Ind. J. Pharm. Edu. Res., 2026; 60(4):1409-1415.
https://www.ijper.org

Original Article

Development and Characterization of Ranolazine-Loaded Solid Lipid Nanoparticles for Enhanced Angina Therapy

Prasanna Shirgaonkar[1], Rutuja Chougale[2], Kiran Patil[1,*], Vibhuti Thakur[1], Firoj Tamboli[3], Somnath Bhinge[4], Shailendra Gurav[5]

[1]Department of Pharmaceutical Quality Assurance, Tatyasaheb Kore College of Pharmacy, Warananagar, Warana University, Warananagar, Kolhapur, Maharashtra, INDIA.
[2]Department of Pharmaceutics, Bharati Vidyapeeth College of Pharmacy, Near Chitranagari, (Affiliated to Shivaji University), Kolhapur, Maharashtra, INDIA.
[3]Department of Pharmacognosy, Bharati Vidyapeeth College of Pharmacy, Near Chitranagari (Affiliated to Shivaji University), Kolhapur, Maharashtra, INDIA.
[4]Department of Pharmaceutical Quality Assurance, Krishna Institute of Pharmacy, Krishna Vishwa Vidyapeeth (Deemed to be University), Karad, Maharashtra, INDIA.
[5]Department of Pharmacognosy and Phytochemistry, Goa College of Pharmacy, Goa University, Goa, INDIA.

ABSTRACT

Background: The study focuses on the development and characterization of Ranolazine-loaded Solid Lipid Nanoparticles (RNZ-SLNs) to enhance therapeutic efficacy and safety in angina therapy. **Materials and Methods:** RNZ-SLNs were synthesized using a heated homogenization process followed by ultrasonication. The formulation was characterized for particle size, zeta potential, % entrapement efficiency, and *in vitro* drug release profile. Biocompatibility was evaluated using *in vitro* hemolysis studies. **Results and Discussion:** The results of the study demonstrated that the formulated Ranolazine-loaded Solid Lipid Nanoparticles (RNZ-SLNs) exhibited favorable physicochemical properties essential for effective drug delivery. The particle size of the RNZ-SLNs was found to be 254.1±2.4 nm, indicating their suitability for nanoparticle-based drug delivery systems. The zeta potential of -15.3±1.8 mV reflected sufficient stability of the formulation, while the % entrapement efficiency of 75.15±3.1% confirmed the effective incorporation of Ranolazine within the lipid matrix. The *in vitro* drug release profile revealed a significantly enhanced release rate for RNZ-SLNs, achieving 61.807±2.51% over 24 hr, compared to the plain Ranolazine dispersion, which released only 36.807±2.08% within the same period. Furthermore, *in vitro* hemolysis studies indicated a marked improvement in biocompatibility for RNZ-SLNs, with a hemolytic effect of 9.17%, compared to 19.23% observed for plain Ranolazine. These findings collectively highlight the potential of RNZ-SLNs to improve the therapeutic efficacy and safety profile of Ranolazine for angina therapy. **Conclusion:** RNZ-SLNs demonstrated superior therapeutic potential, including improved drug release and biocompatibility, suggesting their promise as an effective and safe delivery system for Ranolazine in angina therapy.

Keywords: Angina, Pluronic F108, Ranolazine, Solid lipid nanoparticles, Stearic acid.

Correspondence:
Dr. Kiran Patil
Department of Pharmaceutical Quality Assurance, Tatyasaheb Kore College of Pharmacy, Warananagar, Warana University, Warananagar, Kolhapur, Maharashtra, INDIA.
Email: kspatil.tkcp@gmail.com
ORCID: 0000-0002-3248-6063

Received: 15-12-2025;
Revised: 09-01-2026;
Accepted: 27-03-2026.

INTRODUCTION

Angina, a common cardiovascular condition, occurs due to reduced blood supply to the heart muscles, leading to chest pain or discomfort.[1] It is a key indicator of coronary artery disease, which involves the narrowing or blockage of blood vessels supplying oxygen and nutrients to the heart.[2] Angina affects quality of life and raises the risk of serious events, highlighting the need for effective treatments.

Ranolazine (RNZ), a Biopharmaceutics Classification System (BCS) class II drug, has shown promise in treating angina by selectively inhibiting the late sodium current in heart cells, reducing myocardial oxygen demand.[3] This helps alleviate chest pain and improve exercise tolerance without significantly affecting heart rate or blood pressure, making it suitable for patients with cardiovascular comorbidities.[4]

Despite its potential, RNZ faces challenges due to poor water solubility and a short duration of action, leading to reduced absorption and frequent dosing.[5] Previous efforts to enhance RNZ's pharmaceutical properties include the development of cubosomes, which improved solubility and sustained drug release but faced issues like environmental sensitivity and difficulties in large-scale production.[6] Similarly, solid dispersions

DOI: 10.5530/ijper.20261392

with hydrophilic polymers like Soluplus improved solubility but encountered problems with drug release and stability.

