

Advancing Lovastatin Drug Delivery: Formulation and Evaluation of Polymeric Nanoparticles for Enhanced Bioavailability

Rajeshwar V^{1,*}, Prasanna Kumar Desu², Praveen Kumar CH³, Naga Aparna T⁴, Vasudha B¹

¹Department of Pharmaceutics, School of Pharmacy, Anurag University, Hyderabad, Telangana, India

²Department of Pharmaceutics, Dr Samuel George Institute of Pharmaceutical Sciences, Markapur, India

³Department of Pharmaceutics, Sasikanth Reddy College of Pharmacy, India

⁴Department of Pharmaceutics, Pulla Reddy College of Pharmacy, India

Received February 21, 2025; Revised December 5, 2025; Accepted January 15, 2026

Cite This Paper in the Following Citation Styles

(a): [1] Rajeshwar V, Prasanna Kumar Desu, Praveen Kumar CH, Naga Aparna T, Vasudha B, "Advancing Lovastatin Drug Delivery: Formulation and Evaluation of Polymeric Nanoparticles for Enhanced Bioavailability," *Advances in Pharmacology and Pharmacy*, Vol. 14, No. 2, pp. 175 - 181, 2026. DOI: 10.13189/app.2026.140205.

(b): Rajeshwar V, Prasanna Kumar Desu, Praveen Kumar CH, Naga Aparna T, Vasudha B (2026). *Advancing Lovastatin Drug Delivery: Formulation and Evaluation of Polymeric Nanoparticles for Enhanced Bioavailability*. *Advances in Pharmacology and Pharmacy*, 14(2), 175 - 181. DOI: 10.13189/app.2026.140205.

Copyright©2026 by authors, all rights reserved. Authors agree that this article remains permanently open access under the terms of the Creative Commons Attribution License 4.0 International License

Abstract The present investigation formulated the lovastatin-loaded polymeric nanoparticles (LV-PNPs) by utilizing the modified nanoprecipitation technique. Lovastatin (LV) belongs to the class of BCS type II which has the low solubility and directly affects the bioavailability after oral administration. To overcome this problem LV-PNPs were developed by using chitosan as a polymer and poloxamer 407 as a surfactant. LV-PNPs were formulated by using the different drug: polymer ratios like 2:1, 4:1, 6:1, 8:1 and 10:1. A total of five formulations of LV-PNPs were formulated and evaluated for various evaluation parameters like Particle size, zeta potential, entrapment efficiency (EE), percent yield, drug loading and *in vitro* drug release studies. Later the LV-PNPs were characterized for morphological studies and compatibility studies. Among the total five formulations, LN5 exhibited the lowest particle size i.e., 124 nm, EE was 97.145 and % cumulative drug release was 99.36% over 12 hrs. The drug release from the nanoparticles following the zero-order release kinetics was found by the curve fitting method. Furthermore, morphological studies reveal that LV-PNPs have the spherical shape and porous nature. Drug and excipient compatibility studies validated that there was a lack of drug-polymer interactions. In conclusion, the formulated LV-PNPs increased the solubility and bioavailability at the laboratory level.

Keywords Lovastatin, Chitosan, Polymeric Nanoparticles, Poloxamer 407, Particle Size, *In vitro* Drug Release Studies

1. Introduction

Lovastatin reduces cholesterol levels by reversible and competitive suppression of 3-hydroxy-3-methylglutaryl coenzyme A reductase, an enzyme essential for cholesterol production. It demonstrates low oral bioavailability (G5%) due to fast metabolism in the gastrointestinal tract and liver [1]. Cytochrome P450 3A4 catalyzes the conversion of the lactone form of lovastatin into hydroxy acid and its metabolites. To circumvent hepatic first-pass metabolism and improve bioavailability, the intestinal lymphatic transport of drugs may be utilized. The transport of medications through the intestinal lymphatics via the thoracic duct to the systemic circulation at the confluence of the jugular and left subclavian veins circumvents presystemic hepatic metabolism, hence increasing bioavailability [2]. Highly lipophilic substances, such as long-chain triglycerides, enter systemic circulation through the lymphatic system. Lovastatin, with a water solubility of

