

NANOEMULSIONS: PREPARATION TECHNIQUES AND PHARMACEUTICAL APPLICATIONS – A COMPREHENSIVE REVIEW

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ABSTRACT

Nanoemulsions (NEs) are advanced colloidal drug delivery systems consisting of nanosized droplets of one immiscible liquid dispersed within another liquid phase and stabilized using surfactants and co-surfactants. Due to their small droplet size (approximately 20–200 nm), large interfacial area, improved kinetic stability, enhanced solubilization capacity, and ability to protect encapsulated molecules, nanoemulsions have gained considerable importance in pharmaceutical research. Poor aqueous solubility and limited bioavailability remain major challenges for many therapeutic agents, particularly Biopharmaceutical Classification System (BCS) class II and IV drugs. Nanoemulsion-based systems provide an effective approach to overcome these limitations by improving dissolution rate, permeability, absorption, and therapeutic performance. Nanoemulsions can be prepared using high-energy approaches such as high-pressure homogenization,

ultrasonication, and microfluidization, or low-energy approaches including spontaneous emulsification, phase inversion temperature, and phase inversion composition methods. The selection of preparation technique depends on formulation composition, desired droplet characteristics, drug stability, and scalability requirements. This review focuses on the formulation principles, preparation techniques, characterization parameters, and pharmaceutical applications of nanoemulsions. Particular emphasis is placed on oral, topical,

ocular, parenteral, pulmonary, nasal, anticancer, antimicrobial, and targeted drug delivery applications. The potential of nanoemulsions as versatile carriers for improving drug solubility, bioavailability, stability, and therapeutic efficacy is discussed.

KEYWORDS: Nanoemulsion; Nanocarrier; Drug delivery; Solubility enhancement; Pharmaceutical applications; SNEDDS; Bioavailability enhancement.

1. INTRODUCTION^[1-3]

Nanotechnology has revolutionized pharmaceutical formulation development by providing innovative approaches for overcoming conventional drug delivery limitations. Among various nanocarrier systems, nanoemulsions have emerged as promising delivery platforms because of their unique physicochemical properties and wide pharmaceutical applicability.

A nanoemulsion is a kinetically stable dispersion system containing two immiscible liquids, generally oil and water, stabilized by surfactants and co-surfactants. The dispersed phase exists as nanosized droplets, resulting in increased surface area, improved drug dissolution, enhanced permeability, and improved biological performance.

Unlike conventional emulsions, which generally possess droplet sizes in the micrometer range, nanoemulsions exhibit significantly smaller droplet dimensions, resulting in improved physical stability and optical transparency. They are extensively investigated for delivery of poorly water-soluble drugs, peptides, proteins, vaccines, herbal molecules, and bioactive compounds.

The pharmaceutical importance of nanoemulsions arises from their ability to:

- Increase aqueous solubility of hydrophobic drugs
- Improve dissolution rate
- Enhance gastrointestinal absorption
- Protect drugs against chemical degradation
- Improve drug targeting
- Reduce dose frequency
- Enhance therapeutic index

Recent research has demonstrated nanoemulsions as promising systems for oral, transdermal, ocular, pulmonary, nasal, and parenteral drug delivery.

2. Concept and Structure of Nanoemulsions^[4,5]

Nanoemulsions consist of:

1. **Dispersed phase**

- Oil droplets containing lipophilic drug molecules

2. **Continuous phase**

- Usually aqueous phase

3. **Interfacial layer**

- Surfactant and co-surfactant molecules surrounding droplets

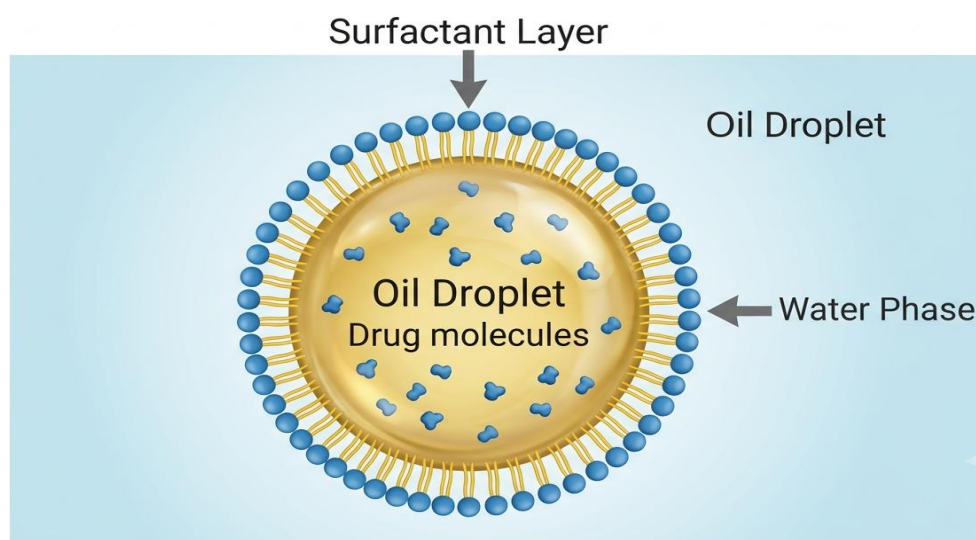


Figure 1: Basic Structure of Nanoemulsion.

3. Classification of Nanoemulsions^[6,7]

Nanoemulsions are mainly classified based on the arrangement of oil and water phases.

3.1 Oil-in-Water Nanoemulsion (O/W)

In O/W nanoemulsions

- Oil droplets are dispersed in aqueous medium
- Suitable for poorly water-soluble drugs
- Commonly used for oral and parenteral delivery

Applications

- Oral drug delivery
- Injectable formulations
- Nutraceutical delivery

3.2 Water-in-Oil Nanoemulsion (W/O)

In W/O systems

- Water droplets are dispersed in oil phase

Applications

- Transdermal delivery
- Cosmetic formulations

3.3 Bicontinuous Nanoemulsions

Both oil and water phases form continuous networks.

Advantages.

- Increased drug loading
- Enhanced transport properties

Table 1: Classification of Nanoemulsions.

Type	Continuous Phase	Dispersed Phase	Pharmaceutical Application
O/W Nanoemulsion	Water	Oil	Oral, injectable delivery
W/O Nanoemulsion	Oil	Water	Topical and transdermal
Bicontinuous	Oil + Water	Interconnected	Advanced drug delivery

4. Components of Nanoemulsions^[7,8]

4.1 Oil Phase

The oil phase determines drug solubilization capacity.

Table 2: Common pharmaceutical oils used in Nanoemulsions.

Oil	Function
Medium chain triglycerides	Solubilization of lipophilic drugs
Oleic acid	Improves permeability
Labrafac PG	Lipid carrier
Capryol 90	Solubility enhancement
Miglyol 812	Pharmaceutical oil vehicle

4.2 Surfactants

Surfactants reduce interfacial tension between oil and water phases.

Examples:

- Tween 20
- Tween 80
- Cremophor RH40
- Labrasol

Functions

- Droplet stabilization
- Prevention of aggregation
- Improved emulsification

4.3 Co-Surfactants

Co-surfactants increase interfacial flexibility.

Examples

- PEG 400
- Ethanol
- Propylene glycol
- Transcutol P

Table 3: Role of Nanoemulsion Components.

Component	Examples	Pharmaceutical Role
Oil	Labrafac PG, Capryol 90	Drug solubilization
Surfactant	Tween 80, Cremophor	Reduce surface tension
Co-surfactant	PEG 400	Improve flexibility
Water phase	Purified water	Continuous medium

5. Preparation Techniques of Nanoemulsions^[9-12]

Nanoemulsion preparation methods are divided into.

1. High-energy methods
2. Low-energy methods

5.1 High-Energy Methods

High-energy methods utilize mechanical energy to reduce droplet size.

5.1.1 High Pressure Homogenization

Principle

A coarse emulsion is passed through a narrow homogenization valve under high pressure resulting in droplet disruption.

