NANOEMULSION-BASED DRUG DELIVERY SYSTEMS: FORMULATION STRATEGIES, THERAPEUTIC APPLICATIONS, AND FUTURE PERSPECTIVES

Mann Singh Jadaon , M.PHARM 3RD SEM ,Pacific College of Pharmacy

Guided by: Dr. Shweta Jain, Associate Professor, ,Pacific College of Pharmacy

ABSTRACT

Nanoemulsion-based drug delivery systems have emerged as one of the most promising lipid-based nanotechnological approaches for addressing solubility, stability, and bioavailability challenges associated with poorly water-soluble drugs [1]. Nanoemulsions are characterized by nanoscale droplet sizes, high interfacial surface area, optical transparency, and kinetic stability, which collectively contribute to enhanced drug solubilization and absorption [2,3]. This review provides an in-depth and comprehensive discussion on nanoemulsion systems, including formulation components, preparation techniques, characterization methods, stability aspects, mechanisms of drug release, and pharmaceutical applications via multiple routes of administration. In addition, safety considerations, regulatory perspectives, marketed products, current challenges, and future research directions are critically analyzed to highlight the translational and clinical potential of nanoemulsion-based drug delivery systems [4–6].

Keywords: Nanoemulsions; Drug Delivery Systems; Bioavailability Enhancement; Lipid-Based Formulations; Nanotechnology; Pharmaceutics

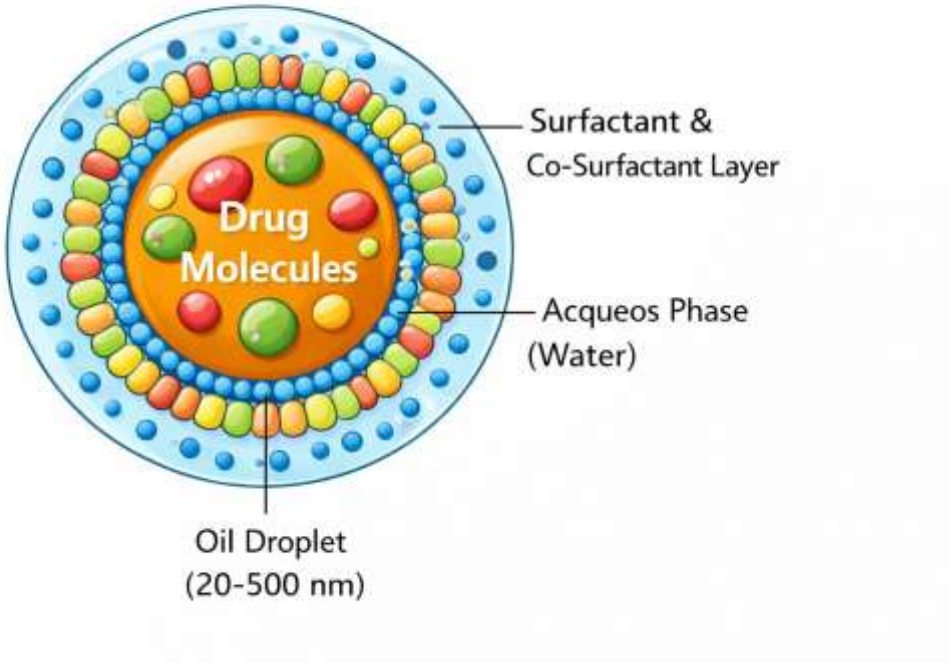
1. INTRODUCTION

The development of effective drug delivery systems remains a critical challenge in pharmaceutical sciences due to the increasing number of newly discovered drug molecules exhibiting poor aqueous solubility and limited permeability [7]. It is estimated that approximately 60–70% of newly developed chemical entities belong to Biopharmaceutics Classification System (BCS) class II or IV, which are associated with low dissolution rates and poor oral bioavailability [8]. As a result, conventional dosage forms often fail to achieve desired therapeutic outcomes.

To overcome these formulation challenges, nanotechnology-based drug delivery systems such as nanoparticles, liposomes, solid lipid nanoparticles, and nanoemulsions have gained increasing attention [9]. Among these, nanoemulsions offer several advantages, including ease of preparation, high drug-loading capacity, improved stability, and versatility for multiple routes of administration [10].

