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Research progress of nanoemulsion based drug delivery system: A review

Fu Yu

Leicester International College, Dalian University of Technology, Dalian 116024, China

ABSTRACT
Nanoemulsions, as an emerging drug delivery system, exhibit significant advantages in enhancing drug bioavailability, targeting efficiency, and reducing side effects due to their small particle size and excellent stability. Particularly in the field of intranasal drug delivery, nanoemulsions can effectively deliver drugs directly to the central nervous system, enhancing therapeutic efficacy and minimizing systemic side effects. This paper reviews the basic composition and preparation methods of nanoemulsions and summarizes their applications across various drug delivery routes, with a particular focus on the latest advancements in intranasal delivery systems. Through this technology, the potential of nanoemulsions in the treatment of neurological diseases is further expanded.

KEYWORDS
Nanoemulsions; Drug delivery system; Preparation methods; Applications

1 Introduction

With the continuous advancement of drug delivery technologies, traditional drug delivery systems face numerous challenges, particularly in enhancing drug solubility, stability, and bioavailability[1-2]. Nanoemulsions, as a novel drug carrier, have gradually emerged as an effective solution to address these issues due to their unique physicochemical properties. The small particle size and high surface activity of nanoemulsions enhance drug solubility and biocompatibility, improving drug absorption efficiency and prolonging the retention time of the drug within the body[3].

In terms of drug delivery routes, nanoemulsions have been widely applied across various delivery methods due to their flexibility and versatility, including oral, topical, transdermal, and intranasal administration. In particular, intranasal delivery, as a non-invasive route that enables rapid onset of therapeutic effects, has garnered increasing attention[4]. By precisely controlling drug release, nanoemulsions can reduce dosing frequency, enhance patient compliance, and, compared to traditional drug delivery methods, better meet the needs of patients.

This paper will explore the fundamental composition and preparation methods of nanoemulsions, as well as their applications across various drug delivery routes. Additionally, it will discuss the broad potential and future clinical applications of nanoemulsion-based drug delivery systems.

2 Construction of nanoemulsion systems

2.1 Nanoemulsion

Nanoemulsions are homogeneous dispersion systems that form spontaneously from water, oil, surfactants, and co-surfactants, with particle sizes ranging from 1 to 100 nm. Generally, nanoemulsions are classified into three types: oil-in-water (O/W), water-in-oil (W/O), and bicontinuous nanoemulsions (B.C.)[5]. Its structure is shown in Fig.1.

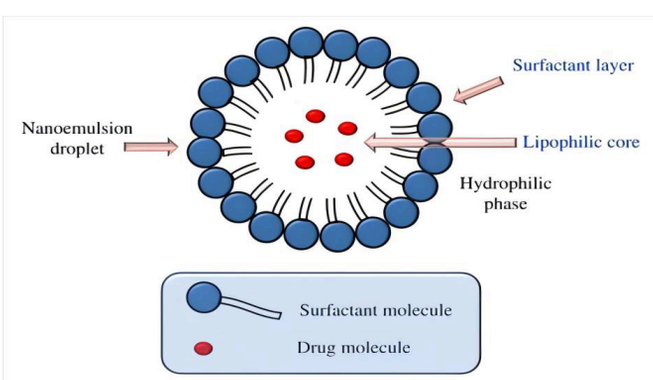

Fig.1 Schematic diagram showing structure of O/W nanoemulsion [6].

Correspondence: 2830048644@mail.dlut.edu.cn

2.2 Composition of the nanoemulsions

The selection of appropriate components is critical for the preparation of nanoemulsions, with the component structure illustrated in Figure 2. Currently, commonly used ingredients are generally safe, natural, and of low toxicity. To enhance the chemical stability of nanoemulsions, three strategies are typically employed: the incorporation of antioxidants or chelating agents, adjustment of interfacial properties, and control of environmental factors. The application of different materials in nanoemulsion preparation exhibits distinct characteristics[7]. The nanoemulsions are primarily composed of four key components:

Oils: Oils help to improve surfactant-co-surfactant interactions, thereby increasing the solubility of hydrophobic drugs in the oil droplet core. For example, oil components such as acrylic acid and triglycerides are commonly used to improve emulsion stability and drug solubility and optimize drug carrier properties[8, 9].