A study aimed to enhance RNZ solubility using solid dispersions with hydrophilic polymers (HPMC, PEG 6000, PVPK 30K, Soluplus). Soluplus showed the highest solubility, with a 10-fold increase in solubility and dissolution rate. However, challenges included inadequate drug release, instability, poor solubility with PEG 6000, and excipient incompatibilities. PVP K30 had limited solubility and caused degradation. Soluplus formulations faced manufacturing difficulties and failed to achieve the desired drug release, affecting stability and bioavailability.[7]

In addition to enhancing solubility through solid dispersions, another research which focused on developing a solid Self-Emulsifying Drug Delivery Systems (SEDDS) for RNZ to improve its oral bioavailability. This suggests that SEDDS could be the best approach to enhance the oral bioavailability of RNZ, thereby improving therapeutic efficacy.[8] However, SEDDS face various challenges during their formulation and development. Drug precipitation, emulsion instability, and incompatibility with excipients can impact their effectiveness and stability. Scaling up SEDDS from laboratory to commercial production poses additional complexities, and their rapid self-emulsification in the gastrointestinal environment may affect drug release profiles.

Solid Lipid Nanoparticles (SLNs) are an advanced nanotechnology used in pharmaceutical research, composed of biocompatible lipids in a solid state at room temperature. SLNs enhance drug solubility, making them a promising option for delivering hydrophobic drugs like Ranolazine to treat angina.[9] By encapsulating RNZ in a lipid matrix, SLNs provide controlled, sustained drug release, prolonging its therapeutic effect and reducing dosing frequency. The high surface area-to-volume ratio of SLNs also improves drug loading and absorption, optimizing RNZ's efficacy in angina management.[10]

This research focuses on the formulation and characterization of Ranolazine-loaded Solid Lipid Nanoparticles (RNZ-SLNs) as a novel drug delivery system to enhance its bioavailability. By optimizing the release kinetics, SLNs can provide controlled and sustained drug release, potentially reducing dosing frequency and minimizing side effects. Improved drug delivery via SLNs is expected to enhance the therapeutic efficacy of Ranolazine in angina management, offering more consistent plasma drug levels and better symptom control. Ultimately, this approach aims to contribute to improved clinical outcomes and patient care by addressing the limitations of conventional drug formulations.

MATERIALS AND METHODS

Materials

RNZ was procured from Yarrow Chem Products, Mumbai. Pluronic F108 was obtained from Sigma-Aldrich, and stearic acid was obtained from Molychem Lab, Mumbai. Soya lecithin, Methanol, Chloroform, and DW were purchased from Fine Chemical, Mumbai.

Methods

Solubility studies

Achieving optimal % and drug loading in SLNs requires careful selection of lipids and surfactants. RNZ's solubility in various surfactants was tested by dissolving excess drug in each surfactant, vortexing, and agitating for 72 hr, followed by centrifugation and UV spectroscopy analysis of the supernatants. These solubility studies helped identify suitable surfactants for formulating RNZ-loaded SLNs, optimizing the drug delivery system.[11]

Ranolazine-loaded Solid Lipid Nanoparticle preparation and optimization

A Ranolazine-loaded Solid Lipid Nanoparticle (RNZ-SLN) formulation was developed using the solvent evaporation method. RNZ was dissolved in methanol (Mixture A), while stearic acid and Pluronic F 108 were dissolved in chloroform (Mixture B). Both mixtures were combined, followed by the addition of soya lecithin. Using a rotary evaporator, the solvent was removed at 70 °C, forming a thin lipid film. To produce SLNs, an aqueous solution was added to the film, which was then homogenized for 10 min.[12]

A 3^2 full factorial design optimized the formulation, with lipid amount (X_1) and PF108 concentration (X_2) as the independent variables. The response variables assessed were % entrapment efficiency (%EE) (Y_1) and particle size (Y_2). Initial screening set the variable levels at -1, 0, and +1. This was performed using Design Expert® VR software (Version 13) to identify optimal conditions for the formulation.

