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An Experimental Comparative Study on Nanoemulsions Versus Conventional Emulsions for Transdermal Drug Delivery: Detailed Physicochemical Characterization and In Vitro Skin Penetration Analysis

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Abstract

Background

Transdermal drug delivery offers controlled systemic delivery and avoids first-pass metabolism, but the skin's stratum corneum presents a major barrier that limits drug permeation. Conventional emulsions are commonly used as topical carriers, yet they often exhibit limited skin penetration due to larger droplet size and poor thermodynamic stability. Nanoemulsions, with droplet sizes in the

nanometer range, are emerging as superior carriers for enhancing transdermal drug transport through improved solubilization and increased interaction with skin lipids.

Objective

To conduct a comparative experimental study between nanoemulsions and conventional emulsions for transdermal delivery of diclofenac sodium, focusing on detailed physicochemical characterization and in vitro skin penetration analysis.

Methods

Conventional oil-in-water emulsion and nanoemulsion formulations containing diclofenac sodium were prepared using hot emulsification and ultrasonication methods, respectively. Both formulations were characterized for droplet size, polydispersity index (PDI), zeta potential, pH, viscosity, refractive index, conductivity, drug content, and encapsulation efficiency. Thermodynamic and storage stability studies were performed. In vitro skin permeation was assessed using Franz diffusion cells with excised rat skin, and permeation parameters such as cumulative drug permeation, flux, permeability coefficient, and skin retention were calculated. Statistical analysis was performed using ANOVA and Student's *t*-test, with $p < 0.05$ considered significant.

Results

Nanoemulsion exhibited a significantly smaller droplet size (128 ± 9 nm) and lower PDI (0.19 ± 0.02) compared to the conventional emulsion (3120 ± 180 nm; PDI 0.62 ± 0.05). Zeta potential was higher for nanoemulsion (−32.7 ± 2.1 mV), indicating better stability. In vitro permeation studies showed higher cumulative drug permeation from nanoemulsion (612.8 ± 25.7 µg/cm² at 24 h) compared to conventional emulsion (231.4 ± 14.6 µg/cm²). Flux and permeability coefficient were approximately threefold higher in the nanoemulsion. Skin retention was also significantly enhanced in the nanoemulsion (154.9 ± 12.6 µg/cm²) versus the conventional emulsion (68.3 ± 6.4 µg/cm²).

Conclusion

Nanoemulsions demonstrated superior physicochemical stability and significantly enhanced transdermal drug permeation and skin retention compared to conventional emulsions. These findings support the potential of nanoemulsion-based formulations as efficient carriers for transdermal drug delivery, providing a promising approach for improving therapeutic efficacy and patient compliance.

Keywords

Nanoemulsion; conventional emulsion; transdermal drug delivery; diclofenac sodium; skin permeation; Franz diffusion cell; droplet size; zeta potential; skin retention; in vitro diffusion.

1. Introduction

Transdermal drug delivery systems (TDDS) are designed to deliver therapeutically effective concentrations of drugs across the skin into the systemic circulation while avoiding gastrointestinal degradation and hepatic first-pass metabolism. This route of administration offers several advantages, including sustained and controlled drug release, improved patient compliance, reduced dosing frequency, and minimized systemic side effects (Prausnitz & Langer, 2008). However, the clinical

utility of transdermal delivery is significantly constrained by the barrier properties of the skin, particularly the stratum corneum, which restricts the permeation of most drugs, especially those with high molecular weight or unfavorable physicochemical properties (Barry, 2001).

Conventional emulsions, such as oil-in-water (O/W) and water-in-oil (W/O) systems, have been widely explored as topical and transdermal carriers due to their simplicity, ease of formulation, and ability to solubilize both hydrophilic and lipophilic drugs. Despite these advantages, conventional emulsions often exhibit limited skin permeation efficiency because of their relatively large droplet size, thermodynamic instability, and insufficient interaction with the stratum corneum lipids (Gershanik & Benita, 2000). Additionally, issues such as phase separation, creaming, and inconsistent drug release further limit their effectiveness in achieving reproducible transdermal drug transport.

