ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

Quality-by-Design Based Development and Physicochemical Characterization of Nanostructured Lipid Carrier Systems for Enhanced Systemic Delivery in the Management of Systemic Lupus Erythematosus

Ritesh Fule[1*]; Prajakta Awachat[2]

[1]Associate Professor

[1,2]Department of Pharmaceutical Quality Assurance, Dadasaheb Balpande College of Pharmacy, Rastrasant Tukadoji Maharaj Nagpur University, Besa Nagpur 440037, Maharashtra, India

[1]ORCID ID- 0000000318982957

Corresponding Author: Ritesh Fule[*]

Publication Date: 2026/03/19

Abstract: Nanostructured lipid carriers containing celecoxib were prepared to treat arthritis-associated Systemic Lupus Erythematosus. CLX-NLC was formulated using hot emulsion ultrasonication method. In preparation of CLX-NLC, stearic acid (solid lipid), oleic acid (liquid lipid), and tween 80 (surfactant) were used. A three-level three-factor box Behnken design was adopted to optimize the formulated nano-structured lipid carrier system. The independent factors were solid lipid amount (X_1), liquid lipid amount (X_2), and surfactant amount (X_3). The examined responses were entrapment efficiency (Y_1, %), and particle size (Y_2, nm). The optimum formula showed high entrapment efficiency of 81%, a small particle size of 138 nm, and a low polydispersity index of 0.248. FTIR spectroscopy shows that the celecoxib is compatible with other excipients like stearic acid, oleic acid, and tween 80. In DSC the melting endothermic peak of celecoxib was not observed in the thermogram of CLX-NLC showed the developed CLX-NLC formulation. The X-ray diffractogram of CLX-NLC showed decrease in intensity of the peaks which leads to amorphization of drug. SEM micrographs revealed that the surface was smooth of prepared NLC formulation and was in spherical shape nature. The in-vitro dissolution study showed a longer retention time of 15 hours in CLX-NLC. In the storage stability study, optimized CLX-NLC was found to be stable for 3 months of storage in a room and accelerated stability conditions. In vivo pharmacokinetic research in Sprague- Dawley rats displayed that the C_{max}, T_{max}, MRT, and AUC_{0-36} hrs were increased two times as compared to pure drug. Current study confirms that CLX-NLC will be an effective medication therapy for SLE patients.

Keywords: *Systemic Lupus Erythematosus, Celecoxib, Nano Lipid Carrier System, Sustained Release.*

How to Cite: Ritesh Fule; Prajakta Awachat (2026) Quality-by-Design Based Development and Physicochemical Characterization of Nanostructured Lipid Carrier Systems for Enhanced Systemic Delivery in the Management of Systemic Lupus Erythematosus. *International Journal of Innovative Science and Research Technology*, 11(3), 1342-1355. https://doi.org/10.38124/ijisrt/26mar275

I. INTRODUCTION

Systemic lupus erythematosus (SLE), an autoimmune illness which encourage the production of autoantibodies. SLE affects different organs and tissues all over the body, can cause the creation and deposition of immune complexes(1). SLE affects 20-150 people out of every 100,000 worldwide, and women are nine times more likely than men to have the condition.(2) In its complicated aetiology, genetic and environmental elements are acknowledged. Numerous drugs have the potential to exacerbate SLE, detect clinically silent SLE, or, in most cases, generate lupus-like symptoms.(3)

Systemic symptoms include excessive and intrusive weariness, chilblains, cognitive fog, fever, swollen lymph nodes, mouth ulcers, and weight loss (4). SLE typically

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

manifests as rashes, which may be transient or disfiguring. Rashes are often induced by sunshine and may lead to alopecia and scarring(5). The word "lupus" comes from the usual malar clean of redness over the cheekbones, which resembles a butterfly. Arthritis, nodules, or contractures may occur when the joints, tendons, and muscles get inflamed. This can also cause pain and impairment (6)(7).

SLE has many complications same as that of rheumatoid arthritis. There are very less treatments available for RA related SLE. Lupus is a chronic disease with very less available treatments. Rheumatoid arthritis complications were prevalent in Lupus patients for which NSAID conventional dosage regimen of higher dosage is preferred(8)(7). To solve the problems associated with conventional delivery systems, Celecoxib loaded nanocarrier lipid system could be developed. Developed NLC system helps to enhance the solubility of drug as well as it increases the absorption which will proactively benefit the patient therapy effectively. Subsequently prolonged retention of drug for more than 12 hours helps to reduce the higher dose toxicity(9)(10).

The innovative colloidal carriers in the latest generation of lipid nanoparticles, known as nanostructure lipid carriers (NLC), have come to the fore in recent developments. Potentially improving the efficacy of pharmaceuticals, nutraceuticals, and other materials, this method for delivering drugs boasts an optimized release profile, drug targeting, high stability, good retention efficiency, incorporation of hydrophobic and hydrophilic drugs, low biotoxicity of the carrier, prevention of solvent-based substances, and good scalability.(11) Liquid lipid, which can disrupt the extremely regular lattice structure, generate an irregular matrix structure, and increase the area for tolerating pharmaceuticals, is inserted into NLCs as a means of overcoming the limitations of SLN. NLC also includes relatively low drug payloads and probable drug expulsion.(12) They have a unique nanostructure, which improves DL and solidly encapsulates the medicine, extending storage time.(13)

The intent of the present research was to formulate CLX-NLC using the hot emulsification-ultrasonication technique. The formulated CLX-loaded NLCs were evaluated utilizing stearic acid as the solid lipid, oleic acid as the liquid lipid, and Tween 80 as the surfactant. The objective was to maintain the distribution of CLX. The optimization of CLX-NLC focused on reducing particle size and improving entrapment efficiency. The optimized formula was further assessed for morphological characteristics, both in vivo and in vitro.

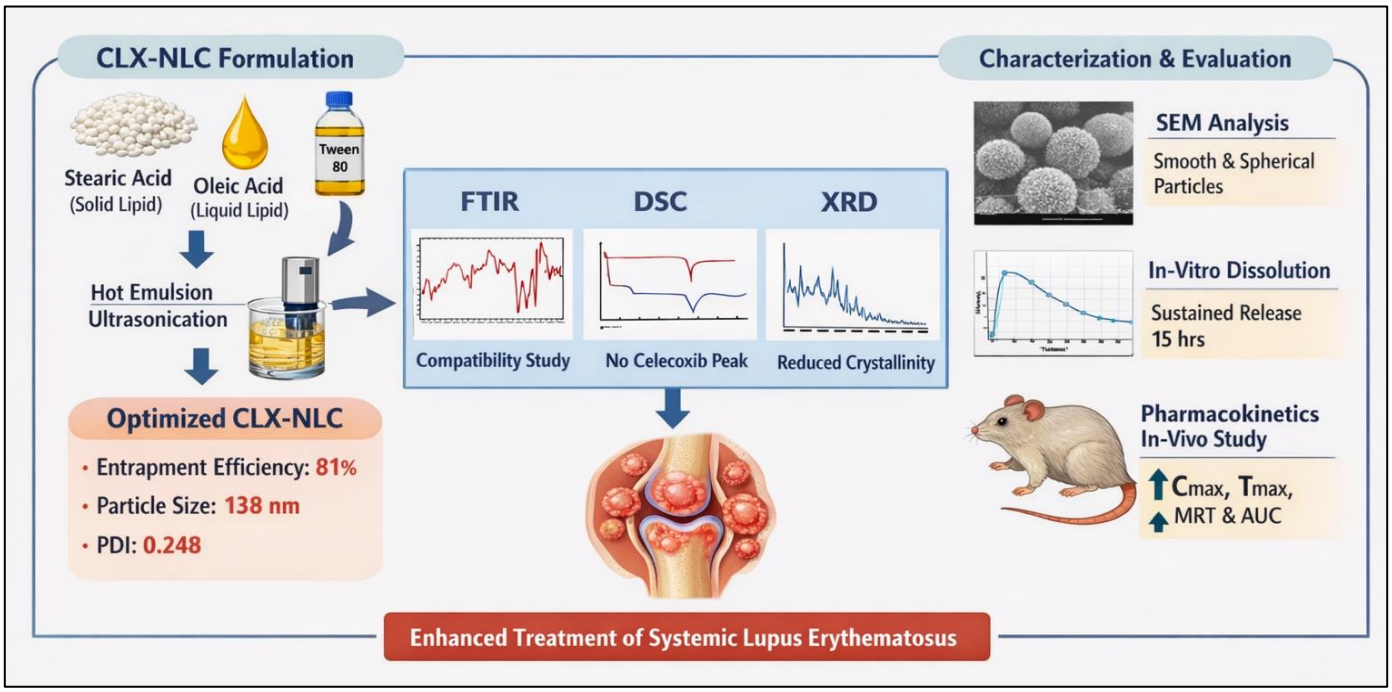


Fig 1 Graphical Abstract

II. MATERIALS AND METHODS

➢ *Materials*

Yucca Enterprises Mumbai supplied celecoxib. Stearic acid was procured from Research Lab Fine Chem Industries, located in Mumbai, India. Oleic acid along with organic solvents including ethanol, methanol, and acetone was acquired from Loba Chemie Pvt Ltd., Mumbai, India. All additional reagents and substances used were of scientific quality.

➢ *Methodology*

To check the solubility of solid lipids, a variety of solid lipids including stearic acid, bees wax, Compritol 888 ATO, cholesterol, and palmitic acid were examined. The solid lipid was precisely weighed into glass vials and heated to 70 °C. 10 mg celecoxib was added to these vials with continuous stirring. After being cooled to room temperature, it was checked for precipitation. Solid lipids that did not show any precipitation were selected for further studies(13).

