Contents lists available atIOCS

Science Midwifery

journal homepage:www.midwifery.iocspublisher.org

Formulation and characterization of nanostructured lipid carriers of curcumin and their development in topical gel preparations for drug delivery systems

Garnadi Jafar[1]*, Choerrunisa[2], Ika Kurnia Sukmawati[3], Al-fira Putriyanti[4]
[1,2,3,4]Faculty of Pharmacy, Universitas Bhakti Kencana, Bandung, Jawa Barat, Indonesia

ARTICLEINFO

Article history:

Received Apr 8, 2026
Revised Apr 15, 2026
Accepted Apr 23, 2026

Keywords:

Curcumin
Lipid Nanoparticles
Nanostructured Lipid Carriers
Physicochemical Characterization
Topical Gel

ABSTRACT

Curcumin is a bioactive compound derived from Curcuma longa with anti-inflammatory and antioxidant activities; however, its topical application is limited due to poor solubility and stability. The development of nanoparticle-based delivery systems such as *Nanostructured Lipid Carriers* (NLC) can enhance drug stability and skin penetration. This study aimed to formulate curcumin-loaded NLC, evaluate its physicochemical characteristics, and develop a gel dosage form based on the optimized NLC formulation. The research methods included preliminary solubility testing of curcumin in various lipid and surfactant components, compatibility analysis using *Differential Scanning Calorimetry* (DSC), formulation of five NLC formulations using hot homogenization and probe sonication methods, and characterization including particle size, polydispersity index, zeta potential, entrapment efficiency, and morphology using *Transmission Electron Microscopy* (TEM). The selected NLC formulation was subsequently incorporated into a gel system and evaluated for pH, viscosity, and spreadability. The results demonstrated that the curcumin NLC exhibited nanoscale particle size with relatively uniform distribution, stable zeta potential values, and high entrapment efficiency. TEM analysis confirmed spherical particle morphology. The NLC-based gel formulation showed acceptable physicochemical properties, including skin-compatible pH, suitable viscosity, and optimal spreadability. In conclusion, curcumin was successfully formulated into an NLC system and further developed into a topical gel formulation with promising physicochemical characteristics as a lipid-based drug delivery system.

Corresponding Author:

Garnadi Jafar,
Faculty of Pharmacy,
Universitas Bhakti Kencana,
Jl. Soekarno Hatta No. 754, Bandung, Jawa Barat, 40614, Indonesia
Email: garnadi.jafar@bku.ac.id

INTRODUCTION

The development of modern drug delivery technology continues to advance in line with the need to improve therapeutic effectiveness and overcome the limitations of the physicochemical

properties of active ingredients. Many drug compounds possess good pharmacological activity but face challenges such as low solubility, poor stability, and limited bioavailability (Vishwakarma *et al*., 2026). These conditions often result in suboptimal therapeutic effectiveness when formulated in conventional dosage forms. Therefore, the development of nanotechnology-based drug delivery systems has become a widely studied approach in the pharmaceutical field (Adepu & Ramakrishna, 2021). Nanoparticle systems can improve drug solubility, stability, and penetration into target tissues. Furthermore, this technology also enables more controlled drug release and increases therapeutic efficiency (Liu *et al*., 2024). Thus, nanoparticle-based approaches are a promising strategy in the development of modern pharmaceutical preparations (Aldeeb *et al*., 2024).

Nanostructured Lipid Carriers (NLC) are a second-generation lipid nanoparticle system developed to address the limitations of *Solid Lipid Nanoparticles* (SLN) (Viegas *et al*., 2023). The NLC system is composed of a mixture of solid and liquid lipids that form an irregular lipid matrix, thereby increasing drug entrapment capacity. This irregular matrix structure can also minimize drug expulsion during storage (Elmowafy & Al-Sanea, 2021). In addition, NLC has better physical stability and more controlled drug release capabilities than previous generations of lipid nanoparticle systems (Mall *et al*., 2024). This system is widely used in topical drug formulations because it can increase drug penetration through the skin layer. The use of lipids as the main component also provides advantages in the form of biocompatibility and relatively low toxicity. Therefore, NLC has become one of the drug delivery systems widely developed in pharmaceutical research (Zhao *et al*., 2023). However, despite these advantages, several scientific gaps remain unresolved, particularly regarding the optimization of lipid–surfactant composition, long-term physical stability, reproducibility of nanoscale characteristics, and the translation of improved physicochemical properties into enhanced therapeutic performance compared with previous curcumin delivery systems.

