Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 30s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Preparation And Characterization Of Solid Lipid Nanoparticles For Topical Delivery Of Curcumin

Vankayala Devendiran Sundar[1*], Magharla Dasaratha Dhanaraju[1], Anilkumar Vadaga[1], Midde Venkatesh[1]

[1]Department of Pharmaceutics. GIET School of Pharmacy, Rajahmundry, AP, India.

[*]**Corresponding author:**
Vankayala Devendiran Sundar
Email ID: sundarvd@yahoo.co.in

Cite this paper as: Vankayala Devendiran Sundar, Magharla Dasaratha Dhanaraju, Anilkumar Vadaga, Midde Venkatesh, (2025) Preparation And Characterization Of Solid Lipid Nanoparticles For Topical Delivery Of Curcumin. *Journal of Neonatal Surgery*, 14 (30s), 702-715.

ABSTRACT

Curcumin, a potent natural polyphenol, exhibits significant therapeutic potential for various inflammatory and skin disorders but faces limitations in bioavailability and stability. To address these challenges, solid lipid nanoparticles (SLNs) were developed as a novel topical delivery system to enhance skin permeation, drug entrapment efficiency, and sustained release properties. This study employed the Box-Behnken design to optimize curcumin-loaded SLNs using Compritol ATO 888, Span 80, and Tween 80 as lipid and surfactant components. Various formulations were evaluated for particle size, polydispersity index (PDI), encapsulation efficiency (EE%), and in vitro drug release behavior. The optimized formulation (F_{12}) demonstrated a particle size of 275.67 nm, a PDI of 0.14, and an encapsulation efficiency of 91.58%, suggesting excellent stability and uniformity. Further drug loading studies (N=3) resulted in a mean ± SD of 15.29 ± 3.56%, confirming high drug entrapment. In vitro drug release studies indicated a sustained release profile, favouring prolonged drug retention in the skin. Excipients such as Compritol ATO 888 provided occlusive effects, enhancing the retention time and bioavailability of curcumin. The study also included Fourier Transform Infrared (FTIR) and Differential Scanning Calorimetry (DSC) analyses, confirming drug-lipid compatibility and stable crystalline structures.

Keywords: *Curcumin, Solid Lipid Nanoparticles, Topical Delivery, Encapsulation Efficiency, Compritol ATO 888, Drug Release, Bioavailability.*

1. INTRODUCTION

Curcumin, the principal bioactive of turmeric (Curcuma longa), is a hydrophobic polyphenol known for its potent anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties, making it highly suitable for dermatological and cosmetic applications[1,2]. Despite its therapeutic potential, curcumin suffers from poor aqueous solubility, rapid degradation, and limited skin permeability, which restricts its effectiveness in conventional topical formulations[3-6]. To overcome these challenges, Solid Lipid Nanoparticles (SLNs) have emerged as an advanced drug delivery system offering enhanced skin penetration, sustained release, and improved physicochemical stability of encapsulated bioactives. SLNs are submicron-sized lipid carriers composed of physiological lipids that remain solid at room and body temperatures, and are stabilized by surfactants. Their ability to form an occlusive film on the skin surface enhances hydration, retention, and drug permeation, making them ideal carriers for curcumin in topical therapy. This study focuses on the formulation, optimization, and characterization of curcumin-loaded SLNs to improve their therapeutic efficacy and bioavailability for topical applications [7,8].

Several studies have reported the successful development and evaluation of solid lipid nanoparticles (SLNs) for topical drug delivery to enhance therapeutic efficacy and skin retention. Kesharwani et al. developed SLN-based gel of Etoricoxib [9], while Ekambaram and Abdul formulated SLNs of Ramipril [10]. Pople and Singh prepared vitamin A-loaded SLNs for topical application [11], and Rahmanian-Devin et al. encapsulated Noscapine in SLNs for anti-psoriatic activity [12]. Begum and Shaik evaluated linezolid-loaded SLNs in gel form [13], and Maiti et al. developed methotrexate-loaded SLNs for psoriasis treatment [14]. Kumar et al. and Panmand et al. formulated topical microemulsion and Acitretin-loaded SLNs, respectively [15,16]. Tacrolimus-loaded SLNs were developed by Khan et al. [17], while El-Housiny et al. conducted clinical

studies using fluconazole-loaded SLNs [18]. Nair et al. optimized clarithromycin SLNs for ocular delivery [19], and Jain et al. formulated SLNs for antifungal therapy [20]. These studies collectively highlight the versatility of SLNs in delivering diverse therapeutic agents via topical routes with enhanced stability and bioavailability.

2. MATERIALS AND METHODOLOGY

The study employed advanced instruments including a UV-Vis spectrophotometer (Shimadzu V-1800), FT-IR (Perkin Elmer), DSC (Perkin Elmer 4000), probe sonicator, zetasizer (Horiba SZ-100), and stability chamber (Thermolab). Equipment for formulation included a mechanical stirrer, homogenizer, centrifuge, and pH meter. Curcumin (gifted by Cipla) and excipients like glyceryl monosterate, stearic acid, various Tweens and Spans, soya lecithin, and HPLC-grade methanol were used from reputed suppliers.

Preformulation studies

Organoleptic properties

The sample of Curcumin was evaluated for its organoleptic properties like color, odor and appearance.

Melting point determination

Melting point was determined by an open capillary method using a melting point apparatus. The Curcumin was taken in a glass capillary and one end of it was sealed by flame. The capillary tube containing drug was dipped in liquid paraffin inside the melting point apparatus equipped with a magnetic stirring facility.

Calibration of Curcumin in Different Solvents

To evaluate the absorbance characteristics of curcumin, calibration was performed in methanol, ethanol, and dimethyl sulfoxide (DMSO). A 100 µg/mL stock solution of curcumin was prepared in each solvent by dissolving 10 mg of curcumin in 10 mL of the respective solvent, followed by sonication for 5 minutes to ensure complete dissolution. From these stock solutions, working dilutions ranging from 1 to 10 µg/mL were prepared. The absorbance of each concentration was measured using a UV-Visible spectrophotometer. In methanol, readings were taken at 425 nm using methanol as the blank; in ethanol, absorbance was measured at 427 nm with ethanol as the blank; and in DMSO, absorbance was recorded at 430 nm using DMSO as the blank.

Fourier transform infrared (FTIR)

The dry sample of pure Curcumin was mixed with potassium bromide (IR grade) in the ratio of 1:100. This mixture was compressed in a form of a pellet by applying 10 tons of pressure in hydraulic press. The pellets were scanned over a wave number range of 4000 to 400 cm-1 in FTIR instrument and spectral analysis was done.