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

- *Screening of Liquid Lipids*

Celecoxib's solubility in various liquid lipids was assessed by dissolving 5 mg of CLX in 5 ml of various oils (oleic acid, castor oil, paraffin oil, and caprylic acid) in small vials. The vials were securely stoppered and mechanically shaken for 72 hours at 25°C to achieve equilibrium. The lipids were then filtered and diluted with buffer solution pH 6.8 and then analyzed via UV spectrophotometer at a wavelength of 251 nm to determine the concentration of CLX in each lipid. The liquid lipid showing the highest solubility was then selected as a liquid lipid for the formulation of CLX-NLC.(14).

- *Selection of Surfactants*

Five surfactants (tween 80, tween 20, span 80, span 20, and tween 60) were examined. To prepare CLX-NLC, varied concentrations of these surfactants were utilised. Particle size and entrapment efficiency were measured. For the CLX-NLC formulation, the surfactant with more drug entrapment and smaller particle size was chosen.(15).

- *Formulation and Optimization of CLX-NLC*

Using Design Expert software 13, a three-level, three-factor box Behnken design was used to examine the effects of three independent variables—solid lipid (X1), liquid lipid (X2), and surfactant (X3)—at three levels (-1, 0, +1) as shown in Table 1 and their actual values (16). We examined particle size (PS, Y1, nm) and entrapment effectiveness (EE, Y2, %). The composition of each of the 15 runs is indexed in Table 2.

The choice of the best fit model was based upon adequate precision ratio, determination coefficient (R^2), and analysis of variance (ANOVA) to recognize the significance of the model and the consequences of each factor at $P \leq 0.05$.

Design Expert 13 software was used to generate 3D, contour, and interaction plots for each plot for each response to study the effect of each factor and show up the interaction between them.

Table 1 Variables in Three Level 3 Factor Box Behnken Design for Preparation of CLX-NLC.

Independent variables	**Levels**		
	Low (-1)	**Medium (0)**	**Medium (1)**
X_1: Concentration of stearic acid	800	1000	1200
X_2: Concentration of oleic acid	400	500	600
X_3: Concentration of tween 80	300	400	500
Responses	Desirability constraints		
Y_1: Particle size	Minimize		
Y_2: Entrapment efficiency	Maximize		

Table 2 The Composition and the Measured Responses of Three Level Three Factor Box Behnken Design for Preparation of CLX-NLC.

Formula Code	**Formulation Independent variables Responses Y_1 Y_2**				
	X_1	**X_2**	**X_3**	**PS (nm)**	**EE (%)**
CLX-NLC 1	-1	-1	0	185	83.15
CLX-NLC 2	1	-1	0	224	81
CLX-NLC 3	-1	1	0	237	77
CLX-NLC 4	1	1	0	305	78
CLX-NLC 5	-1	0	-1	136	80.78
CLX-NLC 6	1	0	-1	159	86
CLX-NLC 7	-1	0	1	112	81
CLX-NLC 8	1	0	1	150	78.21
CLX-NLC 9	0	-1	-1	110	80
CLX-NLC 10	0	1	-1	120	75
CLX-NLC 11	0	-1	1	138	79
CLX-NLC 12	0	1	1	153	71
CLX-NLC 13	0	0	0	182	83
CLX-NLC 14	0	0	0	182	83
CLX-NLC 15	0	0	0	183	83

X1: Concentration of stearic acid

X_2: Concentration of oleic acid

X_3: Concentration of tween 80

- *Preparation of CLX-NLC*

Using the hot emulsion ultrasonication process, CLX-NLC was created. 40 mg of CLX was dissolved in methanol to create solution A. Oleic acid and stearic acid were dissolved in acetone to produce solution B. Solutions A and B were combined at 70°C to create an organic phase. The aqueous phase was developed by disintegrating Tween 80 in

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

water at 70°C. The organic phase was gradually injected into the aqueous phase at 1000 rpm for a duration of 15 minutes. The mixture was sonicated using a probe-type sonicator while positioned in an ice bath to prevent excessive heating from the sonication process. The prepared systems were maintained in an ice bath for 15 minutes to facilitate the solidification of the developed NLCs. The resulting formulations were stored at 4°C for subsequent analysis. All formulations were prepared in triplicate to ensure reproducibility.

- *Physicochemical Characterization of prepared CLX-NLC*

✓ *Determination of Particle Size, Zeta Potential, and Polydispersity Index*

Zeta sizer Anton Paar (Litesizer 500) was used to assess particle size, zeta potential, and polydispersity index (PDI) at 25°C. Samples were prepared by 10 times dilution using distilled water to produce a proper uniform dispersion with good scattering intensity. In order to ensure the reproducibility of the results, each sample was measured three times. (17).

✓ *Determination of Entrapment Efficiency (EE%)*

Drug entrapment performance determines the quantity of drug successfully absorbed into the nanocarrier system. The computation is based on the total quantity of drug utilized during formulation. About 4ml of CLX-NLC formulation was taken in centrifuge tube and was centrifuged for 30 mins at 9500 rpms in cooling centrifuge (Compact Cooling Centrifuge Remi). After centrifugation CLX dissolving in the supernatant was measured using an ultraviolet–visible spectrophotometer (Shimadzu-1800) at a wavelength of 251 nm.(18) Drug entrapment efficiency was calculated by the formula,

$$\% \text{ Entrapment Efficiency} = \frac{\text{Total amount of drug} - \text{amount of free drug} \quad X\ 100}{\text{Total amount of drug}}$$

- *Solid State Characterization of CLX-NLC*

✓ *Fourier Transform Infrared Spectroscopy (FTIR)*

To determine drug-lipid compatibility in NLC production, FTIR spectroscopy was conducted. Shimadzu Affinity 1S FTIR spectrometer was used. A certain amount of sample was combined with potassium bromide (KBr), and pure drug, solid lipid, liquid lipid, and surfactant FTIR signals were seen (19).

✓ *X-Ray Diffraction Study*

X-ray diffraction study was conducted utilizing the Philips Analytical Xperto Pro PW-1710, featuring a resolution of 0.001 Å. The samples' diffraction pattern was captured in stages of 0.01 o/sec using a 2 θ range of 5–60◦. Cu K radiation was employed to power the X-ray source, functioning at 40 kV and 30 mA (20).

✓ *Differential Scanning Calorimetry (DSC)*

DSC is usually used to provide information on physical properties of a compound or formulation, by measuring the heat loss or gain resulting from physical or chemical changes within a sample as a function of the temperature. DSC also gives an insight into the melting and re-crystallization behavior of crystalline materials. CLX and CLX-NLC were subjected by the DSC to assess a possible melting point of the lipid and thermal behavior of the materials(21).

- *In-Vitro Dissolution Study*

We used the USP type I dissolution apparatus (Electrolab Dissolution Tester (USP) TDT-08L) at 50 rpm and a temperature of 37 ± 0.5°C to do in-vitro drug release studies. Phosphate buffer 6.8 was used as the dissolution medium. At various times, 5 ml aliquots were taken. The corresponding volume of dissolving medium replaced samples. UV spectrophotometers evaluated solutions at 247 nm after filtering with Whatman paper. Celecoxib nano lipid carrier system drug release data was fitted to zero-order, first-order kinetics models. Higuchi and Korsmeyer-Peppas to study medication release and mechanism (23).

- *Bioavailability Assessment*

After approval by the institution animal ethics committee (IAEC), the animal studies followed CPCSEA rules. KUSUM Lifesciences, Nanded, provided 220-240 g male Sprague-Dawley rats. For seven days, all animals with unlimited access to food and water were kept in a breeding room (25+2 °C, 60+ 5% RH, fresh air). 10 rats were randomly assigned to test (control) and CLX-NLC groups. CLX and CLX-NLC were given orally at 3.72 mg/kg. At 1, 3, 6, 12, 24, and 48 hours, 3 mL of retro orbital plexus blood was taken in a heparinized tube. Plasma was isolated by centrifuging blood at 9500 RPM for 15 min. Each 100 µL plasma sample received 1 ml of acetonitrile extraction solvent. After vortexing and centrifuging at 9500 RPM for 10 min, nitrogen gas dried the mixture. A 1 ml internal standard (1 µg Zileuton concentration) was applied to measure CLX content. Plasma concentration-time curves provided pharmacokinetic characteristics such AUC0-36h, t1/2, Cmax, and Tmax.

- *Stability Study*

In accordance with ICH guidelines Q1A (R2), the optimized batch of CLX-NLC was incubated at regular (25 ± 2 °C temperature and 60 ± 5% RH) and accelerated (40 ± 2 °C temperature and 75 ± 5% RH) conditions for 3 months in a stability chamber (Remi SC-6 Plus). Stability was determined by formulation appearance, particle size, and entrapment efficiency. (24) Temperature and humidity were measured for 0, 1, and 3 months.

