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Particulate Drug Delivery Systems in Dermal Applications

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Physical form of drug delivery systems can be molecular or particulate. One of the limitations of molecular systems is loading of drug. In contrast, particulate delivery systems can carry a large number of drug molecules in one entity (1). A high potential for drug delivery has been attributed to particulate drug carriers that show promise to obtain systems with optimized drug loading, release properties and low toxicity. The principal factors involved in the localization and/or percutaneous absorption of substances are the properties of the drug, the tissue and the used vehicle. Alteration in chemical structures may lead to alteration in biological activity and there are limitations to the manipulation of the physicochemical properties of the active ingredients as well as the skin. Therefore, the best chance to alter the fate of the topically applied drug is to manipulate the physicochemical properties of the vehicle. Bangham first discovered liposomes in the early 1960s. They were envisioned as ideal drug delivery systems because of their high degree of biocompatibility. They were first shown to be of potential value for topical therapy by Mezei in 1980 (2) and entered the market in 1986 in the cosmetic formulation and the first therapeutically using lipid vesicles on the skin was commercialized shortly before 1990 and contained the antimycotic agent, econazole. During the past decades, there has been wide interest in exploring new techniques to increase drug absorption through skin. Intensive research led to the introduction and development of a new class of lipid vesicles, the highly deformable (elastic or ultraflexible) liposomes that have been termed Transfersomes®, which were first introduced by Cevc in the early 1990s. Elasticity is generated by incorporation of an edge activator in the lipid bilayer structure (3). Ethosome is another novel lipid carrier, developed by Touitou, and it is composed of phospholipid, ethanol and water. Ethanol allows for better solubility of many drugs and also confers a surface negative charge to the liposome which causes high encapsulation efficiency for a wide range of molecules. Ethanol is a well-known permeation enhancer and studies showed that permeation enhancement from ethosomes are much greater than ethanol alone. A synergistic mechanism is suggested between ethanol and vesicle and skin lipids (4). Lipid nanoparticles (solid lipid nanoparticles) were introduced in 1991 and made of solid pure lipids. Their enhanced skin penetration is due to an increase in skin hydration caused by occlusive film formed on skin surface (5). Nano-structured lipid carriers are next generation of lipid nanoparticles, composed of mixture of solid lipids with liquid lipids which leads to the production of an irregular structure resulting in improved drug maintenance and release properties (5). Lipid drug conjugates (LDC) are another class of lipid nanoparticles. Water soluble molecules are transferred to non-water soluble ones by covalent linkage with lipids and produce a lipophilic compound named LDC which has the ability to transform into nanoparticles by high-pressure homogenization (6). Research is still being done on a variety of aforementioned systems and among pharmaceutical companies active in this area, the following can be named:

- IDEA AG (Munich, Germany) has focused on transfersomes and one of its products with the brand name of Diractin® containing ketoprofen has entered the Swiss pharmaceutical market.
- NTT (novel therapeutic technology) in collaboration with University of Jerusalem in US is studying on ethosomes.
- Pharmasol GmbH (Berlin, Germany) has focused on Nano lipid particles.

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