Characterization of RNZ-SLN

percent entrapment efficiency

To determine the %EE in SLNs, a single mL of RNZ-SLN was diluted by using methanol of 10 mL and then centrifuged. The supernatant obtained after centrifugation was spectrophotometrically examined at 273 nm to evaluate the RNZ content.[13] It was calculated with the help of the following formula by substituting the relevant values:

$$\%EE = \frac{Weight\ of\ drug\ in\ SLN}{Weight\ of\ drug\ taken\ initially} \times 100 \quad \ldots\ldots (1)$$

Particle size and zeta potential

Particle size and zeta potential was measured using a Horiba SZ-100 analyzer (version 2.40), with each measurement repeated three times at 25±5°C. This characterization is essential for assessing the stability, dispersibility, and potential therapeutic efficacy of RNZ-SLNs, providing key data for optimizing their formulation.[14]

TEM and SEM Analysis

The morphology of RNZ-SLNs was analyzed using a Jeol JM 2100 TEM. For sample preparation, a small volume of RNZ-SLN suspension was placed on a nitrocellulose-coated copper plate and followed for ambient temperature for 12 hr. The samples were then subsequently treated with 2% w/v phosphotungstic acid. This staining technique improved the visibility of structural features, aiding in the accurate assessment of particle size and morphology.[15]

SEM analysis was done by taping the sample to a brass stump using double-sided glue. To ensure electrical conductivity, it was then plated with a thin layer of platinum. This conductive coating was applied to minimize charging under the electron beam while also boosting image quality by increasing resolution and contrast.[16]

Drug-excipient Compatibility Study

Fourier transform infrared spectroscopy (FTIR)

FTIR spectroscopy was employed to evaluate the compatibility of RNZ with PF108, lipid, and soya lecithin, identifying potential interactions and confirming the chemical stability and integration of the components. This spectrum was analyzed for both pure RNZ and the optimized RNZ-SLN mixture using the FTIR instrument (Agilent Alpha 100508), from range 4000 to 400 cm^{-1}.[17]

Differential scanning calorimetry analysis

It is used to check the thermal responses and correlations of plain RNZ and optimized RNZ-SLN formulations. The analysis was performed using an instrument (SDT Q600 V20.9 Build 20) under an atmosphere of dry nitrogen to prevent oxidation and other atmospheric effects. The thermograms were obtained by heating the RNZ and SLN samples from 0°C to 500°C at a controlled rate of 10°C/min. An empty aluminum pan served as the reference during the analysis, ensuring accurate measurement of thermal transitions.[18]

Powder X-ray diffraction analysis

It was conducted to investigate potential drug-carrier interactions, with diffractograms of pure RNZ and optimized RNZ-SLN obtained using an X-ray Diffractometer (Bruker D8 Advance). Scans were taken in 0.02° increments from 5° to 60° (2θ) with a step time of 1 second per increment, using a zero-background holder for accuracy.[19]

In vitro drug release study

The dialysis tube method using a 12,000 Da MWCO bag was employed to assess RNZ release. The bag containing RNZ was immersed in PBS (pH 7.4) with 0.5% Tween 80, stirred at 37±2°C. Samples were taken at intervals, replaced with fresh buffer, and analyzed spectrophotometrically at 273 nm. For RNZ-SLN, samples were centrifuged, sonicated, and tested. The experiment was repeated three times to ensure reproducibility, providing a precise evaluation of drug release kinetics over time.[20]

In vitro hemolysis study

To assess RNZ-SLN safety, RNZ and RNZ-SLN solutions at 50 µg/mL were added to 2% erythrocyte dispersion, diluted with NaCl (0.9%), and incubated at 37°C for 1 hr. The samples were then centrifuged at 1000 rpm for 10 min. Hemolysis was measured by UV at 420 nm, evaluating the formulations' hemocompatibility and safety for *in vivo* use.[21] Hemolysis percentage was calculated using the appropriate formula:

$$\%hemolysis = \frac{Abs\ of\ sample - Abs\ of\ negative\ control}{Abs\ of\ positive\ control - Abs\ of\ negative\ control} \times 100 \quad \ldots\ldots (2)$$

Lyophilization of RNZ-SLN

Process for lyophilization of RNZ-SLN

A 1-mL volume of the RNZ-SLN formulation was combined with 15% (w/v) lactose and poured into 3 mL vials made of glass. The vials were first frozen for 12 hr at -20°C. Then lyophilized at -42°C and -50°C under a vacuum of 0.1 mBar for 48 hr. The dry mixture was subjected to a vacuum of 0.06 mBar for 12 hr to ensure thorough dehydration. Following this, it was vacuum sealed to maintain its stability and prevent moisture absorption, thereby preserving its integrity for subsequent applications or analysis.[15]

RESULTS

Screening of surfactants for RNZ solid lipid nanoparticles

Selecting the right surfactant is crucial for SLN properties like % efficiency and drug loading. For oral delivery, GRAS surfactants are preferred. Solubility screening of Pluronic F108, Soya lecithin, Tween 80, and Span 80 identified Pluronic F108 and Soya lecithin as having the highest solubility. These two were thus chosen for formulating RNZ-SLNs.[22]

RNZ-SLN preparation and optimization

Initial experiments were conducted, focusing on optimizing the formulation based on two factors: stearic acid concentration (X_1) and PF108 (X_2). The impacts of these variables on the percent EE as well as the particle size (PS) were investigated. The findings are given in Table 1.