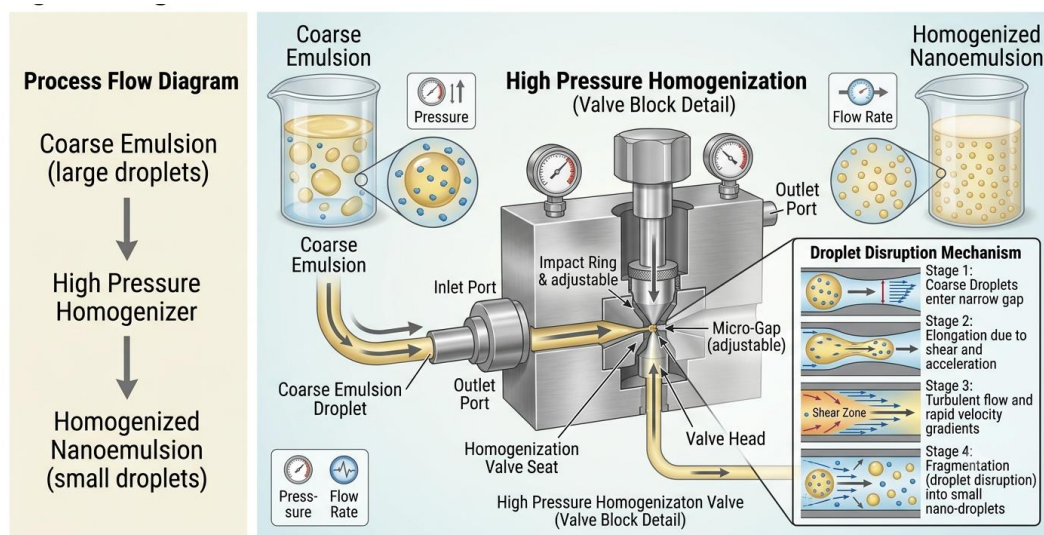


Fig-2: High Pressure Homogenization Process for Nanoemulsion Production.

5.1.2 Ultrasonication

Ultrasonic waves generate cavitation bubbles that break large droplets into nanosized droplets.

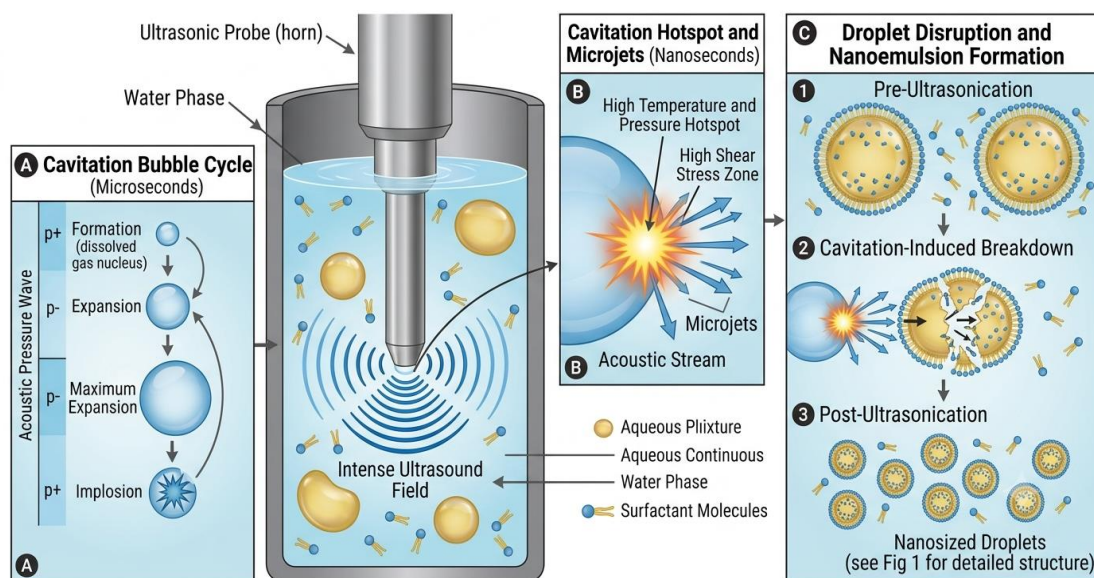


Fig-3: Ultrasonication Process for Nanoemulsion Production.

5.1.3 Microfluidization

Microfluidizers force formulation through microchannels resulting in intensive mixing.