III. RESULTS AND DISCUSSION

➢ *Screening of Solid Lipids:*

The solid lipids were taken in different amount and the solubility of lipids was screened with CLX. It was observed that when solid lipid was taken in more quantity it was not

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

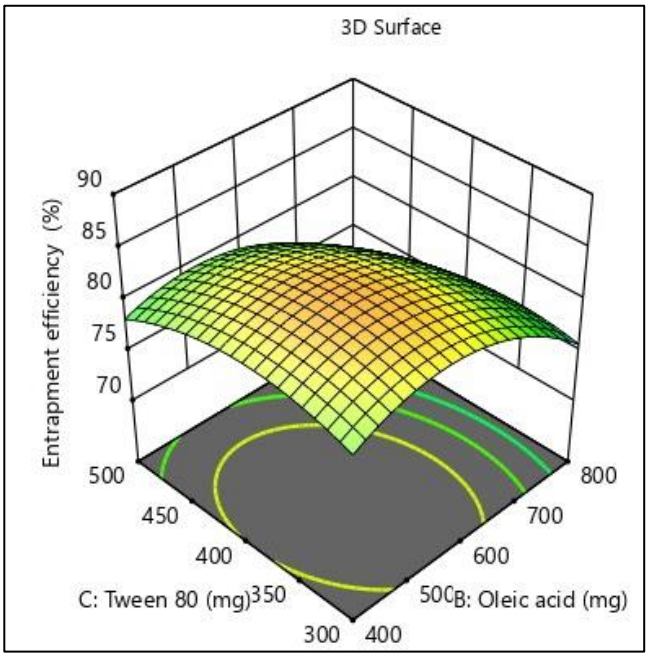
soluble with drug. Hence, solid lipid and CLX were taken in same quantity. From all the lipids, stearic acid showed best solubility with CLX. So, it was selected as a solid lipid.

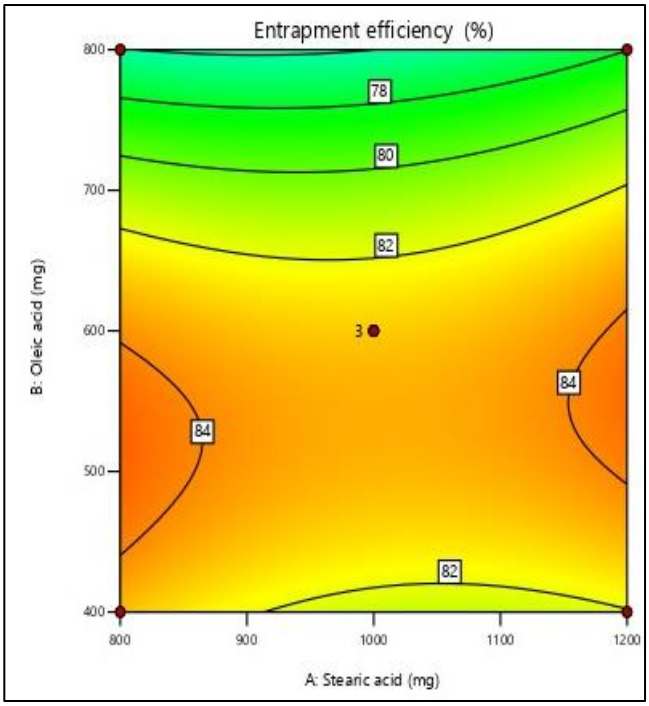
➢ *Screening of Liquid Lipid*

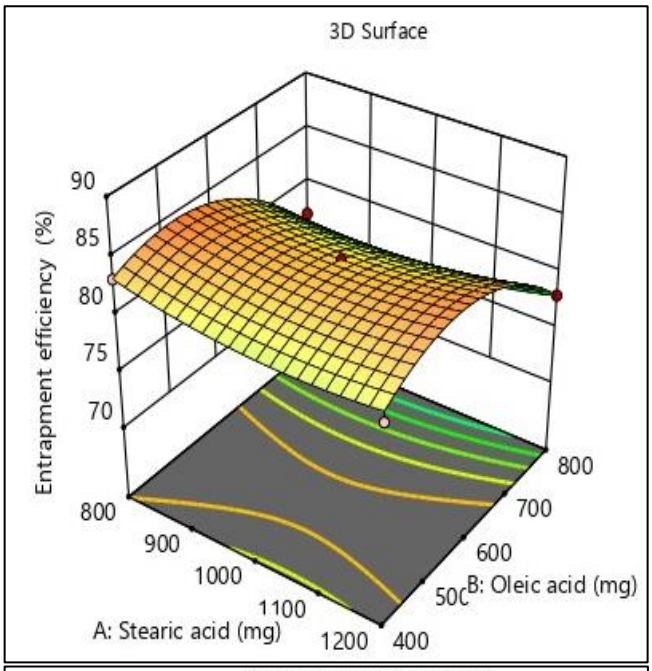
Saturation solubility of CLX with different liquid lipid was done. It was observed that oleic acid was best soluble with CLX and showed good compatibility with stearic acid and tween 80. So oleic acid was selected as liquid lipid.

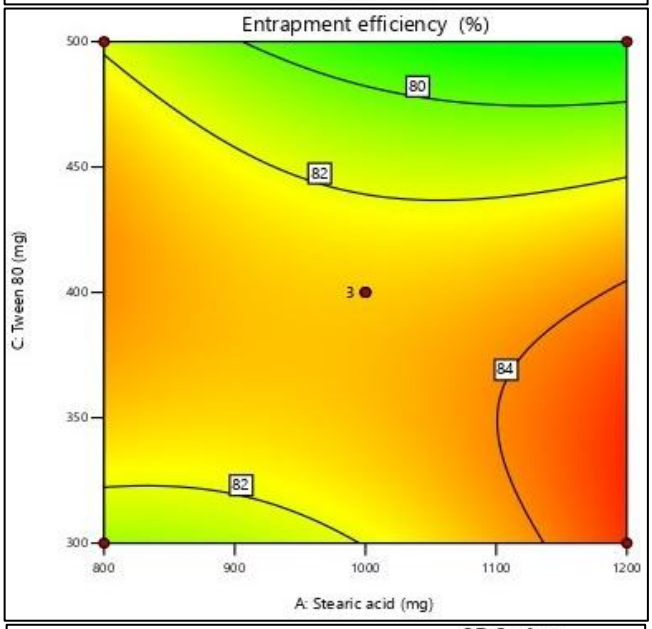
➢ *Screening of Surfactants*

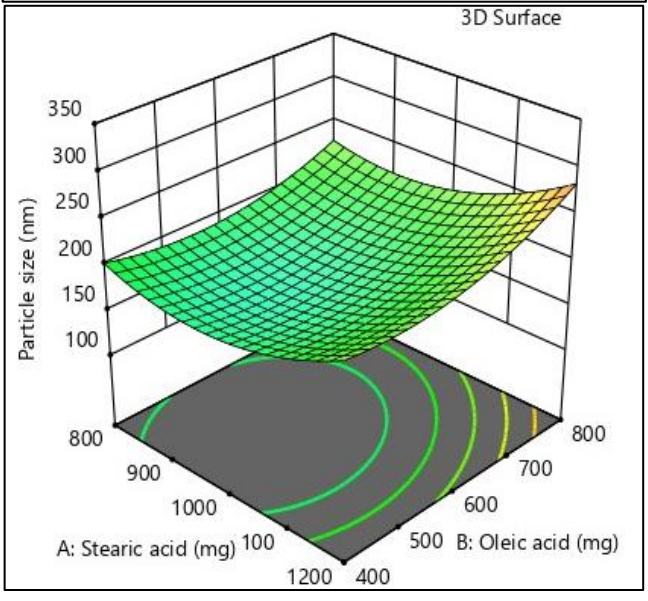
After screening the surfactants, it was found that CLX-NLC which was formulated by using tween 80 as a surfactant, showed the minimum particle size as well as maximum entrapment efficiency. So, it was further selected as a surfactant.











ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

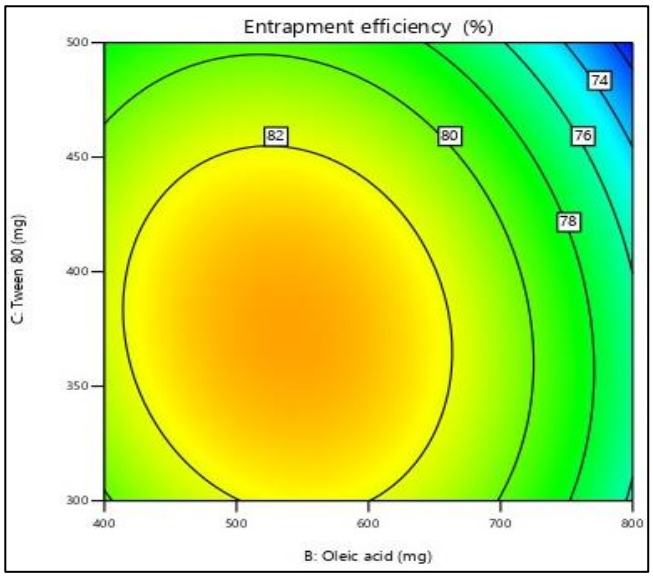
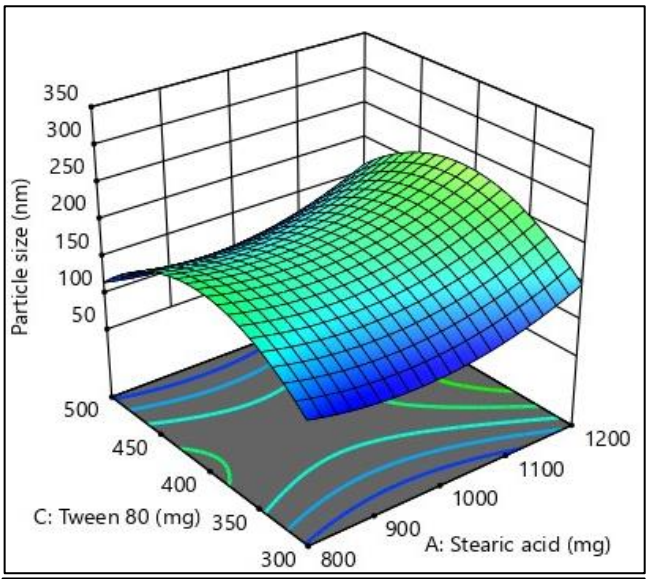
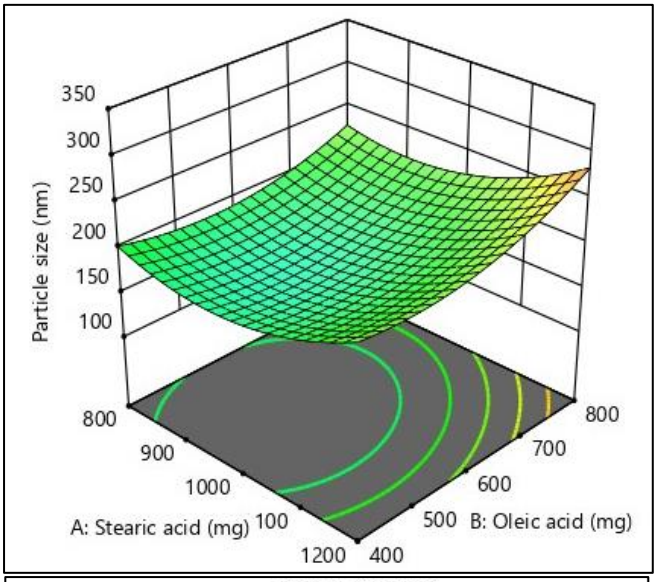
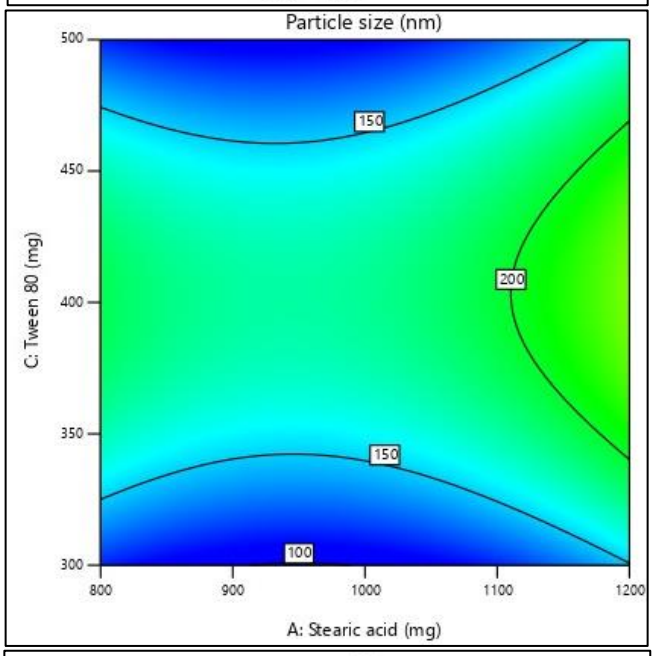
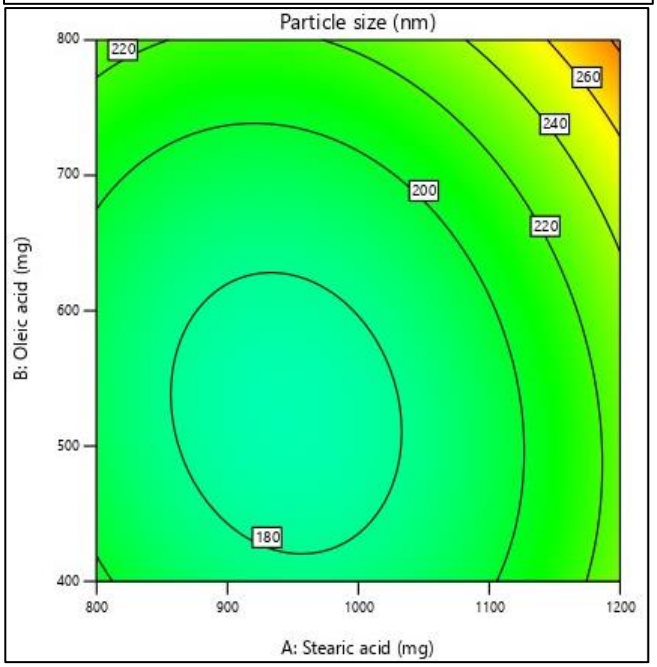


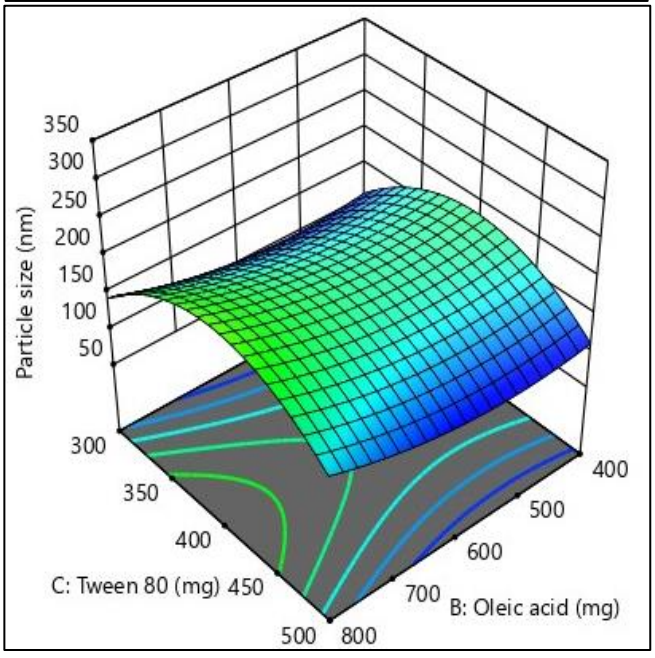
Fig 2 DOE of Formulation Batches with EE Factor











ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

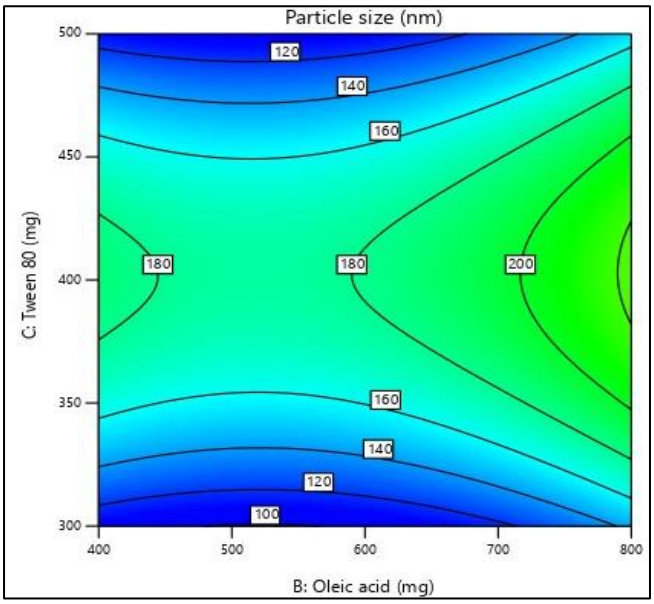


Fig 3 DOE of Formulation Batches with Particle Size Factor

➢ *Development and Optimization of CLX-NLC*

Development of celecoxib nano lipid carrier system of celecoxib was successfully prepared using emulsion evaporation–solidification at low temperature technique.

- *Optimization of NLC:*

Design expert software has generated 15 experimental runs. The value of two dependent variables Y1: Particle size(nm), Y2: Entrapment Efficacy (%) are in the range of 110nm-350nm, 71%-86% respectively. The quadratic model obtained for the formulations was suitably fitted. The effect of independent variables on solid lipid, surfactant concentration, and liquid lipid is presented on a three-dimensional graph.

✓ Response 1 (Y1): Effect of Independent variable on particle size

The average particle size of all the 15 experimental runs was found to be 136 nm, hence these values lie between the minimum and maximum value of the size 110 to 305 nm, respectively.

✓ *Particle Size:*

+182.33+21.00*A+19.75*B+3.50*C+7.25*AB+3.75*AC+1.25*BC+32.21A^2+23.21*B^2-75.29*C^2

Entrapment Efficacy was found to be 71-86%

✓ *Entrapment Efficacy:*

+83.00+0.1600*A-2.77*B-1.57*C+0.7875*AB-2.00*AC-0.7500*BC+1.02*A^2-4.23*B^2-2.52*C

Table 3 Regression Analysis of the Observed Responses According to the Best Fitting Model.

Response	Model	R^2	Adjusted R^2	Predicted R^2	Adequate precision
Y_1	Quadratic	0.9270	0.7955	0.1682	9.1414
Y_2	Quadratic	0.9785	0.9397	0.6553	18.6259

Table 4 Predicted and Observed Responses of Optimized CLX-NLC

Variables	Responses	Predicted value	Actual value	Error (%)
X_1	Y_1: Particle size(nm)	138.48	140.14	1.18
X_2	Y_2: Entrapment Efficiency (%)	78.231	80.421	2.71
X_3				

➢ *Physicochemical Charecterization of CLX-NLC:*

- *Particle Size and Polydispersity Index:*

The nanoparticles revealed size distribution in range of 136 ± 3 nm with PDI 0.298 suggesting that the particle size was evenly distributed throughout the dispersion and have a uniform size.

