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Titre de la thèse : *« Etude du passage cutané des ions inorganiques selon leurs propriétés physicochimiques »*

Résumé

Keywords: skin penetration, ions, Hofmeister series, formulation, skin viability

Human skin forms a unique interface between the body and the external environment whose main role is to protect the internal organs from external factors. Its highly hydrophobic outermost layer, *stratum corneum*, has long been believed impermeable for highly hydrophilic compounds, including ions [1]. Several studies proved this concept wrong [2,3], and recent research by Paweloszek *et al.* [4] demonstrated the important contribution of facilitated transport in permeation of halide anions. In line with these findings, the present work was divided into three main work packages.

Firstly, we developed an adequate survival medium that could be applied for further percutaneous absorption experiments, and we studied mechanisms underlying skin survival *in vitro*. Acidic pH was found to be detrimental to skin viability *in vitro,* and the minimal requirements for satisfactory medium were established as*:* physiological pH, isotonic composition and glucose supply.

Next, we investigated *in vitro* skin penetration of Hofmeister anions (as sodium salts of F^-, Br^-, I^-, SCN, ClO_4^-) alone and in bi- and ternary mixtures in two experimental series. All tested ions permeated viable skin within 24h. Fluoride reduced the penetration of Br^- and I^- in mixtures and synergy between Br^- and I^- was observed. The effects observed within the second group (I^-, SCN^-, ClO_4^-) were related to the inhibition of ClO_4^- penetration in the presence of other ions.

Finally, we studied the impact of formulation of marketed thermal spring water (TSW) into emulsions (TSW/O, O/TSW, TSW/O/W) and liposomes on skin absorption of Ca^{2+} and Mg^{2+}. These experiments revealed a strong impact of formulation on cation distribution after 24h exposure. Liposomes and emulsions promoted retention of Ca^{2+} and Mg^{2+} in skin layers as compared to TSW. Our results demonstrate that the beneficial effects observed during treatment with TSW are associated with penetration of the minerals into and through the skin and are not only a surface action.

To conclude, in this project, we demonstrate the possibility of both anions and cations to penetrate viable skin in vitro, and we disclose the effects of mixing and formulating their aqueous solution on skin penetration profiles.

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