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Nanoemulgel: Introducing a Novel Method for Delivering Substances Topically

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Abstract: The integration of a nanoemulsion system into the hydrogel matrix has a positive impact on skin penetration. Nanoemulgels are formulations that combine nanoemulsion with hydrogel. Nanoemulgel enhances the stability of the nanoemulsion formulation by reducing surface and interfacial tension, resulting in increased viscosity of the aqueous phase. Due to its higher viscosity compared to the nanoemulsion system, nanoemulgel is also referred to as hydrogel-thickened nanoemulsions. Nanoemulgel is highly effective for delivering hydrophobic medications. It offers greater drug loading capacity, improved solubilizing efficiency, enhanced bioavailability through superior permeability, and controlled drug release. As a result, it serves as an efficient alternative delivery technique for treating various disorders. Nanogels provide protection to biomolecules such as enzymes and genetic material, shielding them from destruction. Their macromolecular characteristics enable small molecules to circulate for longer periods and act as a versatile platform for combining therapeutic compounds. The utilization of nanoemulgel has seen a rise in recent years due to its improved acceptability among patients, attributed to its non-greasy nature, convenient spreadability, easy application, and favorable therapeutic and safety profile. Despite facing various challenges, nanoemulgel shows great promise as the primary topical delivery method for lipophilic medications in the future.

Keywords: Nanoemulgel, Nanoemulsion, Bioavailability

I. INTRODUCTION

Throughout history, emulsions have played a crucial role in drug delivery systems. Due to their unique ability to not swell in other solid dosage forms, our ancestors had no choice but to rely on emulsions to administer medications to the elderly and children. Over time, significant advancements have been made in emulsion technology to enhance its safety, effectiveness, patient adherence, and minimize potential side effects. Nowadays, emulsion preparations are not only administered orally but also transformed into gel formulations for topical application [1].

The concept of combining emulsion and gel in a novel way has been devised to create nanoemulgel preparations. This innovative approach has gained widespread acceptance globally, as it serves both medicinal and cosmetic purposes. Scientists have recently taken a keen interest in developing nanoemulgel preparations due to their ability to provide sustained effects. The entire system acts as a reservoir for the drug, allowing for controlled release over an extended period. The release mechanism is influenced by factors such as the crosslink density and the type of polymer chains in the network [2]. The ability of a drug to diffuse through the vehicle and penetrate the skin barrier plays a crucial role in its therapeutic release.

Topical administration systems, which act as drug reservoirs, have an impact on the release of drugs from the inner phase to the outer phase and eventually onto the skin. The release mechanism is influenced by the density of crosslinks and the type of polymer chains in the network [3]. The ability of a drug to diffuse out of the vehicle and pass through the barrier affects its ability to enter the skin and release therapeutic molecules. The therapeutic effect of the drug is achieved by releasing it in droplet form from the gel network, allowing it to reach the stratum corneum, penetrate it, and enter the systemic circulation [4].

The process of creating nanoemulgel involves a straightforward method similar to emulsions such as water in oil and oil in water emulsion, but with a gel foundation. Nanoemulgels present an attractive option for drug delivery due to their dual characteristics, combining a nanoscale emulsion with a gel base in one formulation. This allows the oil droplets to effectively penetrate the stratum corneum of the epidermis, bypassing the hydrophilic phase of nanoemulsions and delivering the medication molecules directly to the stratum corneum [5]. The nanoemulgel offers numerous advantages compared to other topical formulations that have been researched.

One notable benefit is its ability to bypass first-pass metabolism, making it a preferred option. Patients find it easy to use and it is completely safe for self-medication. Moreover, discontinuing the medication is a simple process. The nanoemulgel is well-tolerated by the skin and has been proven to be an effective, well-regulated, and durable method of administering medication [6].

