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Biomedical applications of microemulsion through dermal and transdermal route

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ABSTRACT

Microemulsions are thermodynamically stable, transparent, colloidal drug carrier system extensively used by the scientists for effective drug delivery across the skin. It is a spontaneous isotropic mixture of lipophilic and hydrophilic substances stabilized by suitable surfactant and co-surfactant. The easy fabrication, 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 topical administration of most of the active compounds is impaired by limited skin permeability due to the presence of skin barriers. In this sequence, the microemulsion represents a cost-effective and convenient drug carrier system which successfully delivers the drug to and across the skin. In the present review work, we compiled various attempts made in last 20 years, utilizing the microemulsion for dermal and transdermal delivery of various drugs. The review emphasizes the potency of microemulsion for topical and transdermal drug delivery and its effect on drug permeability.

1. Introduction

The drug delivery through skin offers an alternative and attractive route of drug administration over the oral and parenteral drug delivery. 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 is a non-invasive and convenient route of drug administration hence preferred over the parenteral route [1]. In spite of such 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 skin is the primary defense layer of the body, henceforth it considers all the drug and excipients as an external component and restricts its entry inside the body. This phenomenon is a significant obstacle to skin drug delivery. The human skin consists of three layers of epidermis, dermis, and subcutaneous tissues. The 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 (Fig. 1) [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. The follicular or transappendageal path provide the direct and rapid transfer of contents to the infundibulum region while the intracellular transport facilitates the permeation of lipophilic drug substances (Fig. 2) [7,8]. To enhance the drug permeation across the skin and improve the therapeutic efficacy of the drug, a suitable carrier system is highly desirable. In this sequence, 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.

The term microemulsion or nanoemulsion used for a

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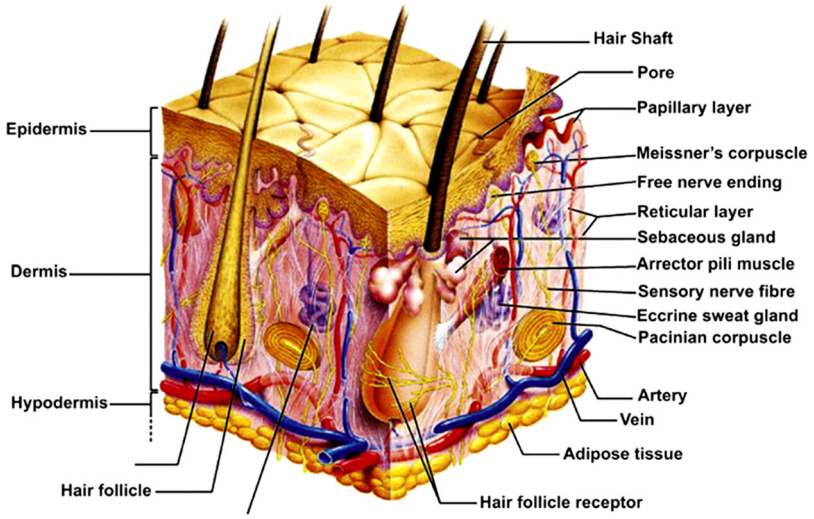

Fig. 1. Structure of skin elucidating the main components of the epidermis, dermis, and hypodermis (adopted from Alexander et al. 2012).

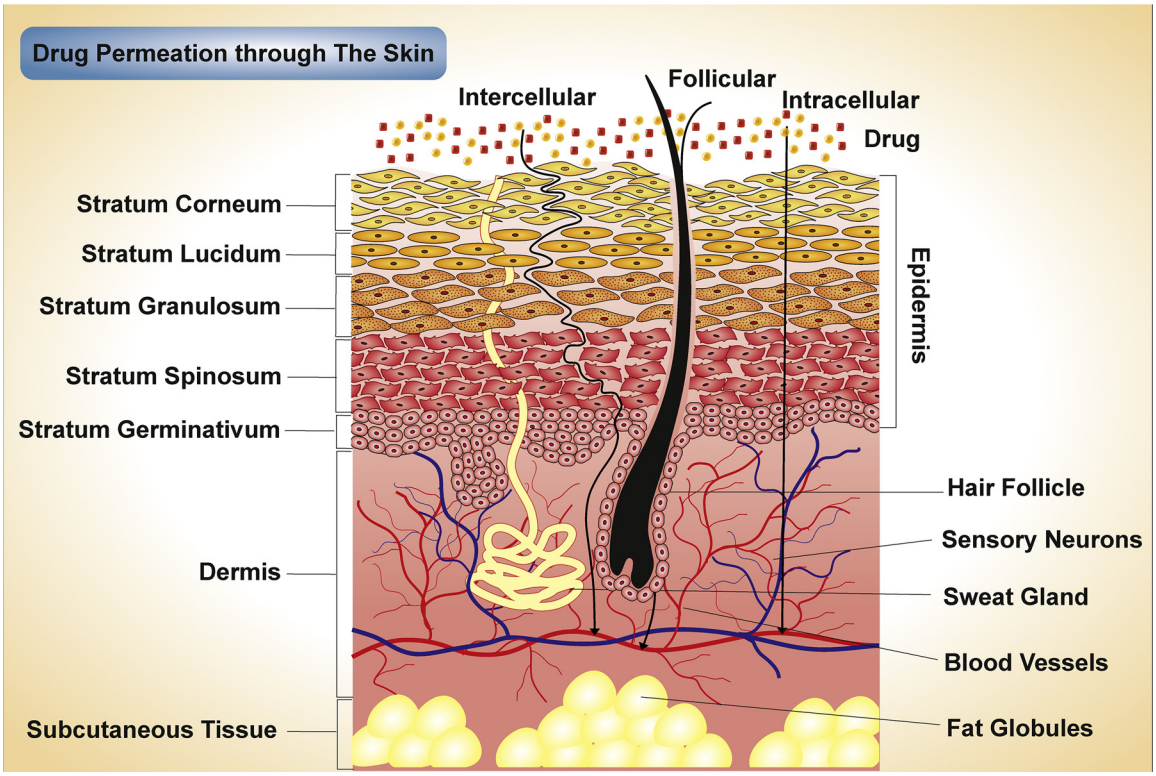

Fig. 2. The graphics illustrate various pathways of drug penetration through different layers of skin including intracellular, intercellular and follicular pathways.

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 Danielsson and Lindman "microemulsion are a system of water, oil, and amphiphile which is a single optically isotropic and thermodynamically stable liquid solution" [11]. The microemulsion is a 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]. Basically, the microemulsion is the emulsions having droplet size less than 0.1 μm. 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 drug carrier 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].

2. Mechanism of drug permeation and permeation enhancer

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 restrict the entry of pathogen or any other foreign material inside. Such defensive

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