. GRDFs help to improve bioavailability and increase the gastro-retention of drugs. From various approaches of GRDF, the bioadhesive drug delivery system (BDDS) shows more interest in developing the dosage form, as it adheres to the mucous membrane of the stomach leading to gastro-retention for longer intervals of time to improve bioavailability.[4-6] The pulsatile drug delivery system (PDDS) is designed as a precautionary measure that has advantages over conventional pharmaceutical formulation. It developed on account of circadian rhythm of the body. PDDS represents as quick release of a particular quantity of drug in a less time interval directly later than a programmed off-release session *viz* lags time which depends on disease and which is always greater than the gastrointestinal emptying time. But, just in case of drugs having maximum absorption in the stomach and if the drug is delivered in small intestine or released after gastric emptying, then this leads into poor absorption of the drug which is a disadvantage of PDDS. Combinations of PDDS with BDDS can be preferable to subdue the same.[7,8] The floating PDDS is another method to lengthen gastric emptying time. FPDDS formulation floats over a gastric content but after gastric emptying, there is more probability that the formulation may enter the small intestine. This can be improved by BPDDS.[9,10]

The major goal of BPDD system is to achieve gastro-retention by adhering to the mucous membrane of the stomach using different types of bio-degradable polymer for bio-adhesion followed by pulsed drug release in the stomach. The pulsatile system releases medication at the proper time, at the accurate place of action and in exact quantity, which also

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beneficial compared to the common dosage form. In chrono-pharmacotherapy, the drug is delivered as per the circadian pattern of disease in therapy for diseases like hypertension, rheumatoid arthritis, and cardiovascular disease. The BPDDS has many advantages such as reducing dosing frequency, decrease side effects, and site-specific drug targeting like a colon.[11] In this study BPDDS of an antihypertensive drug of losartan potassium was prepared, which can be taken before bed time (9 pm) and has ability to release drug later 8 hours of lag time.

MATERIALS AND METHODS

Materials

Losartan potassium was attained as a gift sample from Lupin Pharmaceutical Ltd, Palghar, Tarapur, India. Polyvinyl pyrrolidone, microcrystalline cellulose, cross povidone, ethyl cellulose, carbopol 934 and magnesium stearate were gifted from Loba Chemicals, Mumbai, India. Each and every chemical utilised was of analytical grade.

Methods

Experimental design

The formulations for the present research work were optimised utilizing a two-factor, three-level (3^2) factorial design using the Software: Design Expert software (Version 13). Investigational trials were carried out with each of the nine practicable combinations after the two components were examined at all of three different levels (Low, Medium, and High). The quantity of carbopol 934 (X_1) and ethyl cellulose (X_2) was preferred as independent variables and dependent variables were selected as drug release and mucoadhesion time. The amount of losartan potassium was kept constant (100 mg) in the nine batches for the development of tablets.[12] The dependent and independent variables employed in 3^2 factorial design tactic for preparation of losartan potassium tablets are stated in Table 1. Table 2 reflects the composition of bioadhesive pulsatile tablets of losartan potassium (batches F1-F9) in full factorial design.

Preparation of core tablet (CT)

Core tablet of losartan potassium with a dose 100 mg was formulated through direct compression technique using ingredients: polyvinyl pyrrolidone (7 mg), magnesium stearate (1-mg), cross povidone (varying 9/11/13/15/17 mg) and MCC utilized as diluent with adjusting a tablet weight of 200 mg.

Table 1: Independent and dependent variables utilized in the formulation of tablets

Factor	*Levels, actual (coded)*		
	Low (-1)	*Medium (0)*	*High (+1)*
Independent variables			
X1: Carbopol 934 (mg)	96	144	192
X2: Ethyl cellulose (mg)	240	280	320
Dependent variables	Goals		
Y1: %Drug release	Maximum		
Y2: Mucoadhesion time (h)	Maximum		

Table 2: Composition of bioadhesive pulsatile tablets of losartan potassium (F1-F9) in full factorial design

Batch code (X_1, X_2)	*Amount of carbopol 934 (mg)*	*Amount of ethyl cellulose (mg)*
F1 (-1, -1)	96	240
F2 (0, -1)	144	240
F3 (+1, -1)	192	240
F4 (-1, 0)	96	280
F5 (0, 0)	144	280
F6 (+1, 0)	192	280
F7 (-1, +1)	96	320
F8 (0, +1)	144	320
F9 (+1, +1)	192	320