Nanoemulsions are kinetically stable colloidal dispersions of two immiscible liquids stabilized by surfactants and co-surfactants, with droplet sizes typically ranging from 20 to 500 nm [11]. Their small droplet size leads to

increased surface area, enhanced interaction with biological membranes, and improved drug absorption, making them attractive carriers for both systemic and localized drug delivery [12].



2. NANOEMULSIONS: DEFINITION AND KEY FEATURES

Nanoemulsions are isotropic, thermodynamically unstable but kinetically stable dispersions of oil and water stabilized by suitable surfactant systems [13]. Unlike microemulsions, nanoemulsions require external energy for their formation and exhibit long-term stability due to reduced droplet coalescence and Ostwald ripening [14].

Key features of nanoemulsions include nanoscale droplet size, low viscosity, high kinetic stability, enhanced drug solubilization, and improved bioavailability [15]. These properties make nanoemulsions suitable for oral, topical, ocular, nasal, parenteral, and vaccine delivery applications

3. COMPONENTS OF NANOEMULSION FORMULATIONS

The commonly used components in nanoemulsion formulations along with their functional roles are summarized in Table 1

Table 1: Common Components Used in Nanoemulsion Formulations

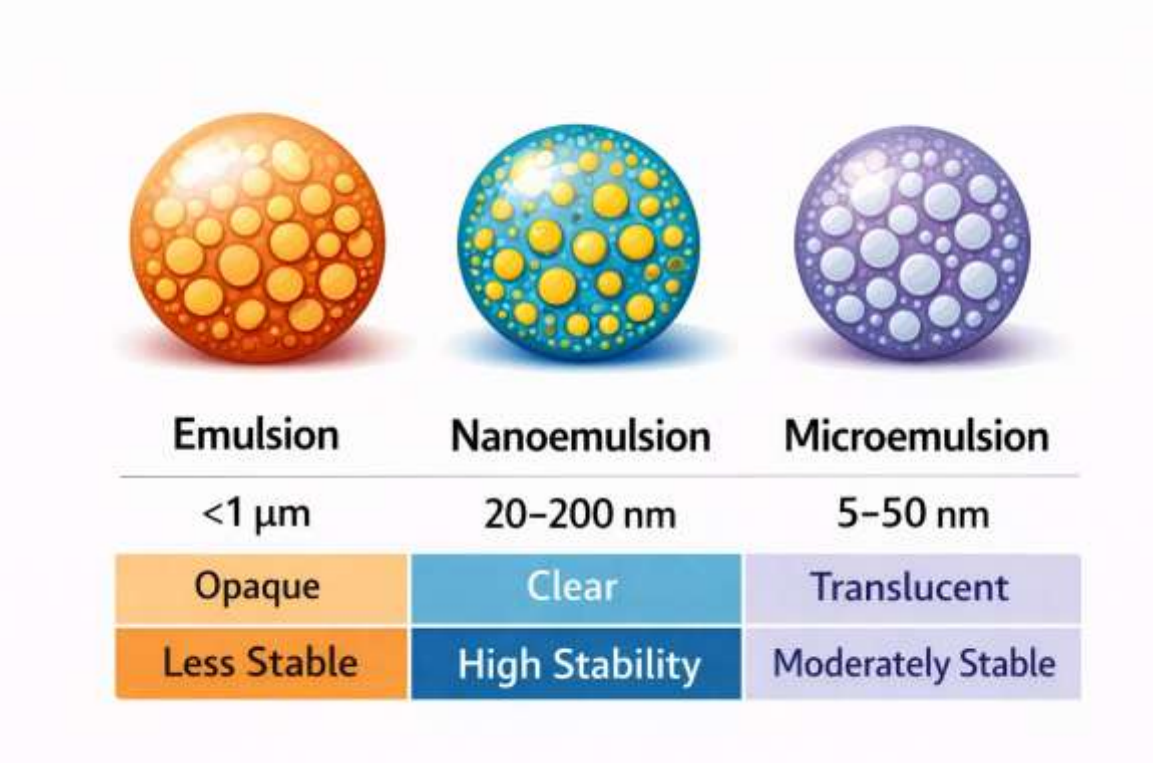
Component	Examples	Role
Oil Phase	MCT, LCT, Oleic oil	Drug solubilization