Among the nine batches, batch P5 was identified as the optimal formulation due to its high encapsulation efficiency of 69.0±2.7%. Additionally, it exhibited a small particle size of 212.0±2.4 nm.

Effect of formulation variables on %EE

The %EE of RNZ-SLNs varied from 32.4±0.9% to 69.0±2.7%, with stearic acid and PF108 concentrations initially improving efficiency, but decreasing beyond optimal levels (19.88 mg for stearic acid and 136 mg for PF108). The regression model

Table 1: 3^2 factorial design batches and results of their characterization.

Formulation code	Drug (mg)	Factor 1 (X_1) Conc. of Stearic acid (mg)	Factor 2 (X_2) Conc. of PF108 (mg)	Response 1 (Y_1) Particle size (nm)	Response 2 (Y_2) %EE (%)
P1	10	13.25	102	264.8±1.2	32.4±0.9
P2	10	13.25	136	228.6±2.3	55.8±1.2
P3	10	13.25	170	259.5±1.4	44.6±3.7
P4	10	19.88	102	252.9±1.8	42.7±1.7
P5	10	19.88	136	212.0±2.4	69.0±2.7
P6	10	19.88	170	281.4± 3.1	37.2±3.4
P7	10	26.51	102	268.2±2.9	60.9±1.5
P8	10	26.51	136	265.8±3.2	66.6±0.7
P9	10	26.51	170	330.8±3.7	36.8±1.8

Values Mean±SD (n=3).

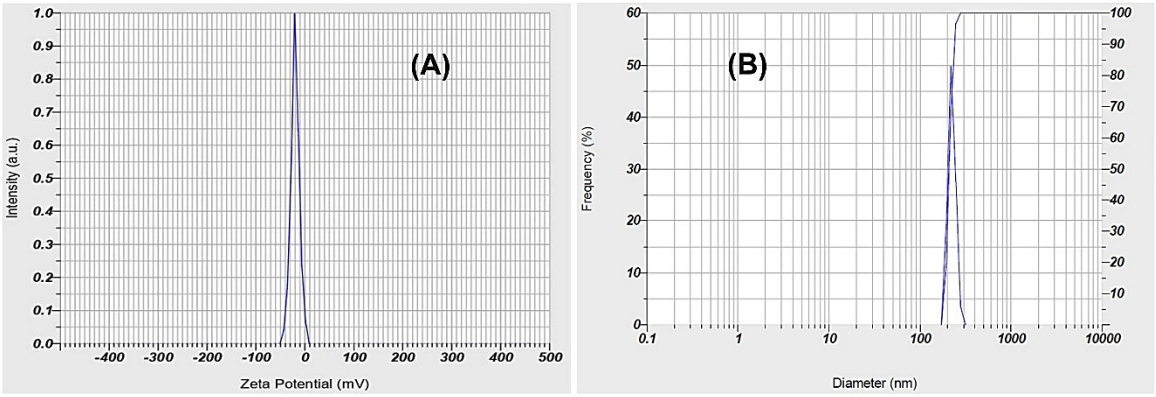

Figure 1: (A) Particle size of optimized Ranolazine-Loaded SLNs (RNZ-SLNs) by Dynamic Light Scattering (DLS) showing particle size distribution. (B) Zeta potential analysis demonstrating the stability of the RNZ-SLNs formulation.

indicates that higher levels of stearic acid (X_1) and PF108 (X_2) reduce %EE, with a statistically significant F-value of 14.76 and p-value<0.05.[18]

$$\%EE = 63.88I+5.24A-2.90B-9.08AB-0.0983A2-21.36B2 \quad \ldots\ldots\ldots\ldots \text{Eq. (1)}$$

Effect of formulation variables on particle size

The particle size of RNZ-SLNs ranged from 212.0±2.4 nm to 330.8±3.7 nm, showing variability in formulation. Increasing stearic acid and PF108 concentrations initially reduced particle size but increased it beyond optimal levels (19.88 mg for stearic acid and 136 mg for PF108). The regression model indicates that higher concentrations of stearic acid (X_1) and PF108 (X_2) increase particle size, with a significant F-value of 25.26 and p-value < 0.05.

$$\text{Particle size} = 221.57I+18.66A+14.32B+17.00AB+20.88A2+40.82B2 \quad \ldots\ldots\ldots\ldots \text{Eq. (2)}$$

Characterization of RNZ-SLN

Particle size and zeta potential

The final batch P5 exhibited a particle size of 212.0±2.4 nm with a PDI of 0.078 and a zeta potential of -19.9±1.7 mV. These metrics, detailed in Figures 1 (A) and (B), reflect excellent colloidal stability and uniformity in the formulation.[23]

Morphology by SEM and TEM

According to Figure 2(A), the TEM images of SLNs were uniformly round, nanometer-sized, and free from aggregation.[24] SEM analysis (Figure 2(B)) revealed that RNZ-SLNs had an irregularly folded and porous spherical shape, likely due to the lipid matrix and manufacturing process.[24]

