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Review

Review Article of Nanoemulsion Drug Delivery System

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Abstract

Emulsions are liquid-liquid dispersions in which tiny droplets of one liquid phase are distributed throughout the other liquid phase. Because of their appealing qualities such as their small size, high surface area per unit volume, improved dispersion of active hydrophobic components, and enhanced absorption nanoemulsions emulsions with sizes ranging from tens to hundreds of nanometers have a wide range of potential uses in pharmaceutics, foods, and cosmetics. Beginning with an introduction to emulsion kinds, preparation, and stability, the article gives a general review of nanoemulsions for drug delivery. Surfactants are essential for creating and maintaining nanoemulsions. Small molecule, particle, phospholipid, peptide, and protein surfactants are among the several forms of surfactants that are enumerated. The uses of nanoemulsions in drug delivery as nanomedicine are then discussed.

Keywords: Nanoemulsion, drug delivery systems, transdermal delivery, bioavailability enhancement, microemulsion, targeted drug delivery.

INTRODUCTION(11,28)

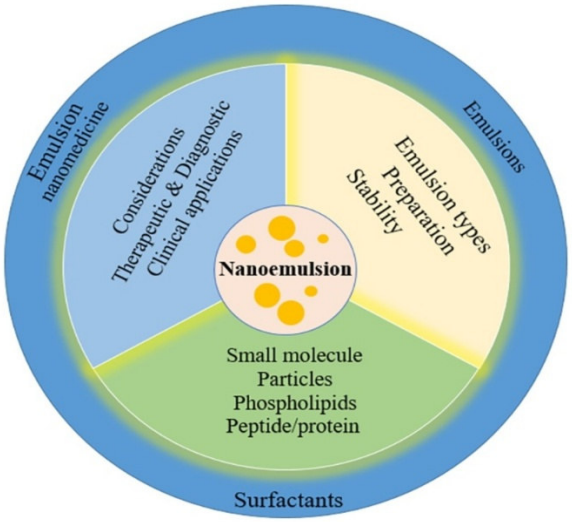
Emulsions are biphasic liquid systems in which the exterior or continuous phase of the liquid is mixed with the interior or dispersed phase, which is distributed as tiny droplets. They may help combine polar and non-polar molecules, alter the texture, taste, and fragrance of items, and increase the effectiveness of medical treatments, which makes them important for the manufacturing of food, medications, and cosmetics. Emulsions offer great potential across a variety of sectors and may be easily adjusted to a wide range of compositions to suit the particular requirements of a process or product, such as dispersing water in oil or oil in water.But, unless surface-active

molecules, also known as emulsifiers, are added to the mixture to stabilize the droplets, emulsions which are thermodynamically unstable systems will quickly split into two distinct phases. Nanoemulsions are emulsions that are nanoscale, with diameters varying from a few tens to hundreds of nanometers. In order to reduce surface tension and prevent emulsion coalescence which is caused by the system's effort to achieve a state of minimal Gibbs free energy surfactants function at the interface between the two immiscible phases.Because they can easily dissolve hydrophobic medications, lessen severe side effects, and be easily transformed into next-generation smart nanomaterials, nanoemulsions hold enormous promise as powerful nanomedicines. An overview of bioinspirednanoemulsions for drug delivery is given in this article, which also covers preparation and stability, introduces various emulsion systems, presents various surfactant types and factors to consider when selecting one, and concludes with emulsion nanomedicine and clinical applications.Nanoemulsions are advanced drug delivery systems featuring nanoscale droplets that improve the solubility, stability, and bioavailability of pharmaceuticals, especially those that are poorly water-soluble. They can be administered via various routes including oral, topical, intravenous, and pulmonary, providing versatile solutions for both medical and cosmetic applications. Nanoemulsion is a type of emulsion consisting of extremely small droplets, typically in the size range of 20–200 nanometers, formed by mixing two immiscible liquids (such as oil and water) with the aid of surfactants or emulsifying agents.

