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Review Article

Micro Emulsion Gel for Treatment of Bacterial Infection by Transdermal Route

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Abstract

Micro emulsions are thermodynamically stable, transparent, colloidal drug carrier system extensively used by the research scholars for effective drug delivery across the skin. These are the spontaneous isotropic mixture of lipophilic and hydrophilic substances stabilized by suitable surfactant and co-surfactant. They are easy to fabricate having long-term stability, enhanced solubilization; biocompatibility, skin-friendly appearance and affinity for both the hydrophilic and lipophilic drug substances make it superior for skin drug delivery over the other carrier systems. The transdermal administration of most of the active compounds is impaired by limited skin permeability due to the presence of skin barriers to overcome this problem, micro emulsion represents a cost-effective and convenient drug carrier system which successfully delivers the drug to and across the skin. In the present review, we compiled various attempts made in last few years, utilizing the micro emulsion for dermal and transdermal delivery of various drugs. The review emphasizes the potency of micro emulsion for topical and transdermal drug delivery and its effect on drug permeability.

Naproxen is a Non-Steroidal Anti-Inflammatory Drug (NSAID) of the propionic acid class and is commonly used for relief of a wide variety of pain, fever, swelling and stiffness caused by conditions including migraine, osteoarthritis, kidney stones, rheumatoid arthritis, psoriatic arthritis, gout, ankylosing spondylitis, menstrual cramps, tendinitis, and bursitis.

Levofloxacin is a fluoro quinolone antibacterial agent with a broad spectrum of activity against Gram-positive and Gram-negative bacteria and atypical respiratory pathogens. It is active against both penicillin-susceptible and penicillin-resistant Streptococcus pneumoniae. Efficacy of levofloxacin in the treatment of infections mainly respiratory tract, genitourinary tract, skin and skin structures are been already popular as studies done in previous years.

Keywords: Micro emulsions; Naproxen; Levofloxacin; Gram-negative bacteria; Gram-positive bacteria; Transdermal route

Introduction

One of the most promising routes of drug administration is through skin which offers an alternative and attractive route of drug administration over the oral and parenteral drug delivery. Sorely it by-passes the hepatic first-pass metabolism and overcomes the limitations of oral drug delivery like GI degradation, hepatic clearance, etc. At the same time, it offers a non-invasive and convenient route of drug administration hence preferred over the parenteral route [1]. Despite of many advantages, the skin drug delivery has several limitations including poor drug permeation hence low bioavailability due to the presence of skin barrier (stratum corneum) [2,3]. As we know skin is the primary defense layer of the body, therefore it considers all the drug and excipients as an external component and restricts its entry inside the body, offering a significant obstacle to skin drug delivery.

As we know human skin consists of three layers of epidermis, dermis, and subcutaneous tissues, epidermis is the outermost layer of the skin, comprises of five layers; 1) stratum corneum, 2) stratum lucidum, 3) stratum granulosum, 4) stratum spinosum and 5) stratum germinativum respectively from outside to inside. This layer consists of keratinocytes, responsible for the production of keratin. The dermis is the middle layer made of collagen fibers. It consists of the sebaceous gland, hair follicles, sweat gland, nerve endings, and blood vessels. This layer ends in the subcutaneous tissues comprises fat globules and adipose tissues [4–6].

Among all the skin layers, the stratum corneum is the primary barrier for drug permeation. However, there are some provisions for transfer of natural compound across the skin including the intercellular, follicular and intracellular pathway. The intercellular path is suitable for the transmission of hydrophilic drug substances, on the other hand the follicular or trans appendageal path provide the direct and rapid transfer of contents to the in fundibulum region while the intracellular transport facilitates the permeation of lipophilic drug substances [7,8]. Therefore, to enhance the drug permeation across the skin and improve the therapeutic efficacy of the drug, we need a suitable carrier system that is highly desirable. In this sequence, micro emulsion represents a potential drug carrier system for trans-

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dermal as well as topical application of the drug to improve the drug transfer across the skin by crossing the skin barriers.

The term microemulsion or nanoemulsion used for a thermodynamically stable or kinetically stable, clear dispersion of two liquid phases in which one is water, and other is oil; stabilized by an interfacial film of surfactant and co-surfactant [9,10]. According to the study done by Danielsson and Lindman "microemulsion are a system of water, oil, and amphiphile which is a single optically isotropic and thermodynamically stable liquid solution" [11]. These are the versatile carrier with their various remarkable properties like enhanced bioavailability of the poorly soluble drugs, high absorption, and permeation because of very low surface tension and small droplet size as well as cost-effective approach [12,13]. We can say that the microemulsion is the emulsions having droplet size less than 0.1µm. These droplets are invisible because of their small size (much smaller than the size of the wavelength of visible light (400–800 nm), they are unable to reflect the light and are not visible through the optical microscope which makes the microemulsion system transparent [14].

As a drug carrier microemulsion represents a suitable system for almost all kind of drugs including both the lipophilic and hydrophilic moieties [9,12,15,16]. Usually, the ternary phase diagram was used to characterize the microemulsion [17,18]. Oil, water, surfactants are the components representing three edges of the ternary phase diagram. Co-surfactant used in microemulsion are grouped with surfactant at a fixed ratio and treated as pseudo-component [18,19].

