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Comprehensive Review of Nanoemulsion Systems

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Abstract: *Nanoemulsions are advanced colloidal dispersions composed of oil, water, surfactants, and co-surfactants, with droplet diameters typically ranging from 20 to 200 nm. Their nanoscale dimensions confer unique physicochemical attributes such as high kinetic stability, enhanced solubilization capacity, optical clarity, and improved bioavailability, distinguishing them from conventional emulsions and microemulsions. Owing to their small droplet size and large interfacial surface area, nanoemulsions enable superior drug dissolution, enhanced permeation across biological membranes, and effective protection of encapsulated actives from chemical and enzymatic degradation. These advantages have positioned nanoemulsions as a highly versatile platform for drug delivery across oral, topical, transdermal, ocular, nasal, pulmonary, and parenteral routes.*

This review provides a comprehensive overview of nanoemulsion systems, covering their fundamental principles, types, formulation components, and preparation techniques—including high-pressure homogenization, ultrasonication, microfluidization, phase inversion temperature (PIT), and spontaneous emulsification. The article further highlights the mechanistic basis of nanoemulsion stability, focusing on destabilization pathways such as coalescence, flocculation, creaming, and Ostwald ripening. In addition to pharmaceutical applications, the review discusses the growing use of nanoemulsions in cosmetics, food technology, agriculture, and biotechnology. Finally, current challenges—including high surfactant requirements, potential toxicity, scalability limitations, and regulatory barriers—are examined alongside emerging strategies aimed at enhancing stability, efficacy, and industrial feasibility. Collectively, this review underscores the broad scientific and commercial relevance of nanoemulsion systems and outlines future directions for their optimized design and application..

Keywords*:* Nanoemulsion, Drug Delivery Systems, Colloidal Stability, High- and Low-Energy Emulsification

I. INTRODUCTION

Nanoemulsions are advanced colloidal delivery systems composed of oil, water, surfactants, and co-surfactants, with droplet sizes typically ranging between 20 and 200 nm. Their extremely small droplet diameter imparts unique physicochemical characteristics—such as high kinetic stability, enhanced solubilization capacity, optical transparency, and improved bioavailability that distinguish them from conventional emulsions and microemulsions. These nanoscale dispersions have emerged as a pivotal technology in modern formulation science, offering significant advantages for drug delivery, cosmetics, food processing, agriculture, and biotechnology.In pharmaceutical applications, nanoemulsions have demonstrated remarkable utility in enhancing the solubility, permeability, and therapeutic efficacy of poorly water-soluble drugs. By encapsulating active pharmaceutical ingredients (APIs) within nanometer-sized droplets, nanoemulsions protect drugs from chemical or enzymatic degradation, improve dissolution rates, enable targeted drug delivery, and facilitate controlled or sustained release. These attributes make them suitable for diverse routes of administration, including oral, topical, transdermal, ocular, nasal, pulmonary, and parenteral delivery.

From a formulation standpoint, nanoemulsions are considered *kinetically stable systems*, resisting sedimentation, creaming, and coalescence for extended durations due to their low interfacial tension and fine droplet size distribution. However, unlike microemulsions, they are not thermodynamically stable and require external energy (e.g., ultrasonication, high-pressure homogenization) or specific phase-inversion methods for their preparation. Their stability is largely governed by the choice of surfactants, co-surfactants, oil phase, and preparation technique.Beyond pharmaceuticals, nanoemulsions are used extensively in cosmetics to enhance skin hydration and dermal penetration; in food technology to improve flavor, stability, and bioavailability of lipophilic nutrients; in agriculture for efficient delivery of pesticides; and in biotechnology as carriers for vaccines, antimicrobial agents, and diagnostic agents. Their versatility across industries highlights their broad relevance and growing commercial significance.Despite their advantages, several challenges persist, including high surfactant requirements, potential excipient toxicity, susceptibility to Ostwald ripening, scalability limitations, and regulatory concerns regarding long-term safety. Ongoing research aims to overcome these issues through improved formulation strategies, newer stabilizers, and advanced manufacturing platforms.

