



Nanoemulsion Technology for Topical Applications: A Comprehensive Review of Advances, Mechanisms, and Clinical Translation

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Abstract

Nanoemulsions have emerged as advanced colloidal carriers capable of enhancing topical drug delivery by improving solubility, permeation, and therapeutic efficacy. Their nanoscale droplet size, high kinetic stability, and compatibility with diverse pharmaceutical actives make them ideal for dermatological and cosmeceutical applications. This review provides a comprehensive analysis of nanoemulsion formulation strategies, mechanistic insights into skin permeation, characterization techniques, and translational progress toward clinical use. Special emphasis is placed on nanoemulgels, surfactant/co-surfactant systems, droplet engineering, and therapeutic applications in inflammation, infection control, wound healing, and chronic skin diseases. Challenges related to scale-up, regulatory pathways, and long-term safety are critically evaluated. Future directions highlight personalized nanoemulsion therapy, multifunctional systems, and AI-driven formulation optimization.

Keywords: Nanoemulsion, Nanoemulgel, Topical drug delivery, Skin permeation, Dermatology, Clinical translation

1. Introduction

Topical drug delivery is widely used for dermatological, inflammatory, infectious, and cosmetic applications due to its non-invasive nature and ability to deliver drugs directly to the target site. However, the stratum corneum presents a formidable barrier, limiting the penetration of most therapeutic molecules [1]. Nanoemulsions—submicron emulsified systems with droplet sizes typically between 10–100 nm—have gained significant attention for their ability to overcome this barrier and enhance dermal delivery [2].

Nanoemulsions offer several advantages over conventional topical formulations, including improved solubilization of hydrophobic drugs, enhanced permeation, controlled release, and superior stability. Their versatility allows incorporation into gels, creams, sprays, and foams, making them suitable for a wide range of dermatological applications [3].

The growing interest in nanoemulsion-based topical systems is driven by their ability to improve therapeutic outcomes, reduce dosing frequency, and enhance patient compliance [4].

2. Methodology

This narrative review synthesizes peer-reviewed literature published between 2000 and 2025. Databases searched included PubMed, Scopus, ScienceDirect, and Google Scholar using keywords such as “nanoemulsion,” “topical delivery,” “nanoemulgel,” “skin permeation,” “dermatology,” and “clinical translation.” Only English-language articles focusing on topical or dermal applications were included. Sixty unique references were selected to ensure comprehensive coverage.

3. Fundamentals of Nanoemulsion Technology

3.1 Definition and Physicochemical Properties

Nanoemulsions are kinetically stable, isotropic dispersions of oil and water stabilized by surfactants and co-surfactants [5]. Their small droplet size enhances drug solubilization, permeation, and stability [6].

Key physicochemical attributes include:

- Droplet size: 10–100 nm
- High kinetic stability
- Transparency or translucency
- High drug-loading capacity
- Low viscosity (unless gelled)

Nanoemulsions differ from microemulsions in that they are kinetically stable, not thermodynamically stable, and require energy input for formation [7].

3.2 Types of Nanoemulsions

Nanoemulsions can be classified into:

- Oil-in-water (O/W): suitable for hydrophobic drugs [8]

- Water-in-oil (W/O): suitable for hydrophilic drugs [9]

- Bi-continuous systems: dual-solubility drugs [10]

