

Development and Optimization of Prazosin Hydrochloride-Loaded Lipid Polymer Hybrid Nanoparticles Using Central Composite Design for Enhanced Oral Bioavailability

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ABSTRACT

Background: Prazosin hydrochloride (PRZ) is a selective α_1 -adrenergic receptor antagonist extensively used in the management of hypertension and associated cardiovascular disorders. Despite its therapeutic efficacy, its oral delivery is limited by poor aqueous solubility, extensive first-pass metabolism, and low oral bioavailability. Lipid polymer hybrid nanoparticles (LPHNs) have emerged as a promising nanocarrier system capable of combining the structural stability of polymeric nanoparticles with the biocompatibility of lipid-based carriers to improve the oral delivery of poorly water-soluble drugs.

Objective: The present study aimed to develop and optimize Prazosin hydrochloride-loaded lipid polymer hybrid nanoparticles using the self-assembly nanoprecipitation technique and Central Composite Design (CCD) to enhance encapsulation efficiency, control drug release, and improve oral bioavailability.

Methods: Prazosin hydrochloride-loaded LPHNs were prepared using Eudragit RLPO as the polymeric matrix, soya lecithin as the lipid component, Tween 80 as the surfactant, and polyethylene glycol (PEG 6000) as the stabilizer. A three-factor, three-level Central Composite Design was employed to optimize lipid-to-drug ratio, polymer-to-drug ratio, and PEG concentration. Particle size, zeta potential, and entrapment efficiency were selected as dependent responses. The optimized formulation was characterized using dynamic light scattering, Fourier Transform Infrared Spectroscopy (FTIR), Differential Scanning Calorimetry (DSC), Scanning Electron Microscopy (SEM), Transmission Electron Microscopy (TEM), in vitro drug release studies, drug release kinetics, and ex vivo intestinal permeation studies.

Results: The optimized formulation produced nanosized lipid polymer hybrid nanoparticles exhibiting high entrapment efficiency, satisfactory zeta potential, and narrow particle size distribution. FTIR and DSC analyses confirmed compatibility between Prazosin hydrochloride and formulation excipients without evidence of chemical interaction. SEM and TEM analyses demonstrated spherical nanoparticles with smooth surfaces and uniform morphology. The optimized formulation exhibited sustained drug release over an extended period and significantly

enhanced intestinal permeation compared with the pure drug suspension, suggesting improved oral bioavailability.

Conclusion: Lipid polymer hybrid nanoparticles prepared using the self-assembly nanoprecipitation method successfully improved the physicochemical characteristics and oral delivery of Prazosin hydrochloride. The optimized formulation demonstrated desirable particle characteristics, controlled drug release, and enhanced intestinal permeation, indicating its potential as an effective oral nanocarrier system for antihypertensive therapy.

KEYWORDS: Prazosin hydrochloride; Lipid polymer hybrid nanoparticles; Central Composite Design; Self-assembly nanoprecipitation; Oral bioavailability; Controlled drug delivery.

1. INTRODUCTION

Hypertension is one of the most prevalent chronic cardiovascular disorders worldwide and remains a leading contributor to morbidity and mortality associated with coronary artery disease, stroke, heart failure, and chronic kidney disease. According to international health organizations, uncontrolled hypertension is responsible for millions of deaths annually and represents a major global healthcare burden. Although numerous antihypertensive agents are available, achieving consistent blood pressure control remains challenging because of poor patient compliance, pharmacokinetic variability, and limited oral bioavailability of several therapeutic agents (1).

Prazosin hydrochloride is a selective α_1 -adrenergic receptor antagonist widely prescribed for the treatment of essential hypertension, benign prostatic hyperplasia, and certain cardiovascular disorders. The drug acts by selectively blocking postsynaptic α_1 -adrenergic receptors, producing relaxation of vascular smooth muscle and subsequent reduction in peripheral vascular resistance. Despite its therapeutic effectiveness, Prazosin hydrochloride belongs to the Biopharmaceutics Classification System (BCS) Class II and exhibits poor aqueous solubility with dissolution-limited absorption following oral administration. Furthermore, extensive hepatic first-pass metabolism reduces systemic drug availability, necessitating frequent dosing and contributing to interpatient variability in therapeutic response (2, 3).

Enhancing the oral bioavailability of poorly soluble drugs remains a significant challenge in pharmaceutical formulation development. Various formulation strategies including solid dispersions, inclusion complexes, lipid-based systems, nanosuspensions, polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers, and lipid polymer hybrid nanoparticles have been investigated to overcome dissolution and permeability limitations. Among these approaches, lipid polymer hybrid nanoparticles (LPHNs) have attracted considerable attention because they integrate the structural advantages of polymeric

nanoparticles with the biological compatibility and membrane interaction properties of lipid carriers (4 - 7).

