RESEARCH PAPER

A Systematic Formulation Approach For The Development Of Olaparib-Loaded Nanostructured Lipid Carriers

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ABSTRACT: Olaparib (OLP), a potent poly(ADP-ribose) polymerase (PARP) inhibitor, exhibits poor aqueous solubility and limited bioavailability, restricting its therapeutic potential. The present study aimed to systematically develop and optimize olaparib-loaded nanostructured lipid carriers (NLCs) using a rational formulation strategy based on drug–lipid miscibility and required hydrophilic–lipophilic balance (rHLB) principles. OLP-loaded NLCs were prepared by the microemulsion–probe sonication method and optimized using a three-factor, three-level Box–Behnken design. Lauric acid and Capmul MCM were selected as the solid and liquid lipids, respectively, through comprehensive solubility, miscibility, and compatibility studies, while the surfactant system was optimized using rHLB-guided formulation design. The formulations were characterized for particle size, polydispersity index (PDI), entrapment efficiency (%EE), zeta potential, drug loading, in vitro drug release, morphology, and anticancer activity. The optimized formulation (F9) exhibited a particle size of 63.7 nm, PDI of 0.50, entrapment efficiency of 99.84%, zeta potential of −34 mV, and drug loading of 11.48%. XRD and FTIR studies confirmed amorphous drug incorporation and compatibility between OLP and excipients. The formulation provided sustained drug release, achieving approximately 90% release within 12 h through a non-Fickian transport mechanism. TEM analysis revealed well-dispersed spherical nanoparticles. In vitro cytotoxicity studies against HeLa cells demonstrated significantly enhanced anticancer activity of OLP-loaded NLCs compared with the conventional formulation. The systematic formulation strategy successfully produced stable, highly efficient OLP-loaded NLCs with superior drug entrapment, controlled release, and enhanced anticancer efficacy, highlighting their potential as an advanced lipid-based delivery platform for cancer therapy.

Keywords: Olaparib, nanostructured lipid carriers. Require HLB, HeLa cells cytotoxicity

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INTRODUCTION:

Nanostructured lipid carriers (NLCs) are among the most effective lipid-based nanocarriers for delivering BCS Class II and IV drugs.(1) Compared with conventional systems such as polymeric nanoparticles, nanoemulsions, and solid lipid nanoparticles (SLNs), NLCs offer higher drug-loading capacity, improved physical stability, and reduced drug leakage during storage.(2) Their partially disordered lipid matrix provides additional space for incorporating poorly water-soluble drugs, leading to improved solubility, dissolution, permeability, and bioavailability.(3) However, successful NLC development requires careful optimization of lipid selection, drug–lipid compatibility, surfactant concentration, and processing parameters, as these factors directly affect particle size, entrapment efficiency, stability, and therapeutic performance.(4)

Olaparib was selected as the model drug for NLC development due to its significant biopharmaceutical limitations. Olaparib is a PARP inhibitor used in the treatment of BRCA-mutated breast, ovarian, pancreatic, and prostate cancers. Despite its proven clinical efficacy, its therapeutic performance is restricted by poor aqueous solubility, limited permeability, and extensive first-pass metabolism. Classified as a BCS Class IV drug, olaparib exhibits pH-dependent solubility and low oral bioavailability, creating a need for advanced delivery approaches.(5,6) The physicochemical characteristics of olaparib make it a suitable candidate for NLC encapsulation. Its lipophilic nature facilitates incorporation into the lipid matrix, resulting in high drug entrapment and sustained release.(7) NLCs can enhance drug solubilization, improve lymphatic transport, reduce hepatic first-pass metabolism, and increase systemic availability. Furthermore, their nanoscale size promotes cellular

uptake and may enhance passive tumor accumulation through the enhanced permeability and retention (EPR) effect, thereby improving anticancer efficacy.(8)

Recent studies have demonstrated the potential of olaparib-loaded NLCs in cancer therapy.(9) Optimized formulations prepared using melt emulsification and ultrasonication exhibited particle sizes below 150 nm, high entrapment efficiencies (>85%), sustained drug release, and significantly improved anticancer activity compared with free olaparib. Enhanced cellular uptake and apoptosis induction in breast cancer cell lines further confirmed the advantages of NLC-based delivery. These findings highlight NLCs as a promising strategy for overcoming the poor biopharmaceutical properties of olaparib and improving its therapeutic effectiveness in cancer treatment.(10)

However, A key strength of the present study is the systematic and science-based formulation strategy adopted for the development of Olaparib-loaded nanostructured lipid carriers (NLCs). In contrast to previously reported Olaparib-NLC formulations, the selection of solid and liquid lipids was guided by detailed drug–lipid miscibility studies to maximize drug solubilization and entrapment within the lipid matrix. Additionally, the surfactant system was optimized using the required hydrophilic–lipophilic balance (rHLB) approach, ensuring efficient emulsification and enhanced formulation stability.

To the best of our knowledge, this work represents the first comprehensive Olaparib-NLC formulation developed using both lipid miscibility assessment and rHLB-based surfactant optimization. This rational design strategy resulted in a formulation with favorable physicochemical properties, high reproducibility, and improved colloidal stability. The study provides a robust framework for the development of lipid-based nanocarriers for poorly water-soluble anticancer drugs and contributes valuable insights into formulation optimization.

MATERIAL & METHODOLOGY:

Olaparib purchased from Sigma Aldrich (Merck), India, Lauric acid, HPLC grade acetonitrile ACN were purchased from Lob chemicals Mumbai, Capmul MCM received as a gift sample from ABITEC, India,

RP-HPLC analytical method development:(11) Following evaluation of the physicochemical properties of olaparib, including its molecular structure, pKa (~9.96), UV absorption maximum (276 nm), high solubility in methanol and acetonitrile, and poor aqueous solubility, RP-HPLC method development was initiated. A stock solution (1000 µg/mL) was prepared and serially diluted to obtain concentrations of 15–75 µg/mL for linearity assessment. Chromatographic analysis was performed using an XTERRA MS C18 column (250 × 4.6 mm, 5 µm) with a mobile phase consisting of acetonitrile and 0.1% trifluoroacetic acid buffer (40:60, v/v). Optimized conditions included a flow rate of 1.0 mL/min, injection volume of 20 µL, and detection at 276 nm using a Spectra 3000 UV–Vis DAD detector.