Drug-excipient compatibility study

FTIR Spectroscopy

FTIR spectra for pure RNZ and the optimized P5 formulation reveal distinct spectral features. The RNZ spectrum shows

characteristic peaks at 2822.455 cm^{-1} (aliphatic C-H stretching), 1684.086 cm^{-1} and 1591.169 cm^{-1} (N-H bending for amine groups), and 1222.076 cm^{-1} and 1251.915 cm^{-1} (C-N stretching). These peaks are also present in the P5 RNZ SLNs spectrum, indicating that the drug's functional groups are preserved in the formulation.[25]

DSC analysis

The DSC analysis of pure RNZ and the P5 batch highlights distinct thermal properties. The thermogram of pure RNZ shows a broad melting point peak at 118.99ºC. In contrast, the excipients used in the P5 formulation exhibit endothermic peaks at 187.75ºC and 227.44ºC. Notably, the RNZ melting point peak is absent in the P5 formulation.[26]

P-XRD analysis

Plain RNZ shows distinct diffraction peaks indicating its crystalline nature. Conversely, for RNZ SLNs, the *P*-XRD pattern exhibited broader peaks with decreased intensities, suggesting that the drug underwent partial amorphization when incorporated into the micellar formulation.[26]

In vitro drug release study

Figure 3 presents the release profiles of RNZ from both the pure RNZ dispersion and RNZ SLNs in a PBS medium. The plain RNZ dispersion shows a slow-release profile, with 36.807±2.08% of the drug released within 24 hr. In contrast, RNZ SLNs exhibit a rapid release behavior, with 61.807±2.51% of the drug released in the same period (p<0.01).[18]

In vitro hemolysis study

This study assessed the hemolytic effects of plain RNZ, blank RNZ SLNs, and optimized RNZ SLNs (P5). The positive control showed complete hemolysis, while the negative control showed minimal hemolysis. Plain RNZ (50 µg/mL) caused more hemolysis compared to both blank SLNs and optimized RNZ SLNs (P5). The *in vitro* hemolysis rates were 19.23% for plain RNZ, 16.47% for blank RNZ SLNs, and 9.17% for optimized RNZ SLNs (P5). The optimized RNZ SLNs (P5) exhibited significantly lower hemolysis (p<0.01) compared to plain RNZ.[16]

Characterization of lyophilized RNZ SLNs

The lyophilized batch of RNZ SLNs with 15% of sucrose as cryoprotectant displayed the following characteristics: a PS of 254.1±2.4 nm, ZP of -15.3±1.8 mV, and 75.15± 3.1 %EE, moisture content of 2.79±0.8%, and a RT is 42±4 sec.[19]

DISCUSSION

The development of Solid Lipid Nanoparticles (SLNs) for the delivery of Ranolazine (RNZ) in the present study was driven by the need to improve the drug's therapeutic efficacy, solubility, and safety profile. Ranolazine, a Biopharmaceutics Classification System (BCS) Class II drug, suffers from poor water solubility and a short half-life, requiring frequent dosing and potentially limiting its effectiveness in angina therapy. Previous efforts to enhance RNZ solubility using various formulations, such as cubosomes, solid dispersions, and SEDDS, showed varying degrees of success but encountered significant challenges such as stability issues, complex preparation, and manufacturing difficulties.

DLS confirmed that the Solid Lipid Nanoparticles (SLNs) are nanoscale, enhancing drug delivery by improving targeting, efficacy, and reducing side effects. They are biocompatible and suitable for both hydrophilic and hydrophobic drugs, enabling controlled and sustained release.

TEM showed that the SLNs were uniformly round and well-dispersed, which is ideal for drug loading and targeted delivery. Scanning Electron Microscopy (SEM) revealed that the