LPHNs consist of a biodegradable polymeric core surrounded by a phospholipid layer and an external hydrophilic stabilizing shell, commonly polyethylene glycol (PEG). The polymeric core provides mechanical strength and sustained drug release, while the lipid shell improves encapsulation efficiency, minimizes drug leakage, enhances intestinal membrane interaction, and promotes oral absorption. PEGylation further improves colloidal stability by reducing particle aggregation and extending nanoparticle residence time within the gastrointestinal tract. These combined characteristics make LPHNs particularly suitable for delivering hydrophobic drugs such as Prazosin hydrochloride (8-9).

Among the available preparation methods, self-assembly nanoprecipitation offers a simple, reproducible, and scalable technique for producing lipid polymer hybrid nanoparticles with narrow particle size distribution and high encapsulation efficiency. During this process, rapid solvent diffusion induces spontaneous polymer precipitation while phospholipids self-assemble around the polymeric core through hydrophobic interactions, producing stable hybrid nanoparticles without the need for complex manufacturing procedures.

Optimization of nanoparticle formulations using statistical experimental designs has become increasingly important in pharmaceutical development. Response Surface Methodology based on Central Composite Design (CCD) enables simultaneous evaluation of multiple formulation variables while reducing the number of experimental runs. This Quality-by-Design (QbD)-oriented approach facilitates identification of optimal formulation conditions by establishing mathematical relationships between formulation variables and critical quality attributes, including particle size, zeta potential, and entrapment efficiency. Such statistical optimization enhances formulation robustness, reproducibility, and product quality while minimizing development time and experimental variability.

Therefore, the present investigation was undertaken to develop, optimize, and characterize Prazosin hydrochloride-loaded lipid polymer hybrid nanoparticles using the self-assembly nanoprecipitation method combined with Central Composite Design. The optimized nanoparticles were comprehensively evaluated for physicochemical characteristics, morphological properties, thermal behavior, drug release profile, release kinetics, and ex vivo intestinal permeation to establish their potential as an advanced oral drug delivery system capable of improving the bioavailability and therapeutic efficacy of Prazosin hydrochloride.

2. MATERIALS AND METHODS

2.1 Materials

Prazosin hydrochloride (PRZ) was obtained as a gift sample from a reputed pharmaceutical manufacturer. Eudragit RLPO was used as the polymeric carrier because of its excellent film-

forming ability, permeability, and sustained-release characteristics. Soya lecithin served as the lipid component to improve biocompatibility and facilitate formation of lipid polymer hybrid nanoparticles. Polyethylene glycol (PEG 6000) was incorporated as a steric stabilizer, while Tween 80 was used as a surfactant to reduce interfacial tension and stabilize the nanoparticle dispersion. Methanol and acetone of analytical grade were used as organic solvents. Mannitol was employed as a cryoprotectant during lyophilization. Potassium dihydrogen phosphate, disodium hydrogen phosphate, sodium hydroxide, sodium chloride, potassium chloride, and distilled water were used for buffer preparation and analytical studies. All chemicals were of analytical reagent grade and used without further purification.

2.2 Experimental Design

The formulation was optimized using a three-factor, three-level Central Composite Design (CCD) generated with Design-Expert® software. Response Surface Methodology (RSM) was employed to establish the relationship between formulation variables and critical quality attributes.

Independent Variables

- X₁: Lipid-to-drug ratio
- X₂: Polymer-to-drug ratio
- X₃: PEG 6000 concentration

Dependent Variables

- Y₁: Particle size (nm)
- Y₂: Zeta potential (mV)
- Y₃: Entrapment efficiency (%)

A total of 15 experimental runs comprising factorial, axial, and center points were performed according to the CCD matrix. Quadratic polynomial equations were generated to describe the influence of formulation variables on the measured responses. Statistical significance was evaluated using analysis of variance (ANOVA), and numerical optimization based on desirability functions was employed to identify the optimum formulation.