One of the bioactive compounds widely studied for its various pharmacological activities is curcumin, the main component of the Curcuma longa plant. Curcumin is known to possess various biological activities such as anti-inflammatory, antioxidant, antimicrobial, and anticancer properties (Cozmin *et al*., 2024). This compound has also been widely used in traditional medicine and modern drug development. Despite its broad therapeutic potential, the use of curcumin is often hampered by its unfavorable physicochemical properties (El-Saadony *et al*., 2023). Curcumin has very low solubility in water and limited stability to light and certain environmental conditions. These conditions result in low bioavailability of curcumin when used in conventional formulations (Kaur *et al*., 2024). Therefore, appropriate formulation strategies are needed to increase the stability and effectiveness of curcumin as an active ingredient (Bertoncini-Silva *et al*., 2024).

Lipid nanoparticle-based formulation approaches such as NLCs can be a solution to overcome curcumin's limitations. NLC systems can increase curcumin's solubility in lipid matrices, thereby enhancing its stability and bioavailability (Jafar & Sukmawati, 2025). Furthermore, the nanoscale particle size allows for increased surface area and better penetration into target tissues. In topical applications, lipid nanoparticle systems can also form an occlusive layer on the skin surface, improving skin hydration and aiding drug penetration (Suthar *et al*., 2026). The use of NLCs as a curcumin delivery system has been reported to enhance the compound's stability and pharmacological activity. However, compared with previous approaches such as conventional suspensions, emulsions, liposomes, and SLN systems, many studies still focus only on basic nanoparticle preparation without integrating systematic optimization of component selection, compatibility evaluation, and incorporation into patient-friendly topical dosage forms. Therefore, developing NLC formulations of curcumin is a relevant approach to improving therapeutic efficacy. Further research is needed to determine the optimal composition and characteristics of these formulations (Thuy *et al*., 2022).

In developing a lipid nanoparticle system, a crucial initial step is selecting the appropriate lipid components and surfactants through a solubility test of the active ingredient. The solubility test aims to determine the type of lipid that can optimally dissolve the active ingredient, thereby increasing the efficiency of drug entrapment in the nanoparticle system (Baltz & Scherließ, 2025). Furthermore, a compatibility analysis between the active ingredients and the lipid components is also necessary to ensure that no adverse interactions occur during the formulation process. One method widely used to evaluate this compatibility is *Differential Scanning Calorimetry* (DSC) (Sambhakar *et al*., 2023). This technique can provide information on changes in thermal properties that indicate interactions between components in the formulation. Thus, the results of the DSC analysis can be used as a basis for developing a stable nanoparticle formulation. This stage is crucial in ensuring the success of the NLC formulation process (John *et al*., 2024).

Once the formulation components are determined, the NLC manufacturing process can be carried out using a heat homogenization method combined with sonication (Jafar, Putriyanti, *et al*., 2025). This method is widely used because it can produce relatively homogeneous nano-sized particles. Physicochemical characterization of NLC is an important step in evaluating the quality of the resulting nanoparticle system. Parameters commonly analyzed include particle size, polydispersity index, zeta potential, and active ingredient entrapment efficiency (Alquraisy *et al*., 2026). Furthermore, particle morphology can also be observed using *Transmission Electron Microscopy* (TEM) (Jafar *et al*., 2024). This morphological analysis aims to determine the shape and distribution of particles at the nanoscale. The results of this characterization will determine the most optimal NLC formula for further development (Jafar, Sofian, *et al*., 2025). The novelty of this research lies in the integrated strategy combining solubility-based excipient screening, DSC compatibility assessment, optimized NLC fabrication, and comprehensive physicochemical characterization to obtain a stable curcumin-loaded NLC system with enhanced entrapment efficiency and nanoscale properties that support improved bioavailability.

Further development of the NLC system can be carried out by incorporating nanoparticles into topical dosage forms such as gels. Gel preparations are often chosen because they are easy to apply to the skin, provide a comfortable sensation, and are able to distribute active ingredients evenly on the skin surface (Mindiarto *et al*., 2024). In addition, gels also have the ability to release active ingredients gradually, thereby increasing the effectiveness of topical therapy. Evaluation of gel preparations is necessary to ensure physical characteristics that meet the requirements of topical preparations. Common evaluation parameters include pH, viscosity, and spreadability measurements (Slavkova *et al*., 2023). These parameters play an important role in determining the stability and comfort of the preparation on the skin. Therefore, this study aims to formulate and characterize curcumin NLC and develop NLC-based gel preparations with good physical characteristics. The additional novelty is the transformation of the optimized curcumin-loaded NLC into a topical gel system, expected to improve storage stability, ease of application, skin retention, and curcumin bioavailability compared with previous conventional gel or non-nanoparticle formulations.

