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Nanotechnology in Action: The Rise of Nanoemulsions in Modern Science

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ABSTRACT

Nanotechnology has emerged as a transformative field, offering groundbreaking innovations across various scientific and industrial domains. Among its diverse applications, the development of nanoemulsions has garnered significant attention due to their unique physicochemical properties, such as enhanced stability, high bioavailability, and efficient encapsulation of active compounds. Nanoemulsions, composed of nanoscale droplets dispersed in immiscible phases, have proven instrumental in revolutionizing sectors like pharmaceuticals, cosmetics, food, and agriculture. This review highlights the pivotal role of nanotechnology in advancing the formulation and functionality of nanoemulsions, emphasizing their advantages in drug delivery, targeted therapies, and bioactive compound preservation. Key challenges, including scalability and stability, are also addressed alongside future prospects for integrating nanoemulsion-based technologies into modern science. By exploring recent advancements, this paper aims to underscore the critical contribution of nanotechnology in shaping the next generation of nanoemulsion applications.

KEYWORDS: *Nanoemulsions, Nanotechnology, Drug delivery Phase, Micron*

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INTRODUCTION

Nanoemulsions are submicron-sized colloidal systems that function as carriers for drug molecules, with sizes typically ranging from 10 to 1,000 nm. These carriers are solid spheres with an amorphous, lipophilic surface and a negative charge. To improve site-specific delivery, magnetic nanoparticles can be incorporated.

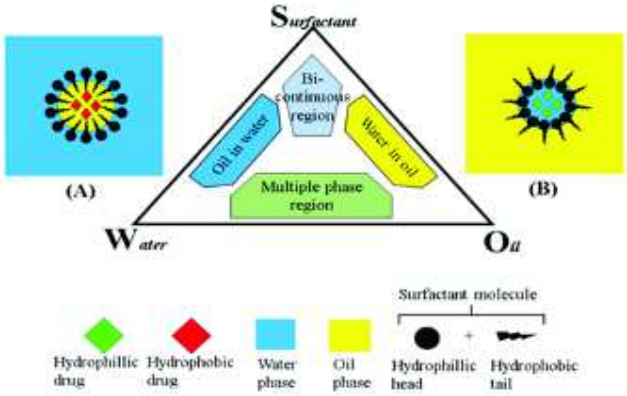
As drug delivery systems, nanoemulsions enhance the therapeutic effectiveness of drugs while reducing adverse effects and toxicity. Their major applications include treating infections in the reticuloendothelial system (RES), enzyme replacement therapy in the liver, cancer treatment, and vaccination.An emulsion is a biphasic system where one phase is finely dispersed within the other in the form of small droplets, typically ranging from 0.1 to 100 µm in diameter. This system is thermodynamically unstable but can be stabilized using emulsifying agents, also called emulgents or emulsifiers. The dispersed phase, also referred to as the internal or discontinuous phase, is distributed within the external or continuous phase, known as the dispersion medium. Emulsifying agents act as intermediates or interphases to maintain stability. The term "nanoemulsion" refers to a miniemulsion, which is a fine dispersion of oil in water or water in oil, stabilized by a surfactant layer, with droplet sizes ranging from 20 to 600 nm.Due to their small droplet size, nanoemulsions appear transparent. They are classified into three types: (a) oil-in-water nanoemulsions, where oil is dispersed in the continuous aqueous phase, (b) water-in-oil nanoemulsions, where water is dispersed in the continuous oil phase, and (c) bi-continuous nanoemulsions, in which both the oil and water phases form continuous structures.

➢ **Advantages of nanoemulsions:**

1. Due to the reduced droplet size, the effect of gravity is minimized, and Brownian motion is sufficient to counteract it. This prevents creaming and sedimentation during storage. Furthermore, the small droplet size inhibits flocculation, maintaining system stability without molecular separation.
2. Surface fluctuations are prevented in small droplets, which helps avoid their coalescence.
3. Nanoemulsions promote the efficient delivery of active compounds through the skin, ensuring quick penetration.
4. Nanoemulsions can be administered via the enteric route and are formulated using surfactants that are generally recognized as safe (GRAS) for human consumption.