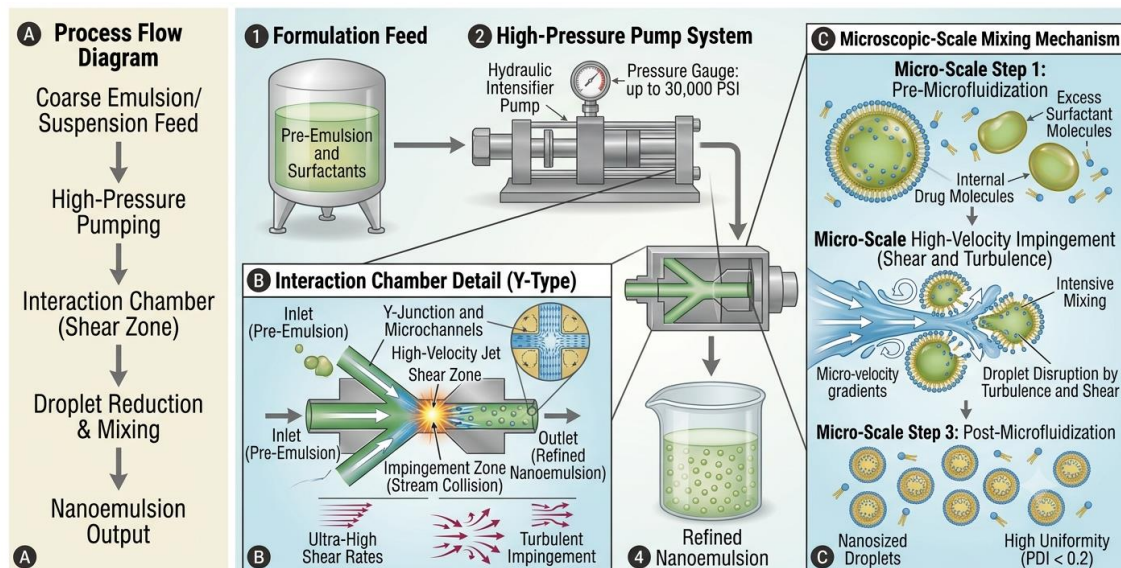


Fig-4: High Pressure Microfluidization Process for Nanoemulsion Production.

5.2 Low-Energy Methods

Low-energy methods utilize physicochemical properties of formulation components.

5.2.1 Spontaneous Emulsification

Formation occurs due to chemical energy released during mixing of components.

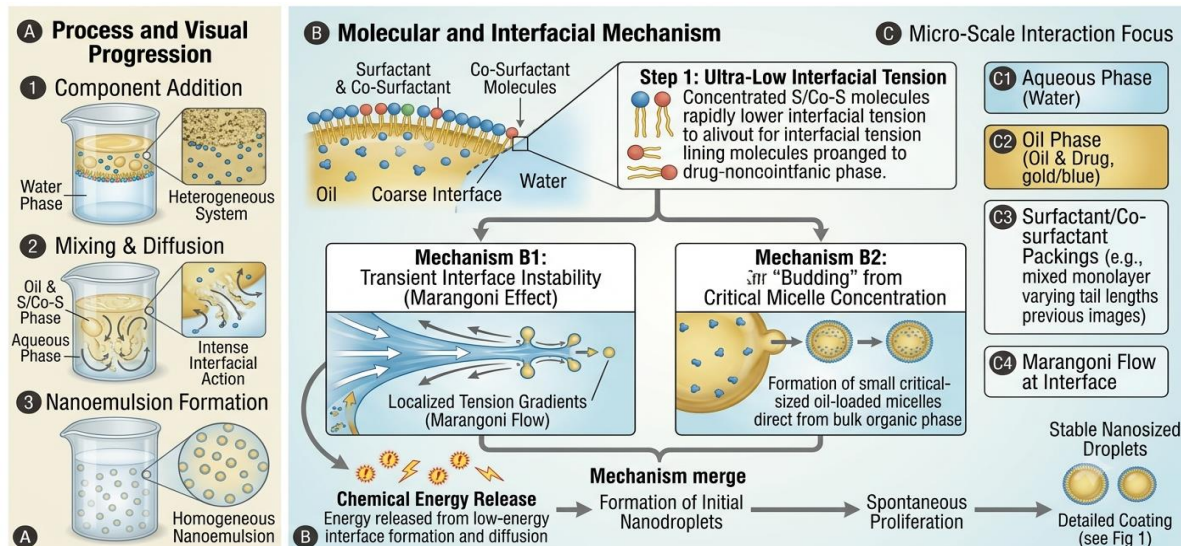


Fig-5- Spontaneous Emulsification Process for Nanoemulsion Production.

5.2.2 Phase Inversion Temperature (PIT)

Based on temperature-dependent alteration of surfactant properties.