0.4×10^{-3} mg/mL, is regarded as a suitable substrate for intestinal lymphatic transport due to its elevated log P value (4.3) and substantial solubility in oils (38 and 42 mg/mL in carbitol and propylene glycol monocaprylate, respectively). Nanoparticle-based drug delivery methods improve the bioavailability of lipophilic drugs like halofantrine and ontazolast through lymphatic transport of biosynthesized chylomicrons linked to the medications. An alternative method for lymphatic transport of nano- and microparticles involves specific absorption by M cells in Peyer's patches. Polymeric nanoparticles enveloped in hydrophobic polymers are readily absorbed by lymphatic cells within the body [3]. Figure 1 represents the structure of lovastatin.

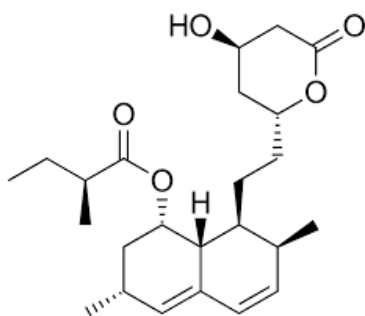


Figure 1. Structure of Lovastatin

In recent years, PNPs have been categorized as biodegradable nanoparticles owing to their excellent entrapment efficiency, controlled release, and reduced toxicity. The nanoprecipitation technique, also known as the solvent displacement method, is a fundamental, quick, and straightforward procedure. The procedure requires the formation of a precipitate from an existing polymer in an organic solution, followed by the diffusion of an organic solvent into an aqueous medium, with or without a surfactant. It requires two water-soluble solvents that do not cause any issues. In an optimal situation, both the polymer and the drug would dissolve in one solvent while remaining insoluble in the other non-solvent. The amalgamation of the polymer solution with the non-solvent triggers a nanoprecipitation process, marked by the swift desolvation of the polymer in the aqueous medium. The polymer precipitates instantly upon the total replacement of the organic solvent with the aqueous medium, leading to the swift trapping of the drug. The rapid creation of a colloidal suspension results from the polymer's accumulation at the interface of the organic solvent and water, aided by the rapid diffusion of the organic solvent. This method is most efficacious for hydrophobic substances that are soluble in ethanol or acetone yet

demonstrate negligible solubility in water [4].

The objective of this study was to formulate and assess lovastatin polymeric nanoparticles utilizing the modified nanoprecipitation technique to enhance the solubility and bioavailability of the drug.

2. Materials and Methods

2.1. Materials

Lovastatin was procured from BMR Chemicals, Hyderabad. Chitosan, sodium tripolyphosphate were obtained from narmadha chemicals, hyderanad. Distilled water was used as the aqueous phase. All chemicals and reagents used were of analytical grade.

2.2. Preparation of LVS-PNPs

The lovastatin-loaded chitosan PNPs were fabricated via a nanoprecipitation technique employing various polymer-to-drug ratios (2:1, 4:1, 6:1, 8:1 and 10:1). Separate beakers were used to dissolve several amounts of chitosan (80, 160, 240, 320, and 400 mg) in a volume of acetone that was around 5mL. The mixture was created by introducing the drug's aqueous solution dropwise into the polymeric organic solution, which was agitated using a magnetic stirrer at 1100 rpm. The solution was subsequently incorporated into 10 mL of an external aqueous solution, agitated, containing 4% (w/v) poloxamer 407 as a suspension stabilizer. Subsequently, the mixture was placed on magnetic stirring for 1 hour at a speed of 600 rpm to removal of the organic solvent. The nanoparticles that had solidified were separated by centrifugation for 45mins at a speed of 1400 rpm. After that, they were washed three times by resuspending them in 5mL of deionized water, and then they were centrifuged to remove any drug that had not been encapsulated [5]. Table 1 summarizes the formulation of nanoparticles in various ratios and nanoparticles preparation is represented in a schematic way in Figure 2.