RESEARCH METHOD

Instrument

The instruments used in this study include an analytical balance (Ohaus), magnetic stirrer (IKA), high-speed homogenizer (Ultra Turrax), probe sonicator (Sonics Vibra Cell), *Differential Scanning Calorimetry* (DSC) (PerkinElmer), dynamic light scattering-based particle size analyzer (Malvern Zetasizer) for particle size analysis, polydispersity index, and zeta potential, *Transmission Electron Microscopy* (TEM) (JEOL) for nanoparticle morphology observation, digital pH meter (Hanna Instruments), Brookfield viscometer for gel viscosity measurement, and spreadability tester. All equipment was calibrated before use to ensure the accuracy and reliability of the measurement results.

Material

The materials used in this study include curcumin as the active ingredient, solid lipids such as glyceryl monostearate, liquid lipids such as oleic oil or isopropyl myristate oil, surfactants such as Tween 80 and Span 80, and appropriate co-surfactants. Other ingredients used for the gel formulation include carbopol as a gelling agent, propylene glycol as a humectant, triethanolamine as a neutralizer, methyl paraben as a preservative, and distilled water as a solvent. All materials used are of pharmaceutical or pro-analysis quality and are obtained from trusted chemical suppliers.

Research Procedures

a. Preliminary Solubility Test, a preliminary solubility test was conducted to determine the type of solid lipid, liquid lipid, and surfactant that had the best ability to dissolve curcumin. A certain amount of curcumin was added gradually to each lipid and surfactant component that had been heated to a certain temperature while stirring using a magnetic stirrer. The additional process was carried out until the curcumin could no longer dissolve completely in the system. The mixture was then visually observed to determine the clarity and homogeneity of the solution. The component that showed the highest ability to dissolve curcumin was selected as the base material in the formulation of *Nanostructured Lipid Carriers* (NLC). The results of this test were used as a basis for selecting the lipid composition at the nanoparticle formulation stage (Li *et al*., 2021).
b. DSC Test, *differential Scanning Calorimetry* (DSC) analysis was performed to evaluate the compatibility between curcumin and the lipid components used in the formulation. The samples analyzed included pure curcumin, solid lipids, liquid lipids, and a mixture of curcumin and lipids. Samples were weighed in certain amounts, then placed in aluminum pans and analyzed using a DSC apparatus at a certain temperature range with a controlled heating rate. Changes in thermal properties such as melting points and endothermic peaks were observed to identify possible interactions between the components. The thermogram data obtained were then analyzed to determine the stability and compatibility of the formulation system. The results of the DSC analysis were used as a basis for developing a stable NLC formula (Agrawal *et al*., 2021).
c. Formula and Characterization of *Nanostructured Lipid Carriers* (NLC), *Nanostructured Lipid Carriers* (NLC) were formulated using a heat homogenization method combined with sonication. Five NLC formulas were prepared with varying compositions of solid lipids, liquid lipids, and surfactants to systematically evaluate the influence of lipid ratio and surfactant concentration on particle size, polydispersity index, zeta potential, and entrapment efficiency. The use of five formula variations was considered sufficient to represent low, medium, and high composition ranges, enabling efficient optimization and selection of the most stable and effective formulation. The solid lipids were melted at a temperature above their melting point and then mixed with liquid lipids and curcumin to form a lipid phase. The aqueous phase containing the surfactant was heated to the same temperature and then slowly added to the lipid phase while homogenizing using a high-speed homogenizer. The hot homogenization method was selected because it allows both lipid and aqueous phases to remain in a molten state during emulsification, ensuring uniform mixing and preventing premature lipid solidification. Probe sonication was subsequently applied to reduce droplet size through high-energy cavitation forces, resulting in smaller and more homogeneous nanoparticles with improved physical stability. The combination of these methods is widely used because it is practical, reproducible, and suitable for producing nanoscale lipid carriers. The formed emulsion was then processed using a probe sonicator to produce nano-sized particles. The obtained NLC systems were then characterized including measurement of particle size, polydispersity index, zeta potential, entrapment efficiency, and observation of

particle morphology using *Transmission Electron Microscopy* (TEM) (Garnadi *et al*., 2024; Wirawan *et al*., 2022).

d. Formulation and Evaluation of Gel Preparations, the selected NLC formula was then formulated into a topical gel preparation. The gel base was prepared by dispersing carbopol in distilled water until a homogeneous dispersion was formed. Propylene glycol, preservatives, and other additional components were then added while stirring until evenly distributed. The NLC dispersion was then slowly added to the gel base while being homogenized until a homogeneous gel was obtained. The gel's pH was adjusted using triethanolamine until it reached a pH range suitable for the skin. Evaluation of the gel preparation included measuring pH, viscosity using a Brookfield viscometer, and a spreadability test to determine the preparation's ability to spread on the skin surface (Taher & Al-Kinani, 2026).