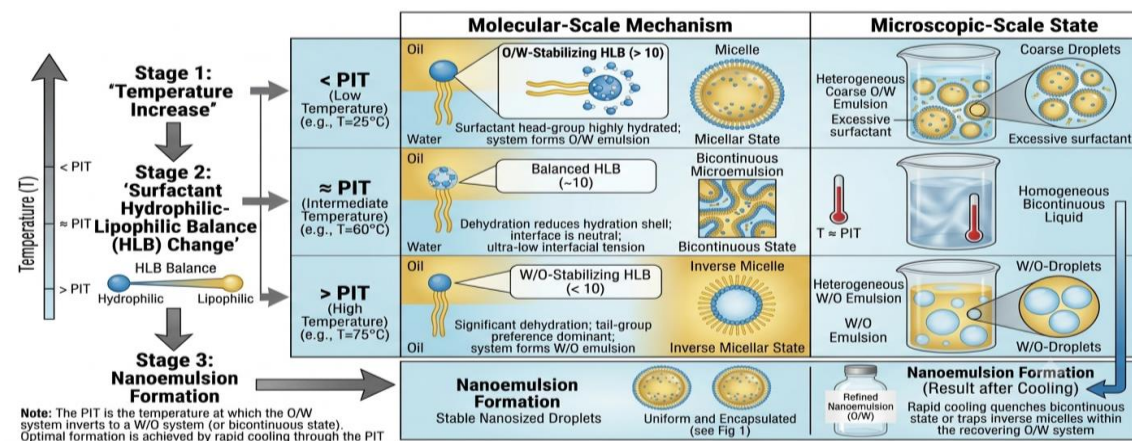


Fig-6: Phase Inversion Temperature (PIT) Process for Nanoemulsion Production.

Table 4: Comparison of Nanoemulsion Preparation Methods.

Method	Energy Requirement	Advantages	Limitations
High pressure homogenization	High	Scale-up possible	Expensive
Ultrasonication	High	Small droplets	Batch process
Microfluidization	High	Uniform size	Equipment cost
PIT method	Low	Good control	Temperature sensitive
Spontaneous emulsification	Low	Simple method	Optimization required

6. Characterization of Nanoemulsions^[13-15]

Characterization is essential to evaluate the physical stability, drug loading efficiency, release behaviour, and biological performance of nanoemulsion systems.

6.1 Droplet Size Analysis

Droplet size is a critical parameter influencing

- Drug dissolution
- Absorption
- Stability
- Biological performance

Common technique

Dynamic Light Scattering (DLS)

Preferred size range

20–200 nm

Smaller droplets provide

- Higher surface area
- Improved drug release
- Better bioavailability

6.2 Polydispersity Index (PDI)

PDI indicates uniformity of droplet distribution.

Interpretation.

PDI Value	Interpretation
<0.2	Excellent uniformity
0.2–0.5	Acceptable distribution
>0.5	Broad distribution

6.3 Zeta Potential

Zeta potential determines electrostatic stability of nanoemulsion droplets.

General indication:

Zeta Potential	Stability
± 10 mV	Low stability
± 20 mV	Moderate stability
$\geq \pm 30$ mV	Good stability

6.4 Entrapment Efficiency

Determines amount of drug incorporated into nanoemulsion droplets.

6.5 Drug Loading Capacity

Represents the amount of drug incorporated per quantity of formulation.

6.6 Morphological Characterization

Techniques

Transmission Electron Microscopy (TEM)

Provides

- Droplet morphology
- Size confirmation
- Surface characteristics

Scanning Electron Microscopy (SEM)

Provides

- Surface structure
- Particle morphology

6.7 Stability Studies

Nanoemulsions are evaluated for.

Physical stability

- Phase separation
- Creaming
- Coalescence

Thermodynamic stability

Tests include

- Centrifugation
- Heating-cooling cycle
- Freeze-thaw cycle

Table 5: Characterization Parameters of Nanoemulsions.

Parameter	Technique	Importance
Droplet size	DLS	Determines nanoscale distribution
PDI	DLS	Measures uniformity
Zeta potential	Electrophoretic mobility	Predicts stability
Morphology	TEM/SEM	Confirms structure
Drug content	HPLC/UV	Determines loading
Stability	Accelerated studies	Shelf-life prediction

7. Key Advantages and Therapeutic Importance^[16,17]

Nanoemulsions have emerged as one of the most versatile and impactful nanocarrier systems in modern pharmaceutical technology. Their unique physicochemical properties—such as nanoscale droplet size, large interfacial surface area, thermodynamic or kinetic stability, and optical clarity—enable them to solve critical drug delivery challenges.

