

Development of Indomethacin Nanostructure Lipid Carrier Incorporated in Emulgel

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Received 1 May 2026 • Revised 8 May 2026 • Accepted 10 May 2026 • Published online 20 October 2026

Abstract:

Objective: This study aimed to develop and optimize an indomethacin (IND)-loaded nanostructured lipid carrier (NLC)-based emulgel for enhanced topical drug delivery.

Material and Methods: IND-loaded NLCs were prepared at varying drug concentrations and characterized for physicochemical properties and colloidal stability. The optimized NLC formulation was incorporated into emulgels with different component ratios and evaluated for rheological properties, drug content, release kinetics, and *in vitro* skin permeation.

Results: The NLCs containing 5.0 % w/w IND exhibited optimal physicochemical characteristics, with a particle size of 160.50 ± 1.10 nm and a narrow size distribution (PDI <0.3), along with good stability. The formulation also demonstrated good stability. The optimized emulgel and the formulation (S1; NLC: gel base: emulsion ratio of 4:2:4) demonstrated desirable rheological behavior, controlled drug release, and enhanced skin permeation.

This paper was from The 8th Current Drug Development International Conference 2026 (May 21–23, 2026).

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J Health Sci Med Res 2027;45(1):e20261469

doi: 10.31584/jhsmr.20261469

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Conclusion: The developed IND–NLC emulgel exhibits good stability, controlled release, and improved skin permeation, highlighting its potential as an effective topical delivery system for enhanced therapeutic efficacy.

Keywords: emulgel, indomethacin, nanostructured lipid carrier, topical drug delivery

Introduction

Indomethacin (IND), a widely used nonsteroidal anti-inflammatory drug (NSAIDs), is commonly prescribed for the treatment of musculoskeletal pain. Topical administration provides localized therapeutic effects while minimizing systemic adverse effects compared with oral delivery^{1–3}. However, its clinical efficacy is often limited by insufficient skin penetration due to its hydrophobic nature⁴. Therefore, advanced drug delivery systems are required to improve its solubility, stability, and overall therapeutic performance.

Nanostructured lipid carriers (NLCs) have emerged as promising drug delivery systems owing to their high encapsulation efficiency, enhanced skin penetration, and controlled release properties^{5,6}. NLCs are second-generation lipid nanoparticles composed of a mixture of solid and liquid lipids, forming a disordered amorphous matrix that enhances drug solubilization⁷. These attributes make NLCs highly suitable for topical delivery, offering high drug-loading capacity, improved stability, and effective skin permeation^{8,9}.

Emulgels are hybrid delivery systems that combine the advantages of gels such as enhanced viscosity, physical stability, and ease of application with those of emulsions, including improved drug solubility and skin penetration. This dual functionality makes them highly attractive for transdermal drug delivery¹⁰. The incorporation of NLCs into an emulgel matrix may further enhance drug retention at the application site, improve spreadability, and promote patient compliance¹¹.

Therefore, this study aimed to develop and optimize an IND-loaded NLCs emulgel for enhanced topical

delivery. The formulations were systematically evaluated for physicochemical properties, drug release kinetics, and *in vitro* skin permeation, integrating nanotechnology with emulgel systems to improve therapeutic performance.

Material and Methods

Materials

IND and excipients, including cetearyl alcohol–sodium cetearyl sulfate, PEG–40 hydrogenated castor oil (Cremophore®RH40), poloxamer 188, Tween 80, and glycerin, were purchased from commercial suppliers in Germany. Montanov 68 (cetearyl alcohol–cetearyl glucoside) was obtained from SEPPIC (Paris La Défense Cedex, France). Miglyol 810N (caprylic/capric triglyceride) and Carbopol ETD 2020 were purchased from Sasol (Johannesburg, South Africa) and Noveon (Cleveland, Ohio, US), respectively.

Preparation of IND–NLCs

IND-loaded NLCs were prepared using a hot nanoemulsion technique followed by probe sonication. IND was first dispersed in Cremophor®RH40 (100 mg/mL) to obtain a homogeneous solution. The oil phase was maintained at 70 °C, while the aqueous phase was heated to 72 °C and added to the oil phase under continuous stirring. The resulting pre-emulsion was homogenized at 15,000 rpm for 10 min, followed by probe sonication (30% amplitude, 5 min) to reduce particle size and obtain IND–NLCs. The dispersion was subsequently cooled to room temperature and stored at 4 °C until further use.