Screening of lipids: A critical step in NLC development is the selection of suitable solid and liquid lipids based on their ability to solubilize the active pharmaceutical ingredient (API). The chosen lipids must be mutually miscible to create imperfections within the solid lipid matrix, thereby enhancing drug incorporation and loading capacity. At the same time, the lipid blend should remain solid at room and physiological temperatures, typically requiring a melting point above 40°C. Since incorporation of liquid lipids generally lowers the melting point of the solid lipid matrix, careful lipid screening is essential to achieve optimal drug loading while maintaining the desired physical stability of the NLC system.

Selection of Liquid and Solid Lipids(2)

Liquid lipids:

The solubility of olaparib (OLP) in various natural and semi-synthetic oils was evaluated by dispersing excess drug in 5 mL of each oil and shaking the mixtures at 250 rpm for 24 h. Oils showing complete drug dissolution were further saturated with additional OLP and shaken for another 24 h. After centrifugation (1000 rpm, 5 min), the supernatant was suitably diluted with a methanol:diethyl ether (1:1) mixture and analyzed for drug content. This solvent system was selected because it effectively solubilizes OLP and is miscible with the tested oils.

Solid lipids:

Drug solubility in solid lipids was assessed using the melt dispersion method. Briefly, 100 mg of each solid lipid was melted slightly above its melting point, and OLP was added incrementally with continuous vortex mixing. The lipid melt was examined for clarity after each addition. Drug incorporation was continued until turbidity appeared or drug crystals were observed after solidification, indicating the solubility limit of OLP in the lipid.

Optimization of solid lipid: drug ratio using Solvent Evaporation Approach & XRD study: In separate test tubes, 10mg of OLP dissolved in methanol & 90 mg of selected lipid (Lauric acid) were dissolved in diethyl ether. Both solution were mixed & vortexed for 2 min. The solution were poured in a clean petri dish for solvent evaporation in order to get 10% w/w blend of OLP in selected lipid (Lauric acid). Similarly 20% & 30% w/w blend were prepared. Gathered the remainder and analyzed by XRD.

Selection of ratio of Solid lipid-liquid using homogeneity test (Filter Paper Test): Nicely miscible solid lipid-liquid lipid facilitates the formation of

imperfections in the solid lipid's crystal lattice structure, thereby simplifying API loading. The mixture of selected solid lipid to liquid lipid (Lauric acid: Capmul MCM) was heated just above the melting point of solid lipid and subsequently chilled to room temperature in varying proportions of 1:9 to 9:1. In order to visually evaluate miscibility, an aliquot was applied to filter paper. Mixtures that exhibited droplets were supposed to unstable due to the poor miscibility that was indicated by the presence of visual droplets.

Drug-lipid compatibility studies: The FTIR spectrophotometer (Jasco 410) was used to collect the IR spectra of the drug-lipid and lipid-lipid mixture in order to assess the drug's compatibility and integrity in the formulation. As well as the mixture of were dissolved in methanol: diethyl ether 1:1 and scanned in the range of 200- 400nm & spectra was observed & compared with standard of OLP.

Selection of Surfactants & ratio of surfactants:(12,13) selected by calculating 'required HLB' (R-HLB) of the formulation.

Selection of concentration of selected ratio of surfactant co-surfactants by constructing Pseudo-ternary phase diagram: Formulation development: A pseudo-ternary phase diagram was constructed using the selected lipid mixture, S-mix (Poloxamer 188:Span 80, 1:2), and water. Various lipid:S-mix ratios were titrated with distilled water under gentle stirring, and compositions forming clear, stable systems were identified after equilibration. The corresponding component percentages were then plotted on a ternary diagram to determine the nanoemulsion region.

Implementation of Design of experiment (DOE):(14) A three-factor, three-level Box–Behnken design (BBD) was employed using Design-Expert® software (v13.0) to optimize the NLC formulation. BBD was selected because it efficiently evaluates the individual and interactive effects of formulation variables while minimizing the number of experimental runs. Seventeen formulations were generated by varying lipid amount (X_1), surfactant concentration (X_2), and sonication time (X_3), with particle size (Y_1) and polydispersity index (Y_2) selected as the critical quality attributes (CQAs).

Formulation of NLCs: (Micro-emulsion formation followed by probe sonication method):(15) OLP-loaded NLCs were prepared by the microemulsion method followed by probe sonication. Lauric acid and Capmul MCM were heated to 50°C and mixed with a preheated surfactant blend of Poloxamer 188 and Span 80. The aqueous phase was added to the lipid phase under stirring to form a pre-emulsion, which was subsequently probe-sonicated and cooled to 4°C to obtain NLCs. The prepared formulations were then characterized for particle size, PDI, entrapment efficiency, and other physicochemical properties.

Evaluation of formulation:(16,17)

Particle Size & zeta potential: The particle size study was carried out for all batches we are prepared and zeta potential study was carried out or checked for optimized batch.

Polydispersity Index (PDI): It measures the uniformity of particle size distribution in a sample (like nanoparticles, polymers, lipid carriers).

Entrapment efficiency (EE%): Entrapment efficiency (%EE) was determined by separating free drug from OLP-loaded NLCs using cold ultracentrifugation (typically 15,000 to 25,000 rpm). The amount of unentrapped OLP present in the supernatant was quantified by a validated HPLC method. The %EE was calculated using the equation: EE (%) = [(Total drug − Free drug) / Total drug] × 100.

Drug loading (DL %): The following formula was used to determine the proportion of DL based on the %EE results:

$$DL\% = (\text{Amount of drug entrapped} / \text{Total weight of nanoparticles}) \times 100$$

In-vitro Drug release study: In vitro drug release from OLP-loaded NLCs was evaluated using the dialysis bag diffusion method. NLC dispersion equivalent to 100 mg of OLP was placed in a dialysis bag and immersed in 900 mL of simulated vaginal fluid (pH 4.2) maintained at 37 ± 0.5°C with stirring at 50 rpm. Samples were withdrawn at predetermined intervals, replaced with fresh medium to maintain sink conditions, and analyzed by HPLC after filtration.

Morphology Studies: Transmission electron microscopy (TEM) was used to examine the morphology of the optimized NLC.