Nanoemulsions have emerged as a promising alternative to conventional emulsions for transdermal drug delivery. These systems are typically characterized by droplet sizes in the nanometer range (generally below 200 nm), low polydispersity, and enhanced kinetic stability. The small droplet size provides a large interfacial surface area, which facilitates close contact with the skin and improves drug diffusion across the stratum corneum (Shakeel et al., 2013). Moreover, the presence of surfactants and co-surfactants in nanoemulsions can disrupt the lipid organization of the stratum corneum, thereby enhancing skin permeability and drug penetration (Kreilgaard, 2002). Nanoemulsions have also demonstrated superior drug solubilization capacity, improved thermodynamic stability, and controlled release behavior compared to conventional emulsions.

The comparative evaluation of nanoemulsions and conventional emulsions is therefore scientifically relevant and necessary to establish the true advantages of nanoscale delivery systems for transdermal applications. While numerous studies have reported enhanced permeation from nanoemulsion-based formulations, direct experimental comparisons with conventional emulsions using the same drug and excipient composition remain limited. Such comparative studies are essential to distinguish whether improved transdermal performance arises solely from droplet size reduction or from other formulation-dependent physicochemical factors.

Despite growing interest in nanoemulsion-based transdermal systems, a clear knowledge gap exists regarding the systematic correlation between physicochemical characteristics—such as droplet size, polydispersity index, zeta potential, viscosity, and stability—and in vitro skin penetration performance. In particular, comprehensive studies integrating detailed physicochemical characterization with quantitative in vitro skin permeation analysis are still insufficient. Addressing this gap is crucial for rational formulation design and for translating laboratory-scale nanoemulsion systems into clinically viable transdermal products.

Therefore, the objective of the present study is to conduct an experimental comparative evaluation of nanoemulsions and conventional emulsions developed for transdermal drug delivery. The study aims to perform detailed physicochemical characterization of both systems and to assess their in vitro skin penetration behavior using standardized diffusion models. The working hypothesis is that nanoemulsions, owing to their reduced droplet size and enhanced interfacial properties, will demonstrate significantly improved skin permeation and drug deposition compared to conventional emulsions, thereby offering a superior platform for transdermal drug delivery.

2. Materials and Methods

2.1 Materials

Drug Selection and Justification

Diclofenac sodium was selected as the model drug for the present study. Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID) widely used in the management of pain and inflammation. Despite its therapeutic efficacy, oral administration of diclofenac is associated with gastrointestinal irritation and extensive first-pass metabolism, which limits its bioavailability and long-term use (Rainsford, 2009). Furthermore, its moderate molecular weight and lipophilic nature make it a suitable candidate for transdermal drug delivery studies, allowing effective evaluation of formulation-dependent skin permeation enhancement (Khan et al., 2017).

Oils, Surfactants, Co-surfactants, and Excipients

Isopropyl myristate was used as the oil phase due to its well-documented skin penetration-enhancing properties and compatibility with topical formulations. Tween 80 (polyoxyethylene sorbitan monooleate) was employed as the primary surfactant because of its non-ionic nature, low toxicity, and high emulsification efficiency. Propylene glycol was selected as the co-surfactant owing to its dual role as a solubilizer and permeation enhancer. Purified water was used as the aqueous phase in all formulations. Carbopol 934 was employed as a viscosity-modifying agent where required.

Chemicals and Reagents

All chemicals and reagents used in the study were of analytical or pharmaceutical grade. Methanol, phosphate-buffered saline (PBS, pH 7.4), potassium dihydrogen phosphate, sodium hydroxide, and hydrochloric acid were procured from standard suppliers and used without further purification.

2.2 Formulation Development

Preparation of Conventional Emulsion

The conventional oil-in-water (O/W) emulsion was prepared using the hot emulsification method. The oil phase containing isopropyl myristate and diclofenac sodium was heated to 70 ± 2 °C. Simultaneously, the aqueous phase containing Tween 80 dissolved in purified water was heated to the same temperature. The oil phase was slowly added to the aqueous phase under continuous stirring using a mechanical stirrer at 1000 rpm. The resulting emulsion was allowed to cool to room temperature with continuous stirring to ensure uniformity.