A nanoemulsion is a kinetically stable, thermodynamically unstable, heterogeneous colloidal dispersion composed of oil and water phases stabilized by surfactants and co-surfactants, wherein the dispersed droplets exhibit nanoscale dimensions typically ranging from 20–200 nm. The small droplet size provides increased surface area, improved drug solubilization, optical transparency, and enhanced bioavailability, making nanoemulsions suitable for a wide range of pharmaceutical, cosmetic, food, and industrial applications.

II. TYPES OF NANOEMULSIONS

1. Oil-in-Water (O/W) Nanoemulsions

- Oil droplets dispersed within a continuous aqueous phase.
- Most widely used type.

Applications:

- Oral drug delivery
- Topical formulations
- Intravenous preparations
- Cosmetic creams and serums

Advantages:

High stability, good patient acceptability, safer for parenteral use.

2. Water-in-Oil (W/O) Nanoemulsions

- Water droplets dispersed within a continuous oil phase.

Applications:

- Transdermal systems
- Cosmetics (e.g., moisturizers)
- Controlled-release formulations

Advantages:

- Enhanced skin occlusion
- Better penetration of hydrophilic actives

3. Bi-Continuous nanoemulsions

- Both oil and water phases form interpenetrating continuous networks.

Applications:

- Drug delivery requiring dual solubilization
- Advanced cosmetics
- Specialized biochemical formulations

Advantages:

- High solubilization capacity for both hydrophilic and lipophilic drugs
- Flexibility in formulation

Sr. No.	Author	Paper title	Journal	Conclusion / Summary
1	Vaibhav V. Changediya, RupalbenJani, PradipKakde	*A Review on Nanoemulsions: A Recent Drug Delivery Tool*	Journal of Drug Delivery and Therapeutics (2019)	Provided a comprehensive overview of nanoemulsion (NE) covering preparation methods (high-energy, low-energy), stability, characterization concluded that due to small droplet size, NEs avoid issues like creaming/coalescence; main destabilization remains Ostwald ripening.
2	Nurul Amin, Biswajit Das	*A Review on Formulation and Characterization of Nanoemulsion*	International Journal of Current Pharmaceutical Research (2019)	Described formulation and evaluation of nanoemulsions as drug carriers; defines NE as thermodynamically stable dispersions with droplet size < 100 nm; underscores their use for improving therapeutic delivery.
3	NehaAgnihotri, G. C. Soni, Dilip K. Chanchal, Afrin, Sakshi Tiwari	*A Scientific Review on Nanoemulsion for Targeting Drug Delivery System*	International Journal of Life Sciences and Review (2019)	Highlighted NE as isotropic, sub-micron oil/water dispersions stabilized by surfactants; reviewed formulation, characterization, and stability argued that NEs can overcome poor water solubility of drugs and improve absorption/distribution for better efficacy.
4	Nikhil Dhumal, Vishal Yadav	*Nanoemulsion as Novel Drug Delivery System: Development, Characterization and Application*	Asian Journal of Pharmaceutical Research and Development (2022)	Defined NEs as transparent, isotropic nano-droplet systems (20–200 nm); reviewed types, preparation (high-/low-energy), stability, and applications across oral, topical, parenteral routes; concluded NE is effective, safe, patient-compliant delivery method.
5	P. Bhatt, S. Madhav	*A Detailed Review on Nanoemulsion Drug Delivery System*	International Journal of Pharmaceutical	Covered formulation aspects, methods (microfluidization, homogenization, low-energy), characterization (droplet size, zeta

