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In-silico approach for predicting the pharmacokinetics of dermal exposure

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Animal testing of cosmetic products and ingredients is banned in most countries in the world and there is a great need to develop alternative methods for assessing the efficacy and safety of not only novel cosmetic care products, but also transdermal drugs and hazardous chemicals. Determining the pharmacokinetics of dermal exposure, absorption, disposition and bioavailability is an important step for both efficacy and risk assessment. Here, we present recent progress in developing a multi-phase microscopic *in-silico model* for predicting the pharmacokinetics of dermal exposure, absorption and disposition. With the multiphase microscopic *in-silico model*, the multiple transdermal permeation pathways are considered including the tortuous lipid pathway, transverse corneocyte pathway and shunt pathway of hair follicles and sweat ducts. *In-vitro* methods have been developed for measuring the tissue specific properties of chemical in the stratum corneum (SC) lipids, corneocytes and sebum. Combined with molecular dynamics simulation of solute partition in lipid bi-layers and binding to keratin, quantitative structure-property relationships (QSPR) have been developed for predicting the diffusion and partition properties of chemical solutes in the SC lipids, corneocytes and sebum. Demonstrated are several examples of applying the multi-phase microscopic *in-silico model* for predicting the pharmacokinetics dermal exposure under various *in-vivo* and *in-vitro* conditions. These examples include a large experimental data set of transdermal permeability, reported clinical study of hair-follicular pathway, and subcellular disposition in the SC lipids and corneocytes and systemic bioavailability in blood circulation under *in-vivo* exposure conditions. The model prediction without parameter fitting agreed well with both the *in-vitro* and *in-vivo* experimental data, suggesting that the proposed *in-silico* approach is a cost effective alternative method for predicting the pharmacokinetics and bioavailability of dermal exposure and valuable *in-silico* tool for supporting the safety assurance and efficacy assessment of cosmetic care products and transdermal drugs.

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