NANOEMULSION(7,8,2)

Nanoemulsions are isotropic liquid mixes of water and oil that include nanoscale droplets with special flow and optical characteristics. Because of their resilience against droplet aggregation and their wide interfacial area, they provide benefits, including improved medication delivery and integration. They are distinguished by their capacity to enhance the bioavailability of encapsulated components and may be produced using either high- or low-energy emulsification processes.

- Nanoemulsion is a stable mixture of two immiscible compounds or liquids.
- These formulations are known for their optical transparency, enhanced physical stability, and ability to improve the delivery and bioavailability of hydrophobic and hydrophilic compounds.
- Nanoemulsions find applications in drug delivery, cosmetics, and the food industry by improving solubility, shelf life, and therapeutic efficacy.
- A miniemulsion is a particular type of emulsion. A miniemulsion is obtained by ultrasonicating a mixture comprising two immiscible liquid phases, one or more surfactants and, possibly, one or more co-surfactants.



TYPES OF NANOEMULSION(7,8,1,2)

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

- **OIL-IN-WATER (O/W) NANOEMULSION**

The oil droplets are dispersed in a continuous water phase. The oil droplets are typically in the size range of 20-200 nanometers. **Eg:**Mayonnaise, Cosmetic creams.

- **WATER-IN-OIL (W/O) NANOEMULSION**

Small water droplets (typically 20-200 nm in diameter) are dispersed in a continuous oil phase, stabilized by surfactants or emulsifiers. **Eg:** Butter and Margarine.

- **OIL-IN-WATER-IN-OIL (O/W/O) NANOEMULSION**

An oil-in-water-in-oil (O/W/O) nanoemulsion is a multiple nanoemulsion system where oil droplets containing smaller water droplets are dispersed in a continuous oil phase. **Eg:**Vtamins and Lip balm.

- **WATER-IN-OIL-IN-WATER (W/O/W) NANOEMULSION**

An water-in-oil-in-water (W/O/W) nanoemulsion is a multiple nanoemulsion system where water droplets containing smaller oil droplets are dispersed in a continuous water phase. **Eg:**Ice creams.

PREPARATION OF NANOEMULSION(5,17)

When two immiscible phases are subjected to a shearing mechanical force that splits the dispersed phase into tiny droplets, emulsions are created. The two types of shear force sources used to create emulsions are high energy (using a device to apply the shear force) and low energy (using knowledge of how the physical characteristics of each liquid phase and selected surfactants change from the thermal or chemical energy in the system) methods. A two-step procedure is needed to create nanoemulsions: first, coarse emulsions must be created, and then the large droplets must be broken up into nano-size using high-pressure homogenization or ultrasonication.High-pressure homogenization (HPH), microfluidization, and ultrasonication are examples of high-energy emulsification processes that need to introduce significant mechanical force into the system in order to produce monodisperse droplets. High pressure (>100 MPa) is applied to a coarse emulsion system that has been prepared prior to HPH as part of the homogenization process. In order to decrease droplet size under high shear stress and strong turbulence, the coarse emulsion is compelled to travel through small openings (such as nozzles or valves). The HPH procedure is often carried out several times until the droplet size is consistent in order to create nanoemulsions with the appropriate sizes. Using scalable microfluidic technology, microfluidization prepares nanoemulsions with high oil phase contents by using the ideas of HPH. Single- or dual-channel systems are available for microfluidizers. Compared to conventional methods, single channel microfluidizers produce nanoemulsions with superior dispersity and a smaller size by passing a coarse emulsion via an HPH system. The method's scalability is limited by the requirement for a coarse emulsion feedstock since it depends on mechanical homogenizers that are not very scalable. Dual-channel microfluidizers, on the other hand, may create nanoemulsions with 50% oil phase content by colliding the water and oil phases and then passing them through an HPH system to create a coarse emulsion in situ. Ultrasound has been employed often in nanoemulsion research because of the strong acoustic energy it exerts on the oil phase, which results in finely distributed nanoemulsions. The way ultrasonication works is that the oscillating ultrasound probe produces amplified sound waves that cause fast cavitation bubbles. The acoustic energy tugs and shreds at the scattered phase, finely shearing it into droplets. Although ultrasonication may create well-dispersed nanoemulsions, its significant heat generation, inability to operate with viscous solutions, and limited probe head working distance make it a technology that is not very scalable. Low energy emulsification techniques, such as solvent displacement emulsification, phase inversion temperature method, self-emulsification, and polymorphic phase transition, take use of unique chemical, physical, thermal, and/or solvent circumstances to create a nanoemulsion. In order to create a nanoemulsion, solvent displacement emulsification involves introducing a tiny quantity of miscible dispersed phase to a continuous phase that contains the surfactant. The excess dispersed phase is then removed from the mixture by rotary evaporation. By combining two immiscible phases at a high temperature with a surfactant, the phase inversion temperature technique creates a W/O emulsion that, when cooled, inverts to create an O/W emulsion. The hydrophilic–lipophilic balance of the surfactant, its concentration, the water-to-oil ratio, and the temperature differential between the ambient and phase transition temperatures all stabilize this process.This might also be seen as a high energy approach, depending on the system's particular temperature needs. Self nanoemulsification can greatly increase the bioavailability of poorly soluble drugs and has garnered a lot of interest for oral medication delivery applications. In physiological media, a particular combination of lipid oil, drug, surfactants, and co-surfactants spontaneously creates a nanoemulsion that can regulate drug release and preserve the cargo. Although the high surfactant concentration needed presents a regulatory hurdle, the approach is easily scalable for commercial manufacturing due to the self nanoemulsification mixes' high drug content and simplicity of synthesis.There have been reports of a low-energy technique for creating nanoemulsions from frozen lipid coarse emulsions that have a high drug concentration and little surfactant. Following freezing, the solid lipid passes through a phase change from gel to crystal, where it breaks down spontaneously into solid lipid particles. Following thawing, monodispersenanoemulsions of lipid particles smaller than 100 nm were observed. This method's high drug loading