Surfactants: Surfactants improve the stability of emulsions by reducing the surface tension at the oil-water interface and facilitating the mixing of the oil and water phases. Typically, these surfactants are used in low concentrations. Common surfactants include propylene glycol and taurine, among others, which play a key emulsifying role in emulsions[5, 8].

Co-surfactants: Different co-surfactants can be used in conjunction with surfactants, and are selected primarily for their emulsifying effect. When surfactants are used alone, it is difficult to reduce surface tension significantly, so further reduction of surface tension is usually achieved by adding co-surfactants[5, 8].

Water: In nanoemulsions, water plays an important role as a solvent and carrier. It not only provides a suitable environment for the dispersion of surfactants and oil phases, but also helps to dissolve hydrophilic substances or drugs.

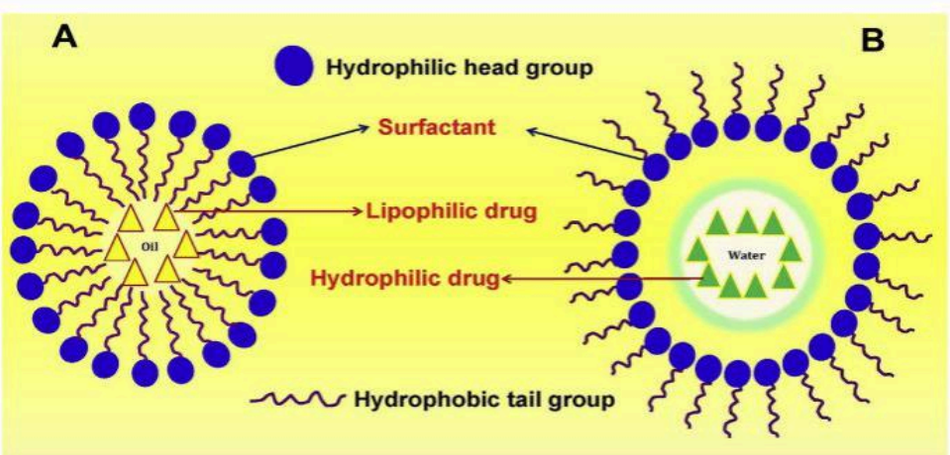

Fig.2 Structure of nanoemulsion [A] oil in water type emulsion (o/w), [B] water in oil type of emulsion (w/o) [10].

3 Route of administration system

The mode of drug administration directly affects its in vivo behavior and therapeutic efficacy. Traditional delivery modes include oral, parenteral (e.g., subcutaneous, intramuscular), and topical administration, as shown in Figure 4, which are widely used because of their proven technology and convenience. In recent years, new delivery systems such as intranasal, ophthalmic, pulmonary, and transdermal modes of drug delivery have gradually gained attention, and intranasal drug delivery in particular has been studied for its potential in brain-targeted therapies[11].

Nanoemulsions, as an efficient drug carrier, can enter the body through various routes such as oral, intravenous, non-intravenous (subcutaneous, intramuscular), topical application and pulmonary delivery. Since the droplet size of nanoemulsions is less than 1μm, it can improve the solubility and absorption of drugs and enhance bioavailability. In addition, nanoemulsions for ophthalmic drug delivery can also improve drug permeability and allow the active ingredient to act more effectively on ocular tissues[12].However, nasal administration and pulmonary delivery, are able to bypass first-pass metabolism and achieve faster drug efficacy. The transdermal route, on the other hand, utilizes the high permeability of nanoemulsions to release the drug slowly and improve the duration of treatment.

From a comprehensive point of view, there are advantages and disadvantages of different drug delivery modes, and a reasonable choice of the appropriate delivery route can optimize drug efficacy, improve therapeutic efficiency, and reduce side effects[13].