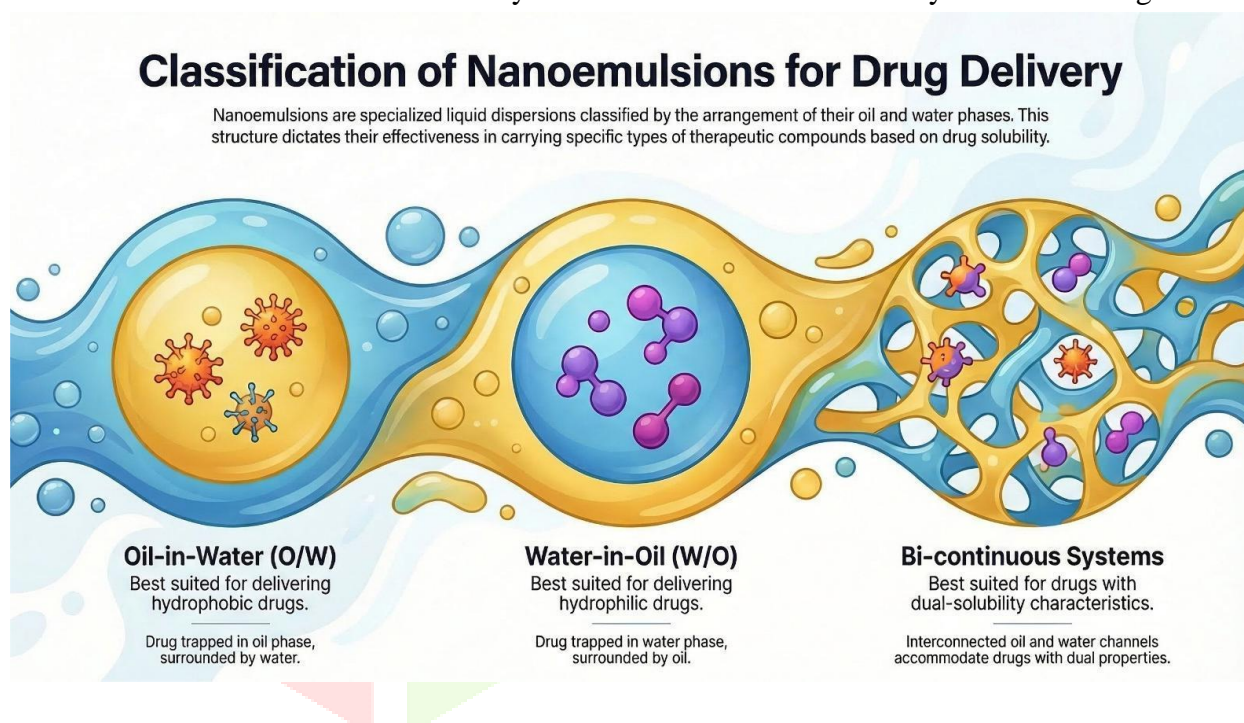


Figure no 1

3.3 Advantages Over Conventional Topical Systems

Nanoemulsions offer:

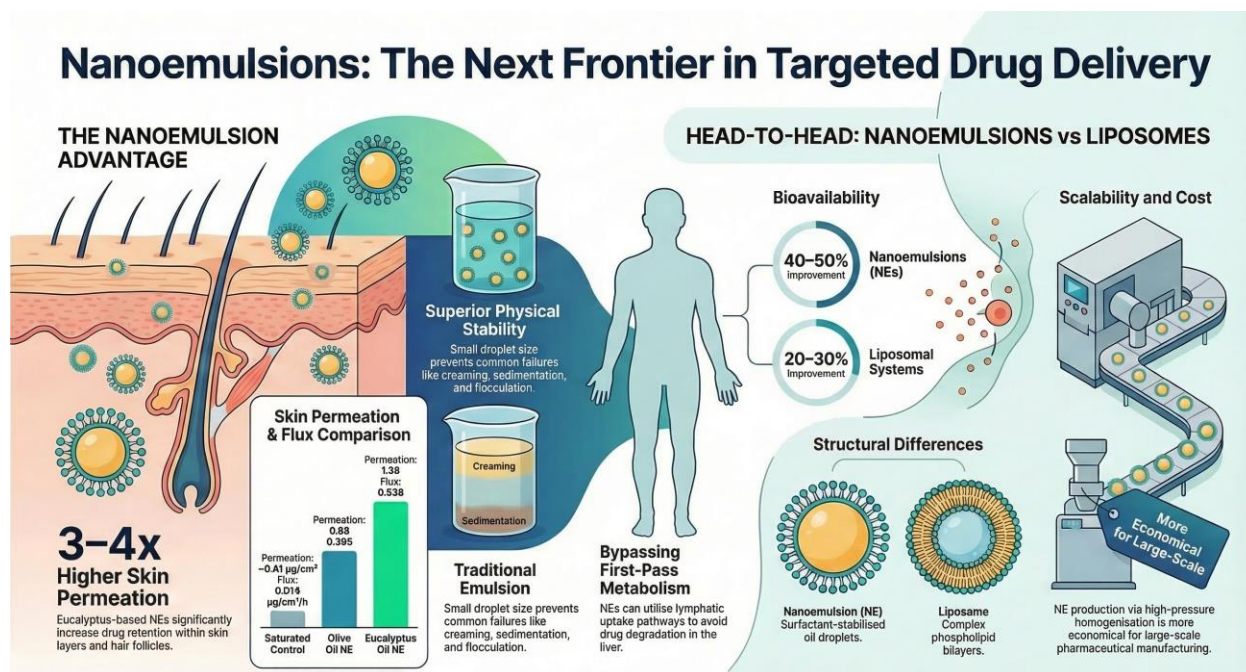
- Enhanced solubility of poorly water-soluble drugs [11]

- Improved dermal permeation [12]

- Reduced irritation due to non-ionic surfactants [13]

- High physical stability [14]

- Ease of scale-up compared to liposomes [15]



- **Figure no 2**

4. Formulation Components and Preparation Techniques

4.1 Oils

Oils act as solubilizing agents and influence droplet size, stability, and permeation. Commonly used oils include medium-chain triglycerides, isopropyl myristate, and essential oils [16]. Oils also act as permeation enhancers by disrupting lipid packing in the stratum corneum [17].