Here is a breakdown of why nanoemulsions are so important across pharmaceutical and biomedical fields.

- **Enhancement of Solubilization & Bioavailability**

- A majority of newly discovered active pharmaceutical ingredients (APIs) suffer from poor aqueous solubility. Nanoemulsions solubilize lipophilic (hydrophobic) drugs within their inner oil core, dramatically increasing dissolution rates and gastrointestinal absorption.

- **Multimodal Administration Routes**

- Nanoemulsions can be formulated for almost every route of administration—including oral, topical/transdermal, ocular, parenteral, pulmonary, and nasal routes.

- **Improved Membrane & Barrier Permeation:**

- The ultra-small droplet size combined with surfactants lowers interfacial tension and allows nanoemulsion droplets to effectively pass through biological barriers, such as the stratum corneum in skin, corneal tissue in the eye, and mucosal linings.

- **Protection of Sensitive Active Ingredients**

- The encapsulated drug core shields labile molecules from chemical degradation (such as oxidation, hydrolysis, enzymatic breakdown, or low pH environment in the stomach).

- **Reduced Systemic Toxicity & Controlled Release**

- Encapsulation allows for targeted or sustained release of potent compounds (e.g., chemotherapeutic agents), reducing non-target exposure and minimizing adverse side effects.

8. Pharmaceutical Applications of Nanoemulsions^[18-20]

Nanoemulsions have gained importance as multifunctional pharmaceutical carriers due to their ability to enhance solubility, permeability, bioavailability, and therapeutic efficiency.

8.1 Oral Drug Delivery

Poor aqueous solubility is one of the major limitations affecting oral absorption of drugs.

Nanoemulsions improve.

- Dissolution rate
- Gastrointestinal absorption
- Drug bioavailability

Examples

Drug	Benefit
Cyclosporine	Improved absorption
Vardenafil	Solubility enhancement
Curcumin	Increased bioavailability
Paclitaxel	Improved dissolution

8.2 Self-Nanoemulsifying Drug Delivery Systems (SNEDDS)

SNEDDS are isotropic mixtures containing

- Oil
- Surfactant
- Co-surfactant
- Drug

They spontaneously form nanoemulsions after contact with gastrointestinal fluids.

Advantages

- Improved oral absorption
- Reduced dose variability
- Enhanced solubility

8.3 Topical and Transdermal Delivery

Nanoemulsions enhance penetration through skin layers.

Advantages

- Increased drug permeation
- Better hydration
- Controlled drug release

Applications

- Antifungal agents
- Anti-inflammatory drugs
- Cosmetic actives

8.4 Ocular Drug Delivery

Conventional eye drops suffer from

- Rapid drainage
- Low residence time

Nanoemulsions provide

- Enhanced corneal penetration
- Longer retention
- Improved therapeutic response

Applications

- Antibiotics
- Anti-inflammatory agents
- Antiglaucoma drugs

8.5 Parenteral Drug Delivery

Nanoemulsions are suitable for injectable delivery of poorly soluble drugs.

Advantages

- Reduced toxicity
- Improved circulation time
- Controlled drug distribution

Examples

- Propofol nanoemulsion injection
- Lipid-based drug carriers

8.6 Pulmonary Drug Delivery

Nanoemulsions improve delivery of drugs through inhalation.

Advantages

- Deep lung deposition
- Enhanced absorption

Applications:

- Respiratory infections
- Asthma therapy

8.7 Nasal Drug Delivery

Nanoemulsions enhance

- Nasal mucosal penetration
- Brain targeting

Applications

- CNS drugs
- Peptides

8.8 Anticancer Drug Delivery

Nanoemulsions provide

- Improved tumour accumulation
- Reduced systemic toxicity
- Enhanced drug protection

Examples

Drug	Application
Paclitaxel	Cancer therapy
Curcumin	Anticancer activity
Docetaxel	Targeted delivery

Table 6: Pharmaceutical Applications of Nanoemulsions.

