Review of the Availability of In Vitro and In Silico Methods for Assessing Dermal Bioavailability

Abstract:
The exposure of the skin to consumer products, drugs, and environmental chemicals can result in their penetrating the skin barrier and entering systemic circulation, potentially resulting in adverse effects in the skin and other organs. The assessment of dermal penetration and bioavailability (including penetration, metabolism, and entry into the systemic circulation) is therefore an important consideration in the risk assessment of chemicals. The skin is a heterogeneous organ with a multilayer structure. Based on its architecture and physiology, substances can penetrate through three major ways but can also be blocked in the different skin layers and in the skin appendages, which act as reservoir. In addition to that, as the skin is a metabolically competent organ, substances can undergo metabolism. After a brief description of the skin architecture, this review will focus on the skin penetration mechanisms and skin metabolic capacities. The skin absorption has traditionally been tested in vivo on animals. However, with the new legislation (i.e., Registration, Evaluation, Authorisation, and Restriction of Chemicals Regulation or Cosmetics Regulation), alternatives to animal testing have to be implemented. In a second part, this review will provide a description of the main in vitro and in silico or computational models available to study skin absorption and skin metabolism (i.e., ex vivo skin models, artificial membrane barriers, primary cells and cell lines, Quantitative Structure–Activity Relationship [QSAR], simulators for the prediction of skin metabolism).

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