Table 1: Observed responses of Prazosin HCl LPHNs using Central Composite design

Runs	A: Polymer(mg) (X1)	B: lipid(mg) (X2)	C:Tween 80 (ml) (X3)	Particle size (nm)	Entrapment Efficiency EE (%)	Zetapotential (mv)
LPHNs-1	22.5	27.5	0.665	160	79	-27

Runs	A: Polymer(mg) (X1)	B: lipid(mg) (X2)	C:Tween 80 (ml) (X3)	Particle size (nm)	Entrapment Efficiency EE (%)	Zetapotential (mv)
LPHNs-2	43.5224	27.5	0.665	172	84	-27.8
LPHNs-3	10	15	0.4	115	65	-23.2
LPHNs-4	35	40	0.4	170	87	-29.4
LPHNs-5	35	15	0.93	145.8	80	-24.8
LPHNs-6	22.5	27.5	1.11068	141	83	-30.8
LPHNs-7	1.47759	27.5	0.665	110	72	-26.5
LPHNs-8	10	15	0.93	105	70.5	-25.6
LPHNs-9	10	40	0.4	135	81	-28
LPHNs-10	22.5	27.5	0.219325	175	73	-21.5
LPHNs-11	10	40	0.93	125	86	-31.5
LPHNs-12	35	15	0.4	155	82	-23.7
LPHNs-13	35	40	0.93	160	90	-31.5
LPHNs-14	22.5	48.5224	0.665	150	92	-32.4
LPHNs-15	22.5	6.47759	0.665	125	77	-25.9

2.3 Preparation of Prazosin Hydrochloride-Loaded Lipid Polymer Hybrid Nanoparticles (10-12)

Prazosin hydrochloride-loaded lipid polymer hybrid nanoparticles (PRZ-LPHNs) were prepared by the self-assembly nanoprecipitation method, which allows spontaneous formation of hybrid nanoparticles through rapid solvent diffusion.

Briefly, accurately weighed quantities of Prazosin hydrochloride, Eudragit RLPO, and PEG 6000 were dissolved in acetone to prepare the organic phase. Soya lecithin and Tween 80 were dissolved separately in distilled water under continuous magnetic stirring to obtain the aqueous phase.

The organic solution was added dropwise to the aqueous phase under constant stirring. Rapid diffusion of the organic solvent into the aqueous medium resulted in precipitation of the polymer and simultaneous self-assembly of phospholipids around the polymeric core through hydrophobic interactions, producing lipid polymer hybrid nanoparticles.

The resulting nanosuspension was subjected to probe sonication to reduce particle size and obtain uniform particle distribution. Continuous stirring facilitated complete removal of the organic solvent. The nanoparticle dispersion was subsequently centrifuged to separate free drug from nanoparticle-associated drug. The optimized formulation was lyophilized using mannitol as a cryoprotectant to improve storage stability and prevent aggregation during freeze-drying.

2.4 Lyophilization

The optimized nanoparticle suspension was mixed with an appropriate concentration of mannitol prior to freeze-drying. Samples were frozen and subsequently lyophilized under reduced pressure to obtain dry nanoparticle powder. The freeze-dried product was stored in airtight containers at room temperature for further characterization. Lyophilization significantly improved the physical stability of the nanoparticles without affecting their physicochemical properties.

2.5 Determination of Particle Size, Polydispersity Index, and Zeta Potential

Particle size, polydispersity index (PDI), and zeta potential of the prepared PRZ-LPHNs were measured using Dynamic Light Scattering (DLS).

The nanoparticle dispersion was diluted with distilled water before analysis to avoid multiple light scattering. Measurements were performed at room temperature, and average values were recorded.

Particle size was used to evaluate nanoparticle dimensions, while PDI indicated the uniformity of particle distribution. Zeta potential measurements were performed to determine surface charge and predict colloidal stability. Nanoparticles exhibiting high absolute zeta potential values were considered more resistant to aggregation during storage.

2.6 Determination of Entrapment Efficiency (13-14)

Entrapment efficiency (%EE) was determined using the indirect centrifugation method.

Freshly prepared nanoparticle suspensions were centrifuged at high speed using a refrigerated centrifuge to separate free Prazosin hydrochloride from nanoparticle-entrapped drug.

The concentration of free drug present in the supernatant was quantified by UV–Visible spectrophotometry using a previously established calibration curve.

High entrapment efficiency indicated successful incorporation of Prazosin hydrochloride within the lipid-polymer matrix.

2.7 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy was performed to investigate possible physicochemical interactions between Prazosin hydrochloride and formulation excipients.

Spectra of the pure drug, physical mixture, and optimized nanoparticle formulation were recorded using the potassium bromide (KBr) pellet method over the appropriate wavelength range.

Retention of characteristic functional group peaks confirmed compatibility between the drug and excipients and indicated successful encapsulation without chemical degradation.

2.8 Differential Scanning Calorimetry (DSC)

Differential Scanning Calorimetry was carried out to investigate the thermal characteristics of the pure drug, physical mixture, and optimized PRZ-LPHNs.