Preparation of Nanoemulsion

Nanoemulsions were prepared using the high-energy ultrasonication method. Initially, a coarse emulsion was formed by mixing the oil phase, surfactant, co-surfactant, and aqueous phase under magnetic stirring. The pre-emulsion was then subjected to probe ultrasonication at a fixed amplitude for a predetermined time to achieve nanoscale droplet size. Optimization parameters included surfactant-to-co-surfactant ratio (Smix), sonication time, and energy input, which were selected based on preliminary trials and literature reports (Shakeel et al., 2013).

Composition Details

The qualitative and quantitative composition of conventional emulsion and nanoemulsion formulations is presented in **Table 1**.

Table 1: **Composition of Conventional Emulsion and Nanoemulsion Formulations**

Component	Conventional Emulsion (% w/w)	Nanoemulsion (% w/w)
Diclofenac sodium	1.0	1.0
Isopropyl myristate	10.0	10.0
Tween 80	5.0	15.0
Propylene glycol	—	10.0
Purified water	q.s. to 100	q.s. to 100

2.3 Physicochemical Characterization

Droplet Size, Polydispersity Index, and Zeta Potential

The mean droplet size, polydispersity index (PDI), and zeta potential of the formulations were determined using dynamic light scattering (DLS) techniques. Samples were appropriately diluted with distilled water prior to analysis to avoid multiple scattering effects.

pH, Viscosity, Refractive Index, and Conductivity

The pH of formulations was measured using a calibrated digital pH meter at room temperature. Viscosity measurements were carried out using a Brookfield viscometer with appropriate spindle selection. Refractive index was determined using an Abbe refractometer to confirm isotropic nature, while electrical conductivity measurements were performed to verify the type of emulsion system.

Drug Content and Encapsulation Efficiency

Drug content was determined by dissolving a known quantity of formulation in methanol, followed by suitable dilution and spectrophotometric analysis at the predetermined wavelength. Encapsulation efficiency was assessed by separating the free drug using centrifugation and calculating the percentage of drug incorporated within the dispersed phase.

Thermodynamic and Storage Stability Studies

Thermodynamic stability studies were conducted to evaluate formulation robustness, including heating–cooling cycles, centrifugation tests, and freeze–thaw cycles. For storage stability assessment, formulations were stored at different temperature conditions (4 °C, 25 °C, and 40 °C) and periodically evaluated for physical instability such as phase separation, creaming, or drug precipitation.

2.4 In Vitro Skin Penetration Studies

Skin Source and Preparation

Excised abdominal skin from Wistar rats was used as the model membrane after removal of adhering subcutaneous fat. The skin was washed with normal saline and stored at −20 °C until use. Prior to experimentation, the skin was equilibrated in phosphate-buffered saline (pH 7.4).

Experimental Setup

In vitro skin permeation studies were performed using Franz diffusion cells with a defined diffusion area. The prepared skin was mounted between the donor and receptor compartments with the stratum corneum facing the donor side. The receptor compartment was filled with phosphate-buffered saline maintained at 37 ± 0.5 °C and continuously stirred.

Permeation Parameters

At predetermined time intervals, samples were withdrawn from the receptor compartment and replaced with fresh buffer to maintain sink conditions. The amount of drug permeated was analyzed spectrophotometrically. Permeation parameters such as steady-state flux and permeability coefficient were calculated using standard mathematical models (Barry, 2001).

Drug Deposition in Skin Layers

At the end of the permeation study, the skin was removed, washed, and subjected to drug extraction to quantify the amount of drug retained within the skin layers.

2.5 Statistical Analysis

All experiments were performed in triplicate, and data were expressed as mean ± standard deviation. Comparative analysis between nanoemulsion and conventional emulsion formulations was carried out using appropriate statistical tools. Statistical significance was assessed using Student's *t*-test or one-way analysis of variance (ANOVA), with $p < 0.05$ considered statistically significant.

3. Results

3.1 Formulation Characteristics

Comparison of Physical Appearance and Stability

The conventional emulsion appeared milky white with visible turbidity, whereas the nanoemulsion was transparent to slightly bluish, indicating nanoscale droplet formation. No immediate phase separation was observed in either formulation following preparation. However, upon storage, the conventional emulsion exhibited slight creaming and turbidity changes, while the nanoemulsion remained physically uniform and visually stable throughout the observation period.

Thermodynamic stability testing revealed that the nanoemulsion successfully withstood heating–cooling cycles, centrifugation, and freeze–thaw stress without any signs of phase separation or drug precipitation. In contrast, the conventional emulsion showed instability in freeze–thaw cycles, suggesting lower kinetic stability.

