Journal of Drug Delivery and Biotherapeutics (JDDB)

(E-ISSN: 3049-1177)

Journal homepage: https://sennosbiotech.com/JDDB/1

Nanoemulsions in Drug Delivery: Advances, Applications, and Future Prospects in Therapeutic Nanomedicine

Dr. Vishal Gurumukhi

[1]Department of Pharmaceutics, Shreeyash Institute of Pharmaceutical Education and Research, Aurangabad, India

ARTICLEINFO

ABSTRACT

Nanoemulsions are kinetically stable, nanometer-sized colloidal dispersions of two immiscible liquids stabilized by surfactants, offering unique advantages in drug delivery such as enhanced solubility, improved bioavailability, and targeted delivery of both hydrophilic and lipophilic drugs. Owing to their small droplet size (typically <200 nm), nanoemulsions exhibit excellent absorption, rapid onset of action, and reduced interpatient variability. This review discusses the recent advancements in the design, preparation techniques, and characterization of nanoemulsions for therapeutic applications. Emphasis is placed on the role of nanoemulsions in oral, parenteral, ocular, transdermal, and pulmonary delivery routes, with detailed analysis of their pharmacokinetic enhancements and clinical relevance. Additionally, the challenges related to formulation stability, toxicity, large-scale manufacturing, and regulatory considerations are highlighted. Future trends such as stimuli-responsive and targeted nanoemulsions for precision medicine are also explored. Overall, nanoemulsions represent a promising nanoplatform in modern drug delivery with wide-ranging pharmaceutical potential.

Keywords: Nanoemulsion, Drug Delivery, Bioavailability, Surfactant Systems, Therapeutic Nanocarriers

Corresponding Author:

Dr. Vishal Gurumukhi

Department of Pharmaceutics, Shreeyash Institute of Pharmaceutical Education and Research, Aurangabad, India

E-mail addresses: hodqa@syppharmacy.org

Received date: 15-Mar-2025 Revised date: 01-Apr-2025, Accepted date: 15-Apr-2025

1. Introduction

The development of novel drug delivery systems has been a central focus in pharmaceutical research, aiming to overcome the limitations of conventional dosage forms such as poor aqueous solubility, low permeability, enzymatic degradation, and systemic toxicity. Among the various nanocarrier systems explored, nanoemulsions have emerged as a promising and versatile platform capable of improving the therapeutic profile of a wide range of drugs [1].

Nanoemulsions are thermodynamically unstable but kinetically stable systems comprising two immiscible phases—typically oil and water—dispersed with the aid of surfactants and co-surfactants. The droplet size of nanoemulsions generally ranges from 20 to 200 nanometers, which allows them to offer several pharmaceutical advantages, including high surface area, improved solubilization of hydrophobic drugs, and enhanced absorption through biological membranes. The optical clarity, low viscosity, and long-term physical stability of nanoemulsions further contribute to their suitability in various administration routes such as oral, topical, ocular, nasal, pulmonary, and parenteral delivery [2-4].

One of the most compelling advantages of nanoemulsions is their ability to enhance bioavailability. Poorly water-soluble drugs, which constitute a significant portion of new chemical entities, benefit substantially from the solubilizing environment provided by nanoemulsion systems. Additionally, nanoemulsions can bypass first-pass metabolism, offer lymphatic uptake, and enable controlled or targeted release, thereby improving therapeutic efficacy while minimizing systemic side effects [5-6].

Recent advancements in formulation science have led to the development of various types of nanoemulsions such as self-nanoemulsifying drug delivery systems (SNEDDS), mucoadhesive nanoemulsions, and stimulus-responsive nanoemulsions. These innovations have extended their application in fields ranging from oncology and neurology to infectious diseases and vaccines.

Despite their potential, challenges remain in achieving large-scale manufacturing, maintaining physical and chemical stability, and navigating the regulatory pathways for approval. Nevertheless, the progress in emulsification technologies, characterization tools, and biocompatible excipients continues to push the boundaries of nanoemulsion-based therapeutics.