Differential scanning calorimetric (DSC)

The DSC thermogram of pure Curcumin was recorded by using a differential scanning calorimeter equipped with a computerized data station. Drug sample was weighed and heated in a closed pierced aluminum pan at a scanning rate of 10°C/min between 50 and 300°C and 40 ml/min of nitrogen flow.

Determination of solubility of Curcumin in different solvents

The solubility of Curcumin was determined in methanol, distilled water, phosphate buffer pH 4.2 and 0.1N HCl. Excess drug was added to known volume of the solvent systems and mixed for 2 min. Mechanical shaker was further used for 24 h to dissolve the drug. The contents were then centrifuged at 10,000 rpm for 15 min. The aliquots of supernatant saturated solvent systems were diluted appropriately with respective solvent and analyzed UV spectrophotometrically.

Formulation and development of Curcumin loaded SLN

The solid lipids selected for the study were Compritol 888 ATO, Precirol ATO 5, Emulcire, stearic acid and glyceryl monosterate. For studying the solubility of Curcumin in solid lipids, 100 mg drug was taken in test tube and solid lipid was added in increments of 0.5 g. The test tube was heated in controlled temperature water bath kept at 80°C or 5°C above the melting point of lipid. The amount of solid lipid required to solubilize drug in molten state was estimated.

Solubility study of drug in various surfactants

The surfactants selected for the study were Gelucire 44/14, Labrafil M2125, Labrafil M1944, Tween 20, Tween 80, Span 20 and Span 80. Excess drug was added to known volume of the surfactant systems and mixed for 2 min. Mechanical shaker was further used for 12 h to dissolve the drug. The contents were then centrifuged at 10,000 rpm for 15 min. The aliquots of supernatant saturated surfactant systems were diluted appropriately with methanol and analyzed UV spectrophotometrically at 425 nm.

Study of stability of pre-emulsion

Different pre-emulsions were prepared using drug, lipid (glyceryl monostearate, Compritol ATO 888 or Precirol ATO 5), lipid phase surfactant (Span 20 or Span 80) and aqueous phase with surfactant (Tween 20 or Tween 80). Briefly, lipid phase consisted of Curcumin, lipid and lipid phase surfactant maintained at 70°C. An aqueous phase was prepared by dissolving aqueous surfactant in distilled water and heated to same temperature as of oil phase. Hot aqueous phase was mixed to oil phase to obtain preemulsion. These pre-emulsions were prepared with different combinations of lipid phase as well as aqueous phase surfactant (Table 5.3) and were kept at ambient temperature for one week to study their stability.

Preparation method of SLN

For preparation of Curcumin loaded SLN, pre-emulsion followed by probe sonication method was selected. Briefly, lipid phase consisted of Curcumin lipid and lipid phase surfactant maintained at 70°C. An aqueous phase was prepared by dissolving aqueous surfactant in distilled water (sufficient to produce 50 ml of preparation) and heated to same temperature as of oil phase. Hot aqueous phase was added to oil phase and homogenization was carried out at 70°C using high speed homogenizer at different speeds for 30 min. Coarse hot 'oil in water emulsion' so obtained was subjected to further size reduction using ultrasonic Probe sonicator for 10-30 min

Preparation of trial batches for selection of homogenization speed and sonication time

On the basis of preliminary solubility and pre-emulsion studies, Compritol ATO 888, Span 80 (lipid soluble surfactants), and Tween 80 (water-soluble surfactant) were selected for formulation of trial batches (Table 1). To select homogenization speed and sonication time, trial batches were prepared using different speeds of homogenization and sonication times and evaluated for particle size and size distribution.

Table 1: Composition of trial batches

Ingredients/Batch	CRN_1	CRN_2	CRN_3	CRN_4	CRN_5	CRN_6
Curcumin (mg)	100	100	100	100	100	100
Compritol ATO 888 (mg)	500	500	500	500	500	500
Span 80 (%)	3	3	3	3	3	3
Tween 80 (%)	3	3	3	3	3	3
Homogenization speed (rpm)	3000	3500	4000	4500	5000	5500
Sonication time (min)	5	10	15	20	25	30

Experimental design

In this study, a Box-Behnken design was introduced to optimize the formulation of solid lipid nanoparticles. Initial studies were undertaken to decide the Experimental excipients and their levels in the experimental design. The choice of lipid was based on the solubility and partitioning of Curcumin in the lipid. Aqueous phase surfactant and lipid phase surfactant were selected based on the stability of the dispersion prepared by using different surfactants. Three factors, the drug: lipid ratio (X1), concentration of Span 80 (lipid phase surfactant) (X2) and sonication time (X3) were used in the design and the responses were the average particle size (PS) (Y1) and % Entrapment Efficiency (EE) (Y2). These three factors that might affect the designed characteristic of nanoparticle formulation were varied over three levels (Table 2).

Table 2: Independent Variables and Their Selected Levels for SLN Formulation

Independent Variable	-1	0	+1
Drug: Lipid Ratio	1:5	1:7	1:9
Surfactant (Lipid Phase) Concentration	3%	4%	5%
Sonication Time	5 min	15 min	30 min

Particle size analysis

The SLN formulations were dispersed in distilled water at appropriate concentrations. The mean particle size of the formulations was measured using particle size analyzer based on the dynamic light scattering method. All measurements

were performed in triplicate.

Determination of entrapment efficiency

The entrapment efficiency of the prepared SLN was calculated by the centrifugation method. About 2 ml of dispersion of SLN and 5 ml of methanol was taken in a centrifuge tube and it was centrifuged at 13,000 rpm for 1 hour. After centrifugation, the supernatant was removed and diluted with appropriate solvent. The concentration of drug (free drug) in the supernatant layer was determined by using UV visible spectrophotometer.

Evaluation of an optimized batch of Curcumin loaded SLN

Particle size analysis and polydispersity index (PI)

The mean particle size and polydispersity index of the optimized batch of drug-loaded SLN were measured using particle size analyzer based on the dynamic light scattering method. The SLN formulations were dispersed in distilled water at appropriate concentrations. All measurements were performed in triplicate. The polydispersity index (PI) indicates the width of the size distribution.

