

Microemulsion Gel for Treatment of Bacterial Infection Using Transdermal Route - A Review

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ABSTRACT

As we know microemulsions are thermodynamically stable, transparent, colloidal drug carrier system extensively used for effective drug delivery across the skin. These emulsions 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 lyophilic drug substances making it superior for skin drug delivery over the other carrier systems. As the previous literature studies done, they show that 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, microemulsion 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 microemulsion for dermal and transdermal delivery of various drugs. This review emphasizes the potency of microemulsion for topical and transdermal drug delivery and its effect on drug permeability.

One of the NSAID Naproxen of propionic acid class, 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 can be a good choice of studies along with Levofloxacin which is a fluoroquinolone antibacterial agent having broad spectrum of activity against both Gram-positive and Gram-negative bacteria including a typical respiratory pathogens, active against both penicillin-susceptible and penicillin-resistant *Streptococcus pneumoniae*, can be used for better results.

Keywords: Microemulsions, Naproxen, Levofloxacin, Gram-negative bacteria, Gram-positive bacteria, Transdermal route

INTRODUCTION

As we have different routes of administration one of the best routes having good patient acceptability is transdermal route which offers an alternative and attractive route of drug administration over the oral and parenteral drug delivery. Not only it by-passes the hepatic first-pass metabolism it also overcome the limitations of oral drug delivery including GI degradation, hepatic clearance, etc. Despite of that, it also offers a non-invasive and convenient route of drug administration hence preferred over other routes [1].

As the two sides of a drug delivery system transdermal routes also has several limitations including poor drug permeation hence low bioavailability due to the presence of skin barrier (stratum corneum) [2,3]. During study of Human skin anatomy, it consists of three layers epidermis, dermis, and subcutaneous tissues, in which 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 also consists of keratinocytes which is responsible for the production of keratin. Moving to dermis that is the middle layer made of collagen fibers consisting of the sebaceous gland, hair follicles, sweat gland, nerve endings, and blood vessels. Finally, layer ends in the subcutaneous tissues comprises fat globules and adipose tissues [4-6].

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The outermost layer stratum corneum is the primary barrier for drug permeation, providing some provisions for transfer of natural compound across the skin including the intercellular, follicular and intracellular pathway. On the other side intercellular path is suitable for the transmission of hydrophilic drug substances and trans appendageal path providing the direct and rapid transfer of contents into the fundibulum region, while the intracellular transport facilitates the permeation of lipophilic drug substances [7,8]. One of the methods to overcome the problem is to enhance the drug permeation across the skin and improving the therapeutic efficacy of the drug, for the same we need a suitable carrier system that is highly desirable. In the same context we can say that microemulsion represents a potential drug carrier system for transdermal as well as topical application of the drug to improve the drug transfer across the skin by crossing the skin barriers.

Out of the many carries available we can say that microemulsion or nano emulsion is thermodynamically stable as well as kinetically stable system. They are clear dispersion of two liquid phases in which one is water, and other is oil which are stabilized by an interfacial film of surfactant and co-surfactant [9,10]. According to the previous literature we can define microemulsion as system of water, oil, and amphiphile which is a single optically isotropic and thermodynamically stable liquid solution [11]. Microemulsions comprise of 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]. The term microemulsion is just because the system is having droplet size less than 0.1 μm and 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].

Microemulsion represents a suitable system for almost all kind of drugs including both the liophilic and hydrophilic moieties [9-16], initially we can use the ternary phase diagram 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

Drug penetration from transdermal route is a challenge in many aspects, 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; to improve the drug permeation across the skin and enhance the percutaneous absorption we can use various novel strategies including the vehicle system, permeation enhancer, novel drug carrier system, transdermal patches, etc. Commonly these strategies enhance the drug permeation by temporary destructing the stratum corneum layer [20]. On the other hand microemulsion reduces the interfacial tension at the skin surface and solubilizes the drug, we can add permeation enhancer mainly surfactant or lipid in the formulation that may dissolve or perturbates the lipid bilayer structure of the stratum corneum minimizing the barrier function of the stratum corneum and opens a pore or passage for drug transfer across skin [21].

One of the FDA-approved API named Levofloxacin can be a good choice when formulated as a microemulsion 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*. [22].

As a promising anti-bacterial agent Levofloxacin which directly inhibits bacterial DNA synthesis, promoting the breakage of DNA strands by inhibiting DNA-gyrase in susceptible organisms, inhibiting the relaxation of super coiled DNA. [23].

Levofloxacin in combination with Naproxen which is also a non-steroidal mitigating medication (NSAID) of the propionic acid class can be excellent combination as Naproxen is used to treat 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 offering a moderate danger of bringing on stomach ulcers as contrasted and ibuprofen, which is okay, and indomethacin, which is high hazard [25].

Despite of several advantages' naproxen, when given orally can cause gastrointestinal problems, such as heartburn, constipation, diarrhea, ulcers and stomach bleeding also undergo extensive first pass metabolism due to which high dose has to be administered [26], reducing the patient compliance.

Out of many available drug carriers we can say microemulsions offers many advantages as they are thermodynamically stable, optically isotropic liquid solutions of oil, water and amphiphile. This carrier system is one of the best candidates as novel drug delivery system offering 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].

CONCLUSION

Despite of several suitable carries available for drug delivery, 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, anti-pyretic, anti-psychotic, anti-depressant, anti-anginal and many more.

This system 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.

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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