Samples were heated under a nitrogen atmosphere at a controlled heating rate. Changes in melting endotherms were analyzed to evaluate alterations in crystallinity following nanoparticle encapsulation.

A reduction in drug crystallinity following encapsulation was considered indicative of successful incorporation within the polymeric matrix.

2.9 Surface Morphology

The surface morphology of the optimized nanoparticles was examined using **Scanning Electron Microscopy (SEM)** and **Transmission Electron Microscopy (TEM)**.

SEM analysis was performed to evaluate surface characteristics, particle shape, and aggregation behavior.

TEM analysis provided detailed information regarding particle morphology, internal structure, and lipid coating surrounding the polymeric core.

2.10 In Vitro Drug Release Study

The in vitro release profile of Prazosin hydrochloride-loaded LPHNs was evaluated using a dialysis bag diffusion method under physiological conditions.

Nanoparticle formulations equivalent to the required drug dose were dispersed in dissolution medium maintained at $37 \pm 0.5^{\circ}\text{C}$ with continuous stirring.

Samples were withdrawn at predetermined time intervals and replaced with equal volumes of fresh dissolution medium.

Drug concentration was determined spectrophotometrically using the calibration curve, and cumulative percentage drug release was calculated.

2.11 Drug Release Kinetics

The cumulative drug release data were fitted into various mathematical models, including:

- Zero-order model
- First-order model
- Higuchi model
- Hixson–Crowell model
- Korsmeyer–Peppas model

The model exhibiting the highest correlation coefficient (R^2) was considered to best describe the release mechanism.

The release exponent (n) obtained from the Korsmeyer–Peppas model was used to determine whether drug release followed Fickian diffusion, non-Fickian diffusion, or Case-II transport.

2.12 Ex Vivo Intestinal Permeation Study

Ex vivo permeation studies were performed using excised intestinal tissue to evaluate intestinal transport of Prazosin hydrochloride from the optimized lipid polymer hybrid nanoparticles.

The optimized formulation and pure drug suspension were evaluated under identical experimental conditions.

Drug permeation across intestinal tissue was quantified spectrophotometrically at predetermined time intervals, and cumulative permeation along with steady-state flux values were calculated.

The ex vivo study was used to assess the capability of PRZ-LPHNs to improve intestinal absorption compared with the conventional drug suspension.

2.13 Statistical Analysis

All experimental data were expressed as **mean $\pm$ standard deviation (SD)**.

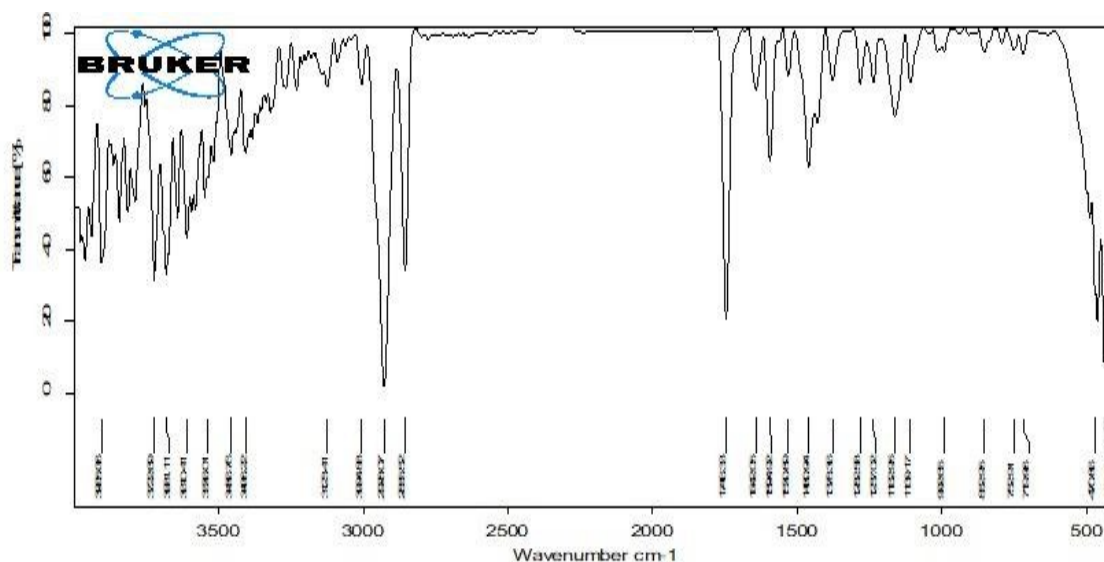
Statistical analysis was carried out using Design-Expert® software. Analysis of variance (ANOVA) was employed to determine the significance of model terms, while response surface methodology and desirability functions were used for optimization.