Determination of entrapment efficiency and drug loading (DL)

The entrapment efficiency of an optimized batch of drug-loaded SLN was calculated by the centrifugation method

Zeta potential

The zeta potential of an optimized batch of drug-loaded SLN was measured by a zeta potential analyzer based on Laser Doppler Micro-electrophoresis. An electric field was applied to the dispersion of particles, which then moved with a velocity related to their zeta potential. This velocity was measured using a laser interferometric technique, which enables the calculation of electrophoretic mobility, and from this, the zeta potential

SEM Analysis

The optimized SLN formulation was freeze-dried to obtain a dry powder, which was then dispersed in distilled water and sonicated for 1-2 minutes to break any agglomerates. A drop of the dispersion was placed onto an aluminum SEM stub and air-dried under vacuum. Since lipid-based nanoparticles are non-conductive, the sample was coated with a 5-10 nm gold layer using a sputter coater under an argon atmosphere to enhance conductivity.

In vitro drug release study

The in vitro drug release study for both pure curcumin and the optimized SLN formulation (F_{12}) was conducted using two different methods. For pure curcumin, a USP Type II paddle dissolution apparatus was used, where 10 mg of drug was dispersed in 900 mL of phosphate buffer (pH 7.4) and stirred at 50 rpm at 37 ± 0.5°C. At specific time intervals (0, 1, 2, 4, 6, 8, 12, and 24 hours), 5 mL samples were withdrawn and replaced with fresh buffer, and drug release was quantified using UV-Vis spectrophotometry at 425 nm. For the SLN formulation (F_{12}), a dialysis membrane diffusion method was employed, where 10 mg equivalent of drug-loaded SLNs was placed inside a pre-soaked dialysis bag and immersed in 100 mL of phosphate buffer (pH 7.4) with 0.5% Tween 80 to enhance solubility. The system was stirred at 100 rpm at 37 ± 0.5°C, and samples were collected at the same time points, with drug content determined using UV-Vis spectrophotometry

Stability studies

The stability studies of the optimized SLN formulation were conducted as per ICH guidelines (Q1A R2) under different storage conditions: accelerated (40°C ± 2°C / 75% RH ± 5%), long-term (25°C ± 2°C / 60% RH ± 5%), refrigerated (4°C ± 2°C), and freeze-thaw cycles (-20°C to 25°C, alternating every 24 hours for 7 cycles). The SLN samples were stored in glass vials, protected from light, and analyzed at 0, 1, 3, and 6 months (accelerated) and 0, 3, 6, and 12 months (long-term).

3. RESULTS AND DISCUSSION

Organoleptic Properties of Curcumin

Curcumin was observed to have a bright yellow color, which is characteristic of its natural pigment properties. It was found to be odourless, indicating the absence of any volatile impurities or degradation products.

Melting Point Determination of Curcumin

The observed melting point of Curcumin ranged between 180°C, which is in accordance with reported literature values, indicating purity and thermal stability of the drug.

Solubility

The solubility of Curcumin was evaluated in different solvents, including organic and aqueous systems. It exhibited higher solubility in organic solvents such as methanol, ethanol, DMSO, and acetone, making them suitable for formulation. In contrast, poor solubility was observed in water and acidic buffers, indicating its hydrophobic nature. These results highlight

the necessity of using surfactants or lipid-based carriers to enhance Curcumin's solubility and bioavailability (Table 3).

Table 3: Solubility of Curcumin in Different Solvents

Solvent	Solubility (mg/mL)
Methanol	12.63 ± 0.12
Ethanol	10.33 ± 0.12
DMSO	25.43 ± 0.12
Acetone	20.23 ± 0.12
Distilled Water	0.0055 ± 0.0004
Phosphate Buffer (pH 4.2)	1.25 ± 0.05
0.1N HCl	0.85 ± 0.05

Calibration data

The calibration of curcumin in methanol, ethanol, and DMSO was performed at different concentrations (2, 4, 6, 8, and 10 µg/mL), and the absorbance values were recorded using UV-Vis spectrophotometry (Table 4). The correlation coefficient (R^2) for all solvents was >0.99, confirming the reliability of the calibration curves. Figures 1 to 3 illustrate the calibration curves.

Table 4: Calibration Data for Curcumin in Methanol, Ethanol, and DMSO

Concentration (µg/mL)	Absorbance (Methanol)	Absorbance (Ethanol)	Absorbance (DMSO)
2	0.210	0.268	0.221
4	0.575	0.542	0.452
6	0.860	0.819	0.687
8	1.135	1.073	0.911
10	1.420	1.340	1.141