RESULTS AND DISCUSSIONS

Preliminary Solubility Test

A preliminary solubility test was conducted to determine the lipid and surfactant components with the best curcumin solubility prior to the *Nanostructured Lipid Carriers* (NLC) formulation process. The results showed that curcumin solubility varied among the lipids and surfactants tested. These differences were influenced by the polarity, chemical structure, and interaction between curcumin and the lipid matrix. Lipids with higher curcumin solubility were selected as the primary components in the NLC formulation because they could enhance the entrapment capacity of the active ingredient within the nanoparticle system (Li *et al*., 2021).

In general, liquid lipids exhibit a higher curcumin-dissolving ability than solid lipids due to their greater molecular mobility. Furthermore, surfactants also play a key role in increasing curcumin solubility by reducing the interfacial tension between the lipid and aqueous phases (Yuan *et al*., 2025). The lipid and surfactant components that exhibited the best solubilization ability were then selected for use in the subsequent NLC formulation stages. The results of this solubility test are presented in Table 1, which shows a comparison of the curcumin-dissolving ability of each tested component.

Table 1. Results of curcumin solubility test in various lipid and surfactant components

Ingredients (mg)		Dissolved substances	Solubility
Curcumin	0.05 mg	0.1446 µg	Practically Insoluble
Chremophor	300 mg		
Curcumin	0.05 mg	0.1014 µg	Practically Insoluble
Plantacare	300 mg		

DSC Analysis

Differential Scanning Calorimetry (DSC) analysis was performed to evaluate the compatibility between curcumin and the lipid components used in the NLC formulation. The DSC thermogram of pure curcumin showed a sharp endothermic peak at a specific temperature, indicating the characteristic melting point of curcumin. This peak indicates that curcumin is in a stable crystalline form. These results are consistent with the thermal characteristics of curcumin reported in various previous studies (Agrawal *et al*., 2021).

When curcumin is mixed with lipids, changes in the thermogram pattern are observed, indicated by a shift or decrease in the intensity of the endothermic peak. This change indicates an interaction between curcumin and the lipid matrix, which can cause a change in the crystalline structure to a more amorphous form (Mankan *et al*., 2025). This transformation is highly advantageous in nanoparticle systems because it can increase the solubility and stability of the active ingredient. Furthermore, the absence of significant new peaks in the thermogram indicates that no adverse chemical reaction occurs between curcumin and lipid components.

The DSC analysis results indicate that curcumin is compatible with the lipids used in the NLC formulation. Therefore, the selected combination of ingredients can be used in the nanoparticle formulation process without causing adverse interactions to the system's stability. The thermogram of the DSC analysis results is shown in Figure 1.

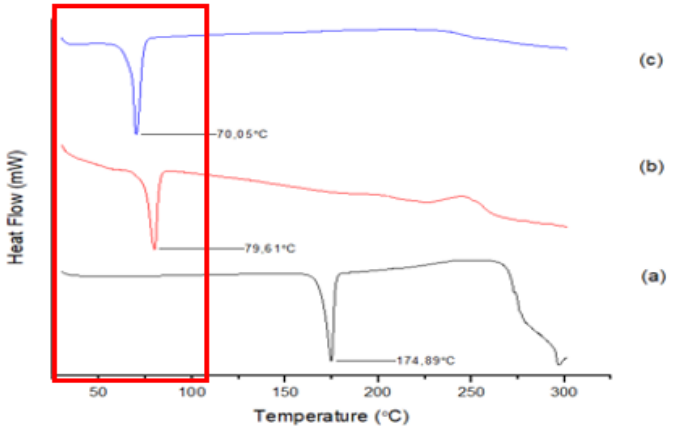

Figure 1. DSC thermograms of curcumin, lipids, and curcumin-lipid mixtures

Formula and Characterization of *Nanostructured Lipid Carriers* (NLC)

Nanostructured Lipid Carriers (NLC) were successfully formulated using a heat homogenization method combined with sonication. This method was chosen because it can produce nano-sized particles with a relatively uniform size distribution. In this study, five NLC formulas were prepared with varying compositions of solid lipids, liquid lipids, and surfactants to determine the most optimal formula. These composition variations aimed to evaluate the effect of the lipid and surfactant ratio on the characteristics of the resulting nanoparticle system (Wirawan *et al*., 2022).