Differences were considered statistically significant at **$p < 0.05$** .

3. RESULTS AND DISCUSSION

3.1 Preformulation Studies

Preformulation studies were conducted to establish the physicochemical properties of Prazosin hydrochloride and to select suitable excipients for the preparation of lipid polymer hybrid nanoparticles. The calibration curve prepared in phosphate buffer (pH 7.4) demonstrated excellent linearity within the selected concentration range, confirming the suitability of the



analytical method for quantitative estimation of the drug. FTIR analysis of the pure drug showed characteristic absorption peaks corresponding to its functional groups, confirming its identity and purity before formulation development.

Figure 1: FTIR of Pure drug

3.2 Screening of Lipid Components

Selection of an appropriate lipid plays a crucial role in determining drug loading, nanoparticle stability, and release characteristics. Solubility screening revealed that the selected lipid provided higher solubilization of Prazosin hydrochloride than the other screened lipids, enabling efficient incorporation into the lipid-polymer hybrid matrix.

The selected lipid also promoted formation of stable nanoparticles during the self-assembly process and minimized drug leakage during preparation. The highest solubility of Prazosin was observed in soya lecithin.

Table 2: Screening of Solid lipids

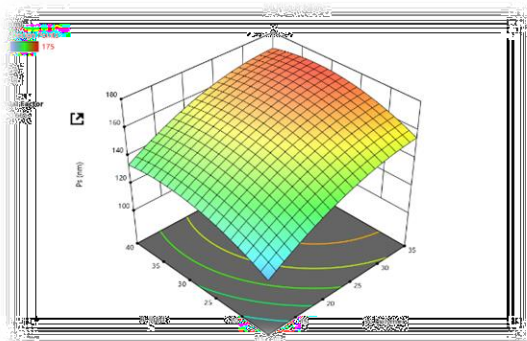
S. No	Solid lipid	Solubility
1	Soya lecithin	26.50 mg
2	Stearic acid	20.60 mg
3	Palmitic acid	18.50 mg

3.4 Effect of Formulation Variables on Particle Size

Particle size is one of the most important quality attributes affecting dissolution rate, intestinal absorption, and nanoparticle stability.

Response surface analysis demonstrated that increasing polymer concentration increased particle size because of greater viscosity of the organic phase and increased polymer deposition during nanoprecipitation. Likewise, excessive lipid concentration produced slightly larger nanoparticles due to formation of a thicker lipid shell around the polymeric core.

PEG 6000 acted as a stabilizer and minimized aggregation by providing steric stabilization. At optimized concentrations, PEG produced nanoparticles with narrow size distribution and improved colloidal stability. The developed quadratic model accurately predicted particle size within the design space, indicating excellent model adequacy.

**Figure 2: Response of Particle Size by 3D Surface plot**

3.5 Effect of Formulation Variables on Zeta Potential

Zeta potential determines electrostatic stability of colloidal dispersions and influences nanoparticle interaction with biological membranes.

The prepared formulations exhibited adequate surface charge, indicating good colloidal stability. The optimized formulation showed a sufficiently high zeta potential to prevent particle aggregation during storage.

Positive surface charge is advantageous because it facilitates interaction between nanoparticles and negatively charged intestinal mucosa, thereby promoting prolonged residence time and improved intestinal uptake following oral administration.

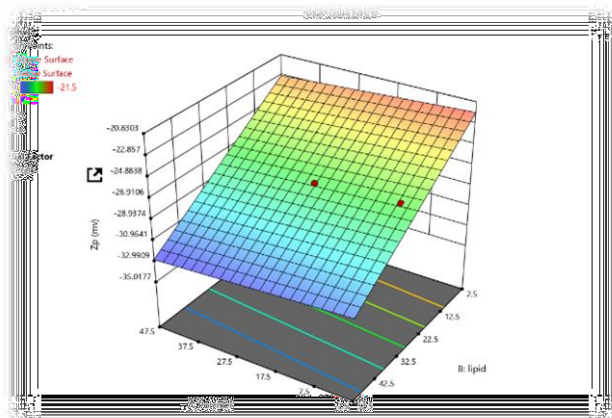


Figure 3: Response of Zetapotential by 3D Surface plot

3.6 Effect of Formulation Variables on Entrapment Efficiency

Entrapment efficiency reflects the capability of nanoparticles to successfully encapsulate the drug within the polymer-lipid matrix.

Increasing lipid concentration enhanced drug entrapment by providing a larger hydrophobic environment for incorporation of Prazosin hydrochloride. Similarly, increasing polymer concentration reduced drug diffusion into the external aqueous phase, thereby improving encapsulation efficiency.