All the constituents were weighed and diversified well for about 15 minutes. In the formulation crosspovidone used as disintegrating agent, polyvinyl pyrrolidine was utilised as binder, magnesium stearate was utilised as a lubricant and microcrystalline cellulose were used as diluents. After mixing powder was compressed into tablet by using rotatory tablet machine (D = 8 mm) (Shakti Pharmatech Pvt. Ltd).[13-15]

Characterization

Fourier transforms infrared spectrometry (FTIR)

Losartan potassium spectrum was recorded using fourier transforms infrared spectrometry (FTIR) [Bruker, Germany (Alpha) Cary 630] and used to illustrate structural modification. Small quantity of sample about 100 mg were taken and then placed on FTIR platform and then spectra were recorded. The sample were analysed in the 4000 and 400 cm^{-1} regions.[16]

Pre-compression evaluation of granules

A quantity of powder weighed accurately and transferred to 100 mL measuring cylinder. Then afterward, transferring initial volume was noted as bulk volume. Tap volume (Vi) which is taken up by powder after the tapping of powder for definite interval of time by using mechanical tapping of container which contain the sample by using graduate measuring cylinder. Then tap density was computed using the formula. Each analysis was performed for two times. Carr's index and Hausner's ratio were computed utilizing bulk density (BD) and tap density (TD) values. The fixed funnel technique was utilized to estimate the granules' repose angle.[17-20]

Post-compression evaluation of tablets

The tablet thickness was determined by utilizing an vernier calliper, weight variation, hardness, friability; disintegration time was performed as per IP and USP. The dissolution study was accomplished through utilizing USP type II dissolution apparatus, 900 mL of 0.1N hydrochloric acid with 0.075 % SLS as a medium at temperature 37 ± 2°C and 100 rpm paddle speed.[14,15,21-23]

Table 3: Formulation of BPRT of losartan potassium

Ingredients (mg)	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*
Core tablet	200	200	200	200	200	200	200	200	200
MCC	228	180	132	188	140	92	148	100	52
Polyvinyl pyrrolidone	30	30	30	30	30	30	30	30	30
Ethyl cellulose	240	240	240	280	280	280	320	320	320
Carbopol	96	144	192	96	144	192	96	144	192
Magnesium stearate	6	6	6	6	6	6	6	6	6
Total weight (mg)	800	800	800	800	800	800	800	800	800

Preparation of bioadhesive pulsatile release tablet by direct compression process

For the formulation dry coating was completed utilizing different concentration of ethyl cellulose and carbopol 934. Also, polyvinyl pyrrolidine, magnesium stearate and microcrystalline cellulose were utilized to coat core tablet (Table 3). All ingredients were weighed and mixed manually to prepare fined blend. The bioadhesive pulsatile release tablet (BPRT) was prepared using 13 mm die and punch set. Initially, 40% of the final blend was added in the die, and core tablet was put on it. Then, the remaining 60% blend was added and the tablet was compressed on a KBr tablet press machine (Hi-labs Ltd. E82664).[24, 25]

Evaluation of various tablet properties of BPRT

The prepared press-coated tablet was assessed for weight variation, hardness, thickness, friability, etc., per official books.[14,15]

In-vitro mucoadhesion test

For the mucoadhesion test, the model was prepared using two pan balances. The two pans of a physical balance were taken out and replaced with beakers of the same weight. This entire setup was raised to fit a glass petri plate beneath the left beaker, keeping a distance between the petri plate and the left beaker of 0.5 cm. Before the mucoadhesion evaluation study, the chicken ileum was removed, cleaned, and equilibrated at 37ºC for 30 minutes in 0.1 N HCl medium. The ileum was tied tightly with thread to the mucus on the glass slide, which was then filled with 0.1N hydrochloric acid kept at 37ºC so as to 0.1N hydrochloric acid just reached the surface of ileum membrane to kept it moist. This glass slide was placed beneath the left beaker and lowered down up to the petri plate of left beaker. The tablet was placed on the left beaker's base using two-way adhesive tape and the balance beam. The left beaker was then covered with the steady weight of 10 gm for the duration of 5 minutes, allowing the tablet to make complete contact with the ileum membrane. The mucoadhesive strength was then measured in terms of the weight (in gm) obligatory to remove the tablet from the membrane by adding weights to the right beaker. Time required to separate tablet from mucus membrane was recorded as an adhesion time.[26] then force of adhesion (N) was determined with the formula:

N = Mucoadhesive strength/100 X 9.81------ (1)

In-vitro dissolution study of BPRT

Dissolution assessment was accomplished using USP type II dissolution apparatus, 900 mL of 0.1N hydrochloride acid with 0.075% SLS as a medium at 37 ± 2°C, 75 rpm. The sample was removed periodically and exchanged with fresh and clean dissolution medium by filtering through Whattman filter paper and then diluting it up to 10 mL using 0.1 N HCl. Then sample were analysed by utilizing UV spectrophotometer.[25,30-32]

Stability study

The optimised formulation was kept at stability chamber at a temperature of 40°C and relative humidity (RH) (75%) for the duration of 45 days. Following a predetermined time period, the placed samples were assessed for weight variation, hardness, thickness, %drug release and drug content.[28-33]

RESULTS

Experimental Design

Effect of independent variables on %drug release (Y1)

Percent drug release is linked to the amount of carbopol 934 and ethyl cellulose of formulation. The increase in carbopol 934 and ethyl cellulose concentration shows increases in %drug release of formulations. The following quadratic equation can be used to explain the impact of independent factors on the % of drug release.

$$\%\text{Drug release } Y_1 = +97.20+3.45X_1+0.3500X_2+0.6250\ X_1X_2-2.35\ X_1^2-4.65\ X_2^2 \text{ ----- (2)}$$

Where Y_1 is the % drug release, X_1 is the concentration of carbopol 934 and X_2 is concentration of ethyl cellulose. The equation shows that amount of ethyl cellulose and carbopol 934 both positively affect %drug release (Figure 1). This has indicated that as amount of carbopol 934 and ethyl cellulose increased, drug release also increased.

Effect of independent variables on mucoadhesion time (Y2)

The mucoadhesion time is of most important to the bioadhesive drug delivery system. As if the tablet shows required adhesion time the drug can easily release in stomach after the 8 hours of lag time which is required for hypertension. In addition, absorption of drug and %drug release is also affected by the mucoadhesion time. The lesser mucoadhesion time was observed for F1 (7:30 h) formulation while the largest mucoadhesion time was obtained for F6 formulation (9:45 h).

The following equation can be used to explain the impact of independent factors on mucoadhesion time.

Mucoadhesion time $Y2 = +8.43+0.6583\ X_1+0.3917\ X_2$ ---- (3)

Where the Y_2 is the mucoadhesion time, X_1 is the concentration of carbopol 934, and X_2 is concentration of ethyl cellulose. The equation displays that the concentration of carbopol 934 positively affects mucoadhesion time, and the concentration of ethyl cellulose also has a positive effect (Figure 2). This clears that the mucoadhesion time of BPRT tablets boosts with an increase in the concentration of carbopol 934 and ethyl cellulose. Figure 3 showed overlay plot which is achieved from the design of experiment (DOE) software which displays design space to choose an optimum concentration of carbopol and ethyl cellulose it shows the optimum value of carbopol which is 157 mg and value of ethyl cellulose is 305 mg. which is also nearer to the design point of the model. Using the software point prediction approach, the optimal BPRT Formulation was selected from nine trial batches made in accordance with a factorial design based on principles of achieving largest %drug release and shortest mucoadhesion time. Following careful analysis, it was discovered that the F5 formulation (Carbopol 934–144 mg and ethyl cellulose- 280 mg) fulfilled the criteria for ideal formulation. The optimized BPRT tablet have %drug release 97.9% with a mucoadhesion time 9:15 hours.

Preparation of core tablet

Formulated core tablets were characterized and assessed for weight variation, hardness, friability, disintegration time (DT) and dissolution.