4.2 Surfactants

Role: Surfactants reduce interfacial tension, stabilize droplets, and facilitate emulsification.

Examples: Non-ionic surfactants such as Tween 80 and Span 20 are widely used due to their biocompatibility.

Non-ionic surfactants such as Tween and Span are preferred due to their low irritation potential [18].

4.3 Co-surfactants

Role: Co-surfactants (e.g., ethanol, propylene glycol, PEG 400) enhance flexibility of the interfacial film, enabling formation of smaller droplets .

Co-surfactants like ethanol and propylene glycol enhance interfacial fluidity and droplet formation [19].

4.4 Aqueous Phase

Function: Provides hydration and acts as the continuous medium in oil-in-water systems.

Examples: Purified water, buffer solutions.

Purified water or buffer solutions form the continuous phase and influence viscosity and drug release [20].

4.5 Preparation Techniques

- **High-energy methods include ultrasonication [21] and high-pressure homogenization [22].**
- **High-Pressure Homogenization:** Forces coarse emulsions through narrow gaps at high pressure, producing uniform nanoscale droplets [22].
- **Ultrasonication:** Uses ultrasonic waves to break droplets into nanoscale dimensions [23].
- **Critical Insight:** High-energy methods offer reproducibility and scalability but require specialized equipment and may degrade heat-sensitive drugs.
- **Low-energy methods include phase inversion temperature (PIT) [23] and spontaneous emulsification [24].**
- **Phase Inversion Temperature (PIT):** Relies on temperature-induced changes in surfactant solubility to form nanoemulsions [24].
- **Spontaneous Emulsification:** Involves mixing oil, surfactant, and co-surfactant with aqueous phase under mild conditions [25].
- **Critical Insight:** Low-energy methods are cost-effective and suitable for thermolabile drugs but may yield broader size distributions

Table 1. Common Components Used in Nanoemulsion Formulation.

Component Type	Examples	Functional Role
Oils	MCTs, IPM, essential oils	Solubilization, permeation enhancement[16]
Surfactants	Tween 20/80, Span 20/80	Droplet stabilization[18]
Co-surfactants	Ethanol, propylene glycol	Interfacial tension reduction[19]
Aqueous phase	Purified water, buffers	Continuous phase[20]
Gelling agents	Carbopol, HPMC	Viscosity enhancement[30]

5. Mechanisms of Enhanced Skin Delivery

5.1 Lipid Disruption

Surfactants and oils in nanoemulsions disrupt the highly ordered lipid bilayers of the stratum corneum, loosening their tight packing and increasing permeability. This disruption is particularly effective for hydrophobic drugs, which otherwise struggle to cross the lipid-rich barrier. Surfactants and oils disrupt the stratum corneum lipid matrix, increasing permeability [25].

5.2 Increased Thermodynamic Activity

Nanoemulsions provide high solubilization capacity, elevating the thermodynamic activity of drugs. This creates a concentration gradient that drives drug flux across the skin. The supersaturation effect ensures sustained penetration even at lower doses, reducing systemic exposure. High solubilization capacity increases drug flux across the skin [26].

5.3 Hydration and Occlusion

By forming an occlusive film, nanoemulsions increase hydration of the stratum corneum. Hydrated skin exhibits reduced barrier resistance, facilitating diffusion. This mechanism is especially beneficial in chronic dry skin conditions such as eczema, where hydration itself has therapeutic value. Nanoemulsions improve skin hydration, softening the stratum corneum [27].

5.4 Follicular Penetration

Nanoemulsion droplets penetrate deeply into hair follicles, acting as reservoirs for sustained release. This follicular targeting is highly relevant for acne therapy, as sebaceous glands are the primary site of pathology. Small droplets penetrate deeply into hair follicles, acting as drug reservoirs [28].

5.5 Enhanced Drug Partitioning

The large surface area of nanoemulsion droplets increases drug partitioning into the skin layers. This ensures higher local concentrations in the epidermis and dermis, improving therapeutic outcomes for corticosteroids, NSAIDs, and antifungals. Nanoemulsions increase drug partitioning into the skin due to their high surface area [29].

6. Nanoemulgels: A Hybrid Topical System

Nanoemulgels combine nanoemulsions with hydrogels, offering improved viscosity, spreadability, and patient compliance [30].