This review provides an in-depth overview of the composition, preparation techniques, characterization methods, pharmaceutical applications, and clinical potential of nanoemulsions. It also discusses the current limitations and future directions in the field, positioning nanoemulsions as a next-generation nanotechnology tool for effective drug delivery [7].

2. Composition and Preparation of Nanoemulsions

Nanoemulsions are composed of three essential components: the oil phase, the aqueous phase, and a mixture of surfactants and co-surfactants. The appropriate selection and proportion of these components are critical in determining the physicochemical stability, drug-loading capacity, and biocompatibility of the final formulation.

The oil phase serves as the reservoir for lipophilic drugs. Commonly used oils include medium-chain triglycerides (MCTs), long-chain fatty acids, castor oil, soybean oil, and ethyl oleate. The solubility of

the drug in the selected oil significantly influences the drug loading efficiency and release behavior. In some formulations, functional oils such as omega-3 fatty acids or essential oils may be used for added therapeutic benefit or bioactivity.

The aqueous phase generally consists of purified water, buffer solutions, or hydrophilic stabilizing agents. Hydrophilic drugs, when incorporated, are dispersed in this phase and rely on emulsification to remain stable within the colloidal system [8].

Surfactants and co-surfactants play a pivotal role in stabilizing the interface between the oil and aqueous phases. Non-ionic surfactants such as Tween 80, Span 20, and Poloxamers are preferred due to their lower toxicity and higher compatibility with biological systems. Co-surfactants, including ethanol, polyethylene glycol (PEG), or propylene glycol, further reduce interfacial tension and facilitate the formation of smaller droplets with enhanced stability.

The method of nanoemulsion preparation is equally vital. Nanoemulsions can be produced using high-energy methods, such as high-pressure homogenization, ultrasonication, or microfluidization, which rely on mechanical forces to break down the oil droplets into nanoscale sizes. Alternatively, low-energy methods, such as phase inversion temperature (PIT), spontaneous emulsification, or solvent evaporation, utilize the intrinsic physicochemical properties of the components to achieve self-assembly into nano-sized emulsions. The choice of method depends on the drug's sensitivity, formulation requirements, and intended route of administration [9].

Regardless of the method used, the optimization of formulation parameters—such as oil-to-surfactant ratio, emulsification temperature, and mixing speed—is essential to produce nanoemulsions with desirable properties like small droplet size, narrow polydispersity index, and long-term physical stability.

Proper formulation and preparation of nanoemulsions ensure enhanced drug solubilization, stability, and targeted delivery, making them a highly adaptable and effective platform in pharmaceutical applications.

3. Characterization of Nanoemulsions

Thorough physicochemical characterization of nanoemulsions is essential to ensure formulation stability, reproducibility, and therapeutic performance. Various analytical techniques are employed to assess critical parameters such as droplet size, surface charge, viscosity, refractive index, and drug encapsulation efficiency [10].

Droplet size and polydispersity index (PDI) are fundamental indicators of nanoemulsion quality. These are measured using dynamic light scattering (DLS) and laser diffraction techniques. Smaller droplet sizes (<200 nm) enhance stability, bioavailability, and permeability, while a low PDI (<0.3) indicates uniformity in the droplet distribution.

Zeta potential is a measure of surface charge, which influences the stability of the nanoemulsion through electrostatic repulsion between droplets. Zeta potential values beyond ±30 mV typically signify good physical stability by preventing aggregation or coalescence.

Viscosity is evaluated using viscometers or rheometers and affects the flow behavior, particularly important for topical or parenteral formulations. Stable viscosity ensures consistency during manufacturing and administration.

Refractive index and transmittance are optical characteristics used to assess isotropic clarity and homogeneity. A high transmittance (>95%) and refractive index close to that of water indicate nano-sized dispersion with minimal light scattering.

Encapsulation efficiency and drug loading are assessed by separating the unentrapped drug through ultrafiltration or centrifugation, followed by spectrophotometric or HPLC analysis. These values are critical in determining the therapeutic efficiency of the formulation [11].