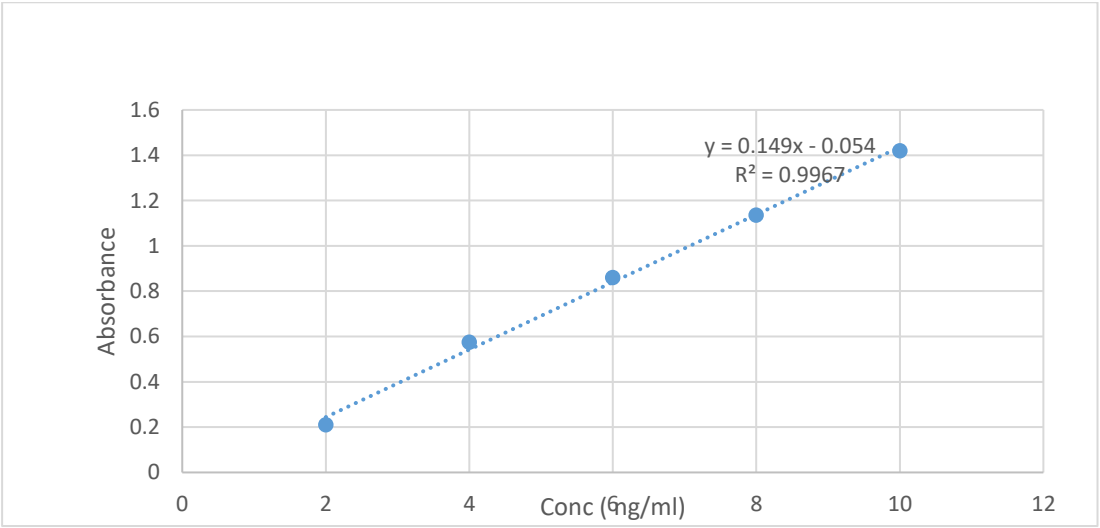

Fig 1: Calibration curve for Curcumin in Methanol

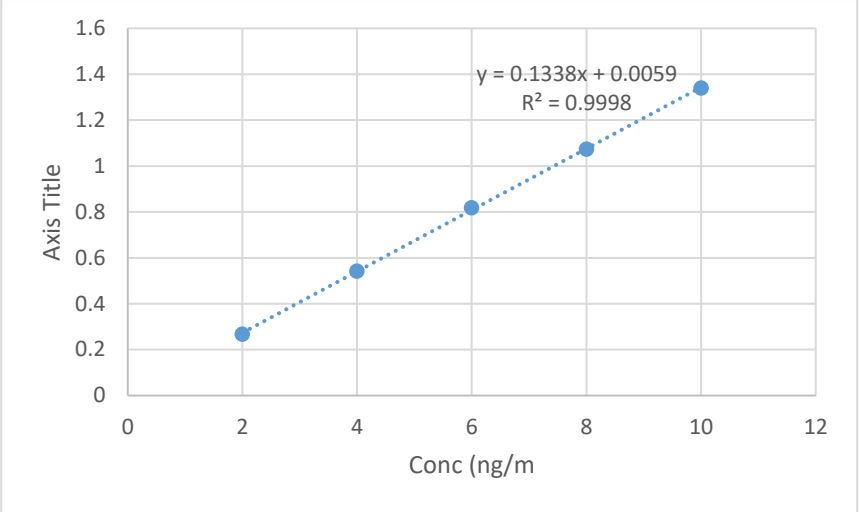

Fig 2: Calibration curve for Curcumin in Ethanol

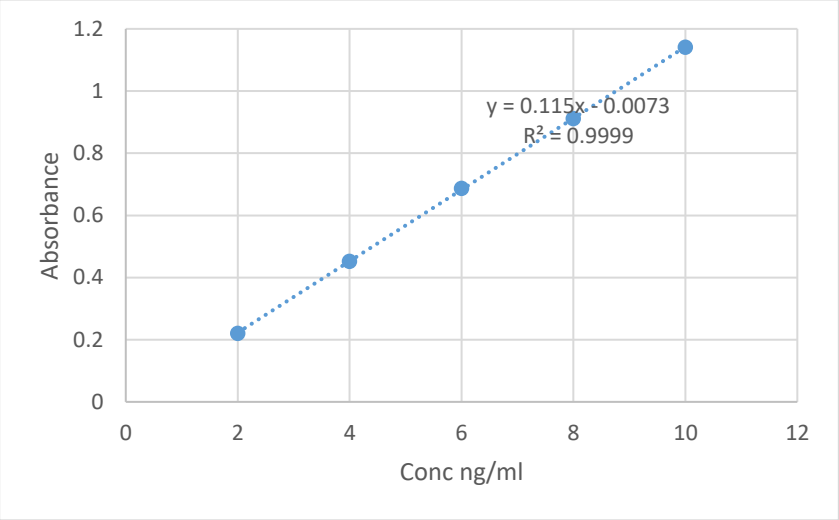

Fig.3: Calibration Data for Curcumin in DMSO

Solubility in solid Lipids

The solubility study of Curcumin in different solid lipids was conducted to determine the most suitable lipid for Curcumin-loaded SLNs. The results showed that Compritol 888 ATO required the least amount (1.15 ± 0.05 g) to solubilize 100 mg of Curcumin, indicating its superior solubilizing capacity and compatibility with the drug. Precirol ATO 5 and Emulcire exhibited moderate solubility, whereas Stearic Acid and Glyceryl Monostearate required a higher lipid amount, suggesting lower solubility and potential limitations in drug loading. Since higher solubility in lipids results in better encapsulation and stability of SLNs, Compritol 888 ATO was selected as the most suitable solid lipid for formulation

Solubility of Curcumin in Surfactants

The solubility of Curcumin in various surfactants was analyzed to select the best stabilizer for SLN formulation. Among all tested surfactants, Gelucire 44/14 exhibited the highest solubility (9.1 ± 0.08 mg/mL), indicating its excellent ability to enhance drug dispersion and stability. Labrafil M2125 and Labrafil M1944 also showed relatively high solubility, whereas Tween 20, Tween 80, Span 20, and Span 80 displayed lower solubility values, making them less effective in solubilizing Curcumin. Since an efficient surfactant ensures better nanoparticle stability and prevents aggregation, Gelucire 44/14 was identified as the optimal surfactant for Curcumin-loaded SLNs.

Optimization by QbD Approach

The Box-Behnken Design (BBD), a type of Response Surface Methodology (RSM) used for optimizing formulation parameters with a reduced number of experimental runs. This design effectively evaluates the influence of three independent variables—X_1 (Drug: Lipid Ratio), X_2 (Surfactant Concentration), and X_3 (Sonication Time)—on critical quality attributes

such as Particle Size (nm), Polydispersity Index (PDI), and Encapsulation Efficiency (%). The response values indicate a significant variation in particle size (162.41–480.29 nm), suggesting the impact of formulation conditions on nanoparticle characteristics. The PDI (0.14–0.31) reflects variations in size distribution, while Encapsulation Efficiency (61.63%–91.58%) highlights the effect of lipid content and processing conditions on drug entrapment. The Box-Behnken Design (BBD) is advantageous in reducing experimental runs while capturing quadratic interactions between variables, making it an efficient approach for SLN optimization (Table 5).

Table 5: Runs generated by Design-Expert® software with recorded responses of the runs

Formulation	X_1	X_2	X_3	Particle Size (nm)	PDI	Encapsulation Efficiency (%)
F_1	0	-1	-1	249.82	0.18	66.99
F_2	0	1	1	480.29	0.17	78.00
F_3	-1	0	1	392.80	0.17	80.73
F_4	1	0	-1	339.46	0.22	61.63
F_5	0	-1	1	162.41	0.31	81.26
F_6	1	0	0	421.58	0.24	65.97
F_7	0	0	0	321.37	0.20	89.34
F_8	-1	0	0	276.90	0.15	74.89
F_9	1	0	1	401.79	0.28	88.41
F_{10}	-1	0	-1	219.45	0.30	70.92
F_{11}	1	1	0	388.15	0.23	72.10
F_{12}	0	1	0	275.67	0.14	91.58
F_{13}	-1	1	0	198.78	0.27	79.45

ANOVA for Particle Size (Y_1):

The analysis of variance (ANOVA) for Particle Size (Y_1) shows that X_1 (Drug: Lipid Ratio), X_3 (Sonication Time), and X_1X_3 (interaction between Drug: Lipid Ratio and Sonication Time) have relatively high F-values, indicating that these factors have a more significant impact on particle size variation. However, none of the individual factors are statistically significant at the $p < 0.05$ level, though X_1X_3 ($p = 0.073$) approaches significance. (Table 6 &7)