			Sciences and Research (2011)	potential, TEM, pH, release, permeation), and applications including drug targeting. Concluded NEs are promising for targeted drug delivery and improved permeation.
6	Navneet Kumar Verma, Asheesh Kumar Singh, VikasYadav, Prem Chand Mall	*A review on nanoemulsion based drug delivery system*	International Journal of Pharmacy and Pharmaceutical Science (2019)	Consolidated information on formulation, characterization (entrapment efficiency, particle size, PDI, zeta potential, DSC, FTIR, TEM), evaluation (in-vitro release, permeation, stability) concluded that NEs offer improved dispersion of hydrophobic agents and enhanced absorption.
7	RupaliJaiswal	*Nanoemulsion as Oral Drug Delivery – A Review*	Current Drug Research Reviews (2020)	Focused on oral delivery applications of nanoemulsions, highlighting improved solubility and bioavailability of poorly water-soluble drugs; concluded NEs provide solutions for conventional dosage limitations.
8	SmitaBorkar	*Nanoemulsion: A Carrier for Drug Delivery*	International Journal of Pharmaceutical Sciences and Research (2024)	Detailed components, methods (high- and low-energy), characterization and applications (pharmaceutical & cosmetic); also discussed advantages and drawbacks of NE systems — reinforcing versatility of NEs.

Nanoemulsion Preparation Nanoemulsions form when two immiscible liquids are subjected to shear forces that break the dispersed phase into nanoscale droplets. Preparation methods are broadly divided into high-energy and low-energy approaches. Typically, a two-step process is used:

1. High-Energy Methods

These techniques apply intense mechanical force to generate fine and uniform droplets.

• High-Pressure Homogenization (HPH):

A coarse emulsion is forced through narrow valves at pressures >100 MPa, generating high shear and turbulence. Multiple cycles are performed until droplet size stabilizes.

• Micro fluidization:

Uses microchannels where two fluid streams collide at high pressure. Dual-channel systems can form coarse emulsions in situ and process high oil contents (up to 50%), making them more scalable.

• Ultrasonication:

Ultrasound waves create cavitation bubbles that collapse violently, breaking droplets into nanoscale sizes. While effective and commonly used in research, scalability is limited due to heat generation and limited probe penetration.

2. Low-Energy Methods These methods rely on internal physicochemical changes rather than mechanical force.

• Solvent Displacement:

A miscible dispersed phase is mixed with an aqueous surfactant solution, followed by solvent removal, spontaneously forming nanoemulsions.

• Phase Inversion Temperature (PIT):

Heating promotes a W/O emulsion formation; cooling below the transition temperature induces inversion to O/W nanoemulsions. Controlled by surfactant HLB, temperature, and water–oil ratio.

• Self-Nanoemulsification (SNE):

A mixture of oil, surfactant, co-surfactant, and drug spontaneously forms a nanoemulsion upon contact with physiological fluids, widely used to improve oral bioavailability. High surfactant content is a regulatory limitation.

• Polymorphic Phase Transition Method:

Freezing a lipid coarse emulsion causes a gel-to-crystal transition that breaks droplets into solid particles. Upon thawing, nanoemulsions <100 nm form with low surfactant (<2%) and high drug loading.

3. Scalability Considerations

HPH is the most industrially adopted method due to its robustness and ability to produce large batches (e.g., milk homogenization). Low-energy techniques offer greater energy efficiency but remain less applied industrially due to incomplete understanding of mechanisms and limited availability of suitable food/medical-grade materials.

III. RESULT AND DISCUSSION

This review highlights the scientific advancements, formulation principles, preparation techniques, stability considerations, and applied potential of nanoemulsion systems across various fields. The analysis of multiple studies demonstrates that nanoemulsions consistently offer significant advantages in drug delivery and related industries due to their nanoscale droplet size, enhanced solubilization capacity, and improved kinetic stability. Across all reviewed papers, droplet sizes in the range of **20–200 nm** emerged as a universal characteristic contributing to superior optical clarity, high surface area, and improved bioavailability of encapsulated compounds.The comparative evaluation of published literature reveals a strong emphasis on the **role of preparation technique**in determining the physicochemical performance of nanoemulsions. High-energy methods such as high-pressure homogenization, microfluidization, and ultrasonication were shown to provide precise control over droplet size and polydispersity, with pressures above 100 MPa and multiple homogenization cycles yielding droplets with high uniformity. Microfluidization, especially dual-channel systems, demonstrated greater scalability and the ability to handle high oil-phase content, making it favorable for industrial applications. Ultrasonication also consistently produced fine droplets but showed limitations in scalability due to heat generation and limited probe capacity.

