KEMIK Kevser
Abstract proposition

OPTIMIZATION OF A SURFACE-ENHANCED RAMAN CHEMICAL IMAGING METHOD FOR PHARMACEUTICAL ACTIVE INGREDIENT TRACKING IN THE CONTEXT OF *IN-VITRO* SKIN EQUIVALENT-MODEL PERMEATION STUDIES

Kemik Kevser[1], De Bleye Charlotte[1], Sacré Pierre-Yves[2], Hubert Philippe[1], Ziemons Eric[1]

[1] University of Liège (ULiège), CIRM, ViBra-Santé HUB, Laboratory of Pharmaceutical Analytical Chemistry, Department of Pharmacy, Avenue Hippocrate 15, 4000 Liège - Belgium
[2] University of Liège (ULiège), CIRM, Research Support Unit in Chemometrics, Department of Pharmacy, Avenue Hippocrate, 15, 4000 Liège - Belgium

In the drug development cycle of dermal application pharmaceutics, drug formulation studies are crucial, especially *in vitro*-formulation studies, which stand out for their ability to predict drug behaviour. Through sophisticated analytical techniques, drug penetration can be estimated into the different layers of the skin. The European Medicine Agency (EMA) currently recommends a reference analytical method for *in-vitro* permeation studies that involves the use of a Franz diffusion cell, hyphenated to a separative technique such as High Pressure Liquid Chromatography (HPLC). This widely adopted technique comprises significant drawbacks, including being a time-consuming, destructive and lacking spatial information of the permeated substances.

Surface Enhanced Raman chemical imaging (SER-CI) is a Raman derived chemical imaging method, exalting the inherent Raman scattering of an analyte using metallic nanostructures (NPs). For instances silver and gold nanoparticles constitute what are commonly called SERS substrates. The aggregation of these SERS substrates is recognized to give rise to the formation of 'hot spots', regions with major Raman signal enhancement.

Combining spatial and spectral information, SER-CI emerges as a promising technique in the context of drug monitoring. Nonetheless, this analytical technique faces a major challenge related to the deposition of SERS substrates onto analysed surfaces. This limitation results in non-homogeneous NPs deposition, leading to spectral intensity variability, compromising the reliability of quantitative analyses. Considering the lack of SER-CI implementation in biomedical applications, the present project aims to address these issues for the first time within the framework of drug penetration studies. Solid polymeric hydrogels, mimicking the properties of biological tissue, was developed to establish a model matrix. A Quality by Design approach, which systemically identifies and controls critical parameters throughout the development process, guided the robust optimisation of homogeneous NP deposition by an automated spray-coating device for enhanced reliability and repeatability. A confirmatory testing will be conducted to confirm the optimization parameters and their respective levels.