Table 1. Formulation of Lovastatin Polymeric nanoparticles

Ingredients	LN1	LN2	LN3	LN4	LN5
Lovastatin (mg)	40	40	40	40	40
Chitosan (mg)	80	160	240	320	400
Poloxomar 407 (%w/v)	4	4	4	4	4
Acetone (mL)	5	5	5	5	5
Aqueous Phase (mL)	10	10	10	10	10

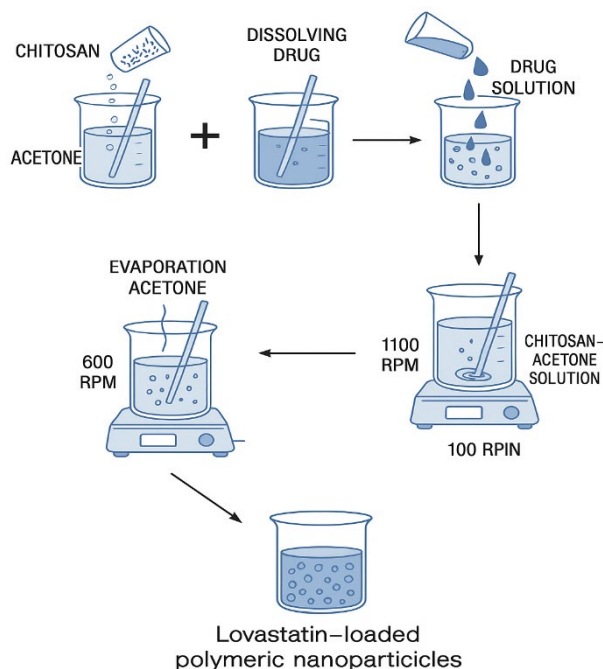


Figure 2. A Schematic diagram of nanoparticles preparation

2.3. Evaluation of LVS-PNPs

2.3.1. Particle Size and Zeta Potential

During the process of conducting the particle size investigation, the technique of dynamic laser scattering was utilized. An instrument called a Zetasizer (Nano ZS, which was manufactured by Malvern Instruments in Malvern, United Kingdom) was utilized in order to ascertain the particle size and PDI of PNPs. In order to make the PNPs suspension more manageable, distilled water was used [6]. Twelve different measurements were taken, and then an average was determined for the outcomes of those measurements.

2.3.2. Entrapment Efficiency

An approach that was not directly involved was utilized in order to determine the effectiveness of the medication's encapsulation within the polymeric nanoparticles. The suspension that contained the PNPs was centrifuged for fifteen minutes at a speed of 1200 revolutions per minute. Following the dilution of the obtained supernatant with methanol, the quantity of free lovastatin was determined by employing a spectrophotometer with a wavelength of 246 nm [7]. The EE was computed using the following formulation:

$$\%EE = \frac{(\text{Amount of drug added in formulation} - \text{Amount present in the supernatant})}{(\text{Amount of drug added in formulation})} \times 100$$

2.3.3. Percentage Yield

In order to determine the amount of nanoparticles that were formed, a comparison was made between the total weight of the nanoparticles that were produced and the

total weight of the copolymer and treatment [8].

$$\% \text{ Yield} = \frac{(\text{Amount of Drug})}{(\text{Amount of drug} + \text{polymer})} \times 100$$

2.3.4. % Drug Load

Following the determination of their mass, drug-loaded PNPs were solubilized in 50 ml of methanol. The medication was sonicated in methanol for 15 minutes to achieve full dissolution. After filtering the solution via Whatman filter paper, the resulting filtrate was subsequently treated with methanol [9]. The aliquot was analyzed at a wavelength of 248 nm using UV-visible spectroscopy to ascertain the concentration of the drug present.