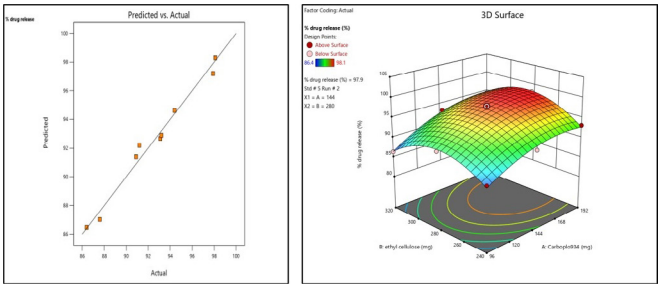

Figure 1: Predicted versus Actual plot and 3D graph of %drug release

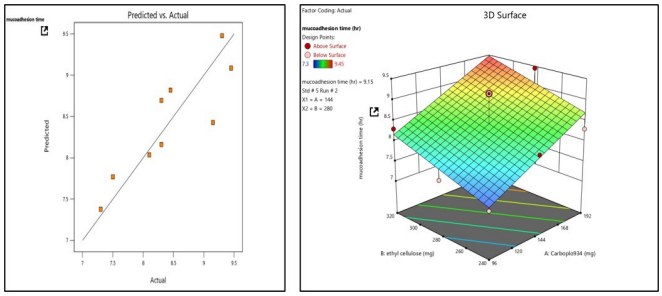

Figure 2: Predicted versus actual plot and 3D graph of mucoadhesion time

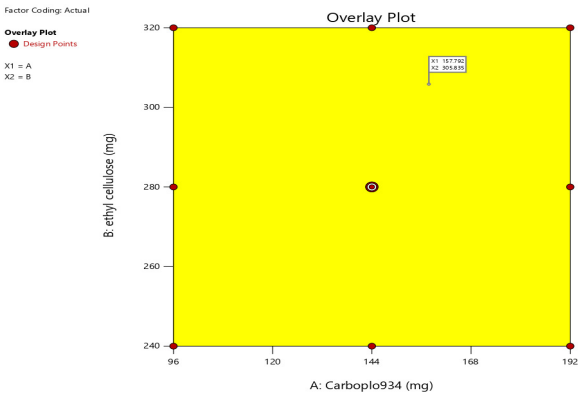

Figure 3: Overlay plot of optimized batch

Characterization

FTIR study

FTIR spectra of pure losartan potassium, losartan potassium with carbopol 934, losartan potassium with ethyl cellulose and drug with all excipients were shown in Figure 4. FTIR spectra of drug and excipients showed that major peaks of functional groups of pure drug were remained intact in final mixture of the preparation, hence it was concluded that the there was no major interface was observed amongst drug and excipients indicated compatibility of drug and excipients.

Pre-compression evaluation of granules

The pre-compression evaluation parameters of final blend are BD, TD, Hausner's ratio and Carr's indexes (CI), as given in Table 4. The result has indicated that all the batches of formulations were suitable for formulation of tablets by direct compression as it has showed optimum flowability and compressibility.

Post-compression evaluation of tablets

The values of post-compression limitations are as given in Table 5. Thickness, hardness, weigh variation, %friability, disintegration time (DT) and drug content were well within the prescribed limit of official books.[14,15] *In-vitro* %drug release of all preparations of C1 to C5 were showed in Figure 5. For formulation, C5 98.10% of drug was released within 10 to 15 minutes so it was considered as burst release as accepted in the pulsatile drug delivery system. Batch C5 has shown all evaluation parameters comparatively better, so it was finalized as an optimized batch for further development of BPRT.

Preparation of bioadhesive pulsatile release tablet by direct compression system

Bioadhesive pulsatile release tablets were formulated through direct compression routine and evaluated for several parameters.

Evaluation of various tablet properties of BPRT

The pre-compression evaluation parameters of final blend are BD, TD, Hausner's ratio and CI, as given in Table 6. The result has indicated that all the batches of formulations were suitable for the formulation of tablets by direct compression as it has showed optimum flowability and compressibility.