ADVANTAGES OF NANOEMULGEL

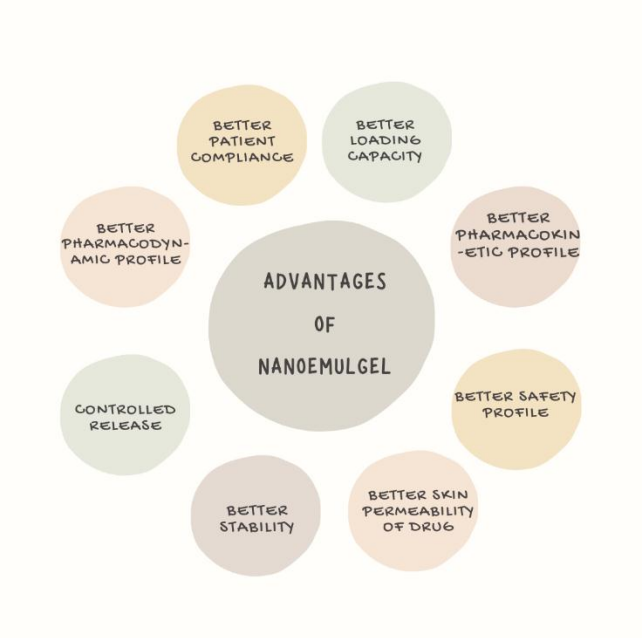

Fig.1: Advantages of Nanoemulgel

EMULSION-BASED NANO-CARRIER IN TOPICAL APPLICATION

The conventional transdermal delivery system faces a significant challenge in delivering lipophilic drugs due to their low therapeutic potential and poor skin permeability capability. Researchers suggest that the utilization of nanoscale-sized transdermal preparations can enhance drug permeability by disrupting the lipid bilayer of the skin [7] and prolonging the drug's retention time at the targeted site [8, 9].

Nanoemulsion has the potential to serve as an effective carrier for hydrophobic drugs due to its superior thermodynamic stability and enhanced ability to solubilize drugs compared to emulsion and other dispersion systems. Additionally, nanoemulsion boasts a longer shelf life and requires minimal external energy during the manufacturing process [10]. This dispersed system comprises nanoscale-sized droplets (with a diameter ranging from 20 to 200 nm) consisting of an oil phase and water phase, which are stabilized by a suitable surfactant.

The drug is trapped within the core, which is surrounded by a layer of emulsifier. In general, when a nanoemulsion is used as a carrier for delivering a lipophilic drug, [11] permeation enhancers are not necessary. This is because nanoemulsions have a lower tendency for phase separation compared to regular emulsions, making them more stable [12]. Several studies have shown that the permeation of drugs into the skin is better with nanoemulsion delivery systems compared to conventional ointments [13], creams [14], gels [15], and emulsions [16]. The type of nanoemulsion, whether it is oil-in-water or water-in-oil, determines its ability to solubilize both hydrophobic and hydrophilic drugs within its structure [17].

Despite numerous benefits, nanoemulsion faces challenges such as limited spreadability, low viscosity, and inadequate skin retention [18]. Consequently, the practical use of topical nanoemulsion is limited [19]. Scientists have addressed this issue by transforming nanoemulsion into nanoemulgel through its integration into a gel matrix.

NANOEMULGEL AS TOPICAL DRUG DELIVERY SYSTEM

Nanoemulgel is the combination of two systems: nanoemulsion system and hydrogel system. Each system has its own drawbacks. For instance, nanoemulsion has limited spreadability and poor retention, while hydrogels cannot incorporate lipophilic molecules [20, 21]. Nanoemulgel consists of various types of polymeric materials, surfactants, and fatty substances of natural, synthetic, and semisynthetic origin, with droplet sizes ranging from 5 to 500 nm [22].

Nanoemulgel possesses the ability to surpass the constraints of both systems. The oil phase of the nanoemulsion effectively dissolves the lipophilic drug, which is subsequently combined with a hydrogel base to create nanoemulgel [23]. This innovative formulation allows for the integration of lipophilic drugs into a hydrogel while simultaneously enhancing the viscosity of the nanoemulsion.