Characterization of IND-NLCs

The physicochemical properties of IND-NLC formulations were evaluated on day 1 and after 7 days of storage. Particle size, polydispersity index (PDI), and zeta potential were measured using dynamic light scattering (Zetasizer Ultra Red, Malvern Instruments, Malvern, UK) at 25 °C. The pH of the dispersions was determined using a calibrated pH meter (Apera™ PH20, Apera Instruments, Wuppertal, Germany).

Stability study of IND-NLCs

The physical stability of IND-NLC formulations was evaluated using a LUMiSizer analytical photocentrifuge (LUM GmbH, Berlin, Germany). Briefly, 1 mL of each sample was transferred into a polyamide LUM cell (optical path length: 2 mm) and centrifuged at 4000 rpm at 25°C under near-infrared laser illumination (870 nm). A total of 500 transmission profiles were recorded at 30 s intervals. The instability index was calculated using SEPView® software (version 3.5.0). In addition, the physical stability of the NLC formulations was further assessed by microscopic observation.

Entrapment efficiency (%EE) and loading capacity (LC) of IND-NLCs

Entrapment efficiency (%EE) and loading capacity (LC) of IND-NLCs were determined using a direct

quantification method¹². Briefly, the NLC dispersion was centrifuged at 15,000 rpm for 2 h at 4 °C (Centrifuge 5430 R, Eppendorf, Germany) to separate free IND from the NLC-associated fraction. Then, the amount of IND in each fraction was quantified by UV-visible spectrophotometer at 320 nm¹³. A calibration curve of IND was constructed over the concentration range of 1–100 µg/mL with good linearity ($r^2 > 0.999$). The %EE and LC were calculated using Eqs. (1) and (2) to evaluate formulation performance.

$$\%EE = \frac{W_n}{W_t} \times 100 \quad (\text{Eq. 1})$$

$$LC = \frac{W_n}{W_{lipid}} \quad (\text{Eq. 2})$$

Where W_n is the amount of IND in the NLCs fraction (µg), W_t is the total amount of IND (µg), and W_{lipid} is the total amount of lipid composition (mg).

Preparation of emulgels

The emulgel was prepared by incorporating IND-NLC into a pre-formed gel, followed by the addition of an emulsion phase. The gel base was obtained by dispersing Carbopol® ETD 2020 and glycerin in distilled water, with pH adjustment using sodium hydroxide. The emulsion phase, consisting of cetearyl alcohol (and) sodium cetearyl sulfate, almond oil, propylene glycol, and water, was prepared as an oil-in-water emulsion. The optimized IND-NLC dispersion

Table 1 Composition of IND-NLC formulations

Phase	Compositions	IND1 (%w/w)	IND2 (%w/w)	IND3 (%w/w)
Oil phase	IND Solution	5.0	10.0	15.0
	Montanov 68	3.0	3.0	3.0
	Miglyol 810N	10.0	10.0	10.0
	Chamomile oil	2.0	2.0	2.0
	Poloxamer 188	3.0	3.0	3.0
Water phase	Tween 80	2.0	2.0	2.0
	Deionized water	75.0	70.0	65.0

IND=indomethacin

was subsequently incorporated into the gel base under gentle stirring to obtain a homogeneous emulgel.

Viscosity measurement of emulgel

The viscosity of the emulgel formulations was measured using a Brookfield DV-II+ Pro Extra viscometer (Brookfield Engineering Lab, Inc., MA, USA) equipped with an SC4-64 spindle (LV4) at 25 °C and a rotational speed of 6 rpm.

In vitro drug release study

The *in vitro* release of IND from the emulgel formulation was evaluated using a dialysis membrane method. Briefly, 5 g of the formulation IND-NLC emulgel was placed in a dialysis membrane (molecular weight cut-off 12,000–14,000 Da) and immersed in 35 mL of phosphate buffer saline (PBS, pH 7.4) containing 0.5% Tween 80. The system was maintained at 32 °C under continuous agitation. At predetermined time intervals, the amount of drug released into the medium was quantified using a UV-visible spectrophotometer at 320 nm. The cumulative release data were analyzed by fitting to various kinetic models to elucidate the drug release mechanism.