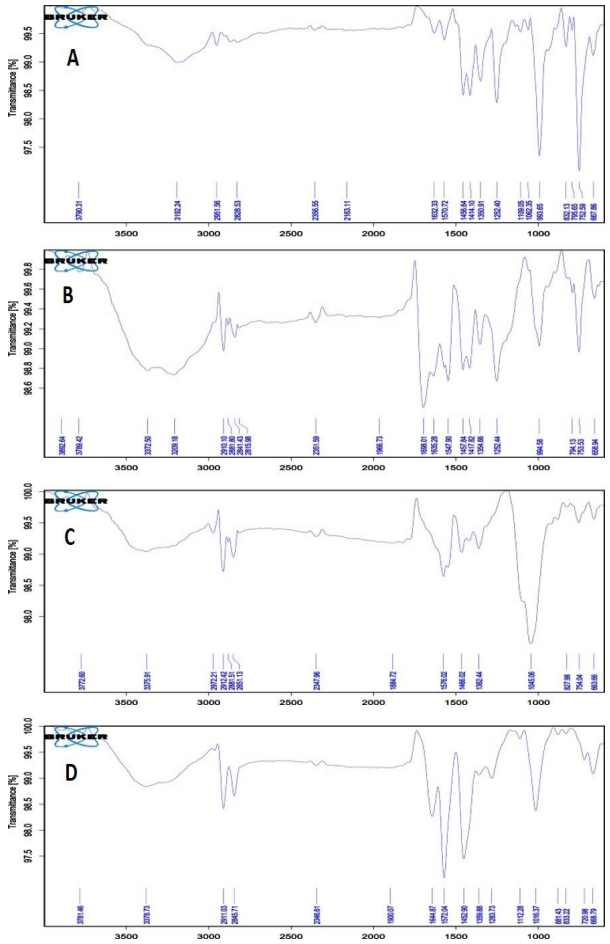

Figure 4: FTIR spectra of A. Pure losartan potassium, B. Drug with Carbopol 934, C. Drug with ethylcellulose, D. Drug with all excipients

The values of post-compression parameters are as specified in Table 7. Thickness, hardness, weigh variation, %friability, disintegration time and drug content were well within the prescribed limit of official books.[14,15]

In-vitro mucoadhesion test

The results of adhesion time, mucoadhesive strength and force of adhesion of all F1 to F9 batches were given in Table 7. Optimized batch F5 showed 9:15 hours of adhesion time, 30.25 gm of mucoadhesive strength and 2.96 N of adhesion force, which is sufficient for a mucoadhesive tablet.

In-vitro dissolution study of BPRT

The formulations of bioadhesive pulsatile tablets of F1 to F9 showed distinct lag times and *in-vitro* %drug release of all

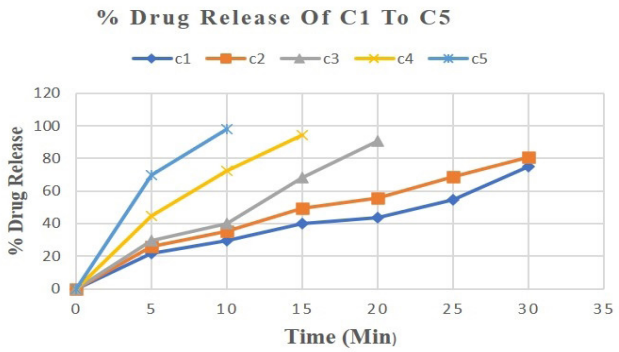

Figure 5: %drug release of C1 to C5

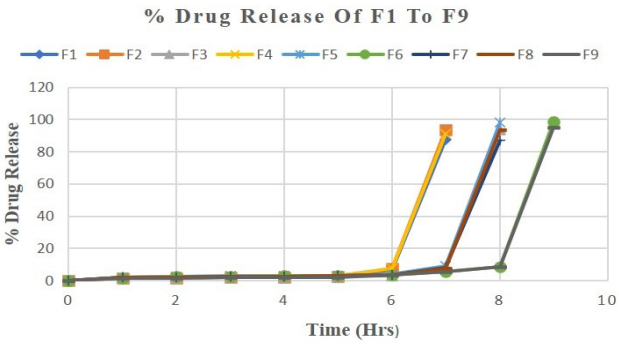

Figure 6: %drug release of F1 to F9

preparations was showed in Figure 6. It has been observed that increased amount of polymers around tablets may have subsidized in the direction of the decreased drug release of losartan potassium caused by an increase in ethyl cellulose and carbopol concentration. For formulation F5 only 8.89% of drug was released up to at 8 hours and after that 97.95% of drug was released for next hour so it was considered as burst release as accepted in pulsatile drug delivery. Also, F5 formulation showed the eight-hour desired lag time for hypertension as per the circadian rhythm.[25] A reduction in lag time was demonstrated when ethyl cellulose and carbopol concentration rises.[26] It may be due to reason of higher concentration of polymer decreases free water volume and increases the viscosity of the tablet coat causing a decline in drug release.[27,28]

Stability study

An optimized check-point batch (F5) was the subject of the stability investigation, which looked at a number of significant characteristics. The stability test results evidently show that the established pulsatile preparation was stable enough