In vitro drug release studies are carried out using dialysis bags, Franz diffusion cells, or USP apparatus to evaluate the release profile and kinetics of the encapsulated drug. Sustained and controlled release behavior is a desirable feature of nanoemulsion-based systems.

Stability studies under accelerated conditions help predict the shelf-life and phase behavior over time. Changes in particle size, phase separation, or drug content during storage are indicators of instability and must be addressed through formulation optimization.

Table 1. Key Parameters for Characterization of Nanoemulsions [12]

Parameter	Technique Used	Purpose / Significance
Droplet Size & PDI	Dynamic Light Scattering (DLS)	Determines uniformity and nanoscale dispersion
Zeta Potential	Electrophoretic Light Scattering	Evaluates physical stability due to surface charge
Viscosity	Brookfield Viscometer, Rheometer	Assesses flow behavior and formulation consistency
Refractive Index	Refractometry	Confirms optical clarity and isotropic nature
Transmittance	UV–Vis Spectrophotometer	Indicates droplet size and homogeneity
Encapsulation Efficiency	Centrifugation + HPLC/UV analysis	Measures drug retention within droplets
In Vitro Drug Release	Dialysis method, Franz diffusion cell	Analyzes release profile and kinetics
Stability Studies	Storage at different temperatures/humidity	Predicts shelf-life and long-term formulation integrity

4. Applications of Nanoemulsions in Drug Delivery

Nanoemulsions have gained immense popularity across a broad spectrum of therapeutic areas owing to their enhanced solubilization, targeted delivery potential, and ability to overcome biological barriers. Their versatility allows them to be administered via multiple routes including oral, intravenous, transdermal, ocular, nasal, and pulmonary delivery [13].

In oral drug delivery, nanoemulsions help improve the solubility and gastrointestinal absorption of poorly water-soluble drugs, such as curcumin, cyclosporine, and paclitaxel. By bypassing first-pass metabolism through lymphatic absorption,

nanoemulsions increase oral bioavailability and reduce dosing frequency.

In intravenous formulations, nanoemulsions provide a safe and stable medium for hydrophobic anticancer or antifungal agents. Their small droplet size minimizes embolism risks and allows efficient distribution within systemic circulation. Lipid nanoemulsions like propofol (anesthetic) are already commercially available and have demonstrated excellent safety profiles [14].

Transdermal and topical nanoemulsions are employed to deliver anti-inflammatory and antimicrobial drugs, as they enhance skin permeability and provide site-specific action. Drugs such as ketoprofen, diclofenac, and clotrimazole have been successfully formulated as topical nanoemulsions.Ocular nanoemulsions increase the residence time and penetration of drugs into intraocular tissues. Drugs like cyclosporine A, which suffers from poor corneal penetration, show improved therapeutic outcomes when delivered as nanoemulsions (e.g., Restasis®).Nasal and pulmonary nanoemulsions allow rapid drug absorption for systemic effects or brain targeting. Nasal nanoemulsions loaded with antidepressants or anti-migraine agents show promising results in bypassing the blood–brain barrier via olfactory and trigeminal pathways.In cancer therapy, nanoemulsions can be engineered to carry chemotherapeutic agents with ligands that target overexpressed receptors on tumor cells, improving therapeutic efficacy and reducing off-target toxicity [15].

Table 2. Examples of Drug Delivery Applications Using Nanoemulsions [16-17]

Route of Administration	Drug(s)	Therapeutic Area	Key Benefits
Oral	Curcumin, Paclitaxel	Cancer, Inflammation	Enhanced solubility and bioavailability
Intravenous	Amphotericin B, Propofol	Fungal infections, Anesthesia	Safe, stable delivery of hydrophobic drugs
Topical/Transdermal	Ketoprofen, Diclofenac	Pain, Inflammation	Improved skin penetration, localized effect
Ocular	Cyclosporine A	Dry eye, Uveitis	Increased corneal retention and penetration
Nasal	Risperidone, Sumatriptan	CNS disorders, Migraine	Brain targeting via nose-to-brain transport
Pulmonary	Budesonide, Salbutamol	Asthma, COPD	Deep lung delivery and rapid onset of action

5. Challenges and Future Prospects

Nanoemulsions, despite their vast pharmaceutical potential, present several formulation and technical challenges. A major limitation is their thermodynamic instability, which can lead to phase separation through Ostwald ripening or coalescence during storage. Ensuring long-term stability requires optimal selection of oils and surfactants [18-19].