(50%) and low surfactant concentration (<2%) show a novel approach to scalable emulsification technology. Industrial methods that can satisfy demand are necessary to translate emulsion science into applications that have a major influence on society and people. The technique's scalability is a measurement of the maximum quantity of product that can be made before the vessel's size distorts its qualities. For large-scale manufacturing, such as homogenizing animal milk, high-pressure homogenization which entails passing the mixture through a small channel under pressure that generates a high shear force to make nanoemulsion has been employed. When compared to earlier techniques, low energy emulsification techniques such solvent displacement and phase inversion temperature approaches provide greater energy efficiency while requiring only small modifications to the reactor's current infrastructure. However, due to a shortage of food or medical grade solvents and surfactants, as well as a lack of knowledge about the underlying mechanisms and process, they are presently not commonly employed in commercial manufacturing.

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NANOEMULSION STABILITY(7,9)

Thermodynamically unstable systems, nanoemulsions gradually tend to separate into two distinct phases. This period is prolonged when stabilized by surfactants, which effectively makes emulsions kinetically stable. This means that a well-designed emulsion can have a longer shelf life and maintain its original characteristics for months or years. The translation of nanoemulsion into other applications is crucial, particularly in emulsion nanomedicine, where formulation modifications over time can have a significant effect on patient health. To guarantee that nanoemulsions are generated and kept correctly, it is crucial to comprehend the mechanisms of emulsion instability and stabilization. Emulsion stability is described by the DLVO theory, which was carried out by Derjaguin and Landau as well as Verwey and Overbeek. It combines two separate forces: repulsive electrostatic double layer forces and attractive van der Waal's interactions. Since the two forces are assumed to be independent, the total energy of interaction (FT) at particular distances may be obtained by simply adding the attracting force (FA) and repulsive force (FR), which provides a fair estimate of stability to around 5 nm.