2.3.5. *In vitro* Drug Release Studies

Utilizing the USP-II apparatus, an investigation into the *in vitro* drug release from the formulation was carried out. In order to achieve the desired dissolving medium, a buffered phosphate solution with a pH of 6.8 was utilized. Take use of the nanoparticles that have been manufactured in a variety of different compositions. A buffer solution must be used in place of the 5mL sample. This is a critical step [10]. Through the utilization of a UV-visible spectrophotometer, conduct an analysis of the absorbance at a wavelength of 246 nm.

2.4. Characterization of LVS-PNPs

2.4.1. SEM Study

SEM was employed to examine the morphology of nanoparticles. Prior to conducting the SEM inspection, an initial procedure involved depositing 100 microliters (μl) of the chitosan nanoparticle formulation onto a 10 millimeter (mm) glass slide and permitting it to dry in a vacuum desiccator at ambient temperature for a duration of 24 hours. Nanoparticles were prepared for analysis in a high vacuum evaporator by affixing enough supports, followed by the application of a gold sputter module for gold coating [11]. The inspection was conducted using specialized magnification at 15 kV.

2.4.2. FT-IR Study

The FT-IR spectrophotometer was employed for the drug excipient compatibility testing conducted (Perkin Elmer). Distinct FT-IR examinations of the drug, polymers, and formulations were conducted, and the findings were connected to assess their compatibility [12].

3. Results and Discussion

3.1. Particle Size and Zeta Potential

Nanoparticles displayed a consistent size distribution, with average particle sizes ranging from around 124 to 248

nm. Eudragit, as a positively charged polymer, confers cationic properties to particles, with the zeta potential values of nanoparticles ranging from 24.5 to 32.8 mV. The particle size and zeta potential of the synthesized lovastatin PNPs are presented in Table 2.

Table 2. Evaluation of Formulated Lovastatin nanoparticles

Formulation Code	Particle Size (nm)	Zeta Potential (mv)	Entrapment Efficiency (%)	Drug Loading (%)	% yield
LN1	248	24.5	84.58	48.75	91.2
LN2	210	26.2	88.43	52.63	93.5
LN3	180	28.5	91.78	58.21	95.3
LN4	150	30.1	94.32	63.12	97.1
LN5	124	32.8	97.14	68.75	98.4

3.2. EE, Drug Loading, % Yield

EE, drug loading and % yield are summarized in Table 2. The actual EE was found to increase with the increasing amount of polymer used for the preparation. The EE was, therefore, found to be between 84.58 and 97.14%. Drug loading increased proportionally with polymer content (48.75% to 68.75%). Higher drug loadings of F5 indicate a tighter interaction between the drug and polymeric matrix, leading to higher retention. The % yield of nanoparticles was in the range of 91.2% and 98.4%, showing effective regaining of nanoparticles. The highest yield was observed in F5 i.e., 98.4%, indicating that increased polymer concentration improves nanoparticle manufacturing efficiency. This tendency suggests that a higher eudragit-to-drug ratio enhances polymeric stability and minimizes loss during preparation [13].

3.3. *In vitro* Drug Release Studies

In vitro drug release studies were conducted, cumulative

drug release could be observed at different time intervals like 0.5, 1, 2, 4, 6, 8, 10 and 12 hours and drug release followed the zero order trough out the 12hr period. In F5 formulation, 99.36% drug release was observed in 12 hrs followed by F4 formulation. It indicated that drug release depended on the polymer concentration. The controlled drug release from the formulation indicated that the nanoparticles were effectively formulated by the rate release retardant polymer [14]. The cumulative drug release of all formulations is tabulated in Table 3 and shown in Figure 3.

