Overcoming the Stratum Corneum: The Modulation of Skin Penetration

A Review

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Abstract
It is preferred that topically administered drugs act either dermally or transdermally. For that reason they have to penetrate into the deeper skin layers or permeate the skin. The outermost layer of the human skin, the stratum corneum, is responsible for its barrier function. Most topically administered drugs do not have the ability to penetrate the stratum corneum. In these cases modulations of the skin penetration profiles of these drugs and skin barrier manipulations are necessary. A skin penetration enhancement can be achieved either chemically, physically or by use of appropriate formulations. Numerous chemical compounds have been evaluated for penetration-enhancing activity, and different modes of action have been identified for skin penetration enhancement. In addition to chemical methods, skin penetration of drugs can be improved by physical options such as iontophoresis and phonophoresis, as well as by combinations of both chemical and physical methods or by combinations of several physical methods. There are cases where skin penetration of the drug used in the formulation is not the aim of the topical administration. Penetration reducers can be used to prevent chemicals entering the systemic circulation. This article concentrates on the progress made mainly over the last decade by use of chemical penetration enhancers. The different action modes of these substances are explained, including the basic principles of the physical skin penetration enhancement techniques and examples for their application.

Structure of the Stratum Corneum and Drug Options to Overcome the Barrier

The skin is the largest human organ. It ensures that harmful substances and drugs released from topically applied formulations cannot intrude into the organism off-hand [1]. The evolutionary development of the human skin as a potential protective barrier keeping water in and noxious substances out of the human body was a requirement for terrestrial life [2]. Figure 1 illustrates the complex structure of the human skin and the several layers schematically [3].

The outermost layer of the skin, the stratum corneum, is of particular interest as it determines this barrier function [4]. The qualification for this is the unique physico-chemical composition of the stratum corneum [5]. The ‘brick and mortar model’ is applied to describe the structure of the horny layer. Corneocytes are the ‘bricks’ em-