In the context of transdermal drug delivery, nanoemulgel serves as a storage unit for the drug. Initially, the drug is discharged from the inner phase to the outer phase and subsequently reaches the skin surface. Upon application to the skin, oily droplets are discharged from the gel matrix of nanoemulgel, which then infiltrate the skin through the stratum corneum, facilitating the direct delivery of the drug moiety [19]. The process of drug release is contingent upon the crosslink density and the composition of the polymer chain network [24].

Fig.2: Numerous emulgels have been introduced in the market for topical application

SCOPE OF NANOEMULGEL FOR TOPICAL DELIVERY

Nanoemulgel is a crucial component in the topical delivery system, serving a significant purpose. The potential applications of nanoemulgel in the topical delivery system are as follows: Due to its superior absorption capabilities, improved pharmacokinetic profile, and consequently heightened therapeutic effectiveness, topical nanoemulsion gel can be considered a more favorable substitute for conventional lipophilic drug formulations. The enhanced patient acceptance of the nanoemulgel formulation, in comparison to other topical administration options, can be attributed to its reduced stickiness and superior spreading qualities [25-34]. Topical nanoemulgels offer a more efficient and convenient approach to medication administration.

Patient adherence is improved due to the gel's non-greasy qualities, resulting in higher compliance rates. The absence of an oily base enhances medication release compared to other formulations. By integrating Nanoemulsion into the gel matrix, issues such as creaming and phase separation commonly associated with traditional emulsions are resolved, along with increased stability. In certain topical conditions, a nanoemulsion-loaded gel proves to be more advantageous [35-44].

Nanoemulsion-gel formulations have the potential to revolutionize the delivery of hydrophobic medications in the future. Many drugs used to treat skin infections are hydrophobic in nature, and these treatments can be effectively administered as nanoemulgels. In this innovative approach, the drug is integrated into the oil phase of the nanoemulsion and then combined with the gel base. Despite a few challenges, nanoemulgel holds great promise as the primary method for delivering lipophilic medicines topically in the future [45, 46]. Nanoemulgel has been found to be a highly effective medium for administering hydrophobic medications. It serves as a powerful alternative delivery system in the treatment of various diseases, offering a high drug loading

capacity thanks to its increased solubilizing effectiveness. Additionally, it enhances bioavailability by improving permeability and possesses the ability to regulate drug release.

The efficacy of nanoemulgel preparation in treating acne, pimples, psoriasis, fungal infections, osteoarthritis, and rheumatoid arthritis inflammation has been proven to be significantly higher [47]. It is suitable for administering medication ophthalmically, vaginally, dentally, and for nose-to-brain delivery to treat a range of local and systemic diseases like alopecia, periodontitis, and Parkinson's disease, as well as for transdermal application.

Nanoemulgel has found application in the cosmetics industry as a UV absorber, effectively safeguarding the skin against sunburn. This technology exhibits significant promise in the treatment of various local and systemic ailments. While certain nanoemulgel preparations are already available in the market, others necessitate further clinical testing before they can be made accessible to the public [48-69].

II. Conclusion:

Nanoemulgels with topical application have proven to be a superior choice for an efficient and convenient drug delivery method. A significant number of medications utilized for treating skin infections are hydrophobic. These drugs can be efficiently administered through Nanoemulgels by initially incorporating them into the oil phase of the nanoemulsion and then blending them with the gel base. Despite encountering some challenges, nanoemulgel stands a strong possibility of becoming the primary topical delivery system for lipophilic medications in the upcoming years. It provides a range of delivery options for topical medications used to treat various ailments. These options include the ability to adjust drug release and achieve high drug loading due to improved solubilizing efficiency. Apart from transdermal application, it can also be used for ocular, vaginal, dental, and nose-to-brain delivery of medicine. This versatile delivery system is effective in treating local and systemic disorders such as alopecia, periodontitis, and Parkinson's disease.

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