NLC characterization was performed by measuring particle size, polydispersity index (PDI), zeta potential, and curcumin entrapment efficiency. The measurement results showed that all formulations produced particle sizes in the nanoscale range, suitable for nanoparticle-based drug delivery systems. The relatively low polydispersity index value indicates a fairly homogeneous particle size distribution (Garnadi *et al*., 2024; Jafar, Sofian, *et al*., 2025). A low PDI value also suggests that the particles were formed with minimal aggregation and narrow size variation, which is beneficial for maintaining dispersion stability, predictable drug release, and reproducible therapeutic performance. In contrast, a high PDI generally reflects heterogeneity and may increase the risk of instability during storage. Meanwhile, the zeta potential value indicates that the NLC system has good colloidal stability due to the repulsive forces between particles that prevent aggregation. The high negative zeta potential values observed in this study indicate strong electrostatic repulsion among particles, which helps prevent particle collision, flocculation, and coalescence. Therefore, these values explain why the NLC dispersions remained physically stable and well-dispersed.

The entrapment efficiency of curcumin in the NLC system also showed high values. This indicates that the lipid matrix in the NLC system is capable of incorporating curcumin effectively (Thuy *et al*., 2022). The irregular matrix structure of the NLC system provides more space to accommodate active ingredient molecules compared to previous generations of lipid nanoparticle systems. Several factors contributed to the very high curcumin entrapment efficiency, including the high lipophilicity of curcumin, its strong affinity toward the lipid matrix, the presence of mixed solid–liquid lipids that create structural imperfections, and the use of surfactants that improve dispersion and reduce drug leakage during preparation. Compared with previous studies on

curcumin-loaded NLC systems, the present formulation demonstrated competitive particle size, favorable zeta potential, and exceptionally high entrapment efficiency, indicating that the selected lipid–surfactant combination was highly effective in maximizing curcumin loading and system stability. The complete characterization results of the five NLC formulas are presented in Table 2.

Table 2. Characterization of *nanostructured lipid carriers* (particle size, PDI, zeta potential, and entrapment efficiency)

	NLC CURCUMIN FORMULA					Z-Ave		ZP	%EE
Code	KUR%	APL%	MRY %	PTC%	CRE%	nm	PdI	mV	%EE
NLCC1	0,05	6	2	-	5	221,4±2,82	0,39±0,07	-60,7±0,67	99,9
NLCC2	0,05	6,75	2	-	4,5	238,3±1,57	0,38±0,02	-39,2±1,19	99,9
NLCC3	0,05	7,5	2	-	4	274,5±3,02	0,33±0,06	-39,8±0,46	99,9
NLCC4	0,05	8,25	2	-	3,5	385,8±4,16	0,28±0,04	-40,9±0,38	99,9
NLCC5	0,05	9	2	-	3	125,6±1,65	0,31±0,05	-45,9±0,15	99,9
NLCP6	0,05	6	2	5	5	175,5±1,10	0,32±0,02	-34,1±2,45	99,9
NLCP7	0,05	6,75	2	4,5	4,5	165,3±2,77	0,27±0,03	-39,2±2,54	99,9
NLCP8	0,05	7,5	2	4	4	180,4±0,78	0,27±0,02	-38,5±0,68	99,9
NLCP9	0,05	8,25	2	3,5	3,5	172,8±3,22	0,27±0,02	-40,4±2,43	99,9
NLCP10	0,05	9	2	3	3	292.2±6.08	0.30±0.19	-38.1±0.91	99.9

Information: NLCC: NLC Chremophore®, NLCP: NLC Plantacare®, Kur: Curcumin, APL: Apifil®, MRY: Myritol®, CRE: Chremophore®, PTC: Plantacare®, PdI: Polydispersity Index, ZP: Zeta Potential

In addition, particle morphology was also observed using *Transmission Electron Microscopy* (TEM). The results showed that the NLC particles had a relatively spherical shape with a uniform size distribution (Jafar, Putriyanti, *et al*., 2025). The spherical particle shape is a general characteristic of lipid nanoparticle systems formed through heat homogenization and sonication methods. The morphology of the resulting NLC particles is shown in Figure 2.