In vitro Anti-cancer activity: MTT assay procedure (HeLa, 96-well plate):(18) HeLa cells (NCCS, Pune) were cultured in MEM supplemented with 10% FBS at 37°C and 5% CO_2. Cells were seeded in 96-well plates (1×10^4 cells/well) and treated with test samples (10–100 µg/mL) for 24 h. Cell viability was then assessed using the MTT assay, where formed formazan crystals were dissolved in DMSO and absorbance was measured at 570 nm using a microplate reader. Percentage cell viability was calculated using the standard formula.

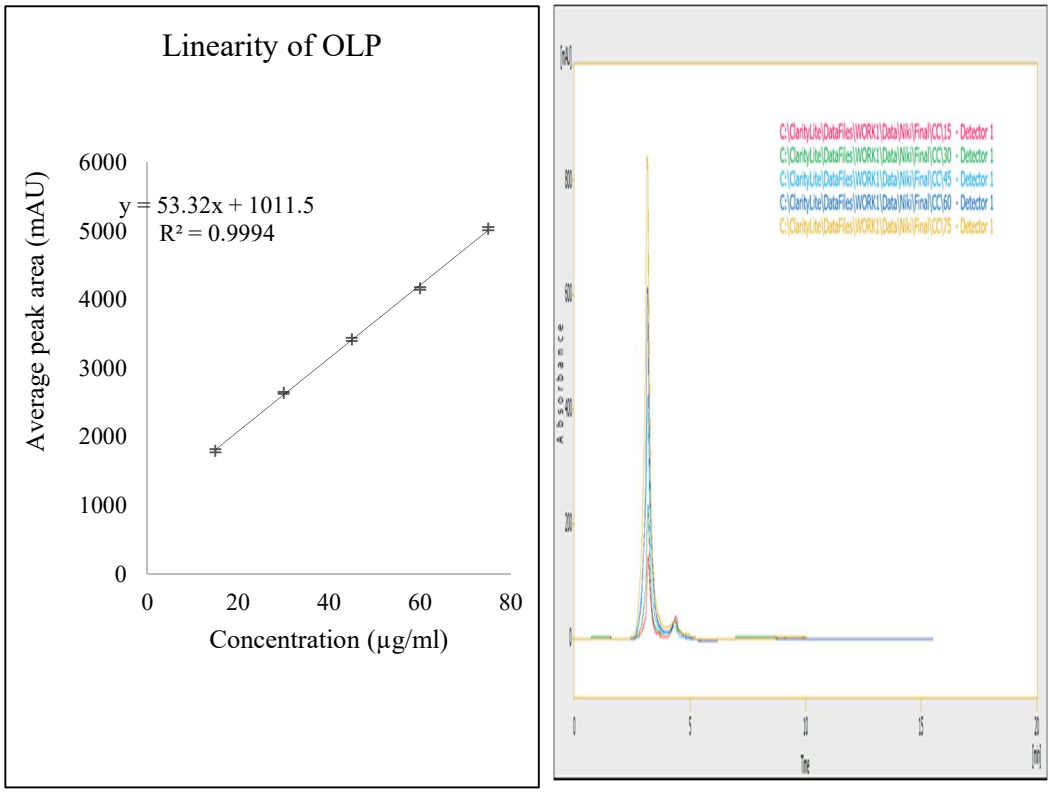
$$\% \text{ cell viability} = \frac{A_{570.\,Sample} - A_{570.\,blank}}{A_{570.\,Test} - A_{570.\,blank}} \times 100$$

RESULTS:

RP-HPLC method development: Linearity was evaluated across the concentration levels, 15–75 µg/ml at 276 nm resulting in a linear equation of Y = 53.32x + 1011.5 (correlation coefficient R^2= 0.999) demonstrating strong linearity. Additionally, the %RSD values were within the acceptable range, (<2) as presented in Table No. 1 and illustrated in Figure 1.

Table No.1 Linearity data of OLP

Conc. µg/ml	Peak area (mAU)			Average peak area (mAU)	SD	% RSD
	1	2	3			
15	1771.162	1804.540	1813.915	1796.540	± 22.47	1.25
30	2654.637	2639.932	2626.310	2640.293	± 14.16	0.53
45	3396.150	3444.471	3420.923	3420.512	± 24.16	0.70
60	4161.762	4182.360	4145.681	4163.270	± 18.38	0.44
75	5032.811	5011.353	5058.033	5034.065	± 23.36	0.46



(A) **(B)**

Figure 1 (A) Linearity data of OLP (B) Overlapped chromatograms of OLP

Screening of lipids: Selection of liquid lipid & solid lipid made by solubility test & melt dispersion or fusion method respectively. Depending upon maximum solubility Lauric acid and Capmul MCM were selected for formulation of NLC of Olaparib (Figure 2)