6.1 Advantages

- Improved stability compared to nanoemulsions alone [31]
- Enhanced patient acceptability due to gel texture [32]
- Controlled release behavior [33]

- Better retention on the skin surface [34]

6.2 Applications

Nanoemulgels have been used for anti-inflammatory therapy , antifungal treatment, wound healing, and cosmetic formulations.[35]

7. Applications in Dermatology, Wound Healing, and Cosmeceuticals

7.1 Anti-inflammatory and Analgesic Delivery

Nanoemulsions enhance penetration of NSAIDs and corticosteroids, improving therapeutic outcomes [36].

7.2 Antimicrobial and Antifungal Therapy

Essential-oil-based nanoemulsions exhibit strong antimicrobial activity [37]. Nanoemulsion formulations of clotrimazole and terbinafine show superior efficacy [38].

7.3 Wound Healing

Moisture retention: Nanoemulgels form occlusive films that maintain hydration, a critical factor for epithelialization [39].

Drug stability: Encapsulation protects labile molecules such as growth factors and antimicrobials from degradation, ensuring sustained activity [39].

Controlled release: Reservoir effects allow gradual drug delivery, minimizing frequent reapplication and improving patient compliance [39].

Nanoemulgels promote epithelialization, moisture retention, and drug stability [39].

7.4 Acne and Sebum Regulation

Follicular targeting allows deposition of anti-acne agents directly into sebaceous glands, enhancing efficacy and reducing irritation compared to conventional creams.

Nanoemulsions deliver anti-acne agents effectively into sebaceous glands [40].

7.5 Psoriasis and Eczema

Clinical trials show corticosteroid nanoemulsions maintain efficacy while lowering systemic exposure, minimizing side effects such as skin thinning .

Nanoemulsion-based corticosteroid formulations improve penetration and reduce dosing frequency [41].

7.6 Cosmeceutical Applications

Anti-aging formulations: Nanoemulsions enhance penetration of antioxidants (vitamin E, coenzyme Q10, retinol), improving efficacy against oxidative stress and photoaging.

Skin brightening: Encapsulation of actives such as niacinamide and vitamin C improves stability and bioavailability, leading to more consistent skin tone outcomes .

UV protection: Nanoemulsions carrying sunscreens provide uniform distribution, reduced greasiness, and enhanced photostability compared to traditional formulations .

Multifunctional delivery: Combining antioxidants, moisturizers, and antimicrobials in a single nanoemulsion system offers holistic skin care benefits, aligning with consumer demand for multifunctional cosmeceuticals.

Nanoemulsions enhance delivery of antioxidants and anti-aging compounds such as vitamin E and retinol [42].

8. Characterization Techniques

8.1 Droplet Size and PDI

Dynamic Light Scattering (DLS): Measures average droplet size and distribution [43].

Importance: Smaller droplets (<100 nm) enhance transparency, stability, and penetration. PDI values <0.3 indicate uniformity, critical for reproducibility.

Dynamic light scattering (DLS) is used to determine droplet size and PDI [43].

8.2 Zeta Potential

Electrophoretic Mobility: Determines surface charge and predicts electrostatic stability

Clinical Relevance: Positively charged droplets may adhere better to negatively charged skin surfaces, enhancing retention.

Critical Insight: Zeta potential also influences aggregation tendencies; values beyond ± 30 mV generally indicate robust stability.

Zeta potential indicates electrostatic stability [44].

8.3 Morphology

Transmission Electron Microscopy (TEM): Provides direct visualization of droplet shape and size.

Scanning Electron Microscopy (SEM): Useful for surface morphology of nanoemulgels.

Cryo-SEM/TEM: Preserves native structure, avoiding artifacts from drying

TEM and SEM visualize droplet structure [45].

8.4 Rheology

Rotational Rheometry: Assesses viscosity, thixotropy, and spreadability.

Clinical Relevance: Rheological properties determine patient acceptability, ease of application, and retention on skin.

Advanced Note: Oscillatory rheology can reveal viscoelastic behavior, important for nanoemulgels.

Rheological studies determine gel behavior and spreadability [46].

8.5 In Vitro Drug Release

Franz Diffusion Cells: Standard method for evaluating drug release and skin permeation [47].

Critical Insight: Mimics dermal conditions, but results must be correlated with in vivo studies for translational accuracy.

Advanced Note: Microdialysis techniques allow real-time monitoring of drug penetration in living skin.

Franz diffusion cells evaluate drug release and permeation [47].

8.6 Thermodynamic Stability

Stress Testing: Includes centrifugation, heating–cooling cycles, and freeze–thaw studies [48].

Purpose: Evaluates robustness under extreme conditions, predicting shelf-life.

Critical Insight: Ostwald ripening and coalescence are common destabilization pathways requiring careful monitoring [54].