Table 6: ANOVA for Particle Size (Y_1)

Sources	Sum of Squares	df	F Value	p-value
X_1	277.848	1	5.196	0.107
X_2	27.051	1	0.506	0.528
X_3	270.385	1	5.057	0.110
X_1X_2	0.038	1	0.001	0.980
X_1X_3	394.618	1	7.380	0.073
Residual	89.472	7	-	-
Lack of Fit	71.578	5	-	-

Table 7: Fit Statistics data of Regression Metrics for Particle Size (Y_1)

Parameter	Value
R^2	0.902
Adjusted R^2	0.610
Predicted R^2	0.415
Adequate Precision	5.678
Standard Deviation	7.312
Mean	321.472
Coefficient of Variation (%)	2.275

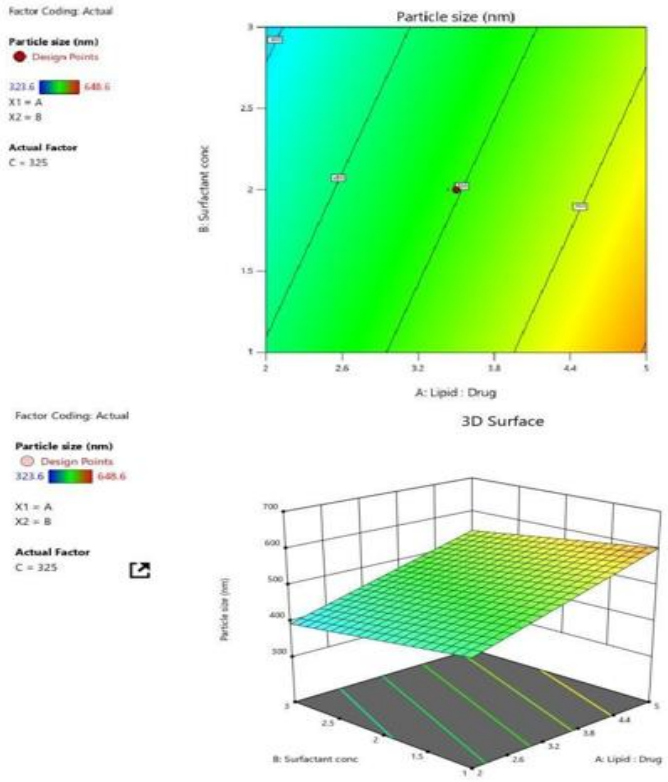

Figure 4: Response of Particle Size by Surface overlay Plot and 3D surface plot

ANOVA for PDI (Y_2):

The ANOVA for Polydispersity Index (Y_2) suggests that X_3 (Sonication Time) has the highest impact among the factors, as indicated by the highest F-value (5.605, $p = 0.097$), although it is not statistically significant at $p < 0.05$. Other factors, including X_1 (Drug: Lipid Ratio) and X_2 (Surfactant Concentration), show lower F-values, suggesting a lesser effect on PDI. (Table 8&9)

Table 8: ANOVA for PDI (Y_2)

Sources	Sum of Squares	df	F Value	p-value
X_1	0.125	1	3.214	0.144
X_2	0.034	1	0.821	0.405

X_3	0.218	1	5.605	0.097
X_1X_2	0.002	1	0.052	0.829
X_1X_3	0.189	1	4.859	0.115
Residual	0.076	7	-	-
Lack of Fit	0.061	5	-	-

Table 9: Fit Statistics data of Regression Metrics for PDI (Y_2)

Parameter	Value
R^2	0.845
Adjusted R^2	0.548
Predicted R^2	0.332
Adequate Precision	4.982
Standard Deviation	0.048
Mean	0.225
Coefficient of Variation (%)	21.333

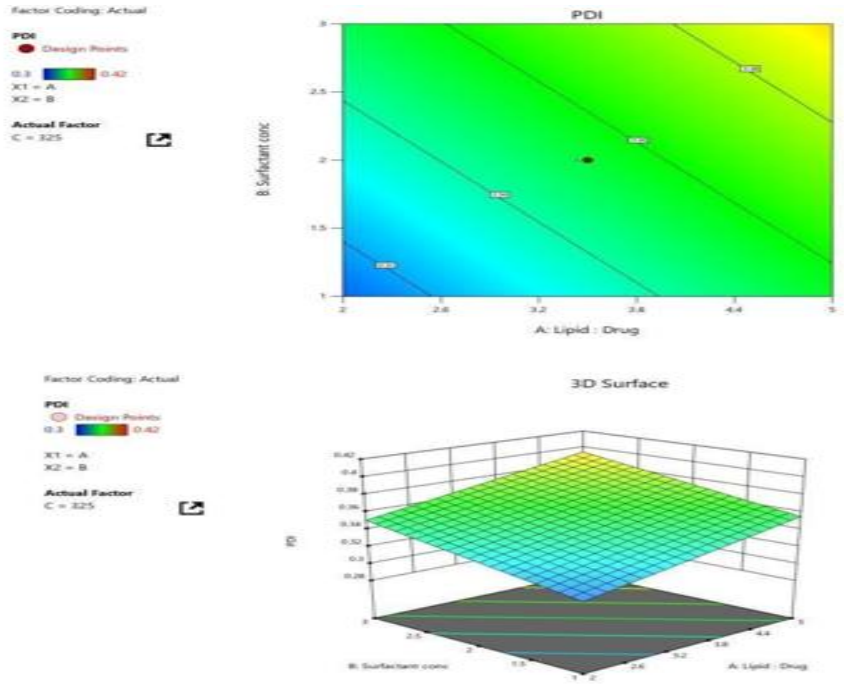

Figure 5: Response of PDI by Surface overlay Plot and 3D surface plot

ANOVA for Encapsulation Efficiency (Y_3)

The ANOVA for Encapsulation Efficiency (Y_3) indicates that X_3 (Sonication Time) has the most substantial effect on encapsulation efficiency ($F = 7.898$, $p = 0.068$), followed by X_1 (Drug: Lipid Ratio, $F = 4.872$, $p = 0.113$). Although these values suggest a notable impact, they do not reach statistical significance at $p < 0.05$. The X_1X_3 interaction also plays a moderate role ($F = 4.391$, $p = 0.126$). (Table 10&11)

Table 10: ANOVA for Encapsulation Efficiency (Y_3)