The toxicity of excipients, particularly surfactants and co-surfactants, is another concern. While they stabilize the nanoemulsion system, high concentrations may cause irritation, hemolysis, or mucosal damage, depending on the route of administration. Therefore, using GRAS-grade and biocompatible agents is essential.Scale-up of production from laboratory to industrial scale remains a significant barrier. Techniques such as ultrasonication or high-pressure homogenization may not be economically feasible or reproducible for commercial batches without advanced equipment and validation [20-22].

Regulatory classification is still ambiguous. Nanoemulsions lie between conventional emulsions and nanocarriers, making it difficult to align them with existing guidelines. More clarity is needed from regulatory authorities on toxicology, biocompatibility, and nanotoxicity assessments.Furthermore, real-time analytical tools that evaluate nanoemulsion performance under biological conditions are still in development. In vitro–in vivo correlation (IVIVC) models for nanoemulsions are often poor, hindering formulation optimization for clinical use [23-24].

Despite these limitations, the future is promising. Stimuli-responsive nanoemulsions, designed to release drugs upon exposure to pH, temperature, or enzymes, are being explored for targeted therapies. Advances in microfluidic technology may also offer more consistent and scalable production.Incorporating targeted ligands into nanoemulsion surfaces, such as peptides or antibodies, could allow site-specific drug delivery, especially in cancer or CNS disorders. Coupled with imaging agents, such systems may evolve into theranostic platforms for diagnosis and treatment in a single formulation.With continued research, innovation, and regulatory alignment, nanoemulsions are expected to become a cornerstone in the next generation of drug delivery technologies [25].

6. Conclusion

Nanoemulsions have emerged as a powerful and adaptable platform for enhancing drug delivery, particularly for poorly soluble or poorly bioavailable compounds. Their unique physicochemical properties—such as small droplet size, high surface area, and improved permeability—enable superior absorption, faster onset of action, and targeted delivery through various administration routes.

They have shown immense potential in oral, parenteral, ocular, transdermal, and nasal delivery, offering advantages like controlled release, reduced dosing frequency, and patient compliance. However, despite their versatility, nanoemulsions face challenges related to formulation stability, excipient toxicity, large-scale manufacturing, and regulatory classification.

Ongoing advancements in emulsification technology, surfactant selection, and functionalization strategies are paving the way for the development of smarter, stimuli-responsive, and targeted nanoemulsions. With increasing research and regulatory support, nanoemulsions are expected to play a vital role in the future of personalized and precision medicine, offering safe, effective, and scalable solutions for complex therapeutic needs.

Conflict of Interest

The authors declare no conflict of interest.

Funding

No Funding was received.