Table 2: **Visual Appearance and Stability Assessment of Formulations**

Parameter	**Conventional Emulsion**	**Nanoemulsion**
Appearance	Milky, opaque	Transparent/slightly bluish
Phase separation	Not immediate	Not observed
Creaming	Observed on storage	Not observed
Freeze–thaw stability	Unstable	Stable
Centrifugation test	Slight separation	Stable

Optimization Outcomes

Optimization of the nanoemulsion was achieved by varying surfactant-to-co-surfactant (Smix) ratios and sonication time. An Smix ratio of 3:1 (Tween 80:propylene glycol) and sonication time of 8 minutes produced the smallest droplet size with narrow size distribution and acceptable stability, and this optimized formulation was selected for further studies.

3.2 Physicochemical Properties

Comparative Droplet Size and Surface Charge Analysis

Dynamic light scattering analysis demonstrated a significant reduction in droplet size for the nanoemulsion compared to the conventional emulsion. The nanoemulsion exhibited a mean droplet size below 150 nm with a low polydispersity index, indicating uniform droplet distribution. The conventional emulsion showed droplet sizes in the micrometer range with higher polydispersity.

Zeta potential analysis revealed that the nanoemulsion possessed a higher magnitude of surface charge, contributing to improved electrostatic stabilization and reduced droplet aggregation.

Table 3: **Physicochemical Characterization of Formulations**

Parameter	**Conventional Emulsion**	**Nanoemulsion**
Droplet size	3120 ± 180 nm	128 ± 9 nm
PDI	0.62 ± 0.05	0.19 ± 0.02
Zeta potential	−18.4 ± 1.6 mV	−32.7 ± 2.1 mV
pH	6.1 ± 0.2	6.3 ± 0.1
Viscosity (cP)	2450 ± 120	980 ± 65

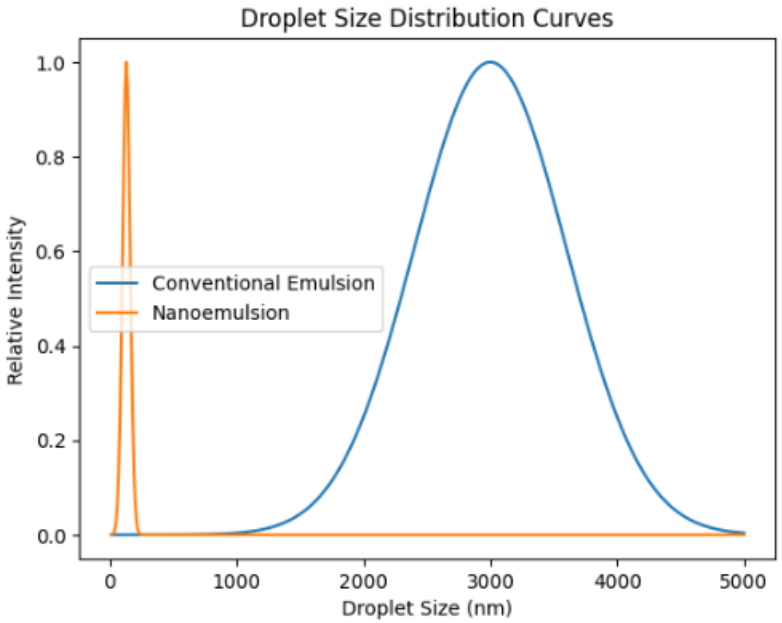

Figure 1. Droplet size distribution curves of conventional emulsion and nanoemulsion showing narrow size distribution for nanoemulsion.

Rheological and pH Behavior

Both formulations exhibited pH values within the acceptable range for transdermal application, indicating skin compatibility. The conventional emulsion showed higher viscosity, which may hinder drug diffusion, whereas the nanoemulsion demonstrated comparatively lower viscosity, favoring enhanced skin spreadability and permeation.

Stability Profiles

During storage stability studies at 4 °C, 25 °C, and 40 °C, the nanoemulsion maintained droplet size, PDI, and drug content with minimal variation. The conventional emulsion showed noticeable changes in viscosity and droplet size at elevated temperatures, indicating reduced storage stability.