Sources	Sum of Squares	df	F Value	p-value
X_1	122.469	1	4.872	0.113
X_2	10.748	1	0.428	0.553
X_3	198.482	1	7.898	0.068
X_1X_2	1.507	1	0.060	0.814
X_1X_3	110.346	1	4.391	0.126
Residual	45.231	7	-	-
Lack of Fit	36.185	5	-	-

Table 11: Fit Statistics data of Encapsulation Efficiency (Y_3)

Parameter	Value
R^2	0.882
Adjusted R^2	0.590
Predicted R^2	0.399
Adequate Precision	5.214
Standard Deviation	5.612
Mean	78.463
Coefficient of Variation (%)	7.155

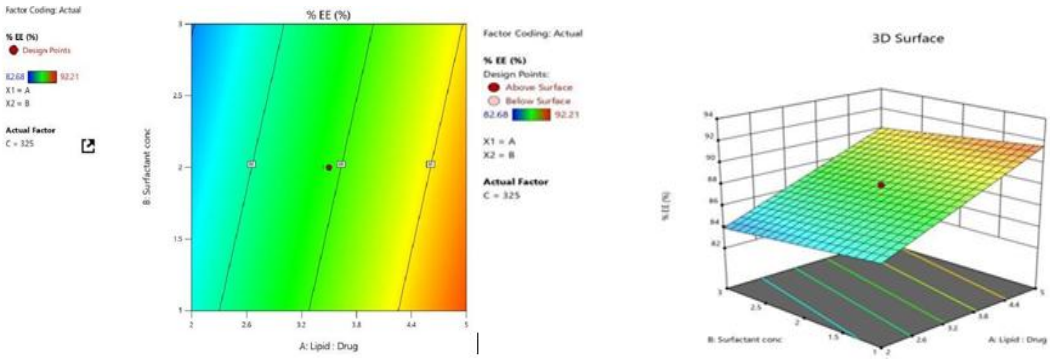

Figure 6: Response of %EE by Surface overlay Plot and 3D surface plot

FTIR of Pure Curcumin and SLNs

The FTIR spectrum of pure curcumin exhibited characteristic peaks at 3500–3200 cm^{-1} (O-H stretching), 1627 cm^{-1} (C=O stretching of the β-diketone structure), 1601 cm^{-1} (C=C stretching of the aromatic ring), and 1274 cm^{-1} (C-O stretching of phenolic groups). These peaks confirm the presence of functional groups characteristic of curcumin. In SLN formulations, a

slight shift and reduced intensity of peaks were observed, particularly in the C=O and O-H stretching regions, indicating molecular interactions between curcumin and the lipid matrix. The absence of new peaks suggests that no significant chemical interactions or degradation occurred, confirming the physical encapsulation of curcumin within SLNs (Figure 7).

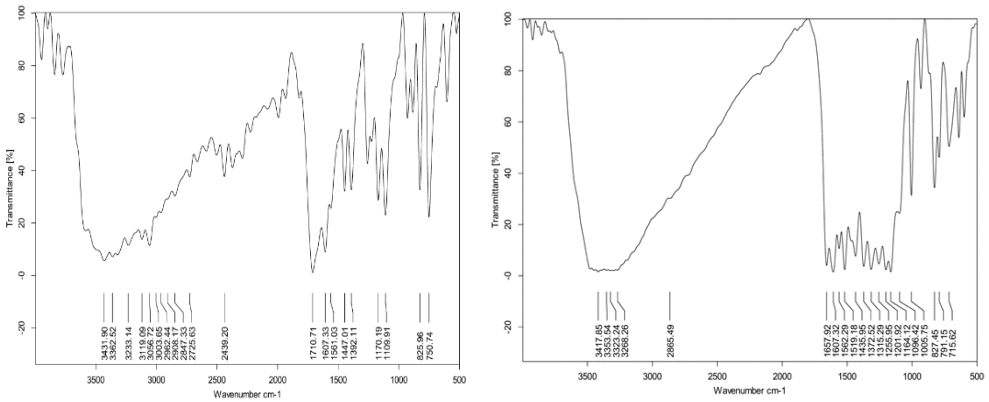

Figure 6.7: FTIR of Curcumin and Optimized Formulation (F12)

DSC Interpretation of Pure Curcumin and SLNs

The DSC thermogram of pure curcumin showed a sharp endothermic peak around 177°C, corresponding to its melting point, confirming its crystalline nature. In contrast, the DSC thermogram of curcumin-loaded SLNs exhibited a broadening or complete disappearance of this peak, indicating a transition from crystalline to an amorphous or molecularly dispersed state within the lipid matrix. (Figure 8).

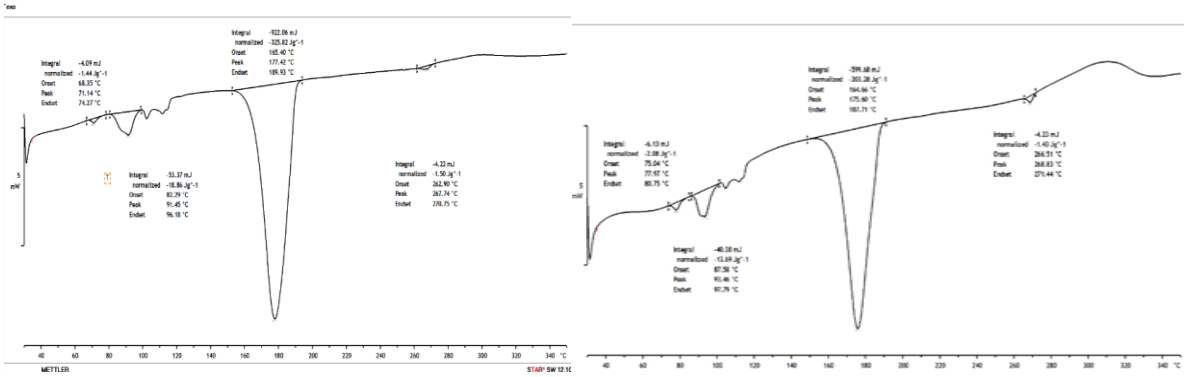

Figure 8: DSC graph of Curcumin and Curcumin –SLNs

SEM

The Scanning Electron Microscopy (SEM) analysis of Curcumin-loaded SLNs revealed that the particles exhibit a spherical shape with a smooth surface morphology. The SEM images confirm the uniform distribution of nanoparticles, indicating successful lipid recrystallization. The absence of crystalline drug particles suggests efficient encapsulation within the lipid matrix, contributing to enhanced drug stability and controlled release (Figure 9).