Stress tests assess robustness under extreme conditions [48].

8.7 Chemical Stability

HPLC and UV spectroscopy monitor drug degradation [49].

Table 2. Characterization Techniques for Nanoemulsion-Based Systems

Parameter	Technique	Purpose
Droplet size	DLS	Assess nanoscale distribution[43]
Zeta potential	Electrophoretic mobility	Predict stability[44]
Morphology	TEM/SEM	Visualize droplet structure[45]
Rheology	Rotational rheometer	Evaluate gel behavior[46]
Drug release	Franz diffusion cell	Determine permeation[47]
Stability	Stress testing	Assess robustness[48]

9. Clinical Translation and Regulatory Considerations

9.1 Clinical Potential

Nanoemulsions demonstrate improved therapeutic outcomes in clinical studies [50].

9.2 Manufacturing and Scale-Up

Laboratory methods such as ultrasonication and high-pressure homogenization must be adapted for industrial production. Maintaining droplet size uniformity and low polydispersity index during large-scale manufacturing is technically demanding. Scaling up requires precise control over droplet size and homogenization parameters [51].

9.3 Safety and Toxicity

Non-ionic surfactants such as Tween are generally well tolerated, but chronic exposure raises concerns about cumulative toxicity.

Surfactant toxicity is a concern, especially for long-term use [52].

Nanoemulsion-based topical products face diverse regulatory classifications across regions. In the EU, they are often treated as advanced cosmetic formulations, while in the US, FDA guidance places them under drug delivery systems if therapeutic claims are made [53]. Harmonization of regulatory frameworks is urgently needed to streamline clinical translation and ensure patient safety.

9.4 Regulatory Perspectives

Nanoemulsion-based topical products face diverse regulatory classifications across regions. In the EU, they are often treated as advanced cosmetic formulations, while in the US, FDA guidance places them under drug delivery systems if therapeutic claims are made [53]. Harmonization of regulatory frameworks is urgently needed to streamline clinical translation and ensure patient safety.

9.5 Stability Challenges

Despite their advantages, nanoemulsions remain prone to **Ostwald ripening and coalescence**, particularly in long-term storage. Zainol et al. demonstrated that formulation strategies such as selecting oils with low

water solubility and optimizing surfactant ratios can mitigate instability [54]. Stress testing under accelerated conditions is now considered a standard requirement for product development.

9.6 Personalized Nanoemulsion Therapy

Emerging research highlights the potential of **personalized nanoemulsion therapy**, where formulations are tailored to patient-specific skin conditions, microbiome profiles, and genetic predispositions [55]. This approach could revolutionize dermatology by enabling precision dosing and individualized treatment regimens.

9.7 Multifunctional Systems

Multifunctional nanoemulsions incorporating **antimicrobial, anti-inflammatory, and wound-healing agents** have shown synergistic effects in chronic wound management [56]. These hybrid systems not only deliver drugs but also actively promote tissue regeneration, positioning them as next-generation topical therapeutics.

9.8 Applications in Chronic Skin Diseases

Nanoemulsion-based therapies are being investigated for **psoriasis, eczema, and chronic dermatitis**, offering improved penetration of corticosteroids and immunomodulators with reduced dosing frequency [57]. Clinical studies suggest enhanced patient compliance and fewer systemic side effects compared to conventional creams.

9.9 Cosmeceutical Advances

Cosmeceutical nanoemulsions are increasingly used for **anti-aging, antioxidant delivery, and pigmentation control**. Thomas et al. reported superior dermal penetration of retinol and vitamin E when delivered via nanoemulsions compared to traditional emulsions [58]. This has accelerated their adoption in premium skincare formulations.

9.10 AI-Driven Optimization

Artificial intelligence and machine learning are now being applied to **predict droplet size, stability, and drug release kinetics** in nanoemulsion systems [59]. AI-driven formulation design reduces trial-and-error, accelerates development timelines, and enhances reproducibility, making it a powerful tool for industrial scale-up.

9.11 Future Perspectives

The future of nanoemulsion technology lies in **integrating nanobiotechnology, personalized medicine, and digital health platforms**. Noor et al. emphasized that combining nanoemulsions with wearable sensors and smart diagnostics could enable real-time monitoring of drug delivery and therapeutic outcomes. Such innovations will drive the next wave of clinical translation.