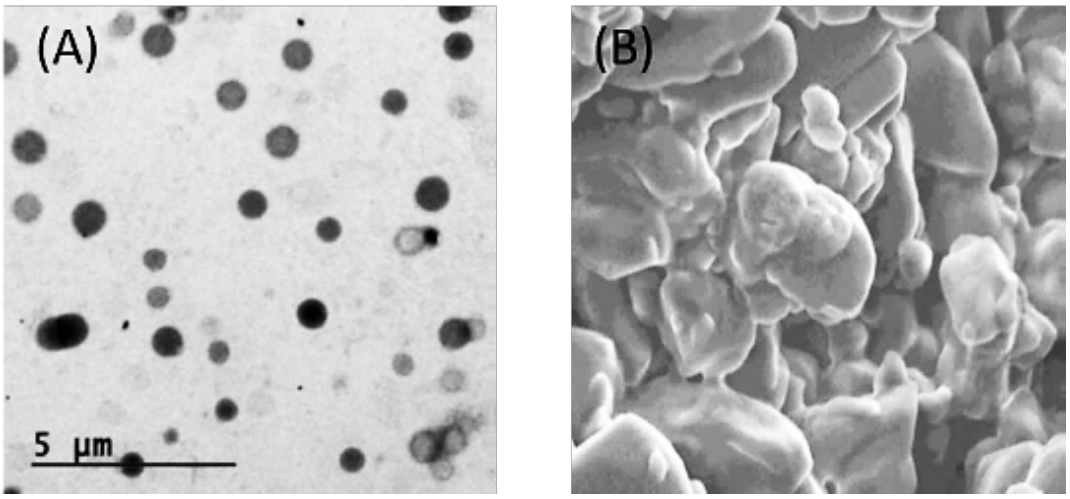

Figure 2: Morphological Analysis of RNZ-SLNs (A) Transmission Electron Microscopy (TEM) image showing the uniform spherical shape and well-dispersed nanoparticles. (B) Scanning Electron Microscopy (SEM) image highlighting the porous structure of RNZ-SLNs, contributing to enhanced drug loading and controlled release.

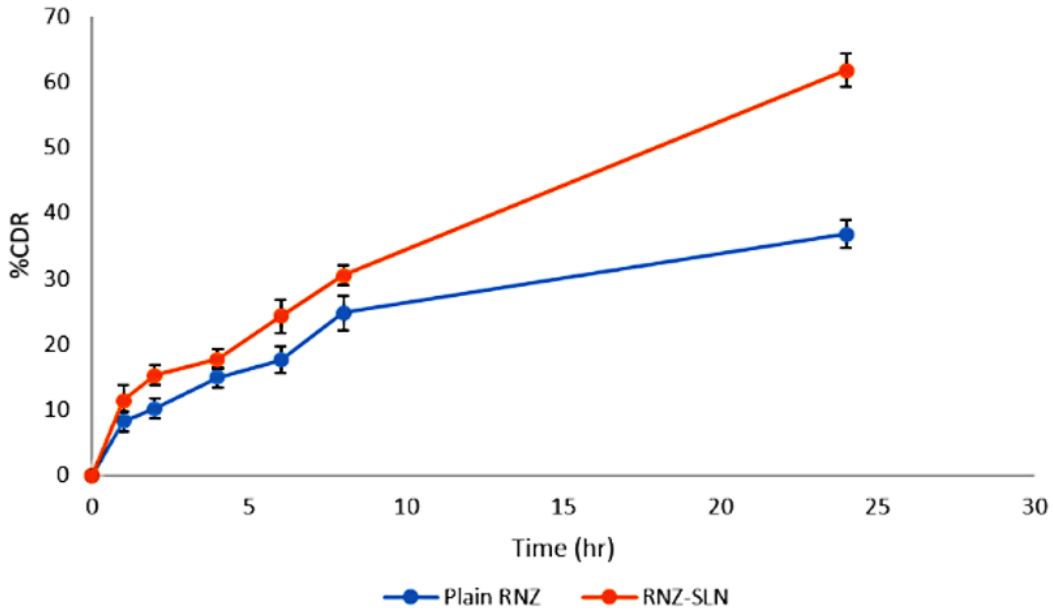

Figure 3: Comparative *in vitro* Drug Release Profile of RNZ-SLNs vs. Plain Ranolazine Dissolution profile of RNZ-SLNs (optimized batch P5) versus plain Ranolazine in Phosphate-Buffered Saline (PBS) at pH 7.4, showing improved drug release kinetics with sustained release over 24 hr.

SLNs had a porous spherical shape, indicating a well-formed lipid matrix crucial for stability.

FTIR confirmed that ranolazine was successfully incorporated into the SLNs without altering its molecular structure, preserving its chemical stability. DSC indicated that ranolazine was either in a disordered crystalline state or molecularly dispersed within the SLNs, suggesting effective entrapment.

The SLNs provided faster drug release compared to plain ranolazine dispersions, leading to quicker symptom relief and improved patient compliance. The hemolysis study showed that the optimized RNZ-SLNs had a lower hemolysis rate, indicating better biocompatibility and safety for intravenous use. The significant reduction in hemolysis rates observed with RNZ-SLNs compared to plain RNZ suggests that the SLN formulation can mitigate the cytotoxic effects associated with ranolazine, making it a safer alternative for intravenous administration. The lyophilization process further ensured the stability and prolonged shelf-life of the SLNs, making them suitable for long-term storage and clinical use. Overall, the study demonstrates the potential of RNZ-SLNs in providing enhanced therapeutic outcomes in angina management by improving drug solubility, stability, and biocompatibility.

Future studies should aim to evaluate the *in vivo* performance of the SLNs, including biodistribution, long-term stability, and therapeutic outcomes. Additionally, exploring alternative lipid matrices or surfactants could further optimize the formulation for different routes of administration or therapeutic targets.