$$F_T = F_A + F_R$$

The system promotes colloid stability when the droplets are far apart because the repulsive forces dominate the interaction energy. However, when the droplets get closer to one another, the attraction forces take over and instability happens. According to the DLVO hypothesis, the emulsion experiences colloidal instability when the attractive forces take precedence. Coalescence, flocculation, creaming/sedimentation, and Ostwald ripening are the four primary processes that cause this. Coalescence is the process by which two or more nearby tiny droplets combine to form a single, bigger droplet. This happens when droplets get close together and distort, creating a thin layer of continuous phase.The passage of the continuous phase and surfactant along the film controls the thinning of the film. When the film thins to a critical point, variations in thickness may cause rupture. The Marangoni effect, which explains mass transport at an interface in reaction to interfacial tension gradients, is responsible for film thinning. When the droplets merge, their combined surface area shrinks, lowering the system's interfacial energy and, ultimately, the Gibbs free energy. The aggregation of scattered, distinct, undisturbed droplets in solution as clusters divided by a thin layer of the continuous phase is known as flocculation. Through electrostatic repulsion, the film's stability delays the emulsion's coalescence; nevertheless, stability against flocculation and stability against coalescence must be taken into account independently, since emulsions may flocculate easily and then coalesce slowly, and vice versa. The intensity of the attractive forces controlling the contact determines whether flocculation is a reversible or irreversible process. Because the droplets are so close together after flocculation, coalescence is more likely to happen. When emulsion droplets of varying densities from the dispersed phase separate to the top or bottom of the solution, creaming and sedimentation of the droplets occur. Creaming/sedimentation, like flocculation, enhances the frequency of contact between droplets, which in turn raises the possibility of droplet coalescence. The inclusion of viscous polysaccharides can inhibit this process, which is particularly important for the food sector and costs billions of dollars annually. Because of improved separation kinetics, creaming can also happen when droplets aggregate into a large floc network, either naturally or as a result of polysaccharide bridging. Diffusion of the dispersed phase through the continuous phase causes bigger droplets to form at the expense of smaller droplets, a process known as Ostwald ripening. The Kelvin effect, which states that particles with a smaller diameter are more soluble in solution, causes this process. It also lowers the Gibbs free energy by decreasing the total surface area of the dispersed phase. By employing a dispersed phase with extremely low solubility in the continuous phase and making sure that the droplets have a monodisperse size distribution, Ostwald ripening may be prevented. The DLVO hypothesis states that two distinct routes that work to resist or limit droplet contact improve emulsion stability by lowering the frequency of destabilization pathways. The first is electrostatic repulsion, in which droplets with similar charges repel one another as they get closer. The second is steric stabilization, in which a thick surface layer that acts as a powerful energy barrier to coalescence prevents droplet contact. Ionic surfactant-coated emulsions

draw counterions from the solution to create an electrical double layer, which allows electrostatic stability through repulsive forces. An electrical double layer is constituted of three separate parts: (1) the charged emulsion surface, (2) the Stern layer of tightly bound counter ions and (3) a diffuse layer of high concentration loosely bound ions and counter ions . The slip plane is the location where the diffuse layer stops moving with the emulsion droplets. An essential metric for assessing an emulsion's stability is the charge at the slip plane, which is where the zeta-potential of an emulsion is measured. Very positive or negative emulsions are more stable. By making the surface layer thicker and more complex, steric hindrance serves as a thermodynamic barrier to droplet contact, which is necessary for destabilization according to the DLVO hypothesis. Long-chain non-ionic surfactants, Pickering particles, or conjugating/coating polymers to the droplet surface can all be used to achieve this. The polymers and side chains interact as droplets get closer, increasing the Gibbs free energy and obstructing the attractive van der Waals forces.

SURFACTANTS (4,8,30)

