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Title: An Image Is Worth A Thousand Words

Abstract: The human skin acts as very effective armour protecting the body against microbial and chemical attacks, ultraviolet light, mechanical insults and water loss. These properties of the skin make delivery of active pharmaceutical ingredients across the skin barrier – and hence achieving the desired effect - a challenging task when developing new topical drug products. A given topical drug product's ability to penetrate depends on many factors like physicochemical properties of the active drug molecule, the presence of penetration enhancers, the saturation degree of the active drug molecule in the formulation, the fraction of active drug dissolved in the formulation and the general condition of the skin.Knowledge about the spatial distribution of the drug molecule in the skin after application is key to successful optimisation of the drug's ability to penetrate the skin and reach the desired target. An imaging technique such as Mass Spectrometry Imaging (MSI) offers the opportunity to study not only distribution of the drug molecule within the skin after topical application of the drug product but also the histology of the skin. Within MSI different techniques are available – e.g. Time of Flight-Secondary Ion Mass Spectrometry (TOF-SIMS) and Matrix-Assisted Laser Desorption/Ionisation (MALDI). Common for the different MSI techniques are that they are very delicate and time consuming and have their own distinctive advantages and disadvantages with respect to properties like: spatial resolution, mass resolution, sensitivity and sample preparation requirements - meaning that e.g. optimising the spatial resolution will negatively impact the sensitivity parameter.

This lecture will demonstrate how the throughput in imaging studies applied to human skin explants can be increased by combining e.g. MALDI MSI studies with cassette dosing. Furthermore it will be demonstrated how MALDI MSI can be used to facilitate the development process of new topical drug molecules by determining quantitative skin distribution profiles. Briefly discussed are the drawbacks accompanying the high spatial resolution and how a combination of TOF-SIMS and Scanning Electron Microscopy (SEM) can be effectively applied to obtain ultra-high spatial resolution images of mouse ears for study of drug distribution and skin histology.