CONCLUSION

This study effectively developed and characterized Ranolazine-loaded Solid Lipid Nanoparticles (RNZ-SLNs), highlighting their potential to enhance the therapeutic efficacy and safety of ranolazine for managing angina. The optimized RNZ-SLNs demonstrated favorable physicochemical attributes. *In vitro* drug release studies revealed a significantly improved drug release from RNZ-SLNs compared to plain RNZ, which is likely due to the increased surface area and enhanced solubility afforded by the lipid matrix. Additionally, the hemolysis study showed lower cytotoxicity for RNZ-SLNs, indicating improved biocompatibility and a safer profile for intravenous use.

Overall, RNZ-SLNs are a potential drug delivery strategy for ranolazine, providing increased solubility, controlled release, as well as decreased hemolytic activity. These findings pave the way for further *in vivo* studies and clinical evaluations to establish the therapeutic benefits of RNZ-SLNs in patients with angina pectoris. The advancements presented in this study highlight the potential of RNZ-SLNs to overcome the limitations of conventional ranolazine formulations, ultimately improving patient outcomes in angina management.

ACKNOWLEDGMENT

The authors sincerely thank Tatyasaheb Kore College of Pharmacy, Warananagar for providing the necessary facilities and support to carry out this research work.

ABBREVIATIONS

BCS: Biopharmaceutics Classification System; **DLS:** Dynamic Light Scattering; **DSC:** Differential Scanning Calorimetry; **EE:** Entrapment Efficiency; **FTIR:** Fourier Transform Infrared Spectroscopy; **MWCO:** Molecular Weight Cut-Off; **PBS:** Phosphate-Buffered Saline; **PDI:** Polydispersity Index; **P-XRD:** Powder X-Ray Diffraction; **RNZ:** Ranolazine; **RNZ-SLNs:** Ranolazine Solid Lipid Nanoparticles; **SEM:** Scanning Electron Microscopy; **SLNs:** Solid Lipid Nanoparticles; **TEM:** Transmission Electron Microscopy; **UV:** Ultraviolet.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

This study developed and characterized Ranolazine-loaded Solid Lipid Nanoparticles (RNZ-SLNs) to enhance therapeutic efficacy and safety for angina therapy. The optimized formulation exhibited a particle size of 212.0±2.4 nm, zeta potential of -19.9±1.7 mV, and encapsulation efficiency of 69.0±2.7%. RNZ-SLNs demonstrated significantly improved drug release (61.807±2.51% over 24 hr) and reduced hemolysis rates (9.17%) compared to plain Ranolazine. Characterization confirmed successful drug incorporation, stability, and ideal morphology for sustained release. These findings suggest RNZ-SLNs as a promising delivery system to overcome the limitations of conventional formulations, warranting further *in vivo* studies.

ETHICAL STATEMENT

This study did not involve human participants or animal subjects. All experiments were conducted in compliance with institutional guidelines for laboratory practices and safety.