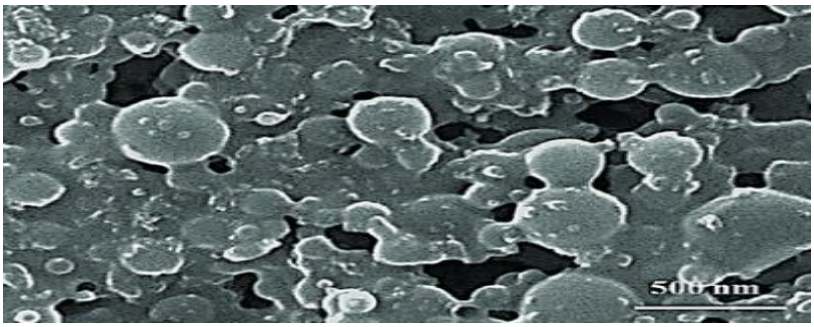

Figure 9: SEM of Optimized Formulation

Particle Size

The particle size of 275.67 nm is within the ideal range for SLN formulations, ensuring efficient cellular uptake and prolonged circulation time. A medium Drug: Lipid ratio (1:7) in F_{12} helps maintain a balance between drug loading and stability. The higher surfactant concentration (X_2 = 1, 5% surfactant) contributes to reducing surface tension and forming smaller particles. PDI is a measure of particle size distribution uniformity, with values <0.3 indicating a homogeneous formulation. The low PDI of 0.14 in F_{12} confirms a narrow particle size distribution, which is crucial for maintaining stability and preventing aggregation (Figure 10).

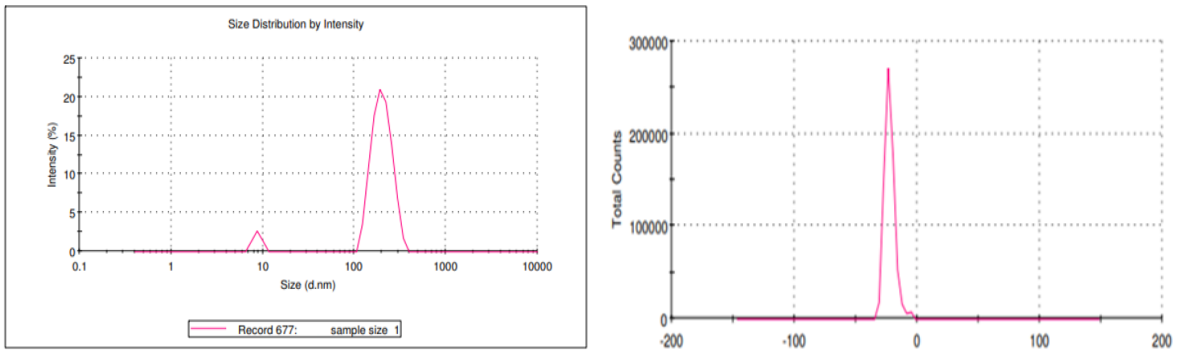

Figure 10: Particle Size and Polydispersity Index of Optimized Formulation

Encapsulation Efficiency

Encapsulation efficiency reflects the percentage of the drug successfully entrapped within the lipid matrix. F_{12} has the highest EE% (91.58%), attributed to the optimal surfactant concentration (5%), which stabilizes the formulation and prevents drug leakage. The intermediate sonication time (X_3 = 0, 15 min) also ensures efficient emulsification without excessive particle breakdown, thereby enhancing drug retention.

Drug Loading Capacity

The drug loading capacity was determined as 15.29 ± 3.56%

in vitro drug release study

The in vitro drug release study compared the pure drug, optimized SLN formulation (F_{12}), and marketed formulation over time. The pure drug showed slow and incomplete release due to poor solubility, while the SLN formulation exhibited a sustained release profile, indicating improved drug retention and controlled release. The marketed formulation showed a moderate release pattern, falling between the pure drug and SLN formulation, demonstrating its conventional drug release characteristics (Table 12).

Table 12: In Vitro Drug Release

Time (Hours)	Pure Drug Release (%) (N=3)	SLN Formulation Release (%) (N=3)	Marketed Formulation Release (%) (N=3)
1	12.0 ± 1.58	34.2 ± 0.62	27.0 ± 1.44
2	18.8 ± 1.11	48.6 ± 2.08	32.17 ± 0.79
4	25.7 ± 1.39	55.0 ± 1.02	38.33 ± 1.76
6	38.1 ± 0.91	66.0 ± 1.41	47.5 ± 0.81
8	42.7 ± 1.42	77.0 ± 2.27	56.67 ± 0.54
12	48.2 ± 1.20	82.0 ± 1.98	65.83 ± 1.37
24	57.2 ± 1.75	91.0 ± 1.56	75.0 ± 1.02

Stability study

The stability study of the optimized Solid Lipid Nanoparticles (SLNs) was conducted under different storage conditions—accelerated (40°C, 75% RH), long-term (25°C, 60% RH), and refrigerated (4°C)—over three months. At 0 months (initial time point), the formulation exhibited a particle size of 275.7 ± 0.37 nm, a PDI of 0.14 ± 0.00, and an encapsulation efficiency

of 91.5 ± 0.08%. After one month under long-term storage conditions, a slight increase in particle size was observed (280.37 ± 0.21 nm), along with a minor increase in PDI (0.15 ± 0.00) and a slight reduction in encapsulation efficiency (90.43 ± 0.12%). At the three-month mark under refrigerated conditions, further changes were noted, with particle size increasing to 285.53 ± 0.21 nm, PDI rising to 0.17 ± 0.00, and encapsulation efficiency slightly decreasing to 88.97 ± 0.12% (Table 13).

Table 13: Stability Study Results for Optimized SLN (F_{12})

Time Point	Storage Condition	Particle Size (nm) (Mean ± SD)	PDI (Mean ± SD)	Encapsulation Efficiency (%) (Mean ± SD)
0 Month	Accelerated (40°C, 75% RH)	275.7 ± 0.37	0.14 ± 0.00	91.5 ± 0.08
1 Month	Long-term (25°C, 60% RH)	280.37 ± 0.21	0.15 ± 0.00	90.43 ± 0.12
3 Months	Refrigerated (4°C)	285.53 ± 0.21	0.17 ± 0.00	88.97 ± 0.12

Drug Release Kinetics

Based on the release kinetics data for the optimized SLN formulation (F12), the First Order Model ($R^2 = 0.983$) provides the best fit, indicating that SLNs primarily follow first-order release kinetics. This suggests that drug release is concentration-dependent, meaning that as the drug is released, the rate of release decreases over time. Additionally, the Higuchi Model ($R^2 = 0.952$) also shows a strong correlation, indicating that diffusion plays a significant role in the drug release process. The Korsmeyer-Peppas Model ($R^2 = 0.934$) suggests that both diffusion and erosion mechanisms may contribute to drug release (Table 14).