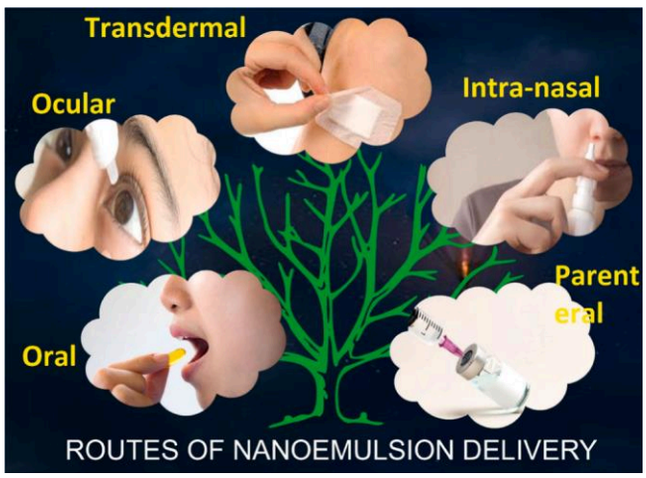

Fig.4 Illustration of different routes of administration of nanoemulsion system [14].

3.1 Oral drug delivery system

Oral drug delivery is the most common non-invasive mode of drug delivery and is widely used in the pharmaceutical field due to its convenience, cost-effectiveness and high patient compliance. However, there are limitations to this method, for example, children, the elderly or psychiatric patients may have difficulty in taking the drug due to difficulty in swallowing. In addition, some drugs are less stable in the gastrointestinal environment, making it difficult for them to be effectively absorbed, thus affecting bioavailability and therapeutic efficacy[15]. To improve the absorption of oral drugs, nanoemulsions have emerged as an effective drug delivery system. Nanoemulsions can be used to reduce the size of drug particles and enhance their gastrointestinal permeability by wet milling technique to improve the absorption efficiency.

In 2015, a Japanese team led by Shoichi Gohtani et al. proposed the preparation of O/W nanoemulsions using isothermal low-energy emulsification and studied the effect of glycerol on their formation, which is important for the preparation of oral nanoemulsions because the low-energy emulsification method reduces the energy consumption and the incorporation of glycerol optimizes the structure of the emulsions, which makes them more suitable for food and drug[16]. It was found that glycerol extends the range of emulsion formation, reduces droplet size and improves stability. It was shown that the method can be prepared directly with water at room temperature without stirring and the drop size range 15.1-2428.5 nm.

A recent study by Tiancheng Jin's team at 2025 highlights the importance of nanoemulsions in oral drug delivery, noting their ability to increase drug bioavailability, prolong the duration of drug action in the body, and improve gastrointestinal absorption. Experimental data showed that nanoemulsions significantly improved drug stability and reduced gastrointestinal degradation compared to conventional oral dosage forms. The study also explored the use of nanoemulsions in cancer, gout and allergy treatment, emphasizing their potential for targeted delivery and reduction of toxic side effects. The study provides theoretical and experimental support for the further development of nanoemulsions for oral drug delivery, while also pointing out the challenges of scale-up and stability optimization, and suggesting that future research should focus on preparation methods, stability control and regulatory approval of nanoemulsions[17].

It has been found that nanoemulsions as drug delivery systems can effectively enhance the solubility, bioavailability and stability of drugs while optimizing oral absorption, especially for difficult-to-solve drugs[18]. Globally, researchers are exploring ways to utilize the properties of nanoemulsions to improve drug formulations for enhanced efficacy. However, despite the success of nanoemulsions in drug delivery, there are still some technical bottlenecks that limit their application in oral drug delivery.