- *Zeta Potential:*

A zeta potential that is both positive (more than 30 mV) and negative (less than 30 mV) is deemed stable. The zeta potential, typically indicates the strength of the bond of attraction or repulsion between particles, impacts the stability of NLCs. A stable formulation was produced, as indicated by the NLC charge measurement of -17.6 ± 5 mV. Nanoparticles' negative charge may originate from the free fatty acids found in the lipids used to make NLCs, which can be either liquid or solid.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

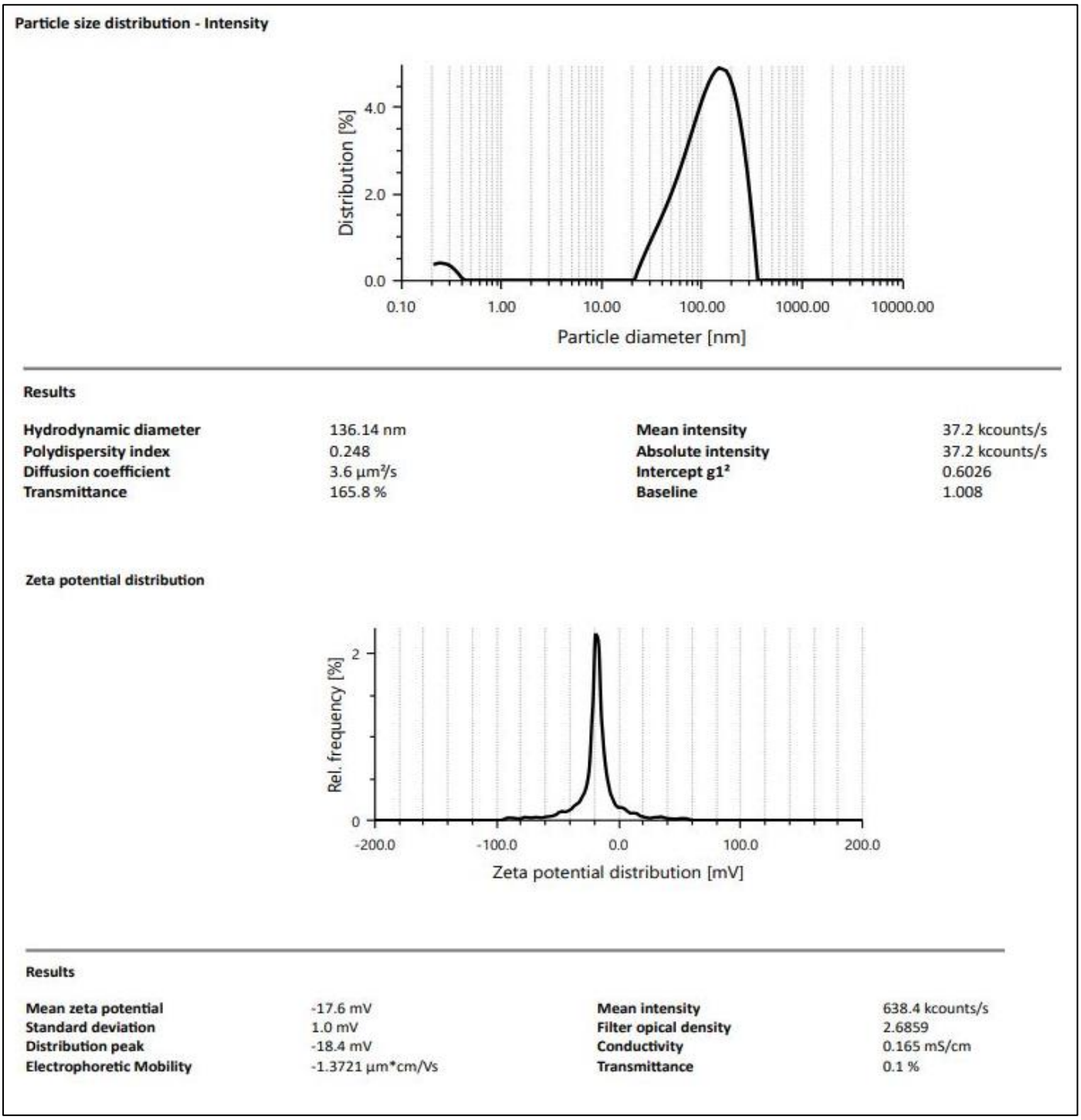


Fig 4 Particle Size and Zeta Potential of Optimized Batch of CLX-NLC

- *Entrapment Efficiency:*

We investigate the amount of celecoxib had become embedded in the lipid matrix (entrapment efficiency). The formulations had an entrapment efficiency of 81.23%. Adding celecoxib makes the rate of entrapment exceedingly high as it is lipophilic in character.

- *Solid State Characterization of CLX-NLC*

✓ *FTIR:*

The FTIR Spectrum showed no significant change in the drug's distinctive absorption bands and linkages of various functional groups. This discovery clearly indicates that the medicine retains its original form and exhibits no alterations in its features, even in physical mixing and formulation. The FTIR spectra showed that there was no interaction between the medication, solid lipid, liquid lipid, and surfactant. The reference range contained all of the distinctive peaks that matched the functional groups in the molecular structures of Celecoxib, Oleic acid, Stearic acid, and Tween 80.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

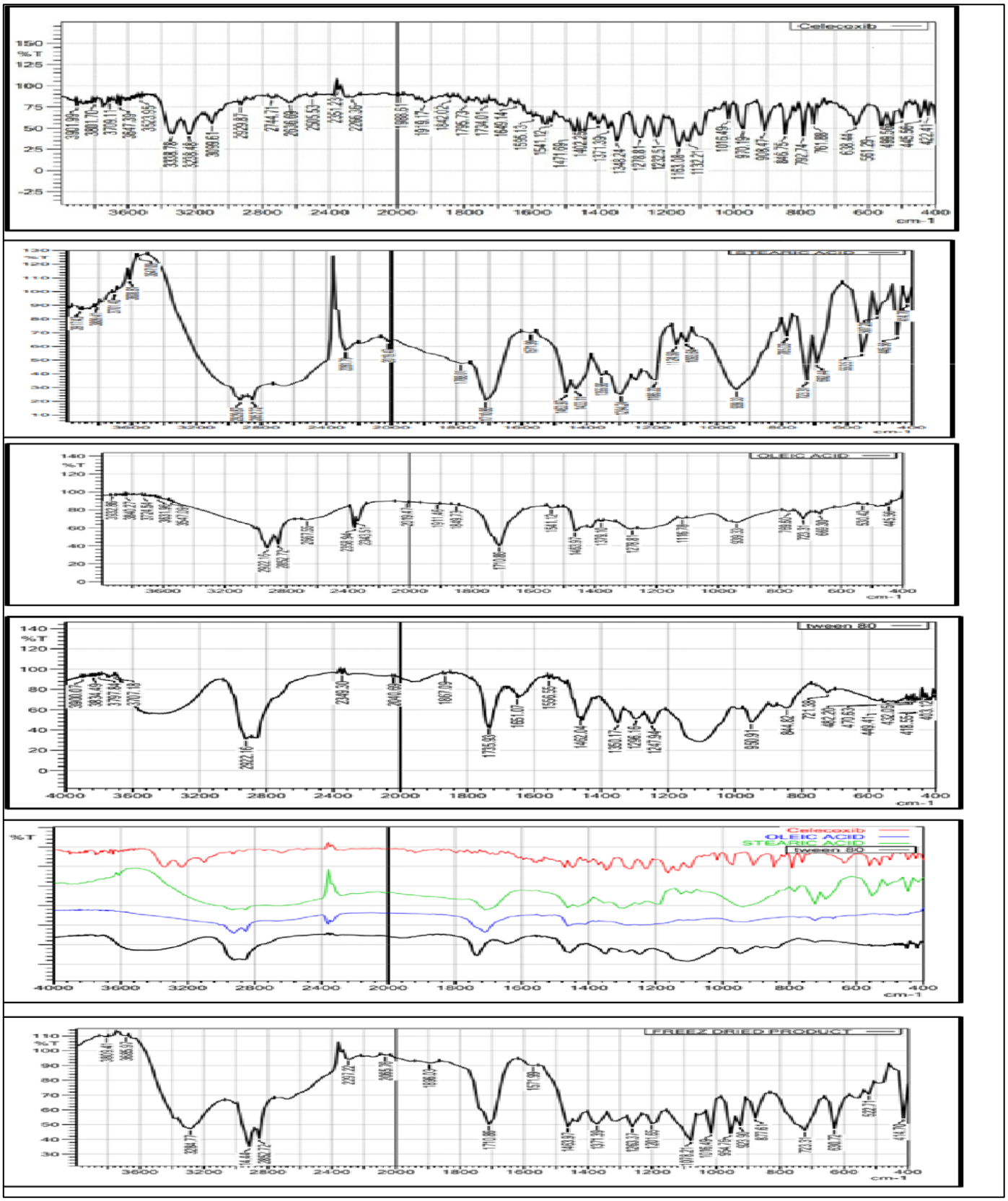


Fig 5 FTIR Overlay Spectra of Pure Drug, Excipients and Optimized Batch of CLX-NLC