Surface active agents, often known as surfactants, are solutes or molecules that are preferentially adsorbed at the liquid's surface or interface and lower the surface or interfacial tension. Every soluble surface active agent has two types of groups: hydrophilic (lipophobic) groups made up of polar groups like carboxylic acid, hydroxide, etc. that have a high affinity for polar solvents, and lipophilic (hydrophobic) groups made up of a long carbon chain that has little affinity for aqueous (polar) solvents. The surfactants are also known as amphiphilic because they include both polar and non-polar groups that contribute to their affinity for both aqueous and non-polar solvents. If the amphiphilic is mostly non-polar in nature, it may be hydrophilicThe majority of surfactants may remain at the interface because they properly balance their hydrophilic and lipophilic characteristics. Components known as surfactants have the capacity to improve ocular penetration. The choice of surfactant has an impact on how the nanoemulsion is formulated. Similar to polysorbates 80, surfactants with a hydrophilic lipophilic balance value of 10 are hydrophilic and form an oil-in-water kind of nanoemulsion. In most cases, the mixture of hydrophilic (high HLB) and lipophilic (low HLB) surfactants may require to form a nanoemulsion under crucial micellar concentrations of the surfactant in solution by allowing areas for lipophilic drug interaction in solution. This increases the solubility of the drug. Surfactant clusters at the crucial micellar concentrations form micelles, as well as the lipophilic core and lipophobic surface. Lipophilic micelles' cores affect the drug's entrapment and hence increase its solubility. It is understood that when the oil content increases, the surfactant concentrates on the oil-water emulsion interface, where the lipophilic medication is dissolved under the hydrophobic core. Small amounts of oil within globules of surfactant, known as nanoemulsions, are created when the oil level is minimal.

DRUG DELIVERY(9,10,15,29)

Pickering emulsions provide superior sustained release for drug administration because they are supported by particles at the water/oil interface, and the particle layer at the interface is far thicker than the molecular layer in emulsions stabilized by molecular surfactants. Pickering emulsions might therefore be used to encapsulate active ingredients in order to regulate their release kinetics and enhance their bioavailability. $Mg(OH)_2$ nanoparticle-stabilized oil-in-water Pickering nanoemulsions might be used to encapsulate hydrophobic medications. Drugs may be released from Pickering emulsions more readily in acidic conditions due to the ability of $Mg(OH)_2$ nanoparticles to dissolve in acidic solutions, demonstrating a pH-dependent release for drug delivery. In Pickering emulsions for drug administration, a variety of particles have been employed as stabilizers, such as silica nanoparticles, cellulose nanocrystals, chitosan nanoparticles, protein nanogels, and starch granules. Water-in-oil Pickering emulsions might be utilized to deliver hydrophilic medications, whereas oil-in-water Pickering emulsions are good for hydrophobic pharmaceuticals. For instance, biodegradable polylactic-co-glycolic acid (PLGA) nanoparticles maintain water-in-oil Pickering emulsions that contain oxaliplatin, a watersoluble chemotherapy medication for liver cancers. The total quantity of oxaliplatin released from colloidal surfactant-stabilized Pickering emulsions after one month is only around 72%, but oxaliplatin contained in molecular surfactant-stabilized emulsions is nearly entirely released within 24 hours.

BIOMEDICAL RESEARCH(3,21)

Biomedical research also makes extensive use of Pickering emulsions. Drugs loaded in Pickering emulsions can swiftly pass through the corneum and then enter the dermis and subcutaneous tissues, preventing further infection and aiding in the skin's recovery. This is because Pickering emulsions without molecular surfactants have a high skin permeability, a high skin penetration depth, and a strong adsorption capacity. For instance, bactericidal Pickering emulsions containing econazole nitrate for topical applications are made using biocompatible cyclodextrins as emulsion stabilizers. The formulation's ability to prevent the development of bacteria

and fungi is demonstrated by the antifungal and antibacterial tests. Apart from cyclodextrin, silica and chitosan particles have also been investigated as topical emulsion stabilizers.

CLINICAL APPLICAATION(4,18)