Application	Major Advantage	Examples
Oral delivery	Increased bioavailability	Cyclosporine, Vardenafil
Topical delivery	Enhanced penetration	NSAIDs, antifungals
Ocular delivery	Increased residence time	Antibiotics
Parenteral delivery	Improved solubilization	Propofol
Pulmonary delivery	Deep lung delivery	Respiratory drugs
Cancer therapy	Targeted delivery	Paclitaxel

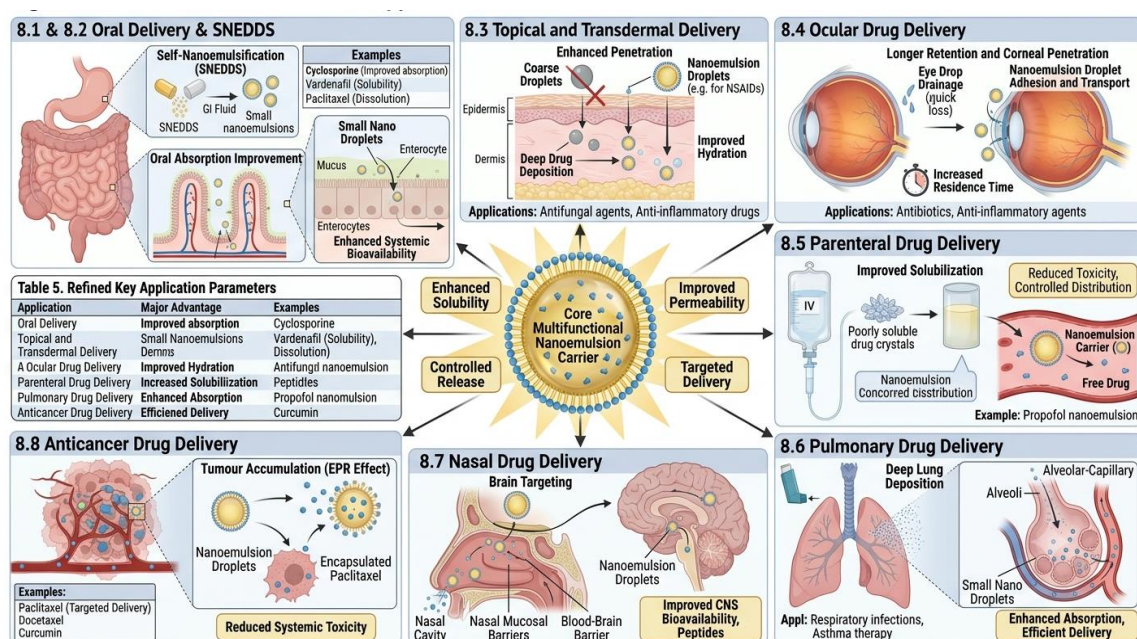


Fig 7: Pharmaceutical Applications of Nanoemulsions.

9. Recent Advances in Nanoemulsion Technology^[19,20]

9.1 Stimuli Responsive Nanoemulsions

These systems respond to

- pH
- Temperature
- Enzymes
- Light

Advantages

- Site-specific drug release
- Improved targeting

9.2 Herbal and Natural Compound Nanoemulsions

Nanoemulsification improves therapeutic potential of:

- Curcumin
- Quercetin
- Essential oils
- Flavonoids

Benefits

- Increased stability
- Enhanced absorption

9.3 Nanoemulsion-Based Vaccines

Advantages

- Antigen protection
- Improved immune response

9.4 Artificial Intelligence-Based Optimization

AI and machine learning approaches are increasingly used for.

- Component selection
- Formulation optimization & Prediction of droplet size

10. Advantages of Nanoemulsions^[19,20]

Table 7: Advantages of Nanoemulsions.

Advantage	Explanation
Enhanced solubility	Improves dissolution of poorly soluble drugs
Improved bioavailability	Enhances absorption
Small droplet size	Increased surface area
Better stability	Reduced sedimentation
Versatile administration	Multiple routes possible

11. CONCLUSION

Nanoemulsions represent an advanced pharmaceutical delivery platform capable of overcoming major limitations associated with conventional formulations, particularly poor aqueous solubility and low bioavailability of therapeutic agents. Their nanoscale droplet size, enhanced surface area, improved drug solubilization capacity, and flexibility for multiple administration routes make them valuable systems in modern pharmaceuticals. Various high-energy and low-energy preparation techniques allow development of optimized nanoemulsion formulations. Proper characterization using particle size analysis, PDI, zeta potential, microscopy, drug loading, and stability evaluation ensures formulation quality and performance. Nanoemulsions have demonstrated significant potential in oral, topical, ocular, pulmonary, parenteral, and targeted drug delivery. Continued advancement in nanotechnology, artificial intelligence-assisted formulation design, and regulatory science will further expand their pharmaceutical applications.

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