✓ *X-Ray Diffraction Study:*

XRD showed that celecoxib had a strong and intense peak. The XRD diffractograms of CLX-NLC exhibited reduced intensity of celecoxib, indicating the amorphization of the medication. The diffractogram of celecoxib peak patterns showed crisp and strong crystalline peaks at 2θ, which proved that the extract was crystalline. But the broad peaks with lower intensity and the broadening of CLX-NLC nanoparticles show that the nanoparticles are completely amorphous and encapsulated.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

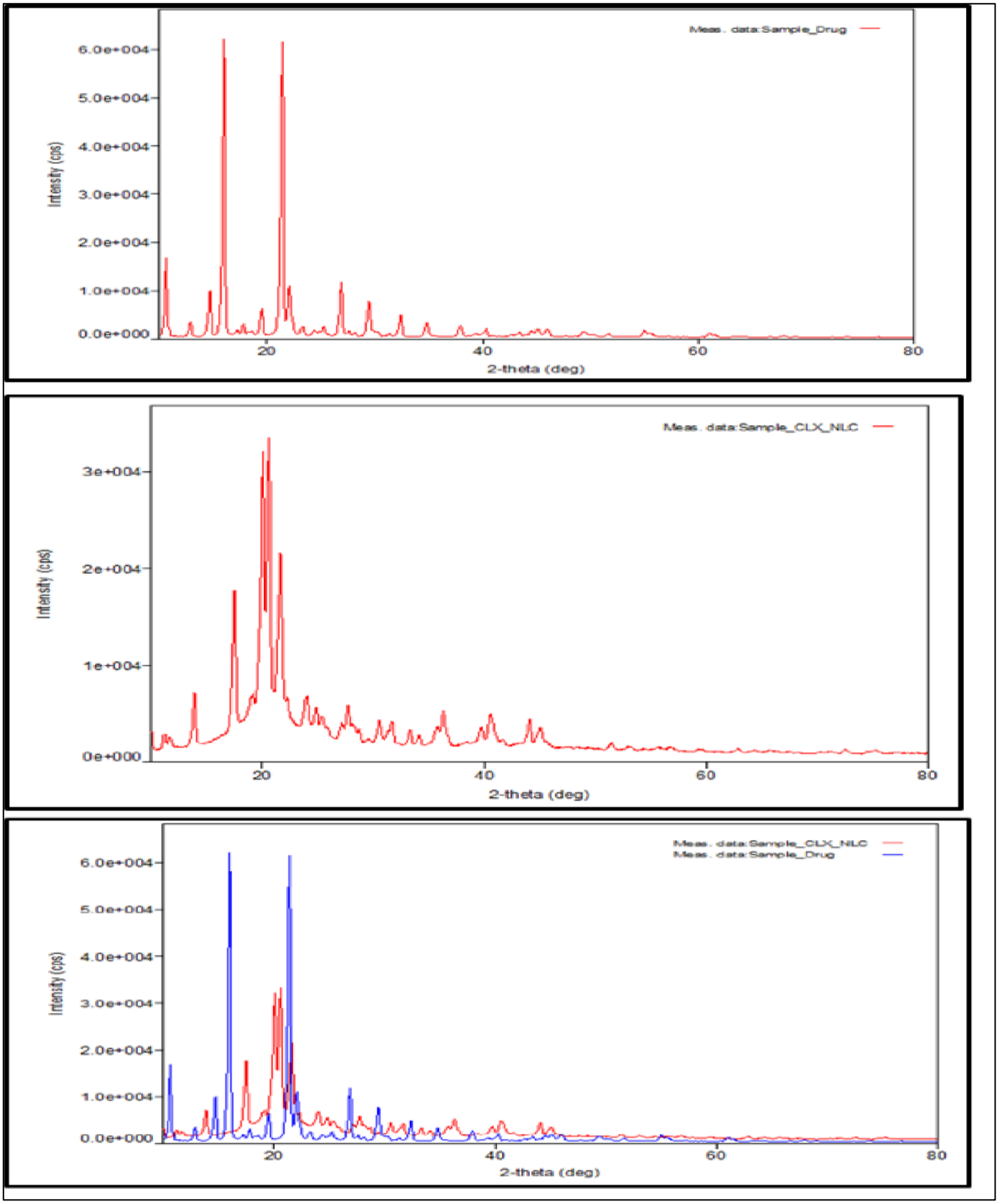


Fig 6 XRD Spectra of Pure Drug and Optimized Batch of CLX-NLC

✓ *Differential Scanning Calorimetry (DSC)*

DSC study demonstrated that celecoxib showed the presence of sharp endothermic peak at 162 ℃which corresponds to its melting point, implying crystallinity as shown in fig. DSC thermogram of CLX-NLC as shown in fig. shows the broad endothermic peak at 166.40 ℃ which is shifted due to the formation of CLX-NLC.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

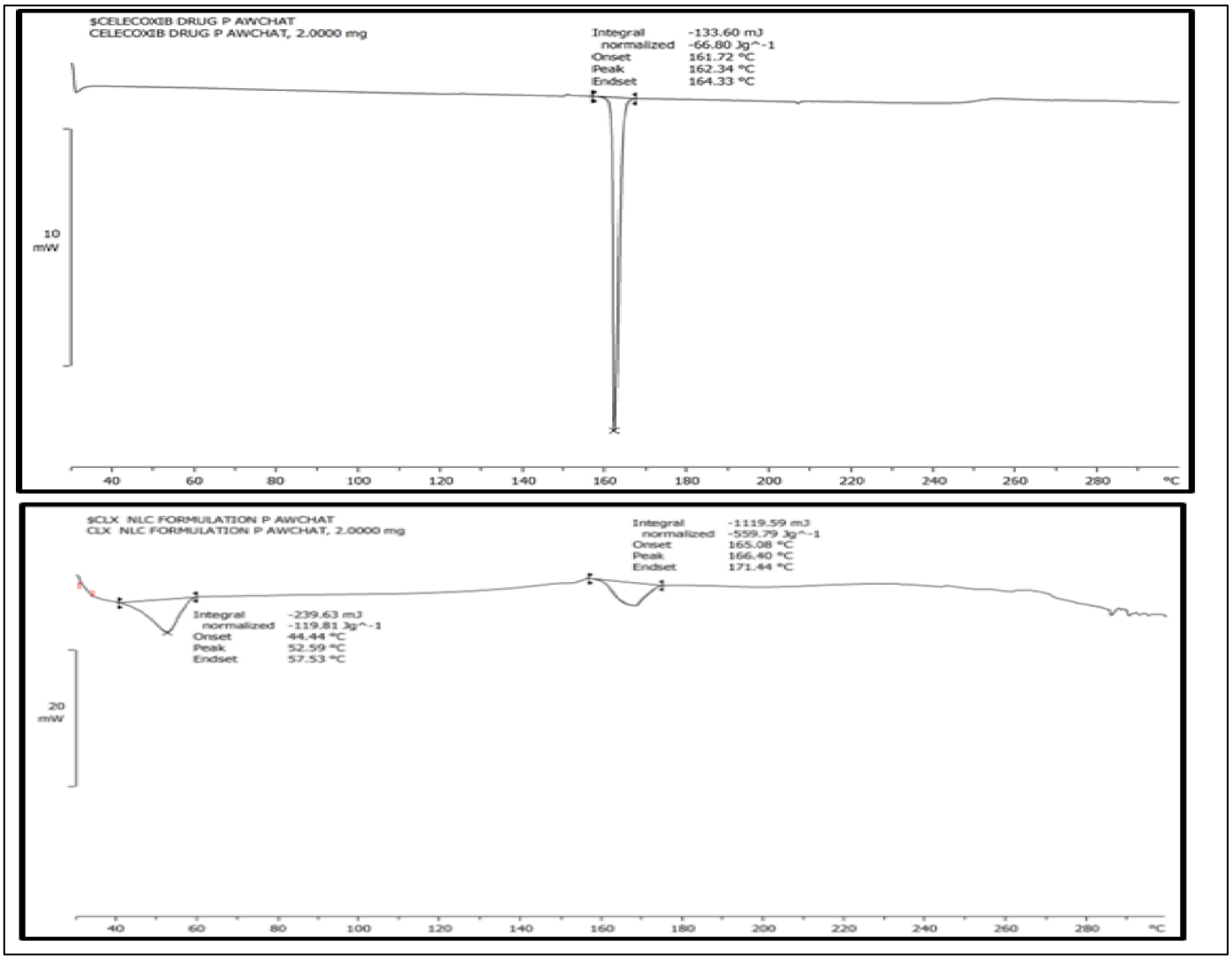


Fig 7 DSC Spectra of Pure Drug and Optimized Batch of CLX-NLC

➢ *In Vitro Release Kinetics Studies*

The in vitro release profile of drug from all the formulations could be best expressed by Zero order model, as the plot shows high linearity (R2 = 0.9654). By performing in-vitro study, it was concluded that there was 100% release of drug at 5 hours whereas formulation showed 100% drug release at 15 hours. Thus, the formulation showed sustained release.

