In-silico and experimental investigation of the thermodynamic change of topical formulations due to evaporation and the impact on skin permeation

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Abstract

In-silico models of skin permeation have been widely explored due to advantages such as in-depth understanding, cost and time saving compared to experimental studies. This work reports the preliminary findings of an investigation, in which we studied the impact of the thermodynamic changes of drug in topical formulations (due to evaporation) on drug permeation to the skin, using integrated modelling and experimental work. A mechanistic model integrating the modelling of both formulation evaporation and physiologically based cutaneous pharmacokinetics has been developed and applied to simulate experimental results. The current model was developed to predict skin permeation in an experimental scenario using a Franz diffusion cell apparatus and where the evaporation is assumed only by the vapour diffusion (the effect of airflow is not presently considered). A commonly used cosolvent, propylene glycol (PG), was mixed with water at variety of concentrations. PG/water formulations containing diclofenac sodium, a model drug, were used in the skin permeation study under un-occluded conditions. The evaporation model predicts how evaporation affects the PG/water ratio and how that will lead to dynamic change of drug solubility, saturation state and activity in the formulation, for different PG/water formulations. The predicted dynamic change of vehicle thickness and diclofenac sodium solubility, saturation state and activity are then set as the exposure condition for the skin permeation model to predict how drug delivery and bioavailability of diclofenac sodium is affected by the interplay of initial cosolvent ratio and evaporation. The model can be applied to simulate both in vitro and in vivo scenarios. Verification of the model with experimental results is planned as the next step of the study.