Components of Nanoemulsions:

Emulsification is mainly governed by several factors, including (1) the nature and concentration of the oil, aqueous phase, surfactants, and co-surfactants, (2) the ratio The aqueous solubility of the oil phase plays a key role in determining the stability profile of a nanoemulsion formulation, with the correct selection of the oil phase helping to prevent Ostwald ripening, a common issue in nanoemulsions. The choice of the aqueous phase is also crucial. For topical nanoemulsions, distilled water is typically used, while for parenteral formulations, the aqueous phase should be iso-osmotic to blood. This can be achieved by adding additives such as electrolytes (e.g., sodium chloride), glycerol, dextrose, and sorbitol. These additives can influence the phase behavior and stability of the nanoemulsion. For instance, electrolytes like sodium chloride reduce the phase inversion temperature (PIT) of non-ionic surfactants. Other additives, such as preservatives, can also affect the nanoemulsion's phase behavior and its area of existence. Preservatives like methyl paraben and propyl paraben can form complexes with surfactants like polysorbates, and such interactions may alter the properties of the nanoemulsionof surfactant to co-surfactant and oil to surfactant, (3) environmental conditions such as pH and temperature, and (4) physicochemical properties of the drug, such as lipophilicity, hydrophilicity, and the pKa coefficient.



A. Oil phase:

Selecting the appropriate oil phase is essential as it directly influences the behavior of other components in nanoemulsions, particularly in oil-in-water (o/w) formulations. The oil phase is typically chosen based on its solubility for the drug candidate, but achieving both high solubility and suitable emulsifying properties in a single oil component can be challenging. Emulsifying oils with long hydrocarbon chains, such as medium-chain triglycerides and fatty acid esters, is particularly difficult, although the solubilization capacity of lipophilic moieties often increases with the length of the oil chains. To balance drug solubilization and the formation of nanoemulsions with the desired properties, a mixture of oils is sometimes used. For example, combining medium-chain triglycerides with fixed oils can provide a better balance between drug loading and emulsification efficiency.

B. Surfactant:

Surfactant selection is a crucial factor in nanoemulsion formulation, as it directly impacts the ability to promote the oily phase and enhance drug solubilization. It is important to note that surfactants may not always be harmless; for example, Tween 20 has virucidal activity. The type and concentration of surfactant must be carefully considered, with a minimum amount being used, regardless of the surfactant's nature, origin, or type. Phospholipids are generally preferred over synthetic surfactants for their beneficial properties, whenever possible. The surfactant choice also depends on the type of nanoemulsion being prepared. For water-in-oil (w/o) nanoemulsions, a low HLB surfactant such as sorbitan monoester is typically used, while a high HLB surfactant like polysorbate 20 is favored for oil-in-water (o/w) nanoemulsions. In some formulations, a combination of lipophilic (low HLB) and hydrophilic (high HLB) surfactants is required. For pharmaceutical applications, several surfactants, including lecithin, poloxamer, and polysorbate 20, are commonly chosen. Additionally, polyoxyl-40 hydrogenated castor oil derivatives like Acrysol® K-

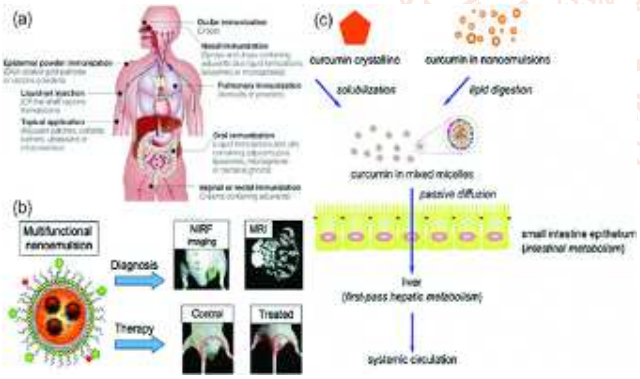
150 and Acrysol EL135 are used in certain co-solvent-based formulations that are marketed today.

C. Aqueous phase:

The aqueous solubility of the oil phase plays a key role in determining the stability profile of a nanoemulsion formulation, with the correct selection of the oil phase helping to prevent Ostwald ripening, a common issue in nanoemulsions. The choice of the aqueous phase is also crucial. For topical nanoemulsions, distilled water is typically used, while for parenteral formulations, the aqueous phase should be iso-osmotic to blood. This can be achieved by adding additives such as electrolytes (e.g., sodium chloride), glycerol, dextrose, and sorbitol. These additives can influence the phase behavior and stability of the nanoemulsion. For instance, electrolytes like sodium chloride reduce the phase inversion temperature (PIT) of non-ionic surfactants. Other additives, such as preservatives, can also affect the nanoemulsion's phase behavior and its area of existence. Preservatives like methyl paraben and propyl paraben can form complexes with surfactants like polysorbates, and such interactions may alter the properties of the nanoemulsion

Applications of nanoemulsions in drug delivery systems:

Nanoemulsions are effective drug delivery systems that enhance the solubility and bioavailability of poorly soluble drugs, offering improved therapeutic effects across various administration routes.