Mechanism of drug permeation and permeation enhancer

As skin is the outermost covering of the body, primarily functions as a protective layer which protects the individual from the harmful external stimuli like light, temperature, radiation, etc. and restricts the entry of pathogen or any other foreign material inside. Such defensive attribute of skin makes the topical or transdermal drug delivery very difficult. As to improve the drug permeation across the skin and enhance the percutaneous absorption there are various novel strategies which have been adapted including the vehicle system, permeation enhancer, novel drug carrier system, transdermal patches, etc. All these strategies enhance the drug permeation by temporary destructing the stratum corneum layer [20]. The micro emulsion reduces the interfacial tension at the skin surface and solubilizes the drug. The permeation enhancer sometime surfactant or lipid, used in the formulation may dissolve or perturbates the lipid bilayer structure of the stratum corneum. By this way, it minimizes the barrier function of the stratum corneum and opens a pore or passage for drug transfer across skin [2,21].

One of the drug named Levofloxacin can be formulated as a microemulsion as it is FDA-approved for the treatment of various bacterial infections including nosocomial pneumonia, community-acquired pneumonia, acute bacterial rhinosinusitis, acute bacterial exacerbation of chronic bronchitis, acute bacterial prostatitis, acute pyelonephritis, urinary tract infection, skin or skin structure infections, prophylaxis, and treatment of plaque due to Yersinia pestis, and to reduce the incidence of disease progression of inhalational anthrax.

Levofloxacin is a broad-spectrum, third-generation fluoroquinolone antibiotic used to treat bacterial infections. Levofloxacin is a safe and effective medicine on the World Health Organization's essential medicines list. It was patented in 1987 and subsequently received FDA approval in 1996 for medical use in the United States [22].

As a promising anti bacterial agent Levofloxacin directly inhibits bacterial DNA synthesis, promoting the breakage of DNA strands by inhibiting DNA-gyrase in susceptible organisms, which inhibits the relaxation of super coiled DNA. The drug is available both for oral tablets and solution and intravenous administration. Levofloxacin is not available for administration through intramuscular, intrathecal, or subcutaneous routes. The marketed oral dosage strengths for levofloxacin are 250 mg, 500 mg, and 750 mg [23].

Another drug of choice can be Naproxen which is a non-steroidal mitigating medication (NSAID) of the propionic acid class and is generally utilized for help of a wide mixed bag of agony, fever, swelling and solidness [24]. It is the favored NSAID for long haul use in individuals with a high danger of cardiovascular entanglements, it offers a moderate danger of bringing on stomach ulcers as contrasted and ibuprofen, which is okay, and indomethacin, which is high hazard [25]. Keeping in mind the end goal to lessen the danger of stomach ulceration, it is frequently joined with a proton-pump inhibitor (a pharmaceutical that decreases the generation of stomach corrosive) amid long haul treatment.

Naproxen, when given orally can cause gastrointestinal problems, such as heartburn, constipation, diarrhea, ulcers and stomach bleeding. Another disadvantage associated with Naproxen is that it undergoes extensive first pass metabolism due to which high dose has to be administered [26]. This again reduces the patient compliance.

Microemulsions are thermodynamically stable and optically isotropic liquid solutions of oil, water and amphiphile. Microemulsions are one of the best candidates as novel drug delivery system because of their long shelf life, improved drug solubilization with ease of preparation and administration [27]. Therefore, to overcome these disadvantages, it is favorable to administer the drug through an alternative route, which is transdermal route. Microemulsion gels are a type of delivery systems in which the drug can be easily administered and absorbed. Topical microemulsion gel shows controlled drug release property. The microemulsion gel could be an effective alternative vehicle for delivering the drug through topical route to avoid side effects associate with oral route [28]. Moreover, this can be applied at the site of action and thus the dosage form becomes site specific.

Conclusion

As we can state that microemulsion are novel carriers provides a superior alternative tool for drug delivery than the simple conventional as well as from the many other novel drug delivery carriers because of its small globular size, high penetration power, increased dissolution rate, improved bioavailability, ease of preparation, stability, capacity to deliver hydrophilic and lipophilic drugs. It also gives potential to provide both lipophilic as well as hydrophilic the drugs of all the categories like anti-cancerous, anti-tubercular, anti inflammatory, antipyretic, anti-psychotic, anti-depressant, anti-anginal and many more.

Microemulsion has also gained the importance because of their versatile nature and successful delivery by various routes like oral, nasal, ocular, topical and parenteral but researchers and industries need to focus their study on patents and marketed products of microemulsions which few are very and require more concentration. After reviewing all the research articles, we came to a favorable inference that by barring all the challenges microemulsion emerges as a promising carrier system to cross the skin barrier and potentially delivers the drug inside.

The present review work concludes that adverse effects of the drug can be reduced if delivered through topical route. Naproxen, a NSAID was selected as the model drug along with Levofloxacin which is a broad-spectrum, third-generation fluoroquinolone antibiotic used to treat bacterial infections. When given orally several G.I. interferences are observed. An attempt was done to formulate microemulsion loaded gel for topical delivery of drug. The particle size was reduced to micro dimensions to facilitate better permeation of the drug through the topical route.

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