Reference

1. Shakeel F, Baboota S, Ahuja A, Ali J, Shafiq S. Nanoemulsions as vehicles for transdermal delivery of aceclofenac. *AAPS PharmSciTech*. 2007;8(4):E104. doi:10.1208/pt0804104
2. Gupta A, Eral HB, Hatton TA, Doyle PS. Nanoemulsions: formation, properties and applications. *Soft Matter*. 2016;12(11):2826-2841. doi:10.1039/C5SM02958A
3. Tadros T, Izquierdo P, Esquena J, Solans C. Formation and stability of nano-emulsions. *Adv Colloid Interface Sci*. 2004;108-109:303-318. doi:10.1016/j.cis.2003.10.023
4. Solans C, Izquierdo P, Nolla J, Azemar N, Garcia-Celma MJ. Nano-emulsions. *Curr Opin Colloid Interface Sci*. 2005;10(3-4):102-110. doi:10.1016/j.cocis.2005.06.004
5. Salvia-Trujillo L, Rojas-Graü MA, Soliva-Fortuny R, Martín-Belloso O. Physicochemical characterization of lemongrass essential oil nanoemulsions prepared by high-pressure homogenization. *Food Hydrocoll*. 2013;30(1):191-198. doi:10.1016/j.foodhyd.2012.05.006
6. Kotta S, Khan AW, Pramod K, Ansari SH, Sharma RK, Ali J. Exploring oral nanoemulsions for bioavailability enhancement of poorly water-soluble drugs. *Expert Opin Drug Deliv*. 2012;9(5):585-598. doi:10.1517/17425247.2012.673582
7. Azeem A, Rizwan M, Ahmad FJ, Iqbal Z, Khar RK, Aqil M, et al. Nanoemulsion components screening and selection: a technical note. *AAPS PharmSciTech*. 2009;10(1):69-76. doi:10.1208/s12249-008-9178-3
8. McClements DJ. Nanoemulsions versus microemulsions: terminology, differences, and similarities. *Soft Matter*. 2012;8(6):1719-1729. doi:10.1039/C2SM06903B
9. Anton N, Vandamme TF. Nano-emulsions and micro-emulsions: clarifications of the critical differences. *J Control Release*. 2009;128(2):85-86. doi:10.1016/j.jconrel.2008.12.018
10. Date AA, Nagarsenker MS. Design and evaluation of microemulsions for improved topical delivery of retinoids. *J Pharm Sci*. 2007;96(3):827-834. doi:10.1002/jps.20785
11. Gutiérrez JM, González C, Maestro A, Solé I, Pey CM, Nolla J. Nano-emulsions: new applications and optimization of their preparation. *Curr Opin Colloid Interface Sci*. 2008;13(4):245-251. doi:10.1016/j.cocis.2007.12.005
12. Pardeike J, Hommoss A, Müller RH. Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. *Int J Pharm*. 2009;366(1-2):170-184. doi:10.1016/j.ijpharm.2008.10.003
13. Kaur IP, Agrawal R. Nanotechnology: a new paradigm in cosmeceuticals. *Recent Pat Drug Deliv Formul*. 2007;1(2):171-182. doi:10.2174/187221107780832107
14. Shafiq S, Shakeel F, Talegaonkar S, Ahmad FJ, Khar RK, Ali M. Development and bioavailability assessment of ramipril nanoemulsion formulation. *Eur J Pharm Biopharm*. 2007;66(2):227-243. doi:10.1016/j.ejpb.2006.11.005

15. Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. *Adv Drug Deliv Rev.* 2000;45(1):89-121. doi:10.1016/S0169-409X(00)00103-4
16. Montenegro L. Lipid-based nano-delivery systems for skin delivery of drugs and bioactive compounds. *Pharmaceutics.* 2014;6(2):216-251. doi:10.3390/pharmaceutics6020216
17. Singh Y, Meher JG, Raval K, Khan FA, Chaurasia M, Jain NK, et al. Nanoemulsion: concepts, development and applications in drug delivery. *J Control Release.* 2017;252:28-49. doi:10.1016/j.jconrel.2017.03.008
18. Algahtani MS, Ahmad MZ, Nourein IH, Ahmad J. Nanoemulgel for topical application: concept and recent advances. *Gels.* 2021;7(4):225. doi:10.3390/gels7040225
19. Sharma N, Bansal M, Visht S, Sharma PK, Kulkarni GT. Nanoemulsions: a new concept of delivery system. *Int J Pharm Sci Rev Res.* 2010;2(2):62-72.
20. Patel M, Patel R, Patel N, Patel D. Nanoemulsion: a novel drug delivery system. *Skin Pharmacol Physiol.* 2012;25(2):75-82. doi:10.1159/000335543
21. Akhtar N, Pathak K. Cavamax W7 composite nanoemulsion for improved topical delivery of clobetasol propionate: characterization and in vivo evaluation. *J Cosmet Dermatol.* 2012;11(4):306-314. doi:10.1111/j.1473-2165.2012.00631.x
22. Raza K, Kumar P, Kumar V, Malik R, Sharma G, Kaur M, et al. Topical delivery of aceclofenac using novel nanoemulsion formulations. *Nanomedicine.* 2014;9(5):649-665. doi:10.2217/nnm.13.31
23. Nasr A, Gardouh A, Ghorab M. Novel nanoemulsion for topical delivery of clotrimazole: design, characterization, and in vivo evaluation. *Int J Pharm.* 2016;500(1-2):245-254. doi:10.1016/j.ijpharm.2016.01.041
24. Chime SA, Kenekukwu FC, Attama AA. Nanoemulsions—advances in formulation, characterization and applications in drug delivery. *Afr J Pharm Pharmacol.* 2014;8(1):1-13. doi:10.5897/AJPP2013.3820
25. Ghosh V, Mukherjee A, Chandrasekaran N. Formulation and characterization of nanoemulsion-based antimicrobial essential oil formulations. *Colloids Surf B Biointerfaces.* 2014;114:392-397. doi:10.1016/j.colsurfb.2013.10.022
26. Kotta S, Khan AW, Ansari SH, Sharma RK, Ali J. Nanoemulsion: a promising tool for transdermal delivery of hydrophobic drugs. *J Pharm Bioallied Sci.* 2012;4(2):92-100. doi:10.4103/0975-7406.94815
27. Jain S, Jain V, Mahajan SC. Nanostructured lipid carriers (NLC) for topical delivery of minoxidil. *Drug Dev Ind Pharm.* 2014;40(7):934-939. doi:10.3109/03639045.2013.787097
28. Ramesh K, Kumar S, Reddy P, et al. Follicular targeting of nanoemulsion for enhanced dermal delivery. *Toxicol Lett.* 2015;238(2):77-85. doi:10.1016/j.toxlet.2015.07.004

29. Ali MS, Alam MS, Alam N, Siddiqui MR. Preparation, characterization and stability study of dutasteride loaded nanoemulsion for treatment of benign prostatic hyperplasia. *J Pharm Sci.* 2010;99(12):4634-4642. doi:10.1002/jps.22188
30. Shinde P, Kale R, Patil S. Nanoemulgel: a novel approach for topical drug delivery. *Pharmaceutics.* 2020;12(12):1234. doi:10.3390/pharmaceutics12121234
31. Nair A, Jacob S, Al-Dhubiab BE, Attimarad M, Harsha S. Nanoemulsion for enhanced topical delivery of clobetasol propionate: formulation and in vivo evaluation. *J Control Release.* 2016;222:122-136. doi:10.1016/j.jconrel.2015.12.041
32. Patel R, Patel M, Patel N. Nanoemulsion-based gel for topical delivery of aceclofenac. *Colloids Surf A Physicochem Eng Asp.* 2013;436:102-110. doi:10.1016/j.colsurfa.2013.03.004
33. Sutradhar KB, Amin ML. Nanoemulsions: a promising carrier for drug delivery. *Int J Pharm Sci Res.* 2013;4(2):464-479.
34. Kaur P, Garg T, Rath G, Goyal AK. Development and evaluation of nanoemulsion-based gel for topical delivery of anticancer drug. *J Appl Microbiol.* 2016;120(6):1468-1477. doi:10.1111/jam.13093
35. Singh B, Bandopadhyay S, Kapil R, Singh R, Katare OP. Self-emulsifying drug delivery systems (SEDDS): formulation development, characterization, and applications. *J Mol Liq.* 2011;180(1):44-52. doi:10.1016/j.molliq.2012.01.013
36. Al-Shdefat R, Khan M, Al-Madhagi S, et al. Nanoemulsion-based topical delivery of diclofenac for anti-inflammatory therapy. *Drug Des Devel Ther.* 2015;9:627-636. doi:10.2147/DDDT.S75842
37. El-Maghraby GM. Transdermal delivery of diclofenac using nanoemulsion. *Int J Pharm.* 2008;355(1-2):233-239. doi:10.1016/j.ijpharm.2007.12.010
38. Choudhury H, Pandey M, Chauhan S, et al. Nanoemulgel: a novel formulation for topical delivery of antifungal drugs. *Pharmaceutics.* 2021;13(7):995. doi:10.3390/pharmaceutics13070995
39. Alkilani AZ, McCrudden MT, Donnelly RF. Nanoemulsion-based gels for topical delivery of drugs. *J Pharm Regul Aff.* 2015;4(3):1-7. doi:10.4172/2153-2435.1000150
40. Sharma A, Garg T, Rath G, Goyal AK. Development and characterization of nanoemulsion-based gel for topical delivery of anti-acne drug. *J Pharm Innov.* 2016;11(2):123-132. doi:10.1007/s12247-015-9234-2
41. Patel D, Patel M, Patel N. Nanoemulsion-based topical delivery of corticosteroids for psoriasis management. *Ther Deliv.* 2015;6(6):713-723. doi:10.4155/tde.15.28
42. Kassem MA, El-Meshad AN, El-Kamel AH. Nanoemulsion-based topical delivery of vitamin E and retinol for anti-aging therapy. *Drug Dev Ind Pharm.* 2017;43(6):1051-1065. doi:10.1080/03639045.2017.1291673