3.2 Parenteral drug delivery system

Parenteral drug delivery is an important non-oral mode of drug delivery that allows for the direct injection of drugs into the circulation, bypassing the gastrointestinal absorption step, making it one of the most effective therapeutic routes for responding to emergencies. This method is suitable for patients with rapid onset of action, poor oral absorption or impaired behavior[19]. However, some drugs limit their application in parenteral administration due to low solubility or poor stability in aqueous solutions. Nanoemulsions can effectively improve these problems. Oil-based nanoemulsions allow hydrophobic drugs to be dissolved in the oil phase and uniformly dispersed in the aqueous phase, improving solubility and stability. In addition, the small particle size and slower clearance rate of nanoemulsions allow for longer residence time in the body and improved drug utilization.

Syed A.A. Rizvi's team explored the use of nanoemulsions in parenteral drug delivery in a study in 2021, noting their

ability to significantly improve the solubility and bioavailability of difficult-to-solubilize drugs, while decreasing the clearance rate of the drug in the body and prolonging the duration of action. Experimental data showed that NE improves drug stability in the bloodstream and enhances cell membrane permeability compared to conventional formulations, resulting in easier absorption of low solubility (BCS-II), low permeability (BCS-III) and low solubility low permeability (BCS-IV) drugs[20]. This study provides theoretical and experimental support for the application of nanoemulsions in parenteral drug delivery and also highlights the challenges of formulation optimization, stability control and regulatory approval.

Nanoemulsion-loaded drugs show greater potential for parenteral drug delivery, which can improve drug solubility and bioavailability. Research has focused on preparation methods, drug loading and release control[21]. Future research will focus on improving stability, reducing toxic reactions and enabling more precise targeted drug release, with a wide range of applications, especially in targeted therapy and personalized medicine.

3.3 Transdermal drug delivery system

Transdermal drug delivery has many advantages, such as controlled release of the drug, ease of self-administration by the patient, and reduction of gastrointestinal discomfort. It has shown good clinical value in the treatment of cardiovascular and neurological diseases[22]. In order to improve the efficiency of drug absorption, it is necessary to regulate the skin barrier and rationally control the distribution of the drug in the body. Nanoemulsions allow the drug to enter the blood circulation more efficiently due to their ability to penetrate the skin pores. In addition, the formulation and carrier properties of the drug play a key role in its transdermal absorption. Since the stratum corneum restricts drug diffusion, efficient delivery is often difficult to achieve with conventional solutions or suspensions, making novel drug delivery systems a superior choice, especially for topical treatments.

Kh. Hussan Reza proposed the concept of nanoemulsion as a transdermal drug delivery system in 2011. His study showed that nanoemulsions, due to their droplet size of less than 100 nm and high surface area, can significantly improve drug transdermal penetration and provide superior drug release efficiency compared to traditional delivery systems (e.g., solid lipid nanoparticles, polymer nanosuspensions)[23]. The experimental results show that nanoemulsions can enhance bioavailability, reduce drug dosage requirements and minimize gastrointestinal side effects, and have a wide potential for application in the treatment of dermatological, analgesic and systemic diseases.

As a transdermal drug delivery system, nanoemulsions can effectively improve the transdermal absorption and bioavailability of drugs and reduce gastrointestinal side effects due to their small droplet size and stability[24]. Nevertheless, the preparation process and transdermal mechanism still need to be optimized. In the future, with technological advances, nanoemulsions are expected to play a greater role in skin therapy and drug delivery.

3.4 Ocular drug delivery system

Ocular drug delivery presents a number of challenges, mainly stemming from the unique physiological environment and pharmacokinetic properties of the eye. The structure and function of the eye make it difficult for drugs to be retained for long periods of time and absorbed efficiently, so improving the bioavailability of ocular drugs, reducing the frequency of administration and enhancing patient compliance are key objectives[25]. To overcome these problems, hydrocortisone nanoemulsions are widely used, which prolong the effect of the drug and improve therapeutic efficacy. Although ophthalmic treatments are usually non-invasive, ensuring sustained drug release and deeper absorption remains a central research challenge due to the short residence time of the drug in the eye socket[26].