1. Nano-emulsions and intranasal drug delivery

The intranasal drug delivery system is increasingly recognized as a reliable alternative to oral and parenteral routes. The nasal mucosa offers a promising pathway for systemic drug administration and helps overcome barriers to direct drug delivery to target sites. This route is also painless, non-invasive, and well-tolerated. In a study by Jursil et al. (2022) on blood-brain barrier permeability through nanoemulsions, the authors investigated the potential of nanoemulsions to cross the blood-brain barrier. The formulation, created using high-pressure homogenization, was characterized for its physicochemical properties. The study found that the optimal composition of virgin coconut oil (VCO)-based nanoemulsion, consisting of 80% water (w/v) and 10% VCO (w/v), resulted in a smaller particle size. This formulation not only crossed the blood-brain barrier but also enhanced the permeability rate in an artificial membrane system

2. Nanoemulsions for transdermal drug delivery

Drug delivery through the skin to systemic circulation is gaining interest for its convenience in treating various clinical conditions. It provides the advantage of controlled, steady-state drug delivery over an extended period, with the added benefit of self-administration, unlike the parenteral route. Patients can easily stop the drug input by removing the transdermal patch. The transparent and fluid nature of nanoemulsions offers a pleasant skin feel, and their nano-sized droplets can penetrate the skin's pores, reaching the systemic circulation for effective delivery. Nanoemulsions have been shown to enhance the transdermal permeation of many drugs compared to traditional topical formulations like emulsions and gels.

3. Nano-emulsions and parenteral drug delivery

Nanoemulsions are ideal vehicles for parenteral drug delivery due to their ability to dissolve large quantities of hydrophobic drugs, protect them from hydrolysis and enzymatic degradation, and ensure compatibility. Their advantages over larger emulsions include the absence of flocculation, sedimentation, and creaming, as well as a large surface area and free energy. These features enhance drug transport, delivery, and targeting to specific sites. In a study by Khalil et al. (2015), a nanoemulsion of a benzimidazole derivative, an anti-tumor drug, was prepared. The results showed physical stability with no phase separation or particle size alteration. The lipophilic anticancer agent chlorambucil, used against breast and ovarian cancer, was loaded into parenteral emulsions prepared by high-energy ultrasonication. In a colon adenocarcinoma mouse model, this nanoemulsion led to a higher tumor suppression rate compared to treatment with the plain drug solution, demonstrating the potential of drug-loaded emulsions as effective carriers for cancer treatment.

4. Nanoemulsions and vaccine delivery

Nanoemulsions are being explored as potential carriers for vaccines, particularly in the context of HIV prevention. Studies suggest that HIV can infect the mucosal immune system, emphasizing the need for developing mucosal immunity with nanoemulsions to fight the virus. Unlike conventional vaccine delivery methods, this oil-based emulsion is administered nasally. Ongoing research indicates that

nasal mucosa vaccination may trigger immunity in the genital mucosa, presenting a promising new strategy for HIV prevention.

Drawbacks of nanoemulsions in drug delivery system

- Stability Concerns: Nanoemulsions can suffer from issues such as phase separation or sedimentation over time, which affects their long-term stability, especially under varying storage conditions.
- High Production Costs: The preparation of nanoemulsions often involves energy-intensive processes like high-pressure homogenization, making them more expensive to manufacture compared to traditional formulations.
- Potential Toxicity: Some surfactants and other components used in nanoemulsion formulations may cause adverse effects or toxicity, raising concerns about their safety in long-term use.
- Limited Drug Loading: Nanoemulsions may not be ideal for loading high amounts of hydrophilic drugs, as their drug-loading capacity can be lower than that of other delivery systems such as liposomes.
- Formulation Complexity: Achieving a stable and effective nanoemulsion requires precise selection of ingredients, making the formulation process more complex compared to conventional drug delivery systems.
- Regulatory Hurdles: Due to their novelty, nanoemulsions may face rigorous regulatory scrutiny, requiring additional testing and approval processes, which can delay their availability in the market.

Conclusion:

Nanoemulsions are commonly utilized in pharmaceutical systems, offering numerous benefits, including the delivery of drugs, biological agents, and diagnostic substances. One of the primary applications of nanoemulsions is to mask the unpleasant taste of oily liquids. Additionally, nanoemulsions provide protection to drugs that are prone to hydrolysis and oxidation.

Nanoemulsions are increasingly utilized for the targeted delivery of anticancer drugs, photosensitizers, and therapeutic agents, offering the added benefit of prolonged drug action. These formulations are considered to be effective, safe, and capable of improving bioavailability. Ongoing research and development are expected to further advance nanoemulsion technology in the future.

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