Refrences

1. Gupta A, Eral HB, Hatton TA, Doyle PS. Nanoemulsions: formation, properties and

applications. Soft Matter. 2016;12(11):2826–2841.
2. Shakeel F, Ramadan W, Shafiq S. Nanoemulsions as vehicles for transdermal delivery of aceclofenac: formulation development and evaluation. Drug Dev Ind Pharm. 2009;35(6):647–655.
3. Solans C, Izquierdo P, Nolla J, Azemar N, Garcia-Celma MJ. Nano-emulsions. Curr Opin Colloid Interface Sci. 2005;10(3-4):102–110.
4. Ahmad J, Mir SR, Kohli K, et al. Nanoemulsion-based drug delivery system for enhancing bioavailability of poorly soluble drugs. Curr Drug Deliv. 2020;17(5):448–461.
5. Tiwari R, Pathak K. Nanostructured lipid carrier versus self-nanoemulsifying drug delivery system: a comparative study for enhancing oral bioavailability of ezetimibe. Drug Deliv. 2011;18(8):593–602.
6. Date AA, Nagarsenker MS. Design and evaluation of microemulsions for improved parenteral delivery of propofol. AAPS PharmSciTech. 2008;9(1):138–145.
7. Wang L, Dong J, Chen J, Eastoe J. Design and optimization of a new self-nanoemulsifying drug delivery system. J Colloid Interface Sci. 2009;330(2):443–448.
8. Shah P, Bhalodia D, Shelat P. Nanoemulsion: a pharmaceutical review. Syst Rev Pharm. 2010;1(1):24–32.
9. Jaiswal P, Gidwani B, Vyas A. Nanotechnology: a review. J Drug Deliv Ther. 2016;6(1):15–27.
10. 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.
11. Constantinides PP, Wasan KM. Lipid formulation strategies for oral delivery of poorly water-soluble drugs. Adv Drug Deliv Rev. 2007;59(7):667–684.
12. Wu H, Ramachandran C, Weiner ND, Roessler BJ. Topical transport of hydrophilic compounds using water-in-oil nanoemulsions. Int J Pharm. 2001;220(1–2):63–75.
13. Azeem A, Rizwan M, Ahmad FJ, Iqbal Z, Khar RK, Aqil M, Talegaonkar S. Nanoemulsion components screening and selection: a technical note. AAPS PharmSciTech. 2009;10(1):69–76.
14. Singh Y, Meher JG, Raval K, Khan FA, Chaurasia M, Jain NK, Chourasia MK. Nanoemulsion: concepts, development and applications in drug delivery. J Control Release. 2017;252:28–49.
15. Nasr A. In vitro and in vivo evaluation of self-nanoemulsifying drug delivery systems of clopidogrel bisulfate. Eur J Pharm Sci. 2014;62:220–231.
16. Hariharan M, Bogue A. In vitro and in vivo evaluation of a nanoemulsion-based drug delivery system of buprenorphine. Int J Nanomedicine. 2009;4:511–519.
17. Rao SV, Agarwal P. Self-nanoemulsifying drug delivery systems (SNEDDS) for oral delivery of hydrophobic drugs. Res Pharm Sci. 2021;16(1):1–10.
18. Zhang Q, Jiang X, Jiang W, Lu W, Su L, Shi Z. Preparation of nimodipine-loaded microemulsion for intranasal delivery and evaluation on the targeting efficiency to the brain. Int J Pharm. 2004;275(1–2):85–96.

19. Lawrence MJ, Rees GD. Microemulsion-based media as novel drug delivery systems. Adv Drug Deliv Rev. 2012;64:175–193.
20. Tadros T, Izquierdo P, Esquena J, Solans C. Formation and stability of nano-emulsions. Adv Colloid Interface Sci. 2004;108–109:303–318.
21. Aqil M, Ahad A, Sultana Y, Ali A. Status of nanoemulsion formulations for oral drug delivery. Curr Drug Deliv. 2013;10(1):87–100.
22. Devarajan PV, Ravichandran V. Nanoemulsions: as modified drug delivery tool. Pharmacie Globale. 2011;2(1):1–6.
23. Baspinar Y, Bodmeier R. Preparation and characterization of poly (lactic acid) nanoparticles containing clobetasol propionate for topical delivery. Int J Pharm. 2004;276(1–2):161–172.
24. Kommuru TR, Gurley B, Khan MA, Reddy IK. Self-emulsifying drug delivery systems (SEDDS) of coenzyme Q10: formulation development and bioavailability assessment. Int J Pharm. 2001;212(2):233–246.
25. Constantinides PP. Lipid microemulsions for improving drug dissolution and oral absorption: physical and biopharmaceutical aspects. Pharm Res. 1995;12(11):1561–1572.