In 2025, research by Avinash Gite's team proposed the use of nanoemulsions in ocular drug delivery. They noted that nanoemulsions, due to their small particle size (10-1000 nm) and high stability, are effective in prolonging the retention time and increasing the bioavailability of drugs in the eye, thereby reducing the frequency of administration and enhancing efficacy. For example, nanoemulsions can be used to deliver drugs for glaucoma (e. g., Timolol and Latanoprost) by improving corneal penetration and duration of action[27]. In addition, the composition of the nanoemulsion (e.g., oil phase, emulsifier and co-emulsifier) plays a key role in the stability and solubility of the drug. These findings provide a theoretical basis for the design of more efficient ocular drug delivery systems, which can help to improve the effectiveness of ocular disease treatment and patient compliance.

With the rapid growth of the ophthalmic drug market and the increasing demand for innovative therapeutic solutions, especially in recent years, the field of ophthalmic therapeutics is facing unprecedented opportunities. Although manufacturers have invested significant resources in the development of non-invasive ophthalmic formulations, there is still a large gap in demand for multi-active ophthalmic drug formulations, especially combination therapy products[28]. Ophthalmic nanoemulsions, as an innovative drug delivery system, offer a new direction to solve this problem by virtue of their superior drug stability, bioavailability and sustained release.

3.5 Intranasal drug delivery system

As an emerging drug delivery system, nanoemulsions have demonstrated broad application prospects in the field of nasal drug delivery. Through their nano-size and stability, nanoemulsions can effectively enhance the residence time of drugs in the nasal cavity and accelerate the penetration of drugs through the nasal mucosa, thus improving the bioavailability of drugs[29]. What's more, nanoemulsions are able to deliver drugs directly to the brain by bypassing the blood-brain barrier, showing unique advantages especially in the treatment of central nervous system diseases. Nanoemulsions can also protect the drug from the external environment, enhancing its stability and efficacy. With the further development of the technology, nanoemulsion drug delivery system is expected to become an important tool in the field of nasal drug delivery, which will promote the progress of CNS disease treatment[30].

Gulshan Sharma's team in 2024 successfully overcame the problems of blood-brain barrier limitations, low drug bioavailability and poor delivery efficiency in Parkinson's disease treatment by combining nasal drug delivery with nanoemulsion technology. The nanoemulsions they developed (e.g., Ibuprofen nanoemulsions with a particle size of 46.3 ± 2.28 nm) were able to significantly increase the concentration of the drug in the brain and reduce the distribution of the drug in the systemic circulation, thereby reducing systemic side effects. Meanwhile, the sustained release properties of the nanoemulsions (e.g., Selegiline nanoemulsions) further enhanced drug efficacy and improved the behavioral deficits in animals with Parkinson's disease models[31].

The main contributions of this study are reflected in the following: on the one hand, the combination of nasal drug delivery and nanoemulsion technology improves drug efficacy, reduces drug dose and administration frequency, and thus enhances patient compliance; on the other hand, the nanoemulsion can reduce the distribution of the drug throughout the body, reduce systemic side effects, and provide a safer and more effective therapeutic pathway for Parkinson's disease. These studies not only provide new ideas for the treatment of Parkinson's disease, but also lay a theoretical foundation for clinical application, which has important scientific and clinical value[31].

Nanoemulsion-loaded drug delivery via the nasal cavity shows great potential in the treatment of central nervous system diseases. Their small size and stability help to improve drug bioavailability, bypass the blood-brain barrier, reduce side effects and enhance therapeutic efficacy[32]. Despite challenges such as stability and production processes, nanoemulsions are expected to become an effective treatment for neurodegenerative diseases as technology develops.

4 Conclusion

Nanoemulsion drug delivery systems have shown promising applications in the field of drug delivery, especially in the treatment of central nervous system diseases. Nasal drug delivery combined with nanoemulsion technology not only improves drug delivery efficiency, but also effectively reduces systemic side effects. Despite the challenges of stability and production process, with the advancement of technology, nanoemulsions are expected to become an important drug delivery method in the future, especially in the treatment of neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. Future research should focus on optimizing preparation methods, improving product stability, and solving problems in clinical applications to promote the widespread use of this technology.

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