REFERENCES

1. Pasternac A, Noble J, Streulens Y, Elie R, Henschke C, Bourassa MG. Pathophysiology of chest pain in patients with cardiomyopathies and normal coronary arteries. Circulation. 1982; 65(4): 778-89.
2. Bhatia SK, Bhatia SK. Coronary artery disease. Biomaterials for Clinical Applications. 2010; 23-49.
3. Guarini G, Huqi A, Marzilli M. Metabolic therapy for the ischemic heart. In: Marzilli M, editor. Cardiac Energy Metabolism in Health and Disease. London: Springer; 2014. p. 237-48.
4. Guarini G, Huqi A, Morrone D, Capozza PF, Marzilli M. Trimetazidine and other metabolic modifiers. Eur Cardiol Rev. 2018; 13(2): 104.
5. Telange DR, Ukey SA, Hemke AT, Umekar MJ, Pethe AM, Kharkar PS. Lipoid SPC-3-based coprecipitates for the enhancement of aqueous solubility and permeability of ranolazine. J Pharm Innov. 2021; 16: 643-58.
6. Mercy P. Formulation, optimization, and characterization of ranolazine-loaded cubosomes for the treatment of angina pectoris [doctoral dissertation]. Chennai (IN): College of Pharmacy, Madras Medical College; 2021.
7. Unnisa A, Chettupalli AK, Alazragi RS, Alelwani W, Bannunah AM, Barnawi J, *et al.* Nanostructured lipid carriers to enhance the bioavailability and solubility of ranolazine: statistical optimization and pharmacological evaluations. Pharmaceuticals. 2023; 16(8): 1151.
8. Desai ND, Mishra S, Chaurasia R, Jat D, More MK, Soni N, Jain DK. Design and evaluation of self-emulsifying mouth-dissolving film of ranolazine by solvent casting method. J Adv Zool. 2023; 44(5): 1433-45.
9. Al-Sayadi GM, Verma A, Choudhary Y, Sandal P, Patel P, Singh D, *et al.* Solid lipid nanoparticles (SLNs): advancements in modification strategies toward drug delivery vehicle. Pharm Nanotechnol. 2023; 11(2): 138-54.
10. Kushwaha AK, Vuddanda PR, Karunanidhi P, Singh SK, Singh S. Development and evaluation of solid lipid nanoparticles of raloxifene hydrochloride for enhanced bioavailability. Biomed Res Int. 2013; 2013: 584549.
11. Potta SG, Minemi S, Nukala RK, Peinado C, Lamprou DA, Urquhart A, *et al.* Development of solid lipid nanoparticles for enhanced solubility of poorly soluble drugs. J Biomed Nanotechnol. 2010; 6(6): 634-40.
12. Nguyen TT, Duong VA. Solid lipid nanoparticles. Encyclopedia. 2022; 2(2): 952-73.
13. Mirchandani Y, Patravale VB, Brijesh S. Solid lipid nanoparticles for hydrophilic drugs. J Control Release. 2021; 335: 457-64.
14. Patil KS, Hajare AA, Manjappa AS, More HN, Disouza JI. Design, development, *in silico*, and *in vitro* characterization of docetaxel-loaded TPGS/Pluronic F108 mixed micelles for improved cancer treatment. J Drug Deliv Sci Technol. 2021; 65: 102685.
15. Kurane A, Chougale R, Thakur V, Patil K, Patki S, D'souza J, *et al.* Design, development, and characterization of lyophilized posaconazole-loaded mixed micelles for improved fungal treatment and stability. FABAD J Pharm Sci. 2024; 49(1): 143-62.
16. Chougale R, Patil K, Disouza J, Hajare A, Jadhav N, Kumbhar P. Development of docetaxel-loaded (Soluplus-PF108) mixed micelles vacuum foam-dried product for improved stability and melanoma treatment by QbD approach. Future J Pharm Sci. 2024; 10(1): 54.
17. Hajare A, Dol H, Patil K. Design and development of terbinafine hydrochloride ethosomal gel for enhancement of transdermal delivery: *in vitro*, in vivo, molecular docking, and stability study. J Drug Deliv Sci Technol. 2021; 61: 102280.
18. Dol HS, Hajare AA, Patil KS. Statistically designed novel ranolazine-loaded ethosomal transdermal gel for the treatment of angina pectoris. J Drug Deliv Sci Technol. 2022; 75: 103574.
19. Kargane S, Chougale R, Mali N, Patil K, Patki S, Disouza J. Statistically developed stable camptothecin-loaded Soluplus/TPGS mixed micelles for improved ovarian cancer treatment. J Dispersion Sci Technol. 2024;[Pagination pending].
20. Sawwashe D, Chougale RD, Gavande G, Patil KS, Patki S. Design, development, and characterization of posaconazole ethosomal *in situ* gel. Thai J Pharm Sci. 2023; 47(4): 5.
21. Winter E, Pizzol CD, Locatelli C, Crezkynski-Pasa TB. Development and evaluation of lipid nanoparticles for drug delivery: study of toxicity *in vitro* and *in vivo*. J Nanosci Nanotechnol. 2016; 16(2): 1321-30.
22. Kovačević AB, Müller RH, Keck CM. Formulation development of lipid nanoparticles: improved lipid screening and development of tacrolimus-loaded nanostructured lipid carriers (NLC). Int J Pharm. 2020; 576: 118918.
23. Shah R, Eldridge D, Palombo E, Harding I. Optimization and stability assessment of solid lipid nanoparticles using particle size and zeta potential. J Phys Sci. 2014; 25(1):[Pagination pending].
24. Hatziantoniou S, Deli G, Nikas Y, Demetzos C, Papaioannou GT. Scanning electron microscopy study on nanoemulsions and solid lipid nanoparticles containing high amounts of ceramides. Micron. 2007; 38(8): 819-23.
25. Göke K, Lorenz T, Repanas A, Schneider F, Steiner D, Baumann K, *et al.* Novel strategies for the formulation and processing of poorly water-soluble drugs. Eur J Pharm Biopharm. 2018; 126: 40-56.
26. Montenegro L, Sarpietro MG, Ottimo S, Puglisi G, Castelli F. Differential scanning calorimetry studies on sunscreen-loaded solid lipid nanoparticles prepared by the phase inversion temperature method. Int J Pharm. 2011; 415(1-2): 301-6.

Cite this article: Shirgaonkar P, Chougale R, Patil K, Thakur V, Tamboli F, Bhinge S, *et al*. Development and Characterization of Ranolazine-Loaded Solid Lipid Nanoparticles for Enhanced Angina Therapy. Indian J of Pharmaceutical Education and Research. 2026;60(4):1409-15.