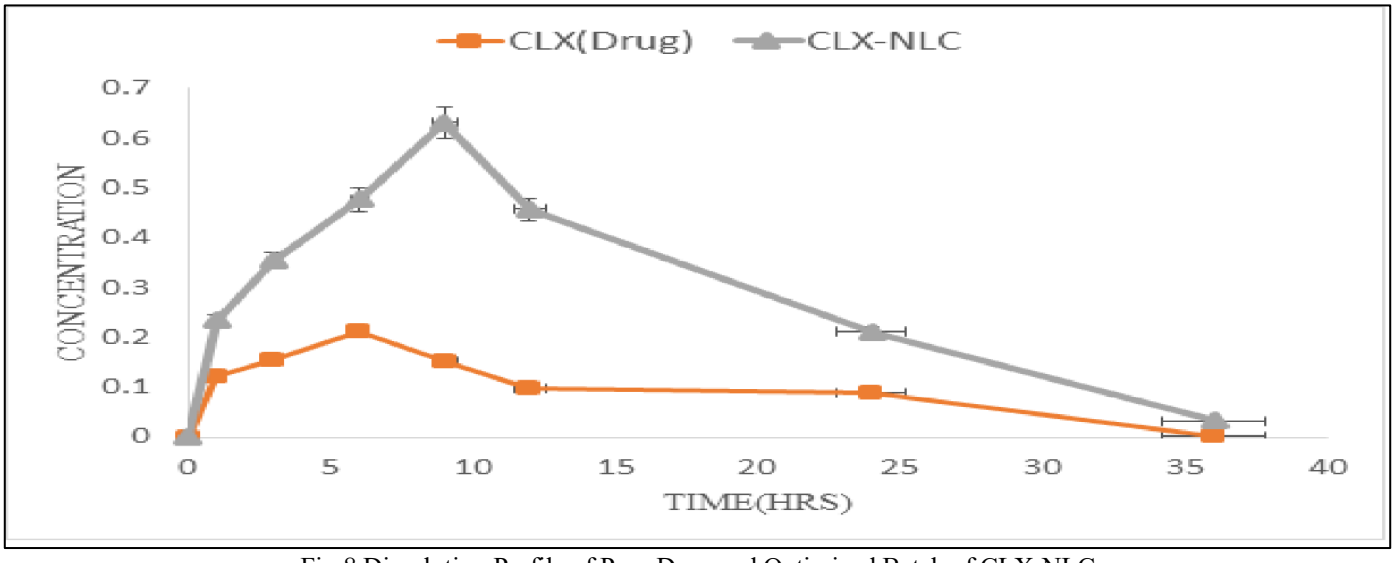


Fig 8 Dissolution Profile of Pure Drug and Optimized Batch of CLX-NLC

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

- *Bioavailability Assessment:*

The table shows the plasma drug concentration time patterns and pharmacokinetic parameters after taking CLX and CLX-NLC by mouth. Using the trapezoidal method for non-compartmental analysis, we found the pharmacokinetic parameters. The results are shown in Table. The results showed that CLX-NLC had a higher AUC and Cmax than CLX, which means that celecoxib was absorbed more quickly in CLX-NLC. The Tmax, half-life (t1/2), and MRT, particularly in CLX-NLC, indicate a substantial enhancement in the oral absorption of celecoxib. CLX-NLC also has a higher bioavailability than the pure medication.

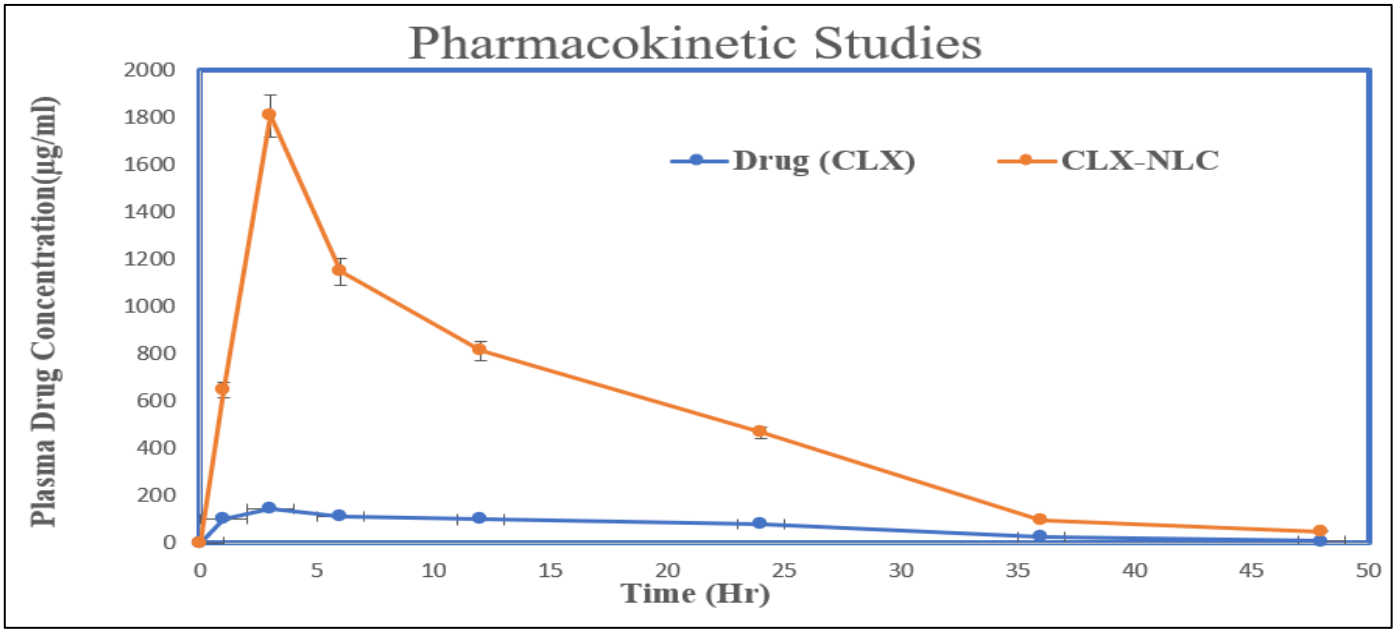


Fig 9 Dissolution Profile of Pure Drug and Optimized Batch of CLX-NLC

- *Stability Study*

ICH recommendations Q1A required an accelerated stability assessment of the resulting formulation's physical appearance, particle size, and drug entrapment efficiency storage settings. As noted, the formulation was observed throughout time. No substantial change in CNL appearance was detected at regular and accelerated temperature and humidity. After 3 months of storage at both settings, particle size increased somewhat and entrapment efficiency decreased. Accelerated changes were slightly higher than usual. Even though the alterations were minor, the optimized formulation was stable throughout the period.

Table 5 Stability Study

Time (month)	25 ± 2 ℃ and 60 ± 5% RH			40 ± 2 ℃ and 75 ± 5% RH		
	Change in Physical apperance	Particle size(nm)	Entrapment efficiency(%)	Change in Physical apperance	Particle size(nm)	Entrapment efficiency(%)
0	No	136	81%	No	136	80%
1	No	136.98	80.54%	No	137.28	79.44%
3	No	137.33	80%	No	139.80	79.23%

IV. CONCLUSION

By emulsion evaporation solidification at low temperature, Celecoxib-loaded NLC was created. Box-Behnken design was used for experimental design and optimization. The work optimized formulation variables to create a cost-effective, biodegradable, stable nanocarrier with increased drug entrapment and prolonged release. 3 level 3 factor Box Behnken experimental design was used to explore how liquid to solid lipid ratio and surfactant concentration affect medication particle size and Entrapment Efficiency. Based on solubility tests, stearic and oleic acids were chosen as solid and liquid lipids, respectively, and tween 80 as a surfactant. The preceding investigation indicated that liquid to solid lipid greatly affects particle size and (%) Entrapment Efficiency. ratio and surfactant concentration significantly. The particle size was found to be 138nm and the zeta potential was found to be -17mV for developed CLX-NLC. PDI was found to be 0.182 which indicates the homogenous population of particles. FTIR spectroscopy shows that the celecoxib is compatible with other excipients like stearic acid, oleic acid, and tween 80. In DSC the melting endothermic peak of celecoxib was not observed in the thermogram of CLX-NLC showed the developed CLX-NLC formulation. The X-ray diffractogram of CLX-NLC showed decrease in intensity of the peaks which leads to amorphization of drug. SEM micrographs revealed that the surface was smooth of prepared NLC formulation and was in spherical shape nature. In vitro drug release study showed the sustained release of drug up to 15 hrs. We found higher entrapment efficiency (86%) and a higher drug release profile with an initial burst and subsequent sustained release. It was concluded from

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

animal studies that CLX-NLC showed more bioavailability in comparison to conventional dosage form. Stability study showed that the formulation possesses good stability at room temperature. CLX-NLC were successfully prepared and can be used an innovative medication therapy which will benefit the SLE patients. The developed CLX-NLCs may confirm to be a good alternative to conventional formulations and could be utilized in the management of Systemic Lupus Erythematosus. This formulation could reduce high dose and dosing frequency of oral celecoxib and could be a new patient friendly alternative therapy for Systemic lupus erythematosus.

ACKNOWLEDGEMENT

The authors gratefully acknowledge the infrastructural facilities and academic support provided by Dadasaheb Balpande College of Pharmacy.

➢ *Declaration*

Authors declares they do not have any conflicts of interest.

REFERENCES

[1]. Fresneda Alarcon M, McLaren Z, Wright HL. Neutrophils in the Pathogenesis of Rheumatoid Arthritis and Systemic Lupus Erythematosus: Same Foe Different M.O. Front Immunol. 2021;12(March).

[2]. Lu X, Wang YH, Zhang J, Pu D, Hu N, Luo J, et al. Patients with systemic lupus erythematosus face a high risk of cardiovascular disease: A systematic review and Meta-analysis. Int Immunopharmacol. 2021;94(January).