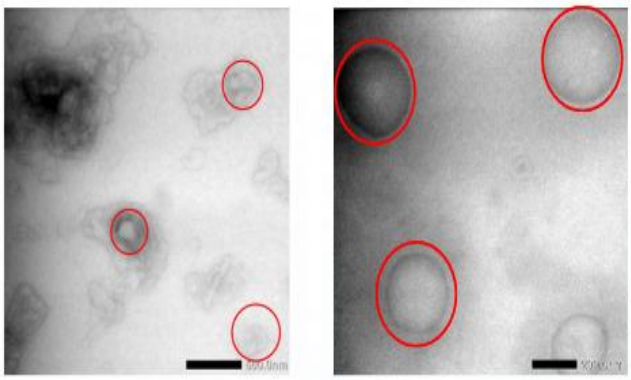

Figure 2. Morphology of nanostructured lipid carrier particles as a result of TEM observations

Formulation and Evaluation of Gel Preparations

The NLC formula that demonstrated the most optimal characteristics was then selected for further development in a topical gel formulation. The gel formulation was chosen due to its advantages in topical application, including ease of application, comfort on the skin, and the ability to distribute the active ingredient evenly (Taher & Al-Kinani, 2026). Furthermore, the gel base can improve the stability of the nanoparticle system and facilitate patient application. The formulation results showed that the resulting gel had a homogeneous appearance, a characteristic yellow color of curcumin, and showed no phase separation during the initial observation process. The physical appearance of the formulated gel preparation is shown in Figure 3.

Figure 3. Physical appearance of gel preparation based on nanostructured lipid carriers

The gel's physical characteristics were evaluated by measuring pH, viscosity, and spreadability. The pH value obtained was within the skin's pH range, making it safe for topical application. The viscosity value indicated that the gel had good consistency and maintained its shape stability during storage (Mointi *et al*., 2025). Meanwhile, the spreadability test results indicated that the gel had good spreading ability on the skin surface, thereby enhancing the effectiveness of active ingredient delivery.

Table 3. Results of gel preparation evaluation (Ph, viscosity, and spreadability)

Formula	NLC Curcumin Eq;0.05%	HPMC%	Carbopol%	pH test	Power Distribution Test	Viscosity Test
FGH1	10mL	1,5	-	5,56 ±0,36	5,80 ±0,23	13,320 ±976
FGH2	10mL	1,75	-	5,61 ±0,25	5,66 ±0,24	16.160 ±829
FGH3	10mL	2	-	5,90 ±0,10	5,30 ±0,16	18.940 ±859
FGH4	10mL	2,25	-	5,84 ±0,15	5,18 ±0,13	20.740 ±926
FGH5	10mL	2,5	-	5,64 ±0,35	5,16 ±0,11	22.540 ±1.643
FGC1	10mL	-	1,5	5,32 ±0,21	5,40 ±0,20	23.300 ±1.367
FGC2	10mL	-	1,75	5,27 ±0,15	5,40±0,10	24.020±1.234
FGC3	10mL	-	2	5,43±0,14	5,26±0,09	27.300±922
FGC4	10mL	-	2,25	5,53±0,11	5,20±0,10	32.300±4.061
FGC5	10mL	-	2,5	5,42±0,13	5,16±0,11	31.760±2.809

Description: FGH (HPMC Gel Formula), FGC (Carbopol Gel Formula)

Overall, the evaluation results in Table 3 show that the NLC-based gel formulation has physical characteristics that meet the requirements for topical preparations.

CONCLUSION

Based on the results of the research that has been conducted, curcumin was successfully formulated in the NLC system using the heat homogenization method combined with sonication. The results of the solubility test and *Differential Scanning Calorimetry* (DSC) analysis showed that curcumin was compatible with the lipid components used in the formulation. NLC characterization showed that the particle size was in the nano range with a relatively homogeneous distribution, a zeta potential value indicating system stability, and high entrapment efficiency, which was supported by the spherical particle morphology based on *Transmission Electron Microscopy* (TEM) observations. The selected NLC formula was then successfully formulated into a topical gel preparation with good physical characteristics, including a pH value that matches the skin pH, stable viscosity, and optimal spreadability. Thus, the curcumin NLC system has the potential to be developed as an effective topical drug delivery system. The practical implications of this study indicate that NLC-based gels can provide improved topical drug delivery through better skin adhesion, enhanced penetration of active compounds, prolonged drug retention at the application site, and improved patient convenience compared with conventional topical formulations.

This research also contributes to the advancement of nanotechnology-based drug delivery systems by demonstrating that lipid nanoparticle carriers can effectively overcome the poor solubility and limited stability of curcumin, while maintaining desirable physicochemical

characteristics for pharmaceutical application. For future research, in vivo studies are necessary to evaluate skin penetration, pharmacological effectiveness, irritation potential, and long-term safety of the curcumin NLC gel. Furthermore, well-designed clinical trials should be conducted to confirm therapeutic efficacy, patient acceptability, and comparative benefits versus currently available topical products.

ACKNOWLEDGEMENTS

The authors would like to thank the Faculty of Pharmacy, Bhakti Kencana University and DKSH Indonesia, for providing research facilities and academic support that contributed to the completion of this study. The authors also appreciate the valuable input from colleagues during the preparation of this manuscript.