In vitro skin permeation study

Skin permeation was evaluated using vertical Franz diffusion cells (effective diffusion area: 1.77 cm²) with excised neonatal porcine abdominal skin as the membrane. The study was approved by the Institutional Animal Care and Use Committee (IACUC) of Prince of Songkla University (Protocol No.: 2026-PHA02-009). The receptor compartment was filled with 6 mL of PBS: isopropanol (1:1, v/v) and maintained at 37 °C throughout the experiment. The test formulation was applied to the donor compartment, and receptor medium samples were collected at predetermined intervals and analyzed for drug

content. An IND aqueous suspension was used as the control. The cumulative amount of drug permeated per unit area was plotted against time to obtain the permeation profile. The steady-state transdermal flux (J) was calculated from the slope of the linear portion, and the permeability coefficient (K_p) was determined using Eq.3.

$$K_p = \frac{J}{c_d} \quad (\text{Eq.3})$$

Statistical analysis

All data are presented as mean±S.D. Statistical analyses were performed using the T-test and one-way analysis of variance (ANOVA), followed by Tukey's post hoc test. Differences were considered statistically significant at p-value<0.05.

Results

Characterization of IND-NLCs

IND-NLCs with varying drug concentrations were developed (Table 1), and their physicochemical characteristics are presented in Table 2. On day 1, all formulations exhibited nanoscale particle sizes and negative zeta potentials. Both IND1 and IND2 exhibited comparable mean particle sizes (160.50±1.10 and 141.17±8.96 nm, respectively) and zeta potentials (−21.46±1.36 and −19.90±5.40 mV, respectively). In contrast, IND3 exhibited the smallest mean particle size (84.79±20.63 nm) but a broader size distribution (PDI >0.3) and a lower absolute zeta potential (−11.28±1.64 mV).

After 7 days, a significant increase in particle size was observed for IND3, indicating particle aggregation and reduced stability. The zeta potential of all formulations decreased over time, with IND1 retaining the highest negative value (−16.71±0.54 mV). All formulations maintained a slightly acidic pH in the range of 4–5 throughout the storage period.

Stability study of IND–NLCs

The results in Table 3 show that IND1 exhibited the lowest instability index, indicating excellent colloidal stability under centrifugal stress. In contrast, IND2 and IND3 displayed instability indices approaching 1, suggesting poor stability. Microscopic analysis revealed clear differences in physical stability among the three formulations. On day 1, all formulations appeared homogeneously dispersed; however, after 7 days, IND2 and IND3 exhibited distinct needle-like particles, whereas IND1 remained uniformly dispersed.

%EE and LC of IND–NLCs

The initial concentrations of IND incorporated into the NLC formulations were 5, 10, and 15 mg/mL for IND1, IND2, and IND3, respectively. The %EE and LC values of each formulation are presented in Table 4. IND1 exhibited the highest %EE, whereas IND2 and IND3 showed lower %EE but higher LC values. Based on the overall physicochemical performance, IND1 was selected for subsequent incorporation into the emulgel formulation.

Preparation and evaluation of IND–NLC emulgel

IND–NLC emulgels were prepared using three different weight ratios of NLC dispersion, gel base, and emulsion phase (Table 5). All emulgel formulations exhibited a milky-white, creamy appearance with a homogenous texture and glossy finish. The pH values of all formulations

were within the range of 4–5. Among the formulations, S3 showed the highest viscosity, followed by S2, whereas S1 exhibited the lowest viscosity and a lighter texture. S2 and S3 also demonstrated greater stickiness. The drug content of S1 was $97.5 \pm 1.2\%$. Based on its overall physicochemical performance, S1 was selected for further evaluation.

In vitro drug release of IND–NLC emulgel

The drug release from the NLC–emulgel formulation (S1) was evaluated using a dialysis membrane method. As shown in Figure 1, the formulation exhibited sustained release behavior, with approximately 40% of IND released over 24 h. The release data were fitted to zero-order, first-order, and Higuchi kinetic models to characterize the release mechanism. The Higuchi model showed the highest correlation coefficient ($R^2=0.994$), followed by the first-order ($R^2=0.971$) and zero-order ($R^2=0.962$) models, indicating that drug release was predominantly governed by diffusion.