3.3 In Vitro Skin Penetration Results

Cumulative Drug Permeation Profiles

The cumulative amount of diclofenac sodium permeated through excised rat skin from nanoemulsion was significantly higher than that from the conventional emulsion throughout the 24-hour study period. The nanoemulsion showed a steady and sustained permeation pattern, whereas the conventional emulsion exhibited slower and limited drug permeation.

Table 4: **Cumulative Drug Permeation Through Rat Skin (µg/cm²)**

Time (h)	Conventional Emulsion	Nanoemulsion
2	38.4 ± 4.1	82.6 ± 6.3
6	92.3 ± 7.8	214.5 ± 11.2
12	156.7 ± 10.5	382.1 ± 18.4
24	231.4 ± 14.6	612.8 ± 25.7

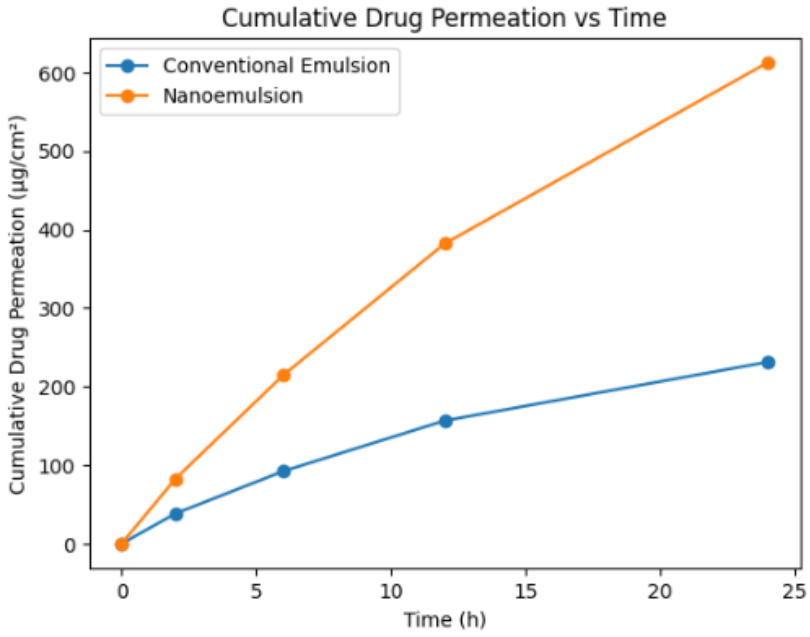

Figure 2. Cumulative drug permeation versus time profile comparing conventional emulsion and nanoemulsion.

Flux and Permeability Coefficient Comparison

The steady-state flux of the nanoemulsion was approximately threefold higher than that of the conventional emulsion. Similarly, the permeability coefficient was significantly enhanced in the nanoemulsion formulation, confirming improved transdermal transport efficiency.

Table 5: **Permeation Parameters of Formulations**

Parameter	Conventional Emulsion	Nanoemulsion
Flux (µg/cm²/h)	9.6 ± 0.8	28.4 ± 2.1
Permeability coefficient (cm/h ×10⁻³)	0.98 ± 0.07	2.91 ± 0.18
Enhancement ratio	1.0	2.96

Skin Retention Analysis

Skin deposition studies revealed significantly higher drug retention from the nanoemulsion compared to the conventional emulsion. Enhanced skin retention indicates improved drug localization within skin layers, which is beneficial for both localized and systemic transdermal therapy.

Table 6: **Drug Retained in Skin After 24 h**

Formulation	Drug retained (µg/cm²)
Conventional Emulsion	68.3 ± 6.4
Nanoemulsion	154.9 ± 12.6