Table 4: Pre-compression parameters of core tablet

Batch code	*BD (gm/cm^3)*	*TD (gm/cm^3)*	*Hausner's ratio*	*CI (%)*	*Angle of repose*
C1	0.35 ± 0.07	0.40 ± 0.08	1.14 ± 0.09	12.51 ± 0.10	29.01 ± 0.50
C2	0.39 ± 0.05	0.46 ± 0.11	1.17 ± 0.08	15.21 ± 1.19	28.19 ± 1.19
C3	0.37 ± 0.09	0.44 ± 0.06	1.18 ± 0.05	15.90 ± 1.10	21.15 ± 0.40
C4	0.38 ± 1.00	0.43 ± 1.07	1.13 ± 0.09	11.62 ± 0.20	26.15 ± 0.15
C5	0.41 ± 0.010	0.47 ± 0.01	1.14 ± 0.04	12.76 ± 0.30	26.9 ± 0.50

Table 5: Post-compression evaluation of CT

Batch code	*Weight variation (mg)*	*Thickness (mm)*	*Hardness (Kg/cm^3)*	*Friability (%loss of weigh*	*DT (sec)*	*Drug content (%)*
C1	199 ± 0.13	3.11 ± 0.10	3.3 ± 013	0.52 ± 0.11	601.5 ± 0.90	97.50 ± 19
C2	200 ± 1.08	3.03 ± 0.05	3.5 ± 0.09	0.45 ± 0.34	510.9 ± 1.20	96.17 ± 0.65
C3	198 ± 0.06	3.07 ± 0.15	3.1 ± 0.19	0.58 ± 0.21	489.8 ± 0.90	98.10 ± 0.50
C4	202 ± 1.09	3.09 ± 0.09	3.9 ± 0.15	0.67 ± 0.32	350.2 ± 0.54	97.31 ± 0.75
C5	201.05 ± 0.2	3.06 ± 0.19	3.6 ± 0.19	0.44 ± 0.21	280.3 ± 0.60	98.15 ± 0.24

Table 6: Pre-compression parameters of BPRT

Batch code	*BD (gm/cm^3)*	*TD (gm/cm^3)*	*Hausner's ratio*	*CI (%)*	*Angle of repose (Θ)*
F1	0.52 ± 0.05	0.69 ± 0.01	1.32 ± 0.02	24.60 ± 0.9	27.01 ± 0.50
F2	0.51 ± 0.03	0.65 ± 0.04	1.27 ± 0.01	21.53 ± 1.2	28.19 ± 1.19
F3	0.55 ± 0.01	0.70 ± 0.01	1.27 ± 0.07	21.42 ± 0.8	29.15 ± 0.40
F4	0.50 ± 0.03	0.66 ± 0.06	1.32 ± 0.06	24.20 ± 0.5	26.15 ± 0.15
F5	0.57 ± 0.01	0.71 ± 0.02	1.24 ± 0.02	19.71 ± 1.1	26.90 ± 0.50
F6	0.53 ± 0.07	0.67 ± 0.09	1.26 ± 0.07	20.89 ± 0.9	28.17 ± 0.25
F7	0.55 ± 0.02	0.72 ± 0.03	1.30 ± 0.01	23.61 ± 1.1	27.51 ± 1.12
F8	0.56 ± 0.07	0.73 ± 0.01	1.30 ± 0.08	23.28 ± 1.3	28.52 ± 1.11
F9	0.57 ± 0.08	0.73 ± 0.03	1.28 ± 0.07	21.91 ± 1.9	29.39 ± 0.50

under accelerated and regulated circumstances. BPRT was determined to be stable beneath accelerated temperature settings since there was no appreciable change in physical appearance or other criteria such as weight variation, hardness, thickness, drug content and %drug release. After some intervals, the outcomes of several parameter studies are mentioned in Table 8.

DISCUSSION

The preparation and optimization of BPRT for delivering losartan potassium present a promising approach for hypertension management, ensuring both controlled drug release and sufficient mucoadhesion time. The study systematically explored the impact of varying carbopol 934 and ethyl cellulose concentrations on two critical parameters: percent drug release (%Y1) and mucoadhesion time (Y2).

The quadratic equations derived from modeling the relationship between the independent variables (concentrations of carbopol 934 and ethyl cellulose) and the dependent variables (%drug release and mucoadhesion time) provided valuable insights into the formulation process. The positive coefficients of the independent variables in both equations indicate that increasing the concentrations of carbopol 934 and ethyl cellulose enhances both drug release and mucoadhesion time. This suggests that higher polymer concentrations lead to better tablet adhesion and controlled release characteristics.