Table 3. *In vitro* Drug Release of all formulations

Time (hrs)	LN1	LN2	LN3	LN4	LN5
0	0	0	0	0	0
0.5	10.12	12.34	15.67	18.23	22.45
1	20.34	22.78	25.45	28.67	32.12
2	35.12	38.45	42.78	46.90	51.23
4	50.34	51.12	58.78	63.45	69.43
6	65.34	69.67	74.12	78.45	82.78
8	75.12	79.45	84.67	89.12	92.56
10	85.34	89.78	93.45	96.12	98.45
12	91.01	93.45	95.67	97.34	99.36

3.4. SEM Studies

SEM examination revealed that the formulated nanoparticles are porous in nature and spherical in shape. That is clearly observed in Figure 4. So, the spherical shape of the nanoparticles increases the solubility and bioavailability after administration. And also the porous nature revealed that drug release can be regulated and achieve the sustained release characteristic which can also be observed in the *in vitro* drug release studies [15].

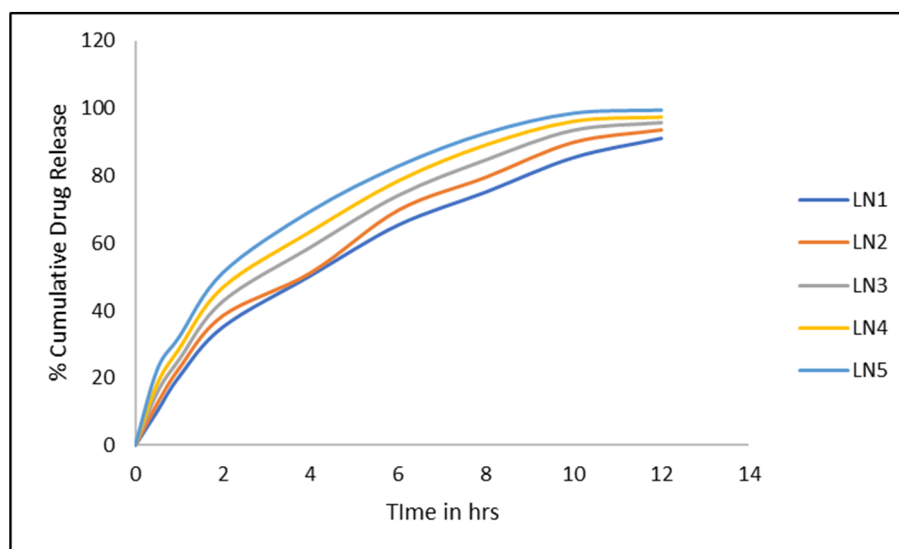


Figure 3. % Cumulative drug release of all formulations

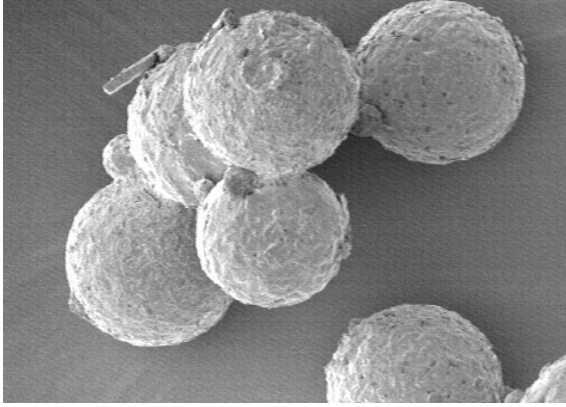


Figure 4. SEM image of F5 formulation nanoparticles

3.5. FTIR Studies

The data from the FT-IR measurements made it very evident that the therapeutic functions, particularly the peak intensities, had not been altered. Based on this information, it appears that the polymer has not created any reactive residues by interacting with the drug at any point during the formulation process [15]. Due to this, it is merely a physical mixture, and there is no interaction between the components. This is a positive aspect since it implies that the formulation process can be carried out without any problems. The FT-IR spectra of the drug and the drug in conjunction with excipients are depicted in Figures 5 and 6, respectively.