[3]. Vaglio A, Grayson PC, Fenaroli P, Gianfreda D, Boccaletti V, Ghiggeri GM, et al. Drug-induced lupus: Traditional and new concepts. Autoimmun Rev [Internet]. 2018;17(9):912–8. Available from: https://doi.org/10.1016/j.autrev.2018.03.016

[4]. Vale ECS do, Garcia LC. Cutaneous lupus erythematosus: a review of etiopathogenic, clinical, diagnostic and therapeutic aspects. An Bras Dermatol [Internet]. 2023;(xx). Available from: https://doi.org/10.1016/j.abd.2022.09.005

[5]. Katz U, Zandman-Goddard G. Drug-induced lupus: An update. Autoimmun Rev [Internet]. 2010;10(1):46–50. Available from: http://dx.doi.org/10.1016/j.autrev.2010.07.005

[6]. Lun Hon K, Leung AKC. Neonatal lupus erythematosus. Autoimmune Dis. 2012;1(1).

[7]. Ruiz-Irastorza G, Bertsias G. Treating systemic lupus erythematosus in the 21st century: new drugs and new perspectives on old drugs. Rheumatol (United Kingdom). 2021;59: V69–81.

[8]. Kuhn A, Bonsmann G, Anders HJ, Herzer P, Tenbrock K, Schneider M. The Diagnosis and Treatment of Systemic Lupus Erythematosus. Dtsch Arztebl Int. 2015;112(25):423–32.

[9]. Obrișcă B, Sorohan B, Tuță L, Ismail G. Advances in lupus nephritis pathogenesis: From bench to bedside. Int J Mol Sci. 2021;22(7).

[10]. Bengtsson AA, Rönnblom L. Systemic lupus erythematosus: still a challenge for physicians. J Intern Med. 2017;281(1):52–64.

[11]. Gururaja D, Hegde V. Ayurvedic Management of Systemic Lupus Erythematosus overlap Vasculitis. J Ayurveda Integr Med [Internet]. 2019;10(4):294–8. Available from: https://doi.org/10.1016/j.jaim.2018.08.007

[12]. Luan J, Zheng F, Yang X, Yu A, Zhai G. Nanostructured lipid carriers for oral delivery of baicalin: In vitro and in vivo evaluation. Colloids Surfaces A Physicochem Eng Asp [Internet]. 2015; 466:154–9. Available from: http://dx.doi.org/10.1016/j.colsurfa.2014.11.015

[13]. Javed S, Mangla B, Almoshari Y, Sultan MH, Ahsan W. Nanostructured lipid carrier system: A compendium of their formulation development approaches, optimization strategies by quality by design, and recent applications in drug delivery. Nanotechnol Rev. 2022;11(1):1744–77.

[14]. Homayouni A, Sadeghi F, Nokhodchi A, Varshosaz J, Garekani HA. Preparation and characterization of celecoxib dispersions in soluplus®: Comparison of spray drying and conventional methods. Iran J Pharm Res. 2015;14(1):35–50.

[15]. Taha E, Nour SA, Mamdouh W, Selim AA, Swidan MM, Ibrahim AB, et al. Cod liver oil nano-structured lipid carriers (Cod-NLCs) as a promising platform for nose to brain delivery: Preparation, in vitro optimization, ex vivo cytotoxicity & in vivo biodistribution utilizing radioiodinated zopiclone. Int J Pharm X [Internet]. 2023;5(November 2022):100160. Available from: https://doi.org/10.1016/j.ijpx.2023.100160

[16]. Cunha S, Loureiro JA, Alves J, Peixoto AF, Forbes B, Sousa M, et al. Double Optimization of Rivastigmine-Loaded Nanostructured Lipid Carriers (NLC) for Nose-to-Brain Delivery Using the Quality by Design (QbD) Approach: Formulation Variables and Instrumental Parameters. 2020;

[17]. Ali AS, Alrashedi MG, Ahmed OAA, Ibrahim IM. Pulmonary Delivery of Hydroxychloroquine Nanostructured Lipid Carrier as a Potential Treatment of COVID-19. Polymers (Basel). 2022;14(13).

[18]. Guo CY, Yang CF, Li QL, Tan Q, Xi YW, Liu WN, et al. Development of a Quercetin-loaded nanostructured lipid carrier formulation for topical delivery. Int J Pharm. 2012;430(1–2):292–8.

[19]. Madane RG, Mahajan HS. Curcumin-loaded nanostructured lipid carriers (NLCs) for nasal administration: design, characterization, and in vivo study. Drug Deliv. 2016;23(4):1326–34.

[20]. Khan AA, Mudassir J, Akhtar S, Murugaiyah V, Darwis Y. Freeze-dried lopinavir-loaded nanostructured lipid carriers for enhanced cellular uptake and bioavailability: Statistical optimization, in vitro and in vivo evaluations. Pharmaceutics. 2019;11(2):1–19.

[21]. Luan J, Zhang D, Hao L, Li C, Qi L, Guo H, et al. Design and characterization of Amoitone B-loaded

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/26mar275

nanostructured lipid carriers for controlled drug release. Drug Deliv. 2013;20(8):324–30.

[22]. Arslan A, Yet B, Nemutlu E, Akdağ Çaylı Y, Eroğlu H, Öner L. Celecoxib Nanoformulations with Enhanced Solubility, Dissolution Rate, and Oral Bioavailability: Experimental Approaches over In Vitro/In Vivo Evaluation. Pharmaceutics. 2023;15(2).

[23]. Rao GD. Studies to enhance dissolution properties of Celecoxib INTERNATIONAL JOURNAL OF COMPREHENSIVE PHARMACY STUDIES TO ENHANCE DISSOLUTION PROPERTIES OF CELECOXIB. 2016;(January 2011).

[24]. Bhatt S, Sharma JB, Kamboj R, Kumar M, Saini V, Mandge S. Design and optimization of febuxostat-loaded nano lipid carriers using full factorial design. Turkish J Pharm Sci. 2021;18(1):61–7.

[25]. Agrawal M, Saraf S, Pradhan M, Patel RJ, Singhvi G, Ajazuddin, et al. Design and optimization of curcumin loaded nano lipid carrier system using Box-Behnken design. Biomed Pharmacother [Internet]. 2021;141(May):111919. Available from: https://doi.org/10.1016/j.biopha.2021.111919

[26]. Chauhan MK, Sharma PK. Optimization and characterization of rivastigmine nanolipid carrier loaded transdermal patches for the treatment of dementia. Chem Phys Lipids [Internet]. 2019;224(May):104794. Available from: https://doi.org/10.1016/j.chemphyslip.2019.104794

[27]. Mishra A, Imam SS, Aqil M, Ahad A, Sultana Y, Ameeduzzafar, et al. Carvedilol nano lipid carriers: formulation, characterization and in-vivo evaluation. Drug Deliv. 2016;23(4):1486–94.

[28]. Madane RG, Mahajan HS. Curcumin-loaded nanostructured lipid carriers (NLCs) for nasal administration: design, characterization, and in vivo study. Drug Deliv. 2016;23(4):1326–34.

[29]. Sakellari GI, Zafeiri I, Batchelor H, Spyropoulos F. Formulation design, production and characterisation of solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for the encapsulation of a model hydrophobic active. Food Hydrocoll Heal [Internet]. 2021;1(August):100024. Available from: https://doi.org/10.1016/j.fhfh.2021.100024

[30]. Homayouni A, Sadeghi F, Nokhodchi A, Varshosaz J, Garekani HA. Preparation and characterization of celecoxib dispersions in soluplus®: Comparison of spray drying and conventional methods. Iran J Pharm Res. 2015;14(1):35–50.

[31]. Khan AA, Mudassir J, Akhtar S, Murugaiyah V, Darwis Y. Freeze-dried lopinavir-loaded nanostructured lipid carriers for enhanced cellular uptake and bioavailability: Statistical optimization, in vitro and in vivo evaluations. Pharmaceutics. 2019;11(2):1–19.

[32]. Uprit S, Kumar Sahu R, Roy A, Pare A. Preparation and characterization of minoxidil loaded nanostructured lipid carrier gel for effective treatment of alopecia. Saudi Pharm J [Internet]. 2013;21(4):379–85. Available from: http://dx.doi.org/10.1016/j.jsps.2012.11.005

[33]. Arslan A, Yet B, Nemutlu E, Akdağ Çaylı Y, Eroğlu H, Öner L. Celecoxib Nanoformulations with Enhanced Solubility, Dissolution Rate, and Oral Bioavailability: Experimental Approaches over In Vitro/In Vivo Evaluation. Pharmaceutics. 2023;15(2).

[34]. G. Nava-Arzaluz M, Pinon-Segundo E, Ganem-Rondero A, Lechuga-Ballesteros D. Single Emulsion-Solvent Evaporation Technique and Modifications for the Preparation of Pharmaceutical Polymeric Nanoparticles. Recent Pat Drug Deliv Formul. 2012;6(3):209–23.

[35]. Arredondo-Ochoa T, Silva-Martínez GA. Microemulsion Based Nanostructures for Drug Delivery. Front Nanotechnol. 2022;3(January):1–21.

[36]. Schubert MA, Müller-Goymann CC. Solvent injection as a new approach for manufacturing lipid nanoparticles - Evaluation of the method and process parameters. Eur J Pharm Biopharm. 2003;55(1):125–31.

[37]. Ren G, Sun Z, Wang Z, Zheng X, Xu Z, Sun D. Nanoemulsion formation by the phase inversion temperature method using polyoxypropylene surfactants. J Colloid Interface Sci [Internet]. 2019; 540:177–84. Available from: https://doi.org/10.1016/j.jcis.2019.01.018