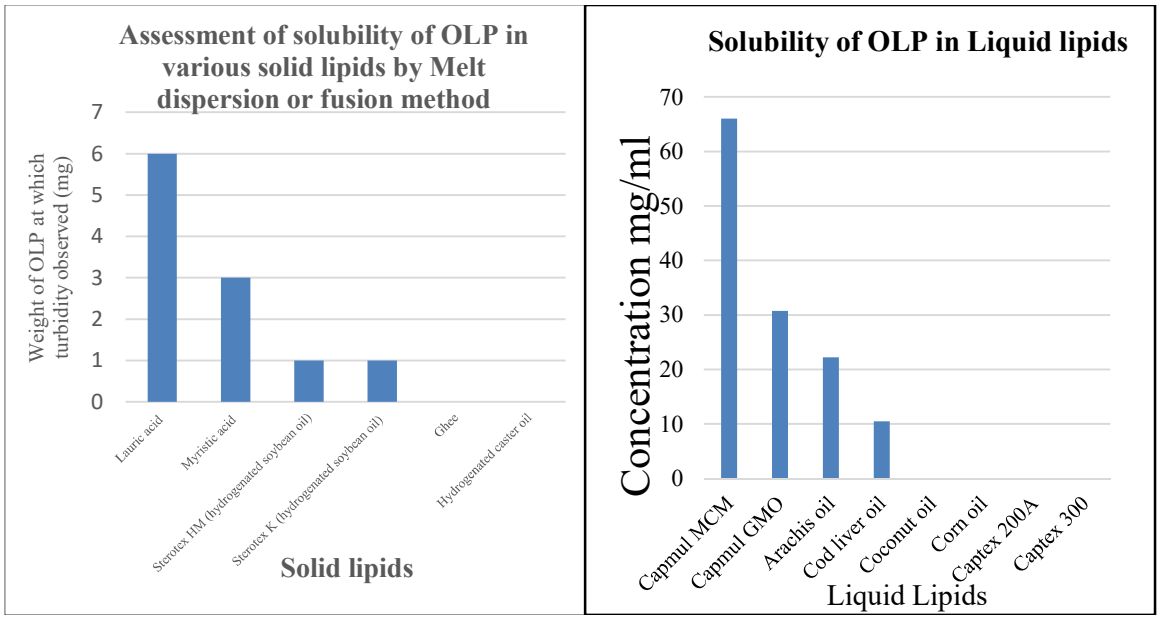


Figure 2 Solubility of OLP in various solid lipids & liquid lipids

However, to improve drug solubility in the lipid matrix, better drug loading, to reduced drug expulsion during storage & possible control over polymorphic transitions of the lipid, 'Solvent Evaporation Approach' were employed & the lipid : drug ratio was optimized using XRD.

Optimization of the lipid: drug ratio using Solvent Evaporation Approach & followed by XRD study: XRD was employed to evaluate the crystallinity of olaparib in Lauric acid dispersions at different drug-to-lipid ratios and to identify the optimal composition for formulation development. The 10% and 20% drug-loaded dispersions showed no characteristic crystalline peaks, indicating that olaparib was predominantly present in an amorphous state. In contrast, the 30% formulation exhibited distinct drug diffraction peaks, suggesting partial crystallization. (Figure 3). These findings were supported by DSC analysis, where the disappearance of the drug melting endotherm confirmed successful amorphization.

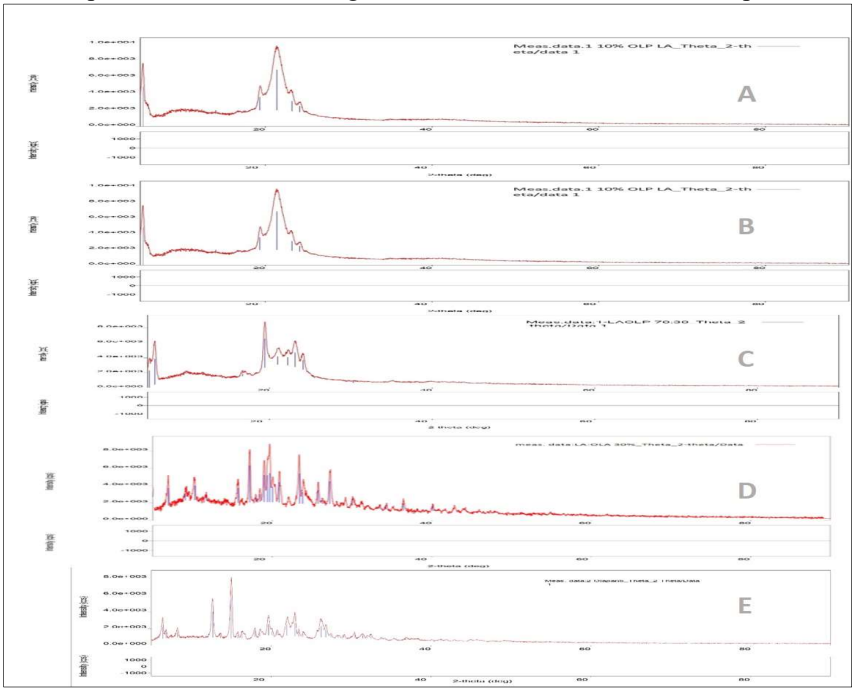
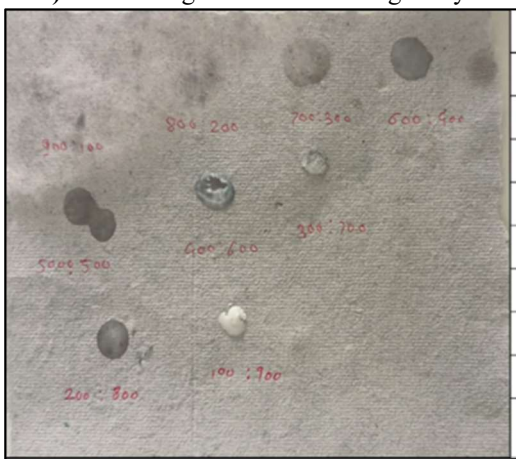


Figure 3 XRD of (A) Pure Lauric acid (B) Lauric acid: OLP (10%), (C) Lauric acid: OLP (20%), (D) Lauric acid: OLP (30%), (E) Pure OLP

Lauric acid–Capmul MCM homogeneity test (Filter Paper Test): Observing results of homogeneity test Capmul MCM:Lauric acid: 1:9 selected for preparation of NLCs. (Figure 4)



Liquid lipid : Solid lipid	Observation's
900:100	Oil spot observed
800:200	Oil spot observed
700:300	Oil spot observed
600:400	Oil spot observed
500:500	Oil spot observed
400:600	Oil spot observed
300:700	Oil spot observed
200:800	Oil spot observed
100:900	No oily spot observed on the filter paper

Figure 4 Observations of filter paper test

Drug excipients compatibility studies:

Infrared absorption spectrum: The FTIR spectrophotometer was used to collect the IR spectra of the drug-lipid and lipid-lipid mixture in order to assess the drug's compatibility and integrity in the formulation. The drug OLP was found to be compatible with selected both lipids (Figure 5)