In vitro skin permeation study of IND–NLC emulgel

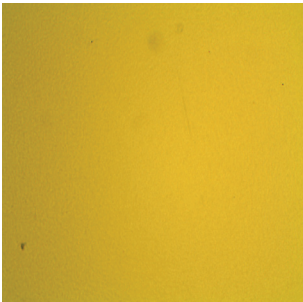
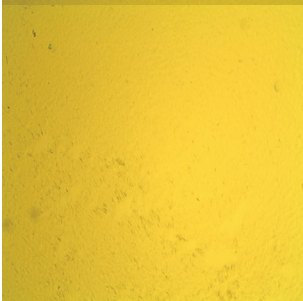
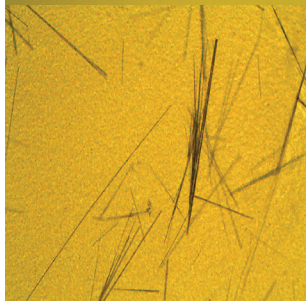
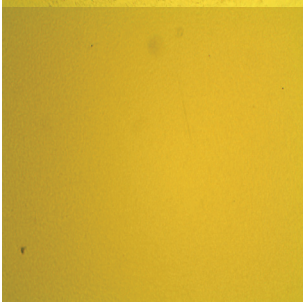
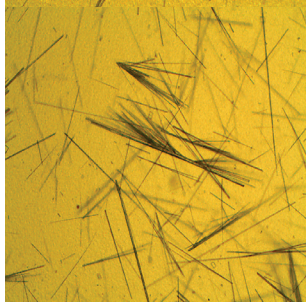
The skin permeation profile, as shown in Figure 2 and summarized in Table 6, demonstrated that the NLC–emulgel significantly enhanced drug permeation across the skin, with an approximately 13-fold increase observed relative to the control formulation.

Table 2 Characteristics of the IND–NLCs on Day 1 and Day 7

		Particle size (nm)	PDI	Zeta (mV)	pH
IND1	Day 1	160.50 $\pm$ 1.10	0.227 $\pm$ 0.004	–21.46 $\pm$ 1.36	5.10 $\pm$ 0.10
	Day 7	165.30 $\pm$ 2.81	0.214 $\pm$ 0.012	–16.71 $\pm$ 0.54	5.20 $\pm$ 0.10
IND2	Day 1	141.17 $\pm$ 8.96	0.326 $\pm$ 0.046	–19.90 $\pm$ 5.40	4.90 $\pm$ 0.00
	Day 7	151.33 $\pm$ 9.54	0.281 $\pm$ 0.013	–14.16 $\pm$ 3.00	4.90 $\pm$ 0.00
IND3	Day 1	84.79 $\pm$ 20.63	0.396 $\pm$ 0.005	–11.28 $\pm$ 1.64	4.70 $\pm$ 0.00
	Day 7	206.73 $\pm$ 58.4*	0.477 $\pm$ 0.018*	–11.43 $\pm$ 0.82	4.80 $\pm$ 0.10

*p-value<0.05 vs Day1 (using T-test), IND=indomethacin, NLCs=nanostructured lipid carrier, PDI=polydispersity index

Table 3 Stability study of IND–NLCs dispersions

Formulations	Instability index	Microscopic images (10x magnification)	
		Day 1	Day 7
IND1	0.028±0.002*		
IND2	1.000±0.006		
IND3	0.738±0.011		

*p-value<0.05 compared with other formulations, as determined by one-way analysis of variance (ANOVA) followed by Tukey's test
 IND=indomethacin, IND–NLCs=indomethacin loaded nanostructured lipid carrier

Table 4 %EE and LC of the IND–NLC

Formulations	%EE	LC (µg/mg)
IND1	71.40±1.42	17.85±0.25
IND2	65.73±0.42	26.29±0.17
IND3	67.46±0.33	33.73±0.16

%EE=entrapment efficiency, LC=loading capacity, IND–NLCs=indomethacin loaded nanostructured lipid carrier