An appealing platform for creating efficient nanomedicines for drug delivery is nanoemulsions. A versatile framework for creating a variety of nanomedicines is offered by the easy production and well-known characteristics of emulsions and surfactants. Their tiny size enables them to have special bio-nano interactions, extend circulation, and get deep into tissues. However, a range of hydrophobic cargo, including medications, photosensitizers, and contrast agents, can be put into the oil core. By loading into the core structure, sensitive materials are shielded from deterioration, poorly adsorbed or soluble drugs become more bioavailable, and cargo is delivered to the illness site more efficiently. Furthermore, nanoemulsions can exhibit strong physiological activity by adorning the surface with hydrophilic polymers, targeting moieties, monoclonal antibodies, and/or diagnostic markers.Nanoemulsion systems are a perfect platform for clinical pipeline research because of their tiny size and logical internal and exterior architectural design. The use of emulsions in clinical diagnosis and therapy has great promise. Over the past 20 years, doctors have frequently recommended lipid emulsion formulations to deliver hydrophobic medications, including immunosuppressants for transplants, anesthetics, and corticosteroids. Numerous potential emulsion nanomedicines have been documented in the literature to administer a range of pharmaceuticals, such as cholesterol-lowering, antipsychotic, anticancer, antimalarial, and antiglaucoma medications. Utilizing the special qualities of nanoemulsions as a delivery vehicle may enhance the new cancer, autoimmune, and chronic disease treatments that have been developed recently, such as immunotherapy, vaccinations, and photo/thermal therapies. By stimulating an immunogenic tumor microenvironment and pro-inflammatory antitumor phenotypic immune cells, immunotherapy is a potential new approach to indirectly treat cancer. Since nanoemulsions have been used extensively in clinical settings and have favorable pharmacokinetic characteristics and safety, they are an appealing adjuvant to improve the immunogenic response. Kim et al. showed that TLR 7/8 agonists encapsulated in a nanoemulsion can effectively reverse immunosuppression at the tumor site, increase and sustain a pro-inflammatory immune environment, activate different immune cell populations, and attract lymphocytes that infiltrate tumors to inhibit tumor growth. Vaccines are very effective in preventing and controlling diseases like influenza outbreaks, which may have a major negative impact on the economy and people's emotions..In order to further enhance immunogenic responses in tumor-specific CD4+ and CD8+ T-cells and promote uptake in dendritic cells, Zeng et al. reported a PEGylated antigen-Clec9A nanoemulsion that utilized conventional targeted nanoemulsion drug delivery without the need for extra adjuvants. This, in turn, suppressed tumor growth. Last but not least, Pellosi et al. have described the creation of a nanoemulsion system for the treatment of dual magnetic hyperthermia and phototherapy that contains magnetic maghemite nanoparticles and chlorine6, a partly hydrogenated porphyrin photosensitizer. According to an in vitro evaluation of the dual action nanoemulsion, the emulsion system prevented the deactivation of the chemically susceptible photosensitizer. When activated with a targeted laser and an alternating electromagnetic field, the nanoemulsion dramatically decreased the viability of MCF-7 breast cancer cell lines in comparison to NHI-3T3 mouse fibroblast cell lines. When conventional diagnostic methods and contrast agents don't work, diagnostic nanoemulsions could give doctors the means to direct their research. They do this by reducing harmful side effects, extending circulation for several scans, and delivering hydrophobic contrast ants to illness areas at diagnostically relevant quantities. Recently, Wallyn et al. created a dual diagnostic imaging nanoemulsion by encapsulating two distinct hydrophobic contrast agents: vitamin E conjugated to an iodinated benzoyl group to improve X-ray images, and iron oxide nanoparticles to improve MRI contrast. MRI and X-ray are two of the most often used diagnostic procedures by physicians. By combining several contrast agents into a nanoemulsion, the need for repeated injections is decreased, biodistribution is enhanced, and concentration in target tissues may be raised, increasing resolution gain. Kennedy's team has also looked at theranostic cancer treatment using nanoemulsions with perfluorinated carbon species and anticancer medications. When subjected to ultrasound, perfluoropentane emulsion undergoes a droplet to bubble transition, selectively releasing the medication while the bubbles improve contrast at the tumor location for a few days. However, because of its thermally driven droplet to bubble transition under physiological settings and its propensity to froth when handled improperly, perfluoropentane(boiling temperature: 29 ◦C) can be challenging to work with. Perfluoro-15-crown-5-ether (boiling temperature: 146 ◦C) emulsions, on the other hand, are extremely stable and show a reversible droplet to bubble transition when exposed to ultrasound, which causes drug release and ultrasound contrast. A single magnetic resonance 19F peak produced by the highly fluorinated perfluorocrown ether functions as a potent MRI contrast agent; nevertheless, the contrast it produces is reliant on the oxygenation and vascularity of the target tissue.