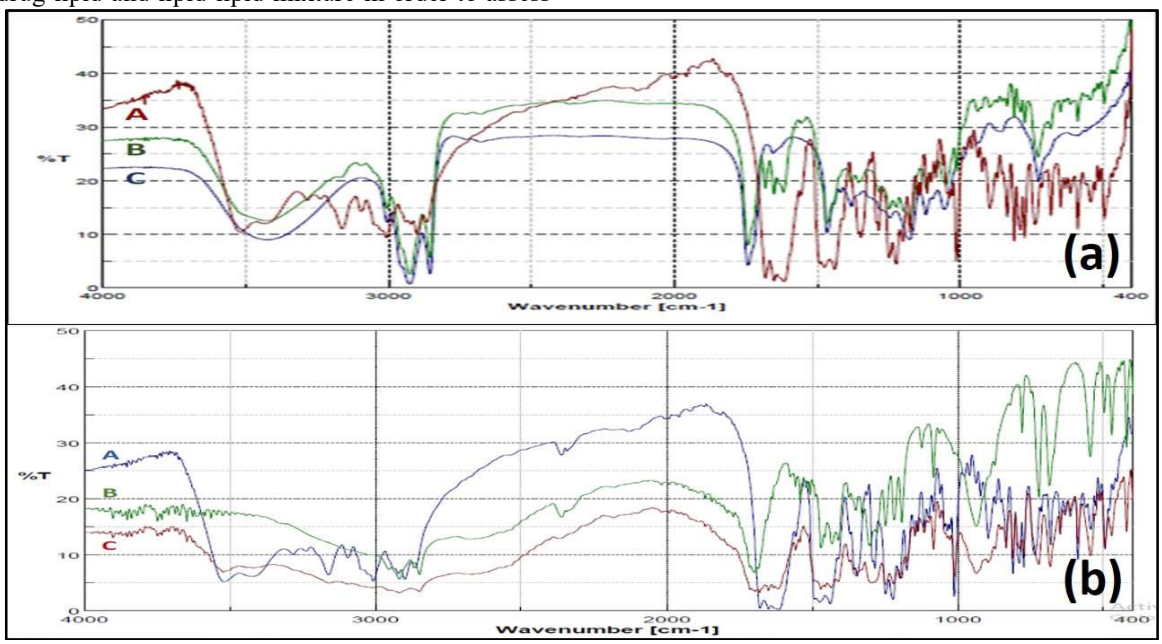


Figure 5 Compatibility of OLA with (a) Capmul MCM by IR spectroscopic method. Overlapped IR spectroscopy of A. Olaparib B. Olaparib+ Capmul MCM C. Capmul MCM (b) Lauric acid by FTIR spectroscopy. Overlapped IR spectra of (A) OLP (B) Lauric acid (C) OLP & Lauric acid mixture

Selection of surfactants: In order to prepare stable emulsion an emulsifier mixture (Surfactant Co-surfactant Mature) having HLB equal to R-HLB of oil phase in the formulation should be used. i.e the HLB value of the surfactant or blend of surfactants (surfactant and co-surfactant) that provides the lowest interfacial tension between oil phase and water phase.

Selection of Surfactants & ratio of surfactant co-surfactant: It is selected by calculating required HLB (R-HLB) of the formulation constructed depending on maximum solubility of OLP in both lipids. (Table no.2). The required HLB of OLP-NLC formulation was found to be ~12.

Table No. 2 Probable formula of the OLP- NLC:

Category	Ingredient	Amount in mg	Amount in %w/v
Drug	OLP	23 mg	0.23%w/v
Solid lipid	Lauric acid	90 mg	0.90%w/v
Liquid lipid	Capmul MCM	10 mg	0.10%w/v
Aqueous solution of Surfactant	Blend of surfactant co-surfactant	QS to 10 ml	98.78%w/v

.For this experiment blend of poloxamer 188 (HLB ≈ 29) and Span 80 (HLB ≈ 4.3) were selected to fulfill the selection criteria of surfactant blend. Blend of Poloxamer 188 ≈ 31.17% & Span 80 ≈ 68.83% gives HLB 12. i.e in ratio 1:21

Selection of concentration of selected ratio of surfactant co-surfactants by constructing Pseudo-ternary phase diagram: Concentration of surfactant bled were selected on the basis of Pseudo-ternary phase diagram. Ideally concentration of surfactant must be as low as possible to avoid toxicity & hemolysis. However it should be sufficient enough to keep the formulation stable for longer period of time.

Pseudo-ternary phase diagrams are essential tools (TernaryPlot.com) for optimizing surfactant co-surfactant concentration at particular ratio of surfactant co-surfactant to form stable NLC formulations. By plotting the oil, surfactant, and water phases, one can identify regions of stable emulsions and select the optimal surfactant concentration. (Figure 6)

This approach allows for the fine-tuning of surfactant concentration to achieve the best particle size**,** stability, and drug encapsulation efficiency**.**

Sr. no.	Lipid Mix %	S-mix %	Water %
1	73.30	10.67	16.09
2	57.97	13.52	28.50
3	46.05	15.81	38.74
4	36.00	17.13	47.2
5	27.72	17.69	54.56
6	20.36	19.57	60.16
7	14.03	21.56	64.29
8	06.20	44.40	49.68
9	02.88	45.98	51.12

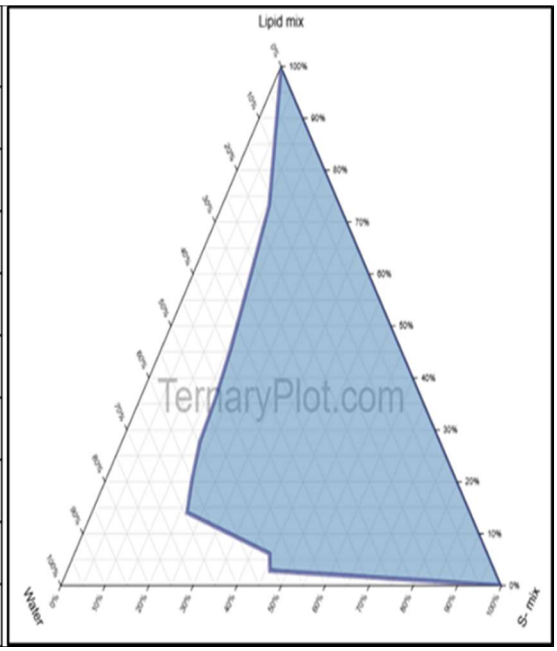


Figure 6 Observations of Pseudo-ternary phase diagram showing micro emulsion area.

Formulation Development: Using Design-Expert® (version 13.0, Stat-Ease Inc.), a 3-level, 3-factor Box–Behnken design (BBD) was applied to optimize the nanostructured lipid carriers (NLCs) of OLP. Trial batches of OLP-loaded NLCs were prepared using the micro-emulsion method followed by probe sonication.