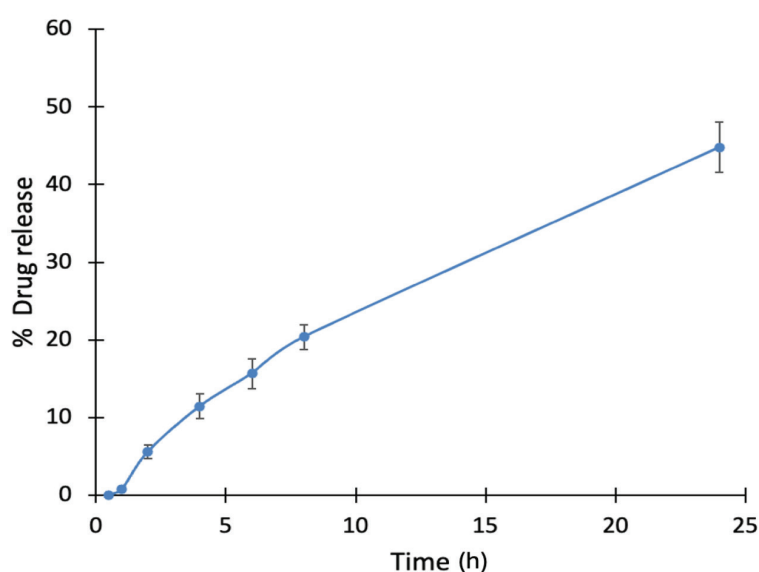
Discussion

All formulations exhibited nanoscale particle sizes, confirming the successful formation of NLCs. Nanoparticulate systems offer advantages for topical delivery by enhancing skin permeation¹⁴, particularly when particle size is ≤300 nm¹⁵. The pH values of all formulations ranged from 4 to 5, indicating suitability for dermal application¹⁶. The optimized formulation (IND1) showed an encapsulation efficiency

Table 5 Formulation and characteristics of the IND–NLC emulgels

Formulation	NLC phase	Gel phase	Emulsion phase	pH	Viscosity (cPs)
S1	4	2	4	5.2±0.2	55,854.67±665.83
S2	4	3	3	5.0±0.2	87,248.00±750.04
S3	4	4	2	4.9±0.1	114,333.33±557.35

IND–NLCs=indomethacin loaded nanostructured lipid carrier



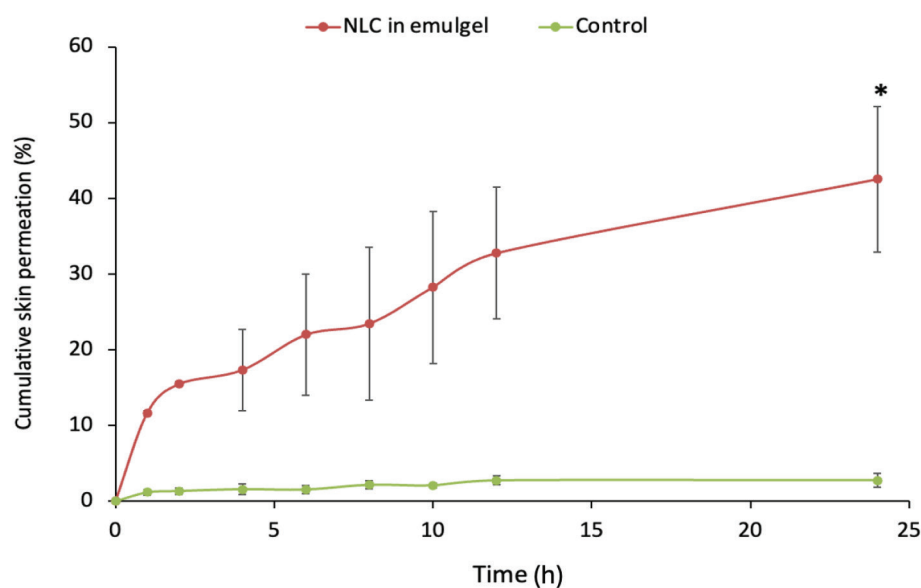
IND–NLCs=indomethacin loaded nanostructured lipid carrier

Figure 1 Drug release profile of IND–NLC emulgel (S1)

of approximately 70%, demonstrating effective drug incorporation within the lipid matrix. An inverse relationship between %EE and LC was observed with increasing IND concentration, whereby higher drug loading increased LC but reduced %EE due to saturation of the lipid matrix.

Surface charge, as indicated by zeta potential, is a key determinant of colloidal stability, with values of approximately ± 30 mV generally required to provide sufficient electrostatic repulsion and prevent aggregation^{17,18}. In this study, IND1 and IND2 exhibited zeta potential values

of around -20 mV, whereas IND3 showed a lower value (-11 mV). Although these values fall below the conventional stability threshold, the stability of NLC systems may also be governed by steric stabilization from nonionic surfactants¹⁹. Poloxamer 188 and Tween 80 likely contributed to steric hindrance, thereby supporting the stability of IND1. This is consistent with particle size distribution results, where IND1 and IND2 exhibited a low polydispersity index (PDI <0.3), indicating homogeneous dispersions, while IND3 showed a higher PDI (~ 0.4), suggesting reduced uniformity.