References

Adepu, S., & Ramakrishna, S. (2021). Controlled drug delivery systems: current status and future directions. *Molecules*, *26*(19), 5905.

Agrawal, M., Saraf, S., Pradhan, M., Patel, R. J., Singhvi, G., & Alexander, A. (2021). Design and optimization of curcumin loaded nano lipid carrier system using Box-Behnken design. *Biomedicine & Pharmacotherapy*, *141*, 111919.

Aldeeb, M. M. E., Wilar, G., Suhandi, C., Elamin, K. M., & Wathoni, N. (2024). Nanosuspension-based drug delivery systems for topical applications. *International Journal of Nanomedicine*, 825–844.

Alquraisy, A., Ramadhani, K., Mohammed, A. F. A., Wilar, G., Osman, W., Elamin, K. M., & Wathoni, N. (2026). Nanostructured Lipid Carrier-Gels for Wound Healing: A Narrative Review of Formulation Strategies, Mechanisms, and Translational Potential. *Nanotechnology, Science and Applications*, *19*, 585159. https://doi.org/10.2147/NSA.S585159

Baltz, N., & Scherließ, R. (2025). Entrapment efficiency methodology for lipid nanoparticles–a literature review. *OpenNano*, 100251.

Bertoncini-Silva, C., Vlad, A., Ricciarelli, R., Giacomo Fassini, P., Suen, V. M., & Zingg, J.-M. (2024). Enhancing the Bioavailability and Bioactivity of Curcumin for Disease Prevention and Treatment. In *Antioxidants* (Vol. 13, Issue 3, p. 331). https://doi.org/10.3390/antiox13030331

Cozmin, M., Lungu, I. I., Gutu, C., Stefanache, A., Duceac, L. D., Şoltuzu, B. D., Damir, D., Calin, G., Bogdan Goroftei, E. R., Grierosu, C., & Boev, M. (2024). Turmeric: from spice to cure. A review of the anti-cancer, radioprotective and anti-inflammatory effects of turmeric sourced compounds. *Frontiers in Nutrition*, *11*, 1399888. https://doi.org/10.3389/fnut.2024.1399888

El-Saadony, M. T., Yang, T., Korma, S. A., Sitohy, M., Abd El-Mageed, T. A., Selim, S., Al Jaouni, S. K., Salem, H. M., Mahmmod, Y., & Soliman, S. M. (2023). Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. *Frontiers in Nutrition*, *9*, 1040259.

Elmowafy, M., & Al-Sanea, M. M. (2021). Nanostructured lipid carriers (NLCs) as drug delivery platform: Advances in formulation and delivery strategies. *Saudi Pharmaceutical Journal*, *29*(9), 999–1012.

Garnadi, J., IRVIANA, P. B., & Fenti, F. (2024). PEMBENTUKAN NANOSTRUCTURED LIPID CARRIER TRETINOIN MENGGUNAKAN COMPRITOL® ATO DAN CREMOPHOR® RH 40 DENGAN METODE SONIKASI PROBE. *PHARMACOSCRIPT Учредители: Universitas Perjuangan Tasikmalaya*, *7*(2), 146–155.

Jafar, G., Putriyanti, A., Muhsinin, S., & Kencana, B. (2025). *Formulation and Characterization of Tretinoin Nanostructured Lipid Carriers Using Apifil and Cremophore*. *5*(3), 477–484.

Jafar, G., Sofian, R., Pratama, R., & Putriyanti, A. (2025). Pengembangan Formula dan Karakterisasi Nanostructured Lipid Carriers Tretinoin Menggunakan Compritol dan Tegocare. *Indonesian Journal of Pharmaceutical Science and Technology*, *12*(3), 289–294.

Jafar, G., Sucipto, Y. K., & Supriadi, D. (2024). *Development of the Formula and Characterization of Tretinoin Nanostructured Lipid Carriers (NLC) With Precirol ® Ato5 Using the Sonicator Probe Method*. *10*(6), 62–67.

Jafar, G., & Sukmawati, I. K. (2025). *Lipid-based nanoparticle delivery system approach for diabetic wounds : A review*. *13*(5).

John, R., Monpara, J., Swaminathan, S., & Kalhapure, R. (2024). Chemistry and art of developing lipid

nanoparticles for biologics delivery: focus on development and scale-up. *Pharmaceutics*, *16*(1), 131.

Kaur, K., Al-Khazaleh, A. K., Bhuyan, D. J., Li, F., & Li, C. G. (2024). A review of recent curcumin analogues and their antioxidant, anti-inflammatory, and anticancer activities. *Antioxidants*, *13*(9), 1092.