Evaluation of formulation:

Particle size, PDI, % Entrapment efficiency: The developed NLC formulations showed particle sizes between 72 and 293 nm, the %EE values, ranging from 41% to 98% & PDI values below 0.5. (Table No. 3)

Table No. 3 Results for average size, PDI, zeta potential, and entrapment efficiency

Batch	Lipid mix	S-mix	Sonication	Particle size (nm)	PDI	EE

no.	(mg)	(%)	Time (mix)					(%)	
1	200	0.3	5	224.40	± 5.5	0.5	±0.02	41.37	±1.20
2	200	0.65	3	117.26	±6.3	0.57	±0.011	69.00	±1.80
3	250	1	3	223.10	± 4.0	0.5	±0.018	95.84	±2.50
4	300	0.65	7	125.83	±3.1	0.61	±0.030	81.88	±1.34
5	250	0.65	5	137.86	±4.5	0.54	±0.018	90.17	±0.89
6	250	1	7	072.50	± 2.9	0.52	±0.015	95.21	±2.01
7	300	1	5	103.43	±6.9	0.64	±0.023	98.99	±0.98
8	250	0.65	5	178.50	±4.2	0.47	±0.012	91.56	±1.45
9	200	1	5	063.70	± 1.3	0.56	±0.02	99.84	±1.40
10	250	0.65	5	165.67	±3.2	0.52	±0.013	91.00	±2.22
11	250	0.65	5	127.10	±3.1	0.45	±0.001	86.36	±2.45
12	250	0.3	3	175.47	±5.1	0.66	±0.014	44.16	±1.89
13	300	0.3	5	133.83	±7.0	0.66	±0.037	64.33	±1.09
14	200	0.65	7	293.95	± 2.1	0.33	±0.019	95.65	±3.02
15	250	0.65	5	121.03	± 4.6	0.45	±0.054	82.31	±2.94
16	250	0.3	7	269.50	± 4.6	0.53	±0.024	80.27	±2.89
17	300	0.65	3	269.83	±3.7	0.62	±0.012	84.65	±3.34

ANOVA and response surface analysis revealed that particle size (Y_1), PDI (Y_2), and entrapment efficiency (%EE) were significantly affected by lipid concentration (X_1), surfactant concentration (X_2), and sonication time (X_3). Quadratic models showed the best fit for all responses with high regression coefficients (R^2 = 0.9500 for particle size, 0.8650 for PDI, and 0.9565 for %EE) and insignificant lack-of-fit values.

The polynomial equations obtained were:

Particle size (Y_1) = $146.03 + 8.3X_1 - 42.5X_2 - 2.9X_3 + 0.94X_1^2 - 15.63X_2^2 + 54.74X_3^2 + 32.58X_1X_2 - 80.17X_1X_3 - 61.16X_2X_3$

PDI (Y_2) = $0.49 + 0.071X_1 - 0.015X_2 - 0.044X_3 + 0.042X_1^2 + 0.063X_2^2 + 0.005X_3^2 - 0.021X_1X_2 + 0.057X_1X_3 + 0.039X_2X_3$

%EE = $88.28 + 3.00X_1 + 19.97X_2 + 7.42X_3 - 4.11X_1^2 - 8.04X_2^2 - 1.37X_3^2 - 5.95X_1X_2 - 7.36X_1X_3 - 9.19X_2X_3$

The results indicated that increasing lipid concentration increased particle size and PDI, whereas higher surfactant levels and longer sonication reduced both responses. Entrapment efficiency increased with all three variables, with surfactant concentration exerting the strongest positive influence.(Figure 7)

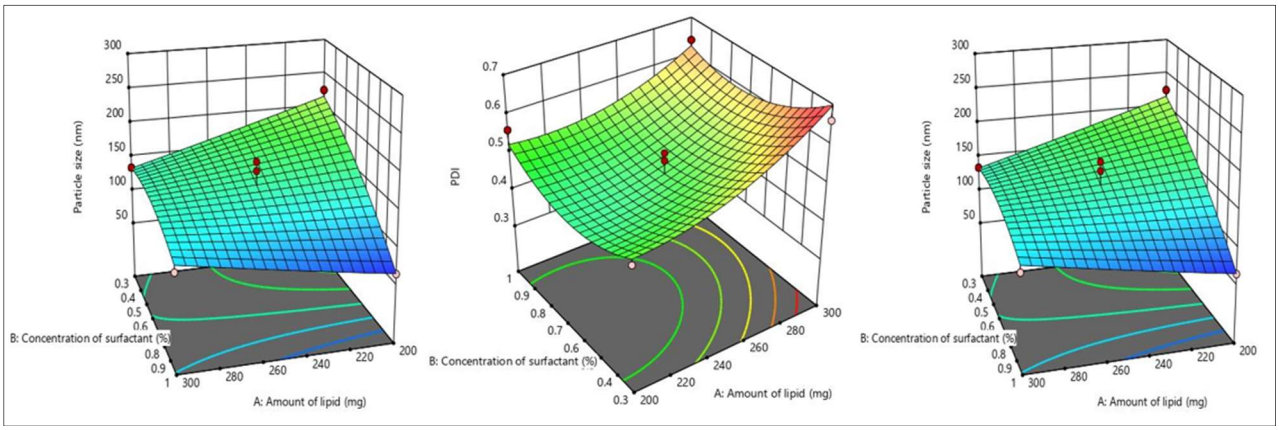


Figure 7 3D Surface response curve for particle size, PDI & % EE

Optimization of batch: By selecting 'in range' goal for L mix, S mix & sonication time formulation F9 batch were found to be optimized batch with desirability 1.00.