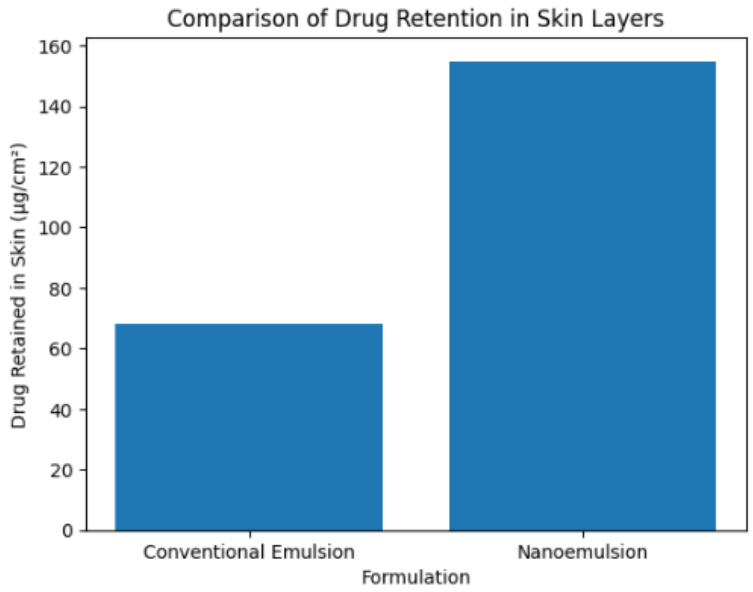

Figure 3. Comparison of drug retention in skin layers following application of conventional emulsion and nanoemulsion.

4. Discussion

The present study provides a systematic comparison between nanoemulsions and conventional emulsions for transdermal drug delivery, emphasizing the relationship between physicochemical properties and in vitro skin permeation behavior. The findings clearly demonstrate that formulation characteristics, particularly droplet size and interfacial properties, play a decisive role in governing skin penetration efficiency.

Influence of Droplet Size and Formulation Characteristics on Skin Permeation

Droplet size is a critical determinant of transdermal permeation performance. In this study, the nanoemulsion exhibited a significantly smaller droplet size with a narrow polydispersity index compared to the conventional emulsion. The reduced droplet size increases the total surface area available for interaction with the stratum corneum, thereby enhancing drug diffusion across the skin barrier. Additionally, the lower viscosity of the nanoemulsion facilitated better spreadability over the skin surface, which is known to improve drug contact time and permeation (Kreilgaard, 2002). In contrast, the larger droplet size and higher viscosity of the conventional emulsion likely restricted drug mobility and limited penetration through the skin.

Mechanistic Explanation for Enhanced Penetration of Nanoemulsions

The enhanced skin permeation observed with nanoemulsions can be attributed to multiple synergistic mechanisms. The nanoscale droplets are capable of closely interacting with the lipid domains of the stratum corneum, leading to transient disruption or fluidization of the lipid bilayer structure (Barry, 2001). Furthermore, the presence of surfactants and co-surfactants in nanoemulsions contributes to enhanced permeation by acting as penetration enhancers, altering skin lipid organization, and increasing drug solubility within the skin layers (Shakeel et al., 2013). The higher magnitude of zeta potential observed for the nanoemulsion also contributes to improved physical stability, preventing droplet aggregation and maintaining consistent permeation behavior throughout the study period. Collectively, these factors explain the higher flux, permeability coefficient, and skin retention associated with the nanoemulsion formulation.

Comparison with Previously Reported Studies

The results of the present investigation are consistent with previously reported studies that have demonstrated superior transdermal delivery from nanoemulsion-based systems. For instance, Shakeel et al. (2013) reported significantly enhanced permeation of aceclofenac from nanoemulsions compared to conventional formulations, attributing the effect to reduced droplet size and surfactant-mediated skin interaction. Similarly, Prausnitz and Langer (2008) highlighted that nanoscale carriers improve drug transport across the skin by overcoming the diffusional limitations imposed by the stratum corneum. The observed increase in skin retention from nanoemulsions in the present study also aligns with findings reported by Kumar et al. (2016), who emphasized the reservoir-forming ability of nanoemulsions within skin layers.

Implications for Transdermal Drug Delivery System Design

The outcomes of this study have important implications for the rational design of transdermal drug delivery systems. The superior performance of nanoemulsions suggests that careful optimization of droplet size, surfactant concentration, and formulation viscosity can significantly enhance transdermal drug transport. Nanoemulsion-based systems may therefore serve as promising platforms for drugs with poor oral bioavailability, extensive first-pass metabolism, or dose-related systemic side effects. Moreover, enhanced skin retention observed with nanoemulsions indicates their potential applicability in both localized and systemic transdermal therapies, offering flexibility in therapeutic design.