However, excessive polymer concentration increased formulation viscosity and slightly reduced encapsulation efficiency because of incomplete solvent diffusion during nanoprecipitation. The optimized formulation exhibited high drug entrapment, demonstrating effective encapsulation within the lipid-polymer hybrid system.

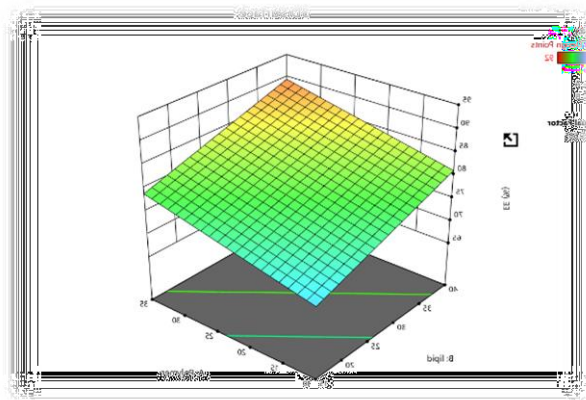


Figure 4: Response of Entrapment efficiency by 3D Surface Plot

3.7 Numerical Optimization and Model Validation

Numerical optimization using the desirability function successfully identified an optimized formulation possessing the desired balance between minimum particle size, maximum zeta potential, and maximum entrapment efficiency. Experimental validation confirmed close agreement between predicted and observed values, demonstrating the reliability and predictive capability of the generated mathematical models.

The small percentage prediction error confirmed that Central Composite Design is an efficient statistical approach for optimization of lipid polymer hybrid nanoparticles.

Table 3: Optimization of formulation based on numerical optimization technique

A: Polymer (X1)	B:lipid (X2)	C: Tween 80 (X3)	Particle size (nm)	Entrapment Efficiency EE (%)	Zeta potential (mv)
10mg	40 mg	0.93 ml	125.315	83.27	-31.2264

3.8 Surface Morphology

Scanning Electron Microscopy (SEM) demonstrated that the optimized nanoparticles possessed smooth surfaces, nearly spherical morphology, and minimal aggregation.

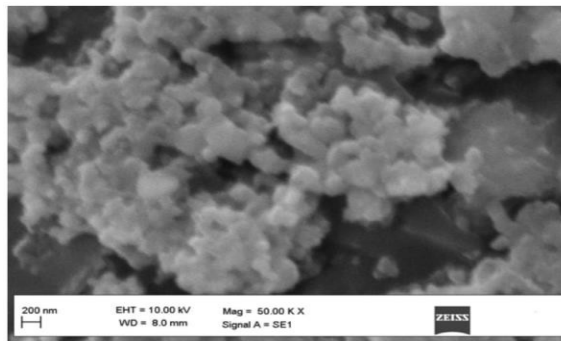


Figure 5: SEM image of LPHNs of Prazosin HCl

Transmission Electron Microscopy (TEM) further confirmed the spherical architecture of the nanoparticles and revealed a distinct lipid layer surrounding the polymeric core, consistent with the structural characteristics of lipid polymer hybrid nanoparticles.

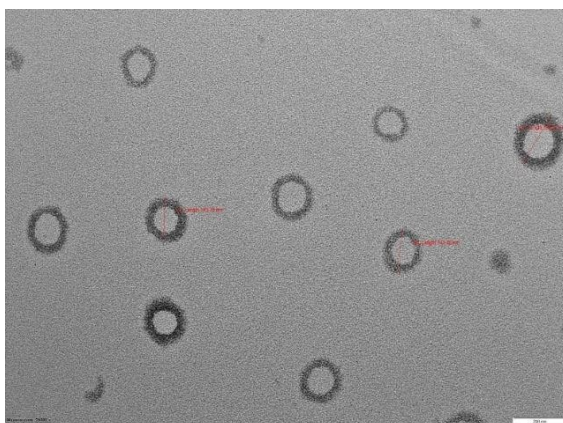


Figure 6: TEM image of LPHNs of Prazosin HCl

The observed particle dimensions closely agreed with Dynamic Light Scattering measurements, confirming successful preparation of uniformly dispersed nanosized particles.

3.9 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra of the optimized formulation retained the characteristic absorption bands of Prazosin hydrochloride without the appearance of additional peaks or significant spectral shifts.

These observations indicate that no chemical interaction occurred between the drug and formulation excipients during nanoparticle preparation.

Minor reductions in peak intensity were attributed to successful encapsulation of the drug within the polymeric matrix rather than chemical degradation. Overall, FTIR analysis confirmed excellent compatibility between formulation components.