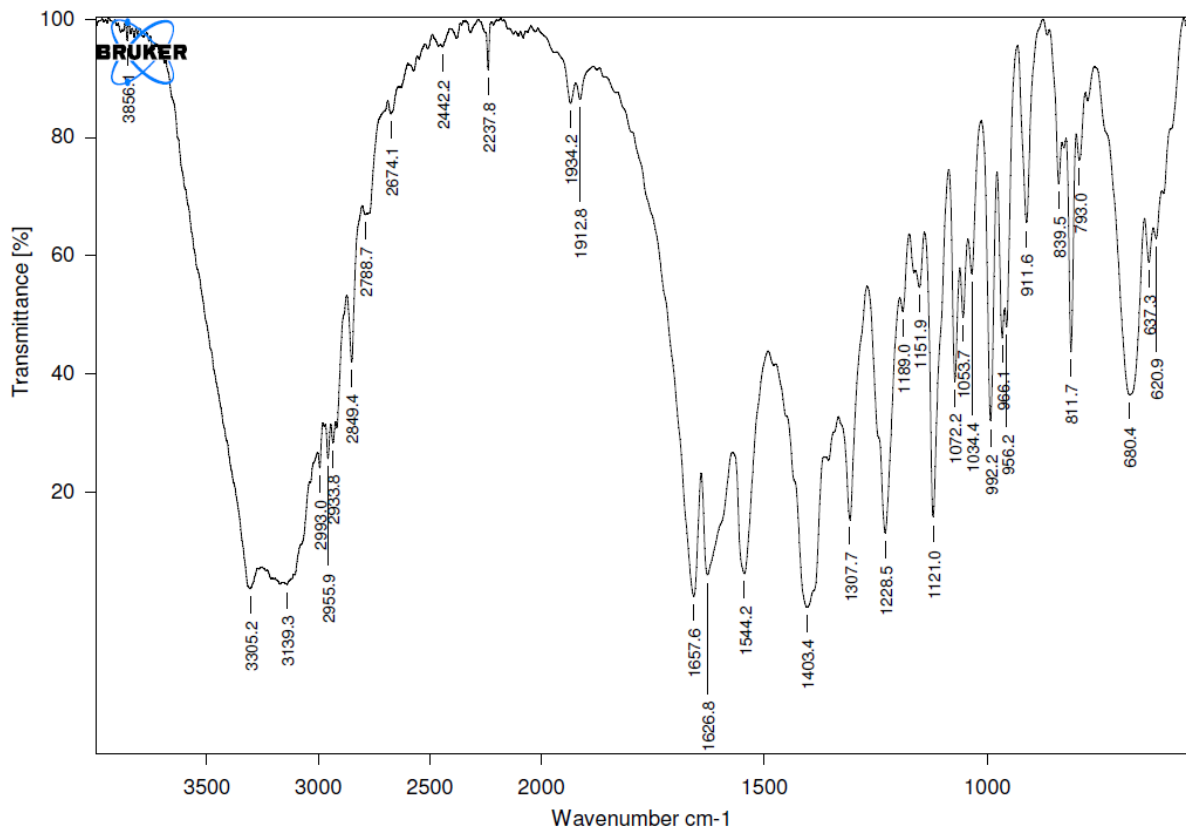


Figure 5. FTIR studies of Pure API

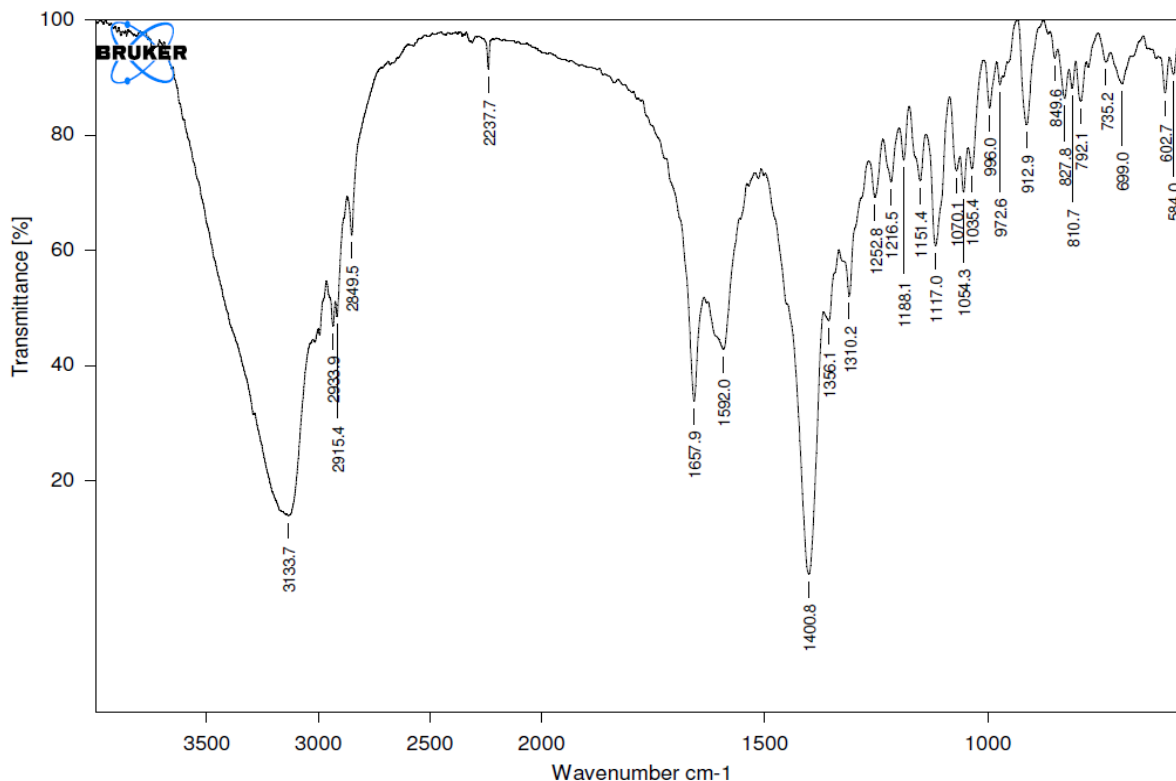


Figure 6. FTIR of Optimized formulation

4. Conclusions

This study effectively developed and assessed lovastatin-loaded chitosan nanoparticles utilizing the nanoprecipitation technique. The optimized formulation (F5) demonstrated the most advantageous attributes, featuring a minimal particle size (124 nm) that enhances surface area and drug solubility, a high entrapment efficiency (97.14%) that guarantees effective drug incorporation, and an improved drug loading (68.75%) that facilitates controlled drug release. The *in-vitro* dissolution investigation demonstrated a sustained drug release profile adhering to zero-order kinetics, with 99.36% drug release attained over 12 hours, indicating its suitability for extended therapeutic applications. The results demonstrate that elevating the polymer concentration markedly improves nanoparticle formation, drug encapsulation efficiency, and dissolution characteristics. The capacity of these nanoparticles to extend drug release while ensuring a consistent and predictable release rate indicates their potential to enhance bioavailability and therapeutic efficacy, positioning them as a promising strategy for sustained drug delivery applications. Subsequent studies must concentrate on *in vivo* pharmacokinetic assessments to substantiate their prospective clinical advantages and determine their viability for pharmaceutical use. This study underscores the efficacy of the nanoprecipitation technique in formulating controlled-release systems for BCS Class II drugs like lovastatin, illustrating its importance in innovative drug delivery mechanisms.

Acknowledgements

We acknowledge all authors for their equal contributions to this work.

Prasanna Kumar Desu: Conceptualization, Formal analysis, Investigation, Methodology, Software, Writing – original draft; **Vasudha B:** Supervision, Project administration, Writing – review & editing; **Naga Aparna T:** Conceptualization, Formal analysis, Investigation, Methodology; **Praveen Kumar CH:** Methodology, Investigation, Data curation; **Rajeshwar V:** Software, Formal analysis, Supervision.

