Evaluation of contamination and quantification of drug penetrations studies using Quantitative Mass Spectrometry Imaging

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Skin penetration and targeting the right tissue (sebaceous or sweat glands, dermis, etc....) are key information for the evaluation of active compounds. Sometimes contamination of the dermis during the sample preparation may occur and interfere for data interpretation. For many years LC-MS have been used as one of the "gold standard" method. In 2011, Quantitative Mass Spectrometry Imaging (QMSI) has been described for the first time and now it is frequently used in preclinical and in clinical studies. Here, we compare the two different techniques and demonstrate the benefits of using the QMSI technique regarding aggregate of 12 drugs penetration studies.

QMSI was applied on human or mice fresh tissues after topical application on 2cm² during 16 hours with a different test compounds on Franz cells. LC-MS/MS approaches were used to compare and validate QMSI results: stratum corneum, epidermis and dermis were isolated and directly analyzed by LCMSMS. The molecular images generated by QMSI on the same skin tissue sections were used to clearly compare the penetration of each compound and confirm their concentration in the different structures of the skin.

QMSI shows great information of localization and quantification of the active compound with similarity with LC-MS (20-25% of similarity). Indeed this multi-imaging platform allows the study of compound distribution and quantification in each histological structure like the hair follicle and the sebaceous gland. It is thus possible to determine the penetration pathway, the compound concentration in each histological region and the target engagement directly within the tissue without any labelling (radioactivity or fluorescence). Moreover, the imaging technique was also able to demonstrate the potential contamination of the dermis (Franz Cell or punch biopsies). QMSI combined with histological staining techniques was confirmed to become an essential multimodal approach in preclinical and clinical studies.