Low-energy methods including spontaneous emulsification, phase inversion temperature (PIT), self-nanoemulsification (SNE), and polymorphic phase transition were identified as energy-efficient and cost-effective alternatives. These methods rely on physicochemical phenomena such as interfacial turbulence, surfactant inversion, or phase-transition mechanisms. While effective for producing nanoemulsions with small droplet sizes, their industrial adoption remains limited due to challenges related to solvent use, high surfactant requirements, and insufficient mechanistic understanding.The discussion of stability elucidates that nanoemulsions, though **kinetically stable,** remain **thermodynamically unstable**, making them susceptible to destabilization pathways such as **coalescence, flocculation, creaming, and Ostwald ripening**. Among these, **Ostwald ripening** consistently appeared as the dominant destabilization mechanism, especially in systems with high oil-water solubility gradients. The incorporation of appropriate surfactants, co-surfactants, ripening inhibitors, and optimized oil phases was shown to enhance resistance to destabilization and extend shelf-life. The reviewed studies support the importance of understanding DLVO theory to predict and mitigate destabilization at the molecular level.

In terms of applications, the compiled evidence illustrates the wide versatility of nanoemulsions across pharmaceutical, cosmetic, food, agricultural, and biotechnological sectors. In pharmaceuticals, nanoemulsions consistently improved the solubility, permeability, dissolution rate, and therapeutic efficacy of poorly water-soluble drugs. Their ability to protect active pharmaceutical ingredients (APIs) from enzymatic and chemical degradation further enhances clinical performance. Cosmetics benefited from improved dermal penetration and hydration properties, while food technology utilized nanoemulsions to deliver flavors, nutraceuticals, and bioactive lipids. Agricultural applications demonstrated improved pesticide efficiency, reduced environmental impact, and enhanced stability. Collectively, these findings emphasize that nanoemulsions represent a robust, multifunctional platform with expanding commercial and industrial relevance.

Despite these strengths, the reviewed literature also highlights several existing challenges. High surfactant concentrations required for stability may pose toxicity risks, particularly in pharmaceutical and food applications. Scalability remains a hurdle for techniques such as ultrasonication and certain low-energy approaches. Regulatory concerns persist regarding long-term safety, excipient selection, and large-scale manufacturing consistency. Ongoing research is focused on reducing surfactant content, improving stability against Ostwald ripening, and developing greener, scalable production technologies.

IV. CONCLUSION

Nanoemulsions represent a highly promising class of colloidal delivery systems with wide-ranging applications in pharmaceuticals, cosmetics, food technology, agriculture, and biotechnology. Their nanoscale droplet size (20–200 nm) imparts superior physicochemical properties—including improved solubilization, enhanced bioavailability, kinetic stability, optical clarity, and efficient encapsulation of both hydrophilic and lipophilic compounds. The literature consistently demonstrates that the success of nanoemulsion formulations depends on the strategic selection of oils, surfactants, and co-surfactants, as well as the choice of an appropriate preparation method.High-energy methods such as high-pressure homogenization, ultrasonication, and microfluidization remain the most effective for producing uniform nano-sized droplets, while low-energy approaches such as PIT, spontaneous emulsification, self-nanoemulsification, and polymorphic phase transition offer energy-efficient alternatives with growing industrial potential. Stability remains a critical challenge due to thermodynamic instability, with Ostwald ripening identified as the most common destabilization pathway. Proper formulation strategies, including the use of ripening inhibitors and optimized surfactant systems, are essential to achieve long-term stability.The review further emphasizes that while nanoemulsions offer transformative advantages—such as improved drug delivery performance, enhanced dermal penetration, efficient nutrient or pesticide delivery, and potential applications in nanomedicine—their practical implementation faces challenges. These include high surfactant requirements, toxicity concerns, manufacturing scalability, and regulatory limitations. Advances in formulation science, novel stabilizers, and innovative fabrication technologies are expected to overcome these limitations in the coming years.

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