Li, N., Li, X., Cheng, P., Yang, P., Shi, P., Kong, L., & Liu, H. (2021). Preparation of Curcumin Solid Lipid Nanoparticles Loaded with Flower-Shaped Lactose for Lung Inhalation and Preliminary Evaluation of Cytotoxicity In Vitro. *Evidence-Based Complementary and Alternative Medicine : ECAM*, *2021*, 4828169. https://doi.org/10.1155/2021/4828169

Liu, Y., Liang, Y., Yuhong, J., Xin, P., & Han, J. L. (2024). *Advances in Nanotechnology for Enhancing the Solubility and Bioavailability of Poorly Soluble Drugs*. *April*, 1469–1495.

Mall, J., Naseem, N., Haider, M. F., Rahman, M. A., Khan, S., & Siddiqui, S. N. (2024). Nanostructured lipid carriers as a drug delivery system: A comprehensive review with therapeutic applications. *Intelligent Pharmacy*.

Mankan, E., Sagdic, O., & Karadag, A. (2025). Development and Characterization of Spray-Dried Curcumin-Lecithin Complexes with Improved Solubility and In Vitro Digestive and Thermal Stability. *Foods (Basel, Switzerland)*, *14*(18). https://doi.org/10.3390/foods14183157

Mindiarto, A. B., Jafar, G., & Putriyanti, A. (2024). Pengembangan Sistem Penghantaran Berbasis NLC (Nanostructur Lipid Carier) sebagai Skin Anti-Aging. *Jurnal Pharmascience*, *11*(2), 452–472.

Mointi, S. S., Kuncahyo, I., & Harmastuti, N. (2025). *Development and optimization of curcumin transfersomes in gel formulations as an antioxidant*. *13*(4).

Sambhakar, S., Saharan, R., Narwal, S., Malik, R., Gahlot, V., Khalid, A., Najmi, A., Zoghebi, K., Halawi, M. A., & Albratty, M. (2023). Exploring LIPIDs for their potential to improves bioavailability of lipophilic drugs candidates: A review. *Saudi Pharmaceutical Journal*, *31*(12), 101870.

Slavkova, M., Tzankov, B., Popova, T., & Voycheva, C. (2023). Gel formulations for topical treatment of skin cancer: a review. *Gels*, *9*(5), 352.

Suthar, M., Malik, A., & Marwal, A. (2026). Role of nanotechnology in cosmetic development and skin care. *Next Nanotechnology*, *9*, 100422. https://doi.org/https://doi.org/10.1016/j.nxnano.2026.100422

Taher, S. S., & Al-Kinani, K. K. (2026). Formulation and characterization of dolutegravir sodium-loaded nanostructured lipid carrier in situ gel for targeted brain delivery via intranasal route. *OpenNano*, *27*, 100270. https://doi.org/https://doi.org/10.1016/j.onano.2025.100270

Thuy, V. N., Van, T. V., Dao, A. H., & Lee, B.-J. (2022). Nanostructured lipid carriers and their potential applications for versatile drug delivery via oral administration. *OpenNano*, *8*, 100064.

Viegas, C., Patrício, A. B., Prata, J. M., Nadhman, A., Chintamaneni, P. K., & Fonte, P. (2023). Solid lipid nanoparticles vs. nanostructured lipid carriers: a comparative review. *Pharmaceutics*, *15*(6), 1593.

Vishwakarma, K., Handa, P., Tawfeeq, W. S., & Hassan, M. A. (2026). Recent advancements in drug nanocrystals: Innovation in formulation and drug delivery. *OpenNano*, *27*, 100277. https://doi.org/https://doi.org/10.1016/j.onano.2025.100277

Wirawan, W., Raharjo, S., & Supriyadi, S. (2022). Formulation and characteristics of nanostructured lipid carrier (NLC) red palm oil (RPO) prepared by high-pressure homogenization and its applications in orange juice. *Indones Food Nutr Prog*, *19*, 31–40.

Yuan, J., Mao, S., Ma, X., Liu, X., & Chen, Y. (2025). Surfactants Significantly Improved the Oral Bioavailability of Curcumin Amorphous Solid Dispersions and Its Underlying Mechanism. In *Pharmaceutics* (Vol. 17, Issue 12, p. 1541). https://doi.org/10.3390/pharmaceutics17121541

Zhao, L., Chen, J., Bai, B., Song, G., Zhang, J., Yu, H., Huang, S., Wang, Z., & Lu, G. (2023). Topical drug delivery strategies for enhancing drug effectiveness by skin barriers, drug delivery systems and individualized dosing. *Frontiers in Pharmacology*, *14*, 1333986. https://doi.org/10.3389/fphar.2023.1333986