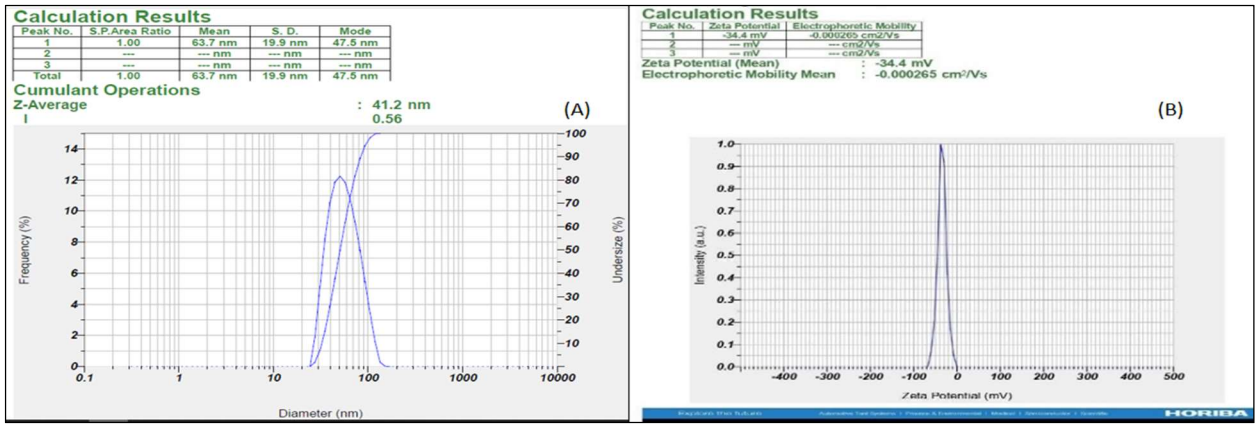


Figure 8 (A) Average particle size & (B) Zeta potential of optimized batch F9

With an average particle size of 63.7 nm and a zeta potential of -34 mV, (Figure 8) OLP-loaded NLCs show a reliable and effective drug delivery method. Strong electrostatic repulsion between particles is suggested by the negative zeta potential, which lowers aggregation and improves colloidal stability.

Drug Loading (%DL): On the basis of results of %EE (99.84%) of optimized batch F9 %DL was determined to be 11.48% based on the overall weight of the nanoparticles (200 mg) and the amount of drug entrapped.

In-vitro drug release study: The significant enhancement in OLP release from OLP-NLCs compared to the OLP can be attributed to several formulation-related factors. In this study, OLP-NLCs achieved approximately 91.56% cumulative drug release in SVF in pH 4.2 over 12 hours, whereas OLP exhibited only about 36% release in the same timeframe. (Figure 9)

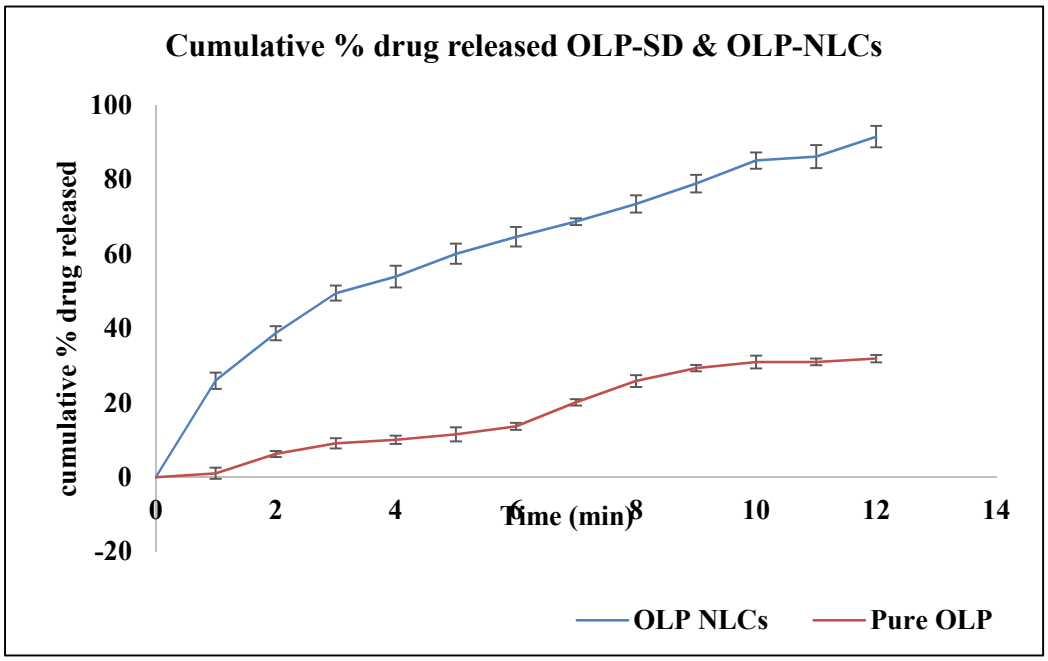


Figure 9 Comparison of Cumulative % drug released OLP-SD & OLP-NLCs

Drug diffusion kinetics study: Kinetic fitting revealed that OLP-NLCs best fitted the Higuchi model ($R^2 \approx 0.996$), suggesting diffusion-controlled release from the lipid matrix for an optimized batch F9 shows n value 0.5 in the Korsmeyer-Peppas model indicates Anomalous (non-Fickian) transport mechanism.