*p-value<0.05, NLCs=nanostructured lipid carrier

Figure 2 The skin permeation profile of IND from NLC-emulgel and control formulation (IND in aqueous suspension)

Table 6 Permeation parameters of NLC-emulgels and control

Formulations	Permeation parameters		
	Transdermal flux ($\times 10^{-3} \mu\text{g}/\text{cm}^2\text{s}$)	Permeability coefficient (K_p) ($\times 10^{-6} \text{cm}/\text{s}$)	Enhancement ratio
NLC-emulgel	$4.35 \pm 1.40^*$	$2.18 \pm 0.70^*$	13.63
Control	0.32 ± 0.04	0.16 ± 0.02	–

*p-value<0.05 vs control (using T-test), NLCs=nanostructured lipid carrier

Stability studies demonstrated that IND3 exhibited the lowest stability, as evidenced by visual inspection, microscopic analysis, and centrifugation testing. IND2 also showed instability, characterized by particle aggregation and a high instability index. The formation of needle-like crystals in IND2 and IND3 suggests drug recrystallization, likely resulting from lipid matrix reorganization during storage. As the lipid matrix transitions to a more thermodynamically stable state, its capacity to retain the drug decreases, leading

to drug expulsion and crystallization. These findings indicate that higher drug loading may exceed the accommodation capacity of the lipid matrix, thereby reducing homogeneity and stability²⁰. In contrast, IND1 maintained stability despite a reduction in zeta potential after 7 days, likely due to steric stabilization provided by nonionic surfactants. Overall, IND1 exhibited the most favorable physicochemical properties and stability, supporting its selection as the optimal formulation for further development.

From our work, the NLC-loaded emulgel exhibited appropriate viscosity, spreadability, and pH, supporting its suitability for topical application¹⁶. The formulation demonstrated controlled drug release behavior consistent with the Higuchi model, with approximately 40% of IND released and permeated through the skin over a 24-h period. The remaining drug was retained within the formulation or potentially within the skin layers, with minor losses attributable to experimental handling. Incorporation of IND-NLCs into the emulgel significantly enhanced skin permeation by approximately 13-fold, which can be attributed to the synergistic effects of the nanocarrier system and the emulgel matrix. The nanoscale size provides a large surface area and promotes close contact with the stratum corneum, facilitating drug partitioning and transfollicular penetration¹⁵. In addition, lipid nanoparticles may interact with and disrupt the stratum corneum, thereby enhancing drug diffusion²¹. The emulgel matrix further contributes by forming a three-dimensional network that increases viscosity, ensures uniform nanoparticle dispersion, and prolongs residence time at the application site, ultimately enabling controlled release and improving drug retention and permeation^{22,23}.

Conclusion

This study successfully developed an IND-loaded NLCs incorporated into an emulgel system. The optimized formulation (IND1) exhibited desirable physicochemical properties and good stability. The resulting emulgel was a homogenous semisolid preparation suitable for topical application. Furthermore, the formulation demonstrated controlled drug release and significantly enhanced skin permeation, indicating its potential as an effective system for topical indomethacin delivery.

Acknowledgement

The authors gratefully acknowledge the Berliner Hochschule für Technik, Berlin, Germany, and the Faculty of Pharmacy, Silpakorn University, Thailand, for providing research facilities. The authors also thank Björn Thomas for his valuable support during the study.

Conflict of interest

The authors declare no conflicts of interest.