Figure 7: FTIR of Pure drug and Optimized LPHNs of Prazosin HCl

3.10 Differential Scanning Calorimetry (DSC)

DSC thermograms of pure Prazosin hydrochloride exhibited a sharp melting endotherm corresponding to its crystalline nature.

The optimized lipid polymer hybrid nanoparticles demonstrated a marked reduction in peak intensity together with broadening of the melting transition, indicating conversion of the crystalline drug into an amorphous or molecularly dispersed state within the nanoparticle matrix.

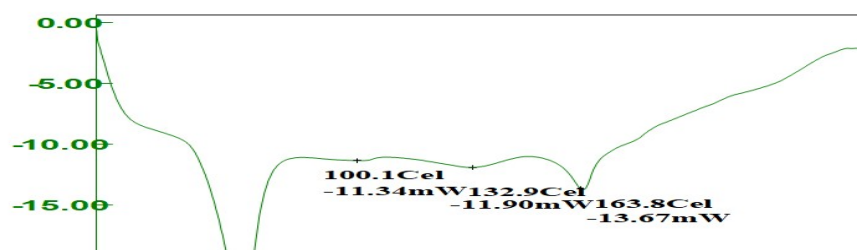


Figure 8: DSC of optimized LPHNs of Prazosin HCl

Reduction of crystallinity is advantageous because amorphous drug forms generally exhibit improved dissolution characteristics and enhanced oral bioavailability.

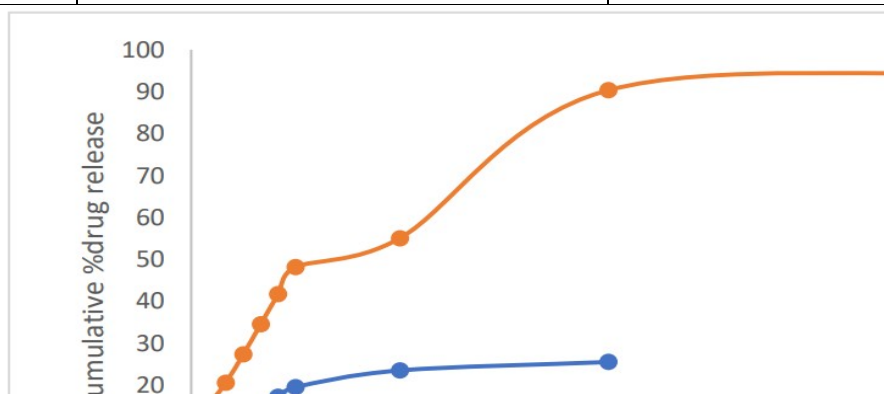
3.11 In Vitro Drug Release

The optimized PRZ-LPHNs demonstrated sustained release of Prazosin hydrochloride over the study period.

Compared with the pure drug suspension, which exhibited relatively rapid release followed by incomplete dissolution, the optimized nanoparticles provided gradual and controlled drug release.

Table 4: Cumulative % DR of PRAZOSIN HCl pure drug and optimized LPHNs formulation

Time(h)	Cumulative % drug release	
	Prazosin HCl pure drug	Prazosin HCl LPHNs formulation
0	0	0
0.5	5.1211	7.11306
1	8.05518	14.7174
2	8.60026	20.6326
3	9.94616	27.389
4	10.82099	34.5424
5	17.22072	41.6958
6	19.5558	48.1898
12	23.5464	55.0538
24	31.5518	90.3564

**Figure 9: % cumulative drug release profile of Prazosin HCl drug suspension and LPHNs formulation**

The sustained release behavior is attributed to diffusion of the drug through both the polymeric core and lipid shell together with gradual polymer relaxation. Such controlled release is expected to maintain therapeutic plasma concentrations for extended periods and reduce dosing frequency.

3.12 Drug Release Kinetics

Release data were fitted into Zero-order, First-order, Higuchi, Hixson–Crowell, and Korsmeyer–Peppas kinetic models.

Among these mathematical models, the optimized formulation exhibited the highest correlation coefficient for the Korsmeyer–Peppas model, indicating that drug release was predominantly governed by anomalous (non-Fickian) diffusion involving both diffusion and polymer relaxation mechanisms.

Table 5: Correlation coefficient (R²) values of different orders

	Zero-order	First order	Higuchi	Hixson Crowell	Korsemeyer Peppas	Release exponent(n)
Pure Prazosin HCl	0.8909	0.8604	0.8431	0.8194	0.9464	0.3789
Prazosin loaded LPHNs	0.9623	0.8423	0.9413	0.9282	0.9546	0.5289

This release behavior is desirable because it provides prolonged therapeutic drug release while minimizing fluctuations in plasma drug concentration.