Table 14: Release Kinetics for SLNs (Optimized Formulation F12)

Kinetic Model	R^2 Value	Rate Constant (k)
Zero Order	0.902	0.040
First Order	0.983	0.021
Higuchi Model	0.952	0.175
Korsmeyer-Peppas	0.934	0.124
Hixson-Crowell	0.872	0.145

4. CONCLUSION

The present study successfully developed and optimized solid lipid nanoparticles (SLNs) of curcumin, demonstrating significant potential for enhancing drug stability, and bioavailability. The optimized formulation (F_{12}) exhibited an ideal particle size (275.67 nm), polydispersity index (0.14), and encapsulation efficiency (91.58%), ensuring effective skin penetration and controlled drug release. The use of Compritol 888 ATO as the lipid carrier and Tween 80 as the surfactant contributed to the stability and uniformity of the formulation. The drug loading capacity of 15.29 ± 3.56% further validated the effectiveness of the formulation in incorporating curcumin within the SLN matrix. Characterization studies, including FTIR, DSC, and in vitro release profiles, confirmed the integrity of the formulation, while in vitro diffusion studies suggested sustained drug release over an extended period. Future studies will focus on in vivo evaluations and clinical trials to establish the clinical applicability of this formulation in treating inflammatory skin conditions.

REFERENCES

[1] Karsten Mader, 187-212. 33. Biswajit Basu, Kevin Garala, Ravi Bhalodia and Bhavik Joshi, Kuldeep Mehta, J. Pharm. Res., 3(1),84-92 (2008).

[2] Vobalaboina Venkateswarlu and Kopparam Manjunath, J. Controlled Rel., 95, 627-638 (2004).

[3] Hania Degobert, Adv. Drug Delivery Reviews, 1688-1713 (2006).

[4] N. K. Jain, Controlled and Novel Drug Delivery, First Edition, CBS Publishers and Distributors, (1997) 3-28.

[5] Lang Sc, Lu L. F, Cai Y and Zhu J. B, Liang BW and Yang CZ, J. Controlled Release, 59, 299-307(1999).

[6] L. Harivardhan Reddy and R. S. R. Murthy, AAPS Pharm. Sci. Tech., 6(2), 24 (2005)

[7] Melike Uner, Gulgun Yener, Int. J. Nanomedicine, 2(3), 289-300 (2007).

[8] Karsten Mader, 187-212. 41. Milan Stuchlík and Stanislav Žák, Biomed, Papers, 145(2), 17-26 (2001).

[9] Kesharwani R, Sachan A, Singh S, Pate D. Formulation & Evaluation of Solid Lipid Nanoparticle (SLN) Based Topical Gel of Etoricoxib. J App Pharm Sci, 2016; 6 (10): 124-131.

[10] Ekambaram P, Abdul HS. Formulation and evaluation of solid lipid nanoparticles of ramipril. J Young Pharm. 2011 Jul;3(3):216-20. doi: 10.4103/0975-1483.83765. PMID: 21897661; PMCID: PMC3159275.

[11] Pople PV, Singh KK. Development and evaluation of topical formulation containing solid lipid nanoparticles of vitamin A. AAPS PharmSciTech. 2006;7(4):91. doi: 10.1208/pt070491. PMID: 17285742; PMCID: PMC2750328.

[12] Rahmanian-Devin P, Askari VR, Sanei-Far Z, Baradaran Rahimi V, Kamali H, Jaafari MR, et al. Preparation and characterization of solid lipid nanoparticles encapsulated noscapine and evaluation of its protective effects against imiquimod-induced psoriasis-like skin lesions. Biomedicine & Pharmacotherapy [Internet]. 2023 Nov 3;168:115823.

[13] Begum M and Shaik NB: Formulation and evaluation of linezolid loaded solid lipid nanoparticles as topical gel. Int J Pharm Sci & Res 2020; 11(10): 4924-33. doi: 10.13040/IJPSR.0975-8232.11(10).4924-33

[14] Debarati Maiti, Mohammed Naseeruddin Inamdar, Mansour Almuqbil, Suresh S, Basheeruddin M, Sultan Alshehri, et al. Evaluation of solid-lipid nanoparticles formulation of methotrexate for anti-psoriatic activity. Saudi Pharmaceutical Journal. 2023 Jun 1;31(6):834–44.

[15] Kumar R, Syed M, Sowmya NT. Development of formulation and evaluation of topical micro emulsion gel loaded with terbinafine HCL micro emulsion. World Journal of Biology Pharmacy and Health Sciences. 2024 Aug 7;19(2):074–89.

[16] P.A. Panmand, P. R. Mahaparale, V. P. Thorat. Development and Evaluation of Acitretin Loaded Solid Lipid Nanoparticles for Topical Drug Delivery System. Research Journal of Pharmacy and Technology. 2024; 17(3):1015-2. doi: 10.52711/0974-360X.2024.00157

[17] Khan AS, Shah KU, Mohaini MA, Alsalman AJ, Hawaj MAA, Alhashem YN, et al. Tacrolimus-Loaded Solid Lipid Nanoparticle Gel: Formulation Development and In Vitro Assessment for Topical Applications. Gels. 2022 Feb 18;8(2):129.

[18] El-Housiny S, Shams Eldeen MA, El-Attar YA, Salem HA, Attia D, Bendas ER, et al. Fluconazole-loaded solid lipid nanoparticles topical gel for treatment of pityriasis versicolor: formulation and clinical study. Drug Delivery. 2017 Dec 14;25(1):78–90.

[19] Nair A, Shah J, Al-Dhubiab B, Jacob S, Patel S, Venugopala K, et al. Clarithromycin Solid Lipid Nanoparticles for Topical Ocular Therapy: Optimization, Evaluation and In Vivo Studies. Pharmaceutics. 2021 Apr 9;13(4):523.

[20] Jain S, Jain S, Khare P, Gulbake A, Bansal D, Jain SK. Design and development of solid lipid nanoparticles for topical delivery of an anti-fungal agent. Drug Delivery. 2010 May 21;17(6):443–51.