CONCLUSION

Nanoemulsions have attracted significant interest in past decades for various applications due to their unique structures and properties. They can be easily produced at large scale using industrial methods including high-pressure homogenization and ultrasonication. By virtue of their small size and easy-to-disperse components with different hydrophobicity (e.g. hydrophobic drugs in the dispersed oil phase and hydrophilic proteins in the continuous aqueous phase), they have great potential in applications including food, cosmetics and pharmaceutics. For example, nanoemulsions have been formulated to deliver hydrophobic drugs, and have been used as adjuvants for vaccines, demonstrating their clinical impacts. Because of these clinical successes, nanoemulsions have been further developed for emerging highend applications such as immunotherapy, targeted therapy by incorporating multiple functions, for example, encapsulating drugs or imaging probes in the oil droplet, and decorating the nanoemulsion surface with targeting ligand or antibodies for targeted delivery and immunotherapy. Although many of these preclinical studies are in very early stage, more systematic studies and fundamental understanding of the complex interactions between nanoemulsions and biological systems from cells to tissues anorgans will accelerate the translation of their real clinical applications.

DECLARATION OF INTEREST STATEMENT
All authors declare no other competing interests.

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REFERENCES

1. Simonazzi A, Cid GA, Villegas M, Romero IA, Palma DS, Bermudez JM. Drug targeting and stimuli sensitive drug delivery systems. *J Drug Deliv Sci Technol*. 2021;61:102011. doi:10.1016/j.jddst.2020.102011.
2. Kadakia E, Shah L, Amiji MM. Mathematical modeling and experimental validation of nanoemulsion-based drug transport across cellular barriers. *Pharm Res*. 2017;34(7):1416-1427. doi:10.1007/s11095-017-2158-7.
3. Ahmad G, Gattacecca F, Sadda EI, Botchkina G, et al. Biodistribution and pharmacokinetic evaluations of a novel taxoid DHA-SBT-1214 in an oil-in-water nanoemulsion formulation in naïve and tumor-bearing mice. *Pharm Res*. 2018;35:91. doi:10.1007/s11095-018-2349-x.
4. Suyal J. Nanoemulsion: a novel approach in various pharmaceutical applications. *J Pharm Sci Bio-scientific Res*. 2017;7(1):153-157.
5. Iwunze MO. The determination of the physico-chemical properties of nanoemulsion. *J Mater Sci Eng-A*. 2017;7(1-2):19-24. doi:10.17265/2161-6213/2017.1-2.003.
6. Ali A, Ansari AV, Ahmad U. Nanoemulsion: an advanced vehicle for efficient drug delivery. *Publons*.
7. Thakur N, Garg G, Sharma PK, Kumar N. Nanoemulsions: a review on various pharmaceutical applications. *Global J Pharmacol*. (Year/Volume/Issue not found).
8. Gupta A, Eral HB, Hatton AT, Doyle PS. Nanoemulsions: formation, properties and applications. *Soft Matter*. 2016;12(11):2826-2841. doi:10.1039/C5SM02958A.
9. Chellapa P, Mohamed TA, Keleb IE, Elmahgoubi A. Nanoemulsion and nanoemulgel as a topical formulation. *IOSR J Pharm*.
10. Chauhan LB, Patil AV, Khutle MN. Nanoemulsion system for topical delivery of tretinoin. *Pharmaceutical Science*. 2015;4:64-80
11. Sun HW, Wei C, Liu SB, Jing H, Feng Q, Tong YN, et al. Induction of systemic and mucosal immunity against methicillin-resistant *Staphylococcus aureus* infection by a novel nanoemulsion adjuvant vaccine. *Int J Nanomedicine*. 2015;10:7275-7290. doi:10.2147/IJN.S91529.
12. Jaiswal M, Dudhe R, Sharma PK. Nanoemulsion: an advanced mode of drug delivery system. *3 Biotech*. 2015 Apr;5(2):123-127. doi:10.1007/s13205-014-0214-0.
13. Patil H, Waghmare J. Nanoemulsion: Current state and perspectives. *Res J Topical Cosmetic Sci*. 2013;4(1):32-40. rjtcsonline.com+1
14. 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. PubMed