REFERENCES

- [1] Pitsiou G, Zarogoulidis P, Petridis D, Kioumis I, Lampaki S, Organtzis J, et al., "Inhaled tyrosine kinase inhibitors for pulmonary hypertension: a possible future treatment," *Drug Des Dev Ther.*, vol. 8, pp. 1753-1763, 2014.
- [2] Xu X, Khan MA, Burgess DJ, "A quality by design (QbD) case study on liposomes containing hydrophilic API: II. Screening of critical variables, and establishment of design space at laboratory scale," *Int J Pharm.*, vol. 423, no. 2, pp. 543-553, 2012.
- [3] Sylvester B, Porfire A, Muntean DM, Vlase L, Lupuț L, Licarete E, et al., "Optimization of prednisolone-loaded long-circulating liposomes via application of quality by design (QbD) approach," *J Lipos Res.*, vol. 28, no. 1, pp.

- 49-61, 2018.
- [4] ICH. Pharmaceutical development Q8. 1st ed, ICH Harmon Tripart Guidel. 2009, pp. 1–28.
- [5] Labiris NR, Dolovich MB, "Pulmonary drug delivery. Part I: physiological factors affecting therapeutic effectiveness of aerosolized medications," *Br J Clin Pharmacol.*, vol. 56, no. 6, pp. 588-599, 2003.
- [6] ICH Expert Working Group. 1st ed, Quality risk management Q9. ICH Harmon Tripart Guidel. 2005, pp. 1–23.
- [7] Roy B, Guha P, Bhattarai R, Nahak P, Karmakar G, Chettri P, et al., "Influence of lipid composition, pH, and temperature on physicochemical properties of liposomes with curcumin as model drug," *J Oleo Sci.*, vol. 65, no. 5, pp. 399-411, 2016.
- [8] Mahmoud M, Labiba N, Khalil EK, Khalafallah N., "Effect of various formulation variables on the encapsulation and stability of dibucaine base in multilamellar vesicles," *Acta Pol Pharm Drug Res.*, vol. 62, no. 5, pp. 369-379, 2005.
- [9] Kulkarni SB, Betageri GV, Singh M, "Factors affecting microencapsulation of drugs in liposomes," *J Microencapsul.*, vol. 12, no. 3, pp. 229-246, 1995.
- [10] Makrilia N, Lappa T, Xyla V, Nikolaidis I, Syrigos K, "The role of angiogenesis in solid tumours: an overview," *Eur J Intern Med.*, vol. 20, no. 7, pp. 663-671, 2009.
- [11] Poss KD, Keating MT, Nechiporuk A, "Tales of regeneration in zebrafish," *Dev Dynam.*, vol. 226, no. 2, pp. 202-210, 2003.
- [12] Schuermann A, Helker CSM, Herzog W, "Angiogenesis in zebrafish," *Semin Cell Dev Biol.*, vol. 31, pp. 106-114, 2014.
- [13] Eyries M, Siegfried G, Ciumas M, Montagne K, Agrapart M, Lebrin F, et al., "Hypoxia-induced apelin expression regulates endothelial cell proliferation and regenerative angiogenesis," *Circ Res.*, vol. 103, no. 4, pp. 432-440, 2008.
- [14] Rathinasamy VS, Paneerselvan N, Jagadeeshan S, Malathi R., "Hypoxia induced angiogenesis and upregulation of VEGF: an in vivo study using zebrafish model," *Int J Sci Eng Res.*, vol. 6, no. 6, pp. 831-839, 2015.
- [15] Xu H, He C, Liu Y, Jiang J, Ma T., "Novel therapeutic modalities and drug delivery—erlotinib liposomes modified with galactosylated lipid: in vitro and in vivo investigations," *Artif Cell Nanomed B.*, vol. 46, no. 8, pp. 1902-1907, 2018.