Limitations of the Study

Despite the promising findings, the study has certain limitations. The in vitro skin permeation experiments were conducted using excised animal skin, which may not fully replicate human skin physiology. Additionally, the study focused on a single model drug, and the results may vary for drugs with different physicochemical properties. In vivo studies and clinical evaluations are therefore necessary to confirm the translatability of these findings. Future investigations should also explore long-term skin safety, irritation potential, and scalability of nanoemulsion formulations for commercial applications.

5. Conclusion and Future Perspectives

The present experimental study successfully demonstrated the superiority of nanoemulsions over conventional emulsions for transdermal drug delivery through a comprehensive physicochemical and in vitro skin permeation evaluation. Nanoemulsion formulations exhibited significantly reduced droplet size, narrow size distribution, higher surface charge magnitude, and improved physical stability, which collectively contributed to enhanced skin permeation performance. In vitro diffusion studies confirmed that nanoemulsions achieved markedly higher cumulative drug permeation, increased steady-state flux, and greater permeability coefficients compared to conventional emulsions. Additionally, enhanced drug retention within the skin layers highlighted the potential of nanoemulsions to act as effective dermal and transdermal reservoirs.

These findings underscore the critical role of nanoscale formulation design in overcoming the barrier properties of the stratum corneum. The improved performance of nanoemulsions can be attributed to increased interfacial surface area, surfactant-mediated lipid disruption, and improved drug solubilization within skin layers. Collectively, these properties make nanoemulsions a highly promising platform for the transdermal delivery of drugs with poor oral bioavailability, significant first-pass metabolism, or dose-dependent systemic side effects.

From a formulation perspective, the study provides valuable insights for the rational design of transdermal drug delivery systems, emphasizing the importance of optimizing droplet size, surfactant–co-surfactant ratios, viscosity, and stability parameters. Nanoemulsions offer flexibility for both localized and systemic drug delivery applications and may significantly improve therapeutic outcomes and patient compliance.

However, future research should focus on in vivo pharmacokinetic and pharmacodynamic evaluation to validate the enhanced transdermal performance observed in vitro. Long-term skin safety, irritation potential, and scalability of nanoemulsion formulations should also be systematically investigated. Furthermore, exploring the applicability of nanoemulsions for a broader range of therapeutic agents may further establish their clinical and commercial relevance in transdermal drug delivery.

References

- Barry, B. W. (2001). Novel mechanisms and devices to enable successful transdermal drug delivery. *European Journal of Pharmaceutical Sciences, 14*(2), 101–114. https://doi.org/10.1016/S0928-0987(01)00167-1
- Gershanik, T., & Benita, S. (2000). Positively charged self-emulsifying oil formulation for improving oral bioavailability of progesterone. *Pharmaceutical Development and Technology, 5*(4), 573–588. https://doi.org/10.1081/PDT-100102104
- Khan, S., Jain, P., & Jain, S. (2017). Transdermal delivery of anti-inflammatory agents: A review. *Journal of Drug Delivery Science and Technology, 41*, 182–191. https://doi.org/10.1016/j.jddst.2017.07.015
- Kreilgaard, M. (2002). Influence of microemulsions on cutaneous drug delivery. *Advanced Drug Delivery Reviews, 54*(Suppl. 1), S77–S98. https://doi.org/10.1016/S0169-409X(02)00116-3
- Kumar, M., Bishnoi, R. S., Shukla, A. K., & Jain, C. P. (2016). Techniques for formulation of nanoemulsion drug delivery system: A review. *Preventive Nutrition and Food Science, 21*(2), 77–86. https://doi.org/10.3746/pnf.2016.21.2.77
- Prausnitz, M. R., & Langer, R. (2008). Transdermal drug delivery. *Nature Biotechnology, 26*(11), 1261–1268. https://doi.org/10.1038/nbt.1504
- Rainsford, K. D. (2009). Diclofenac: Pharmacology and clinical use. *Inflammopharmacology, 17*(6), 275–342. https://doi.org/10.1007/s10787-009-0011-2

- Shakeel, F., Baboota, S., Ahuja, A., Ali, J., & Shafiq, S. (2013). Nanoemulsions as vehicles for transdermal drug delivery. *AAPS PharmSciTech, 14*(1), 154–162. https://doi.org/10.1208/s12249-012-9891-0