Surfactant	Tween 80, Poloxamer 188	Droplet stabilization
Co-surfactant	Ethanol, Propylene glycol	Interfacial flexibility
Aqueous Phase	Purified water	Continuous phase

Nanoemulsion formulations typically consist of four essential components: oil phase, surfactant, co-surfactant, and aqueous phase [16]. The selection of appropriate formulation components is critical for achieving optimal droplet size, stability, drug loading, and in vivo performance.

The oil phase serves as a solubilizing medium for lipophilic drugs and significantly influences drug loading capacity and release behavior. Commonly used oils include medium-chain triglycerides, long-chain triglycerides, fatty acids, and natural oils due to their biocompatibility and ability to enhance lymphatic transport [17].

Surfactants play a crucial role in reducing interfacial tension and stabilizing nanoemulsion droplets. Non-ionic surfactants such as polysorbates, poloxamers, and sorbitan esters are preferred because of their low toxicity and regulatory acceptance [18]. Co-surfactants such as ethanol, propylene glycol, and polyethylene glycol enhance interfacial flexibility and facilitate nanoemulsion formation at lower surfactant concentrations [19].



4. PREPARATION TECHNIQUES FOR NANOEMULSIONS

A comparison of high-energy and low-energy nanoemulsion preparation methods is presented in Table 2.

Table 2: Comparison of Nanoemulsion Preparation Techniques

Method	Advantages	Limitations

High-energy	Uniform droplet size, scalable	High energy consumption
Low-energy	Low cost, mild conditions	Sensitive to formulation variables

Nanoemulsions can be prepared using either high-energy or low-energy emulsification techniques depending on formulation requirements and scalability [20]. High-energy methods include high-pressure homogenization, ultrasonication, and microfluidization, which apply intense mechanical forces to reduce droplet size [21].

Low-energy methods such as phase inversion temperature (PIT), phase inversion composition (PIC), and spontaneous emulsification rely on physicochemical properties of the formulation components and require minimal external energy input [22]. These methods are advantageous for thermolabile drugs but are highly sensitive to formulation parameters.

5. CHARACTERIZATION AND STABILITY EVALUATION

The major characterization techniques employed for nanoemulsion systems are summarized in Table 3.

Table 3: Characterization Techniques Used for Nanoemulsions

Technique	Parameter Measured	Purpose
Dynamic Light Scattering (DLS)	Droplet size, PDI	Particle size distribution
Zeta Potential Analysis	Surface charge	Stability prediction
Transmission Electron Microscopy	Morphology	Structural confirmation
Viscosity Measurement	Flow behavior	Rheological properties

Comprehensive physicochemical characterization of nanoemulsions is essential to ensure quality, stability, and reproducibility [23]. Droplet size and polydispersity index are commonly measured using dynamic light scattering, while zeta potential provides insight into electrostatic stability [24].

Morphological evaluation using transmission electron microscopy or scanning electron microscopy confirms nanoscale droplet formation. Stability studies assess creaming, coalescence, and Ostwald ripening under accelerated and long-term storage conditions [25].

6. PHARMACEUTICAL APPLICATIONS OF NANOEMULSIONS

Route-wise pharmaceutical applications of nanoemulsions are summarized in Table 4.

Table 4: Route-wise Applications of Nanoemulsions

Route	Drug Category	Advantage	Example
Oral	Poorly soluble drugs	Enhanced bioavailability	Cyclosporine
Dermal	Antifungals	Improved skin penetration	Ketoconazole
Ocular	Anti-inflammatory drugs	Increased residence time	Cyclosporine A
Nasal	CNS drugs	Direct brain targeting	Rivastigmine

Nanoemulsions have been widely investigated for oral, dermal, transdermal, ocular, nasal, parenteral, vaccine, and gene delivery applications [26]. Oral nanoemulsions enhance drug solubilization and promote lymphatic uptake, thereby improving systemic bioavailability and reducing first-pass metabolism [27].