The optimization process, guided by the designed experiments and statistical analysis, resulted in the selection of an optimal formulation (F5), comprising carbopol 934 (144 mg) and ethyl cellulose (280 mg). This formulation demonstrated desirable attributes, including a high percent drug release (97.9%) and an extended mucoadhesion time (9:15 hours), meeting the criteria for an ideal BPRT.

Furthermore, the compatibility of the drug with the excipients was confirmed through FTIR spectroscopy, ensuring that the formulation components did not interact adversely. Pre-compression and post-compression evaluations of the tablets, including parameters such as weight variation, hardness, friability, and disintegration time, met the standards set by pharmacopoeial guidelines, indicating the suitability of the direct compression method for tablet manufacturing.

The *in-vitro* dissolution studies provided crucial insights into the release behavior of losartan potassium from the BPRT preparations. The observed lag time monitored through burst releasing aligns with the intended pulsatile drug delivery profile, which is advantageous for achieving therapeutic efficacy in hypertension management, corresponding to the circadian rhythm.

Stability testing over a 90-day period under accelerated and controlled conditions confirmed the robustness and reliability of the optimized BPRT formulation (F5). Minimal changes in physical characteristics and drug release profiles were observed, indicating that the formulation remained stable over the testing period.

In conclusion, the comprehensive scientific discussion underscores the successful development and optimization of bioadhesive pulsatile release tablets for losartan potassium, offering a promising approach for the effective management of hypertension. The systematic formulation approach, supported by rigorous characterization and evaluation, provides a solid foundation for supplementary preclinical and clinical

Table 7: Post-compression parameters of BPRT

Batch code	*Weight variation (mg)*	*Thickness (mm)*	*Hardness (kg/cm^3)*	*Friability (%)*	*Adhesion time (h)*	*Mucoadhesion strength (in gm)*	*N*
F1	800 ± 1.2	7.06 ± 0.01	7.2 ± 0.01	0.62 ± 0.09	7:30	24.15	2.36
F2	801 ± 2.1	7.10 ± 0.06	7.3 ± 0.09	0.65 ± 0.07	8:10	29.30	2.87
F3	799 ± 1.9	7.08 ± 0.07	7.6 ± 0.12	0.61 ± 0.02	8:30	30.15	2.95
F4	800 ± 1.8	7.12 ± 0.09	7.4 ± 0.19	0.59 ± 0.01	7:50	25.30	2.48
F5	800 ± 1.5	7.06 ± 0.04	7.5 ± 0.19	0.54 ± 0.05	9:15	30.25	2.96
F6	798 ± 2.9	7.07 ± 0.05	7.6 ± 0.20	0.56 ± 0.04	9:45	32.15	3.15
F7	800 ± 1.1	7.09 ± 0.06	7.5 ± 0.09	0.55 ± 0.06	8:30	35.45	3.47
F8	801 ± 1.5	7.07 ± 0.09	7.6 ± 0.17	0.53 ± 0.12	8:45	36.10	3.54
F9	802 ± 2.1	7.15 ± 1.23	7.7 ± 0.01	0.52 ± 0.11	9:30	40.15	3.93

Table 8: Stability study of optimized batch (F5)

Time interval (days)	*Weight variation (mg)*	*Hardness (kg/cm^3)*	*Thickness (mm)*	*Drug content (%)*	*%drug release*
0	800 ± 1.3	7.5 ± 0.15	7.06 ± 0.03	98.15 ± 0.50	97.95 ± 0.016
30	800 ± 1.4	7.6 ± 0.14	7.07 ± 0.06	97.10 ± 0.30	96.15 ± 0.027
60	800 ± 1.4	7.7 ± 0.19	7.09 ± 0.05	98.11 ± 0.20	96.55 ± 0.019
90	800 ± 1.5	7.7 ± 0.18	7.09 ± 0.07	98.11 ± 0.25	96.75 ± 0.019

investigations, ultimately leading in the direction of the commercialization of a novel therapeutic formulation.

CONCLUSION

The recent study focused on developing and accessing a BPDDS containing losartan potassium for hypertension treatment. The research showed that losartan potassium optimization was achieved effectively, with batch F5 exhibiting desirable characteristics such as an 8-hour lag time followed by burst release and effective mucoadhesion. Consequently, this formulation holds promise for bioadhesive pulsatile delivery of losartan potassium, potentially improving patient compliance, reducing adverse effects, and ensuring optimal drug delivery to the intended site. Thus, this system could offer significant benefits in the future.

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