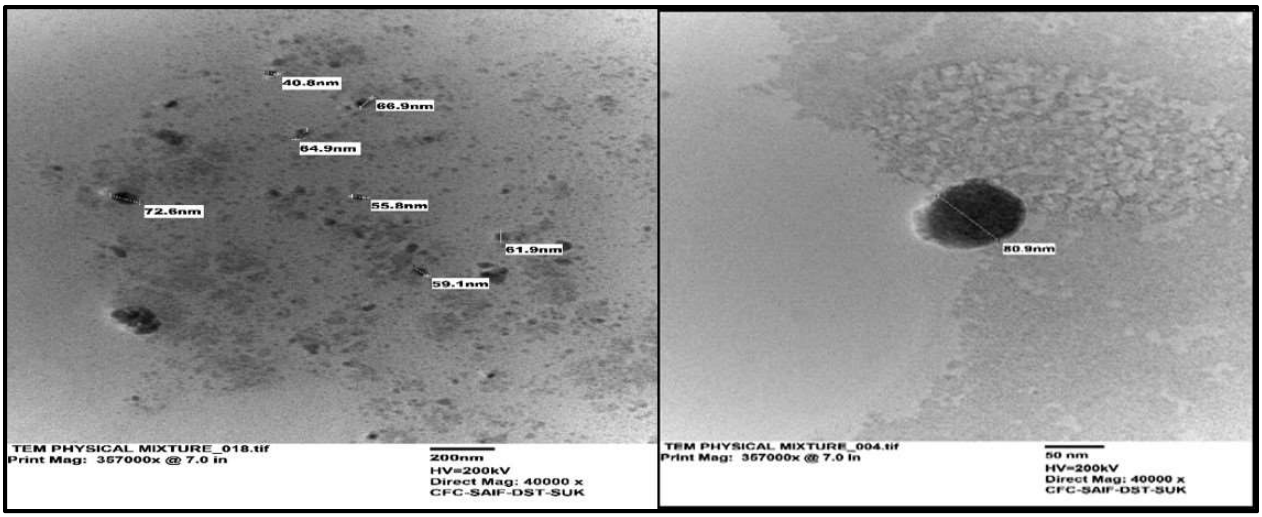
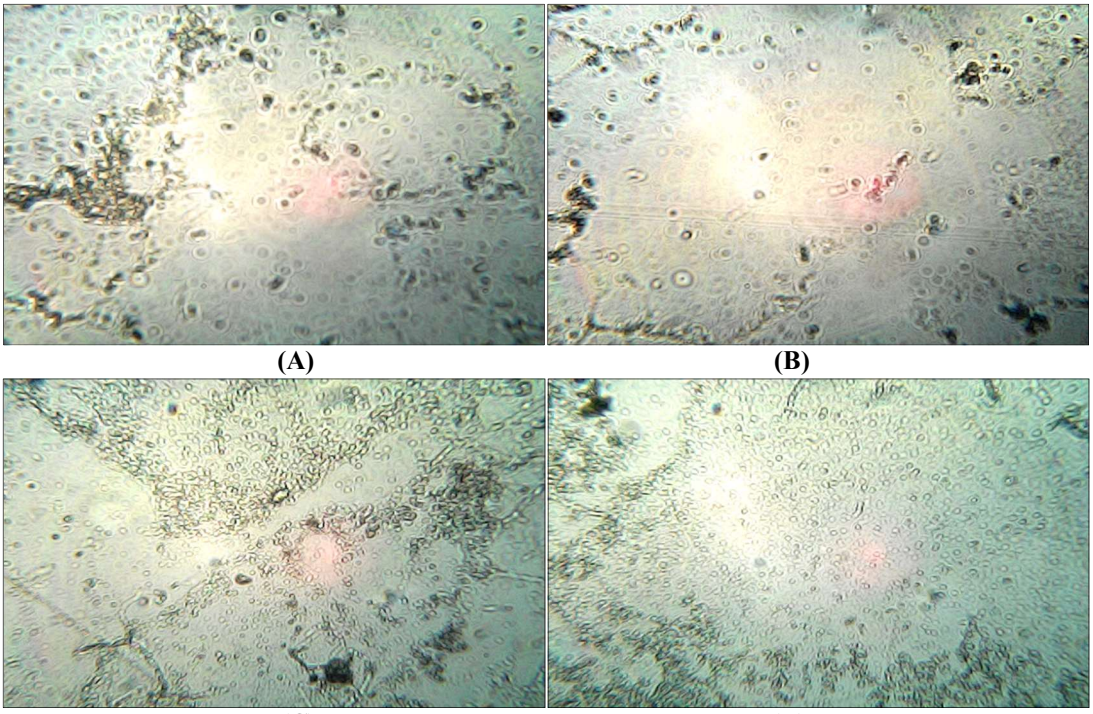


Figure 10 Results of TEM showing morphology of Olaparib -NLCs

The observed particle size range of 40–72 nm confirms the nanoscale nature of the formulation, (Figure 10) which is favorable for enhanced cellular uptake, bioavailability, and tumor penetration. The particles were well dispersed with minimal aggregation, indicating good colloidal stability.

In vitro Anti-cancer activity:

The MTT assay demonstrated a concentration-dependent reduction in HeLa cell viability for both OLP solid dispersion (F1) and OLP-loaded NLCs (F2). However, F2 exhibited significantly greater cytotoxicity, reducing cell viability to 38.63% compared with 70.51% for F1 at higher concentrations. The enhanced anticancer activity of OLP-NLCs may be attributed to improved cellular uptake and more efficient intracellular drug delivery. (Figure 11)



(A) **(B)**

(C) **(D)**

Figure 11 MTT assay results of A) OLP SD drug B) OLP-NLCs C) Standard 5-FU D) Control.

DISCUSSION:

Olaparib-loaded NLCs were successfully prepared by the microemulsion–probe sonication method. Lauric acid and Capmul MCM were selected as the solid and liquid lipids based on their high drug solubilization capacity, while a 9:1 lipid ratio provided optimal miscibility and stable drug incorporation. XRD and FTIR studies confirmed that olaparib remained predominantly amorphous below 20% drug loading and showed no significant drug–excipient interactions.

The developed NLCs exhibited particle sizes of 72–293 nm, entrapment efficiencies of 41–98%, and PDI values below 0.5. Optimization using Box–Behnken design revealed that increasing lipid concentration increased particle size and PDI, whereas higher surfactant levels and longer sonication times reduced both responses and improved formulation stability.

The optimized formulation (F9) showed a particle size of 63.7 nm, PDI of 0.5, entrapment efficiency of 99.84%, zeta potential of −34 mV, and drug loading of 11.48%. It achieved sustained drug release (~90% in 12 h) through a non-Fickian mechanism. TEM confirmed well-dispersed spherical nanoparticles, while MTT studies demonstrated superior cytotoxicity of OLP-loaded NLCs compared with the conventional formulation, highlighting their potential for improved anticancer therapy.

CONCLUSION:

An optimized OLP loaded NLC was successfully prepared by using Lauric acid and Capmul MCM. The formulation showed good nanoparticle characteristics, sustained drug release for 12 h, improved cell infusion, enhanced cytotoxicity against Hella cells and good mechanical properties. The ex vivo, in vitro and stability studies established its potential as a stable and effective drug delivery system for various cancer therapy.

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ABBREVIATIONS:

OLP: Olaparib; NLC: Nanostructured lipid carrier; FTIR: Fourier Transform Infrared Spectroscopy; RP-HPLC: Reverse Phase High Performance Liquid Chromatography; BCS: Biopharmaceutics Classification System; HLB: Hydrophilic-Lipophilic Balance; DSC: Differential Scanning Calorimetry; XRD: X-ray Diffraction; TEM: Transmission Electron Microscopy; PDI: Polydispersity Index; RSD: Relative Standard Deviation; UV: Ultraviolet; ANOVA: Analysis of Variance; MCM medium chain monoglycetride

CONFLICT OF INTEREST:

The authors declare that there are no conflicts of interest regarding the publication of this work.

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AUTHOR CONTRIBUTIONS:

The author N. Gurav carried out the experimental work, data analysis, and manuscript drafting. The co-authors A. Shinde contributed to study supervision, interpretation of results, critical review of the manuscript, and approval of the final version.

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