3.13 Ex Vivo Intestinal Permeation Study

Ex vivo permeation studies demonstrated significantly greater intestinal transport of Prazosin hydrochloride from lipid polymer hybrid nanoparticles than from the pure drug suspension.

Enhanced permeation can be attributed to several synergistic factors:

- Nanoscale particle size increasing surface area.
- Improved wetting and dissolution due to the lipid shell.
- Enhanced mucoadhesion resulting from interaction with intestinal mucus.
- Controlled release maintaining the concentration gradient across intestinal tissue.
- Improved transport through intestinal epithelial pathways.

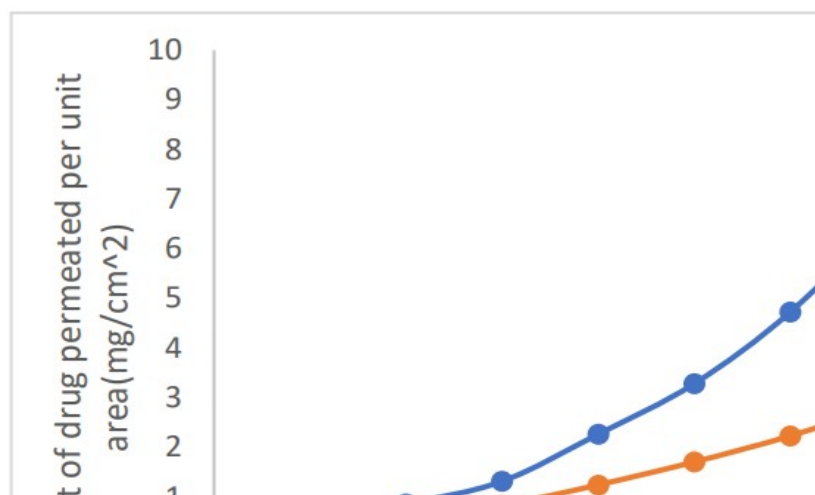


Figure 10: Ex vivo cumulative drug release of Prazosin HCl pure drug and optimized Prazosin.HCL LPHNs

Collectively, these findings indicate that lipid polymer hybrid nanoparticles have considerable potential for enhancing oral bioavailability of Prazosin hydrochloride by overcoming dissolution and permeability limitations associated with conventional formulations.

4. SUMMARY AND CONCLUSION

The present investigation successfully developed and optimized Prazosin hydrochloride-loaded lipid polymer hybrid nanoparticles (PRZ-LPHNs) using the self-assembly nanoprecipitation technique combined with Central Composite Design. The application of Response Surface Methodology enabled systematic optimization of formulation variables and established their influence on critical quality attributes, including particle size, zeta potential, and entrapment efficiency. The optimized formulation demonstrated desirable physicochemical characteristics, confirming the effectiveness of the selected formulation strategy.

The optimized PRZ-LPHNs exhibited nanosized particle dimensions with a narrow size distribution, satisfactory surface charge, and high drug encapsulation efficiency. FTIR and DSC studies confirmed compatibility between Prazosin hydrochloride and formulation excipients while demonstrating successful encapsulation of the drug within the lipid-polymer hybrid matrix. SEM and TEM analyses revealed uniformly distributed spherical nanoparticles with smooth surfaces, confirming the successful formation of a stable hybrid nanocarrier system.

The optimized formulation produced sustained drug release over an extended period compared with the pure drug suspension, while kinetic modeling indicated that drug release followed a diffusion-controlled mechanism involving both diffusion and polymer relaxation. Ex vivo

intestinal permeation studies demonstrated significantly improved drug transport across intestinal tissue, suggesting enhanced oral absorption and bioavailability. The improved performance can be attributed to the combined effects of nanoscale particle size, enhanced wettability, controlled drug release, and efficient interaction of the lipid shell with the intestinal membrane.

Overall, lipid polymer hybrid nanoparticles prepared using the self-assembly nanoprecipitation method represent a promising oral drug delivery platform for Prazosin hydrochloride. The optimized formulation successfully addressed the limitations associated with poor aqueous solubility and limited oral bioavailability while providing sustained drug release and improved intestinal permeation. These findings indicate the potential of lipid polymer hybrid nanoparticles as an advanced nanocarrier system for improving the therapeutic efficacy of poorly water-soluble antihypertensive agents. Future investigations should include long-term stability studies, pharmacokinetic evaluation, scale-up optimization, and clinical assessment to facilitate successful translation of this formulation into pharmaceutical applications.

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