In dermal and transdermal delivery, nanoemulsions improve skin penetration by disrupting the lipid structure of the stratum corneum. Ocular nanoemulsions enhance precorneal residence time and improve corneal penetration, while nasal nanoemulsions facilitate direct nose-to-brain drug delivery [28].

7. SAFETY, TOXICITY, AND REGULATORY CONSIDERATIONS

Although nanoemulsions are generally composed of pharmaceutically acceptable excipients, safety evaluation remains critical [29]. Surfactant concentration, droplet size, and route of administration significantly influence toxicity profiles. Regulatory agencies evaluate nanoemulsions based on quality, safety, efficacy, and stability parameters [30].

8. MARKETED PRODUCTS AND CLINICAL TRANSLATION

Several nanoemulsion-based products have been successfully commercialized, particularly in parenteral nutrition, vaccine adjuvants, and ophthalmic formulations, demonstrating the clinical feasibility of nanoemulsion technology [31].

9. CHALLENGES AND FUTURE PERSPECTIVES

Despite their advantages, nanoemulsions face challenges related to formulation complexity, long-term stability, large-scale manufacturing, and regulatory uncertainties. Future research focuses on targeted nanoemulsions, stimuli-responsive systems, personalized drug delivery, and sustainable manufacturing approaches [32–34].

10. CONCLUSION

Nanoemulsion-based drug delivery systems represent a versatile and promising platform for enhancing the solubility, bioavailability, and therapeutic efficacy of poorly water-soluble drugs. Continued interdisciplinary research and technological advancements are expected to further expand their clinical applications.

11. REFERENCES

1. Shakeel F et al. Nanoemulsions as vehicles for drug delivery. Drug Discov Today. 2008;13:532–543.
2. Gupta A et al. Nanoemulsions: formation, properties and applications. Soft Matter. 2016;12:2826–2841.
3. McClements DJ. Nanoemulsions versus microemulsions. Soft Matter. 2012;8:1719–1729.
4. Anton N, Vandamme TF. Nanoemulsions and microemulsions. Pharm Res. 2011;28:978–985.
5. Tadros T et al. Formation and stability of nanoemulsions. Adv Colloid Interface Sci. 2004;108–109:303–318.
6. Acosta E. Bioavailability of nanoparticles in drug delivery. J Pharm Sci. 2009;98:2591–2608.
7. Kotta S et al. Oral nanoemulsions for bioavailability enhancement. Expert Opin Drug Deliv. 2012;9:585–598.
8. Solans C et al. Nanoemulsions. Curr Opin Colloid Interface Sci. 2005;10:102–110.
9. Date AA et al. Self-nanoemulsifying drug delivery systems. Int J Pharm. 2010;396:1–12.
10. Jaiswal M et al. Nanoemulsion: an advanced drug delivery system. 3 Biotech. 2015;5:123–127.
11. Sarker DK. Engineering of nanoemulsions. Curr Drug Deliv. 2005;2:297–310.
12. Ganta S et al. Nanoemulsions in drug targeting. J Biomed Nanotechnol. 2014;10:2677–2699.
13. Kreilgaard M. Influence of emulsions on cutaneous drug delivery. Adv Drug Deliv Rev. 2002;54:S77–S98.
14. Lawrence MJ, Rees GD. Microemulsion-based drug delivery systems. Adv Drug Deliv Rev. 2000;45:89–121.
15. Pardeike J et al. Lipid nanoparticles for dermal delivery. Int J Pharm. 2009;366:170–184.
16. Kumar M et al. Techniques for formulation of nanoemulsion drug delivery systems. IJPSRR. 2019;56:75–86.
17. WHO. Guidelines on pharmaceutical nanotechnology. WHO Press.
18. FDA. Guidance for industry: nanotechnology. US FDA.
19. Das S et al. Nanoemulsions for brain targeting. Int J Pharm. 2019.
20. Mishra RK et al. Future prospects of nanoemulsions. Drug Deliv Transl Res. 2021.