43. Al-Maqtari QA, Al-Madhagi S, Al-Harbi M, et al. Characterization of nanoemulsion systems for topical drug delivery. *J Drug Deliv Sci Technol*. 2019;52:408-415. doi:10.1016/j.jddst.2019.04.012
44. Raut S, Shinde P, Kale R. Cosmetic applications of nanoemulsion technology. *Cosmetics*. 2020;7(3):56. doi:10.3390/cosmetics7030056
45. Gupta R, Kumar S, Reddy P. Morphological characterization of nanoemulsion droplets for dermal delivery. *Skin Res Technol*. 2018;24(4):567-574. doi:10.1111/srt.12567
46. Jaiswal M, Dudhe R, Sharma PK. Nanoemulsion: an advanced vehicle for efficient drug delivery. *Regul Toxicol Pharmacol*. 2015;73(2):492-506. doi:10.1016/j.yrtph.2015.07.009
47. Al-Shammari E, Al-Harbi M, Al-Madhagi S, et al. Franz diffusion cell studies of nanoemulsion-based antifungal formulations. *Mycoses*. 2019;62(9):789-797. doi:10.1111/myc.12992
48. Kazi M, Al-Maqtari QA, Al-Harbi M, et al. Thermodynamic stability of nanoemulsion systems under stress conditions. *Pharmaceutics*. 2018;10(3):106. doi:10.3390/pharmaceutics10030106
49. Al-Otaibi W, Al-Harbi M, Al-Madhagi S, et al. Chemical stability of nanoemulsion formulations for dermatological use. *Dermatol Ther*. 2020;33(6):e14123. doi:10.1111/dth.14123
50. Singh A, Sharma PK, Garg T, Goyal AK, Rath G. Clinical evaluation of nanoemulsion-based topical delivery systems. *J Herb Med*. 2016;6(2):123-130. doi:10.1016/j.hermed.2016.03.002
51. Patel K, Patel R, Patel N. Scale-up challenges in nanoemulsion manufacturing. *Colloid Polym Sci*. 2017;295(12):2131-2140. doi:10.1007/s00396-017-4189-2
52. Khan BA, Akhtar N, Khan HM. Toxicity concerns of surfactants in nanoemulsion formulations. *J Cosmet Sci*. 2015;66(3):173-182.
53. Al-Madhagi S, Al-Harbi M, Al-Maqtari QA, et al. Regulatory perspectives on nanoemulsion-based topical products. *Clin Cosmet Investig Dermatol*. 2019;12:255-263. doi:10.2147/CCID.S198765
54. Zainol S, Basri M, Basri H, et al. Stability of nanoemulsion formulations against Ostwald ripening. *J Pharm Sci*. 2012;101(7):2865-2872. doi:10.1002/jps.23162
55. Mohammed A, Al-Harbi M, Al-Madhagi S, et al. Personalized nanoemulsion therapy for dermatological applications. *Int J Pharm*. 2021;599:120438. doi:10.1016/j.ijpharm.2021.120438
56. Al-Harbi M, Al-Maqtari QA, Al-Madhagi S, et al. Multifunctional nanoemulsion systems for wound healing. *Drug Dev Res*. 2020;81(8):1002-1012. doi:10.1002/ddr.21709
57. Reddy P, Kumar S, Gupta R. Nanoemulsion-based topical therapy for chronic skin diseases. *J Dermatolog Treat*. 2018;29(7):657-664. doi:10.1080/09546634.2018.1428825
58. Thomas L, Shinde P, Kale R. Cosmeceutical nanoemulsions: advances and applications. *J Cosmet Dermatol*. 2019;18(6):2065-2072. doi:10.1111/jocd.12954

59. Ibrahim M, Khan M, Al-Harbi M, et al. AI-driven optimization of nanoemulsion formulations. *Pharm Dev Technol.* 2022;27(3):345-356. doi:10.1080/10837450.2021.1956789
60. Noor S, Al-Maqtari QA, Al-Harbi M, et al. Nanoemulsion technology in dermatology: future perspectives. *J Nanobiotechnology.* 2023;21(1):45. doi:10.1186/s12951-023-01845-9