15. Valenta C, Schultz K. Influence of carrageenan on the rheology and skin permeation of microemulsion formulations. *J Control Release*. 2004;95(2):257-265. doi:10.1016/j.jconrel.2003.11.020. PubMed
16. Singh R, Chakravorty A, Kumar P, Chaturvedi A. Nanoemulsion: an effective drug carrier for the management of psoriasis. *Res & Rev: Res J Biol*. 2015;4(2):10-15.
17. Roberts MS. *Targeted drug delivery to the skin and deeper tissues: role of physiology, solute structure and disease.Clin Exp Pharmacol Physiol*. 1997 Nov;24(11):874-879. DOI: 10.1111/j.1440-1681.1997.tb02708.x
18. Ng KW, Lau WM. Skin deep: the basics of human skin structure and drug penetration. In: Dragicevic N, Maibach HI, editors. *Percutaneous Penetration Enhancers: Chemical Methods in Penetration Enhancement, Drug Manipulation Strategies and Vehicle Effects*. Berlin/Heidelberg: Springer-Verlag; 2015. p. 3-11. doi:10.1007/978-3-662-45013-0_1.
19. Shaker DS, Ghanem AH, Li SK, Warner KS, Hashem FM, Higuchi WI. Mechanistic studies of the effect of hydroxypropyl-beta-cyclodextrin on in vitro transdermal permeation of corticosterone through hairless mouse skin. *Int J Pharm*. 2003 Mar 6;253(1-2):1-11. doi:10.1016/S0378-5173(02)00625-7. pubmed.ncbi.nlm.nih.gov
20. Shakeel F, Baboota S, Ahuja A, Ali J, Shafiq S. Skin permeation mechanism and bioavailability enhancement of celecoxib from transdermally applied nanoemulsion. *J Drug Target*. 2008 Dec;16(10):733-740. doi:10.1080/10611860802473402.
21. Aldrich DS, Bach CM, Brown W, Chambers W, et al. Ophthalmic preparations. *Pharmacopeial Forum*. 2013 Jan;39(5). Available from: https://www.researchgate.net/publication/288293117_Ophthalmic_preparations
22. Khan W, Vaseem AV, Hussain Z. Self-nano emulsifying drug delivery system (SNEEDS) for ocular administration. *Res J Pharm Technol*. 2020;13(11):5116-5123.
23. Barakat N, Fouad E, Elmedany A. A formulation design of indomethacin-loaded nanoemulsion for transdermal delivery. *Pharmaceutica Analytica Acta*. 2011;2(1):1-8.
24. Scheuplein RJ. Mechanism of percutaneous absorption. II. Transient diffusion and the relative importance of various routes of skin penetration. *J Invest Dermatol*. 1967;48(1):79-88. PMID: 6018244. PubMed
25. Shrestha H, Bala R, Arora S. Lipid-based drug delivery systems. *J Pharm (Cairo)*. 2014;2014:801820. doi:10.1155/2014/801820. PubMed
26. Kawakami K, Yoshikawa T, Moroto Y, Kanaoka E, Takahashi K, Nishihara Y, Masuda K. Microemulsion formulation for enhanced absorption of poorly soluble drugs. I. Prescription design. *J Control Release*. 2002 May 17;81(1-2):65-74. doi:10.1016/S0168-3659(02)00049-4
27. Jadhav PR, Koli WK, Kamble BA, Bhutkar AM. A review on nanoemulsion. *Asian Journal of Research in Pharmaceutical Sciences*. 2012;2(3):52-60.
28. Shakeel F, Ramadan W. Transdermal delivery of anticancer drug caffeine from water-in-oil nanoemulsions. *Colloids Surf B Biointerfaces*. 2010;75(1):356-362. doi:10.1016/j.colsurfb.2009.09.010. PubMed
29. Thakur A, Walia KM. Nanoemulsion in enhancement of bioavailability of poorly soluble drug. *Indian Journal of Pharmaceutical Education and Research*. 2015;49(4):237-246.