References

1. O'Brien M, McCauley J, Cohen E. Indomethacin. In: Florey K, editor. *Analytical Profiles of Drug Substances*. Baghdad: 13: Academic Press; 1984;p.211–38.
2. Sweetman SC, Martindale C. *The complete drug reference*: London: Pharmaceutical Press; 2009.
3. Löbenberg R, Amidon GL. Modern bioavailability, bioequivalence and biopharmaceutics classification system. New scientific approaches to international regulatory standards. *Eur J Pharm Biopharm* 2000;50:3–12.
4. Mikulak SA, Vangsness CT, Nimni ME. Transdermal delivery and accumulation of indomethacin in subcutaneous tissues in rats. *J Pharm Pharmacol* 1998;50:153–8.
5. Naseri N, Valizadeh H, Zakeri-Milani P. Solid lipid nanoparticles and nanostructured lipid carriers: structure, preparation and application. *Adv Pharm Bull* 2015;5:305–13.
6. Müller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Advanced Drug Delivery Reviews* 2002;54:S131–55.
7. Müller RH, Radtke M, Wissing SA. Nanostructured lipid matrices for improved microencapsulation of drugs. *Int J Pharm* 2002;242:121–8.
8. Beloqui A, Solinis M, Rodríguez-Gascón A, Almeida AJ, Prêat V. Nanostructured lipid carriers: promising drug delivery systems for future clinics. *Nanomedicine* 2016;12:143–61.
9. Poonia N, Kharb R, Lather V, Pandita D. Nanostructured lipid carriers: versatile oral delivery vehicle. *Future Sci OA* 2016;2:Fso135.

10. Pooja J, Shaikh D, Rahul D. Emulgel Review – A Novel Topical Drug Delivery System. *Int J Pharm Sci Rev Res* 2024;84.
11. Sharma V, Nayak SK, Paul SR, Choudhary B, Ray SS, Pal K. 9 – Emulgels. In: Pal K, Banerjee I, editors. *Polymeric Gels*: Woodhead Publishing; 2018;p.251–64.
12. Arunprasert K, Pornpitchanarong C, Piemvuthi C, Siraprapapornsakul S, Sripeangchan S, Lertsrimongkol O, et al. Nanostructured lipid carrier-embedded polyacrylic acid transdermal patches for improved transdermal delivery of capsaicin. *Eur J Pharm Biopharm* 2022;173:106169.
13. Sarkis N, Sawan A. Method development for simultaneously determining indomethacin and nicotinamide in new combination in oral dosage formulations and co-amorphous systems using three UV spectrophotometric techniques. *Int J Anal Chem* 2024;2024.
14. Ghasemiyeh P, Mohammadi-Samani S. Potential of nanoparticles as permeation enhancers and targeted delivery options for skin: advantages and disadvantages. *Drug Des Devel Ther* 2020;14:3271–89.
15. Danaei M, Dehghankhold M, Ataei S, Hasanzadeh Davarani F, Javanmard R, Dokhani A, et al. Impact of particle size and polydispersity index on the clinical applications of lipidic nanocarrier systems. *Pharmaceutics* 2018;10.
16. Lukić M, Pantelić I, Savić SD. Towards optimal pH of the skin and topical formulations: from the current state of the art to tailored products. *Cosmetics* 2021;8:69.
17. Azhar Shekoufeh Bahari L, Hamishehkar H. The impact of variables on particle size of solid lipid nanoparticles and nanostructured lipid carriers; a comparative literature review. *Adv Pharm Bull* 2016;6:143–51.
18. Huang G, Xu B, Qiu J, Peng L, Luo K, Liu D, et al. Symmetric electrophoretic light scattering for determination of the zeta potential of colloidal systems. *Colloids Surf A Physicochem Eng Asp* 2020;587:124339.
19. Nguyen VH, Thuy VN, Van TV, Dao AH, Lee B-J. Nanostructured lipid carriers and their potential applications for versatile drug delivery via oral administration. *OpenNano* 2022;8:100064.
20. Syed Azhar SNA, Ashari SE, Zainuddin N, Hassan M. Nanostructured lipid carriers-hydrogels system for drug delivery: nanohybrid technology perspective. *Molecules* 2022;27.
21. Pareek A, Kapoor DU, Yadav SK, Rashid S, Fareed M, Akhter MS, et al. Advancing lipid nanoparticles: a pioneering technology in cosmetic and dermatological treatments. *Colloid and Interface Science Communications. Colloids Interface Sci Commun* 2025;64:100814.
22. Alquraisy A, Ramadhani K, Mohammed AFA, Wilar G, Osman-W, Elamin KM, et al. Nanostructured lipid carrier-gels for wound healing: a narrative review of formulation strategies, mechanisms, and translational potential. *Nanotechnol Sci Appl* 2026;19:1–24.
23. Yılmaz Usta D, Teksin ZS, Tugcu-Demiroz F. Evaluation of emulgel and nanostructured lipid carrier-based gel formulations for transdermal administration of ibuprofen: characterization, mechanical properties, and Ex-Vivo skin permeation. *AAPS PharmSciTech* 2024;25:124.