M8022

Visualization and Investigation of the Flow Behavior and Diffusion of Octyldodecanol Inside Human Skin after Topical Application by Attenuated Total Reflectance Fourier Transform Infrared Imaging (ATR-FTIR Imaging) and Confocal Raman Spectroscopy

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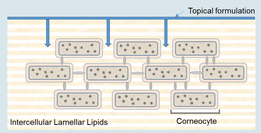
PURPOSE

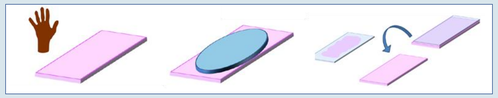
Complete understanding of the behavior of lipidic fluids and their functionality in semi-solid formulations requires that the mechanism by which the excipient interacts with and influences the structures of the skin, both at the surface and inside the stratum corneum (SC) be evaluated. To achieve this understanding, vibrational imaging spectroscopy methods have been employed to study, visualize and measure flow and penetration behavior of a representative long-chain fatty alcohol, octyldodecanol.



METHODS

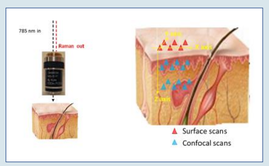
ATR-FTIR Imaging Spectroscopy

In this work, ATR-FTIR imaging spectroscopy is employed to visualize and measure the penetration of Kollicream® OD (octyldodecanol) inside the SC and evaluate the active penetration enhancement potential of this product for the prospective delivery of actives into the SC in ex-vivo human skin. A comparison and visualization of Kollicream® OD deposition and penetration into the human skin was achieved by measuring levels of the excipient at the skin surface and in subsequent layers using ATR-FTIR imaging. Hyperspectral images were collected for each skin sample at the skin surface before treatment (control), on the skin surface after treatment (deposition) and then after eight sequentially tape strips (penetration).The ATR-FTIR imaging system was used at Spectral Resolution: 4 cm^{-1}, Pixel size: 6.25 & 6.25 microns; Accumulation Scans per Pixel: 4; Spectral range: 4000-750 cm^{-1}



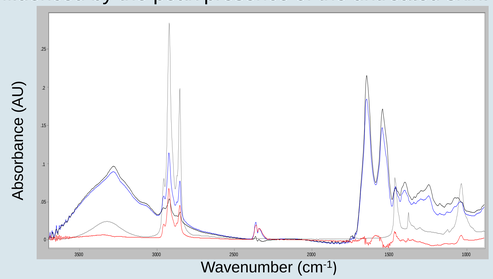
Confocal Raman Spectroscopy

Using a confocal Raman system, 2D images of the skin surface and inside the epidermis of ex-vivo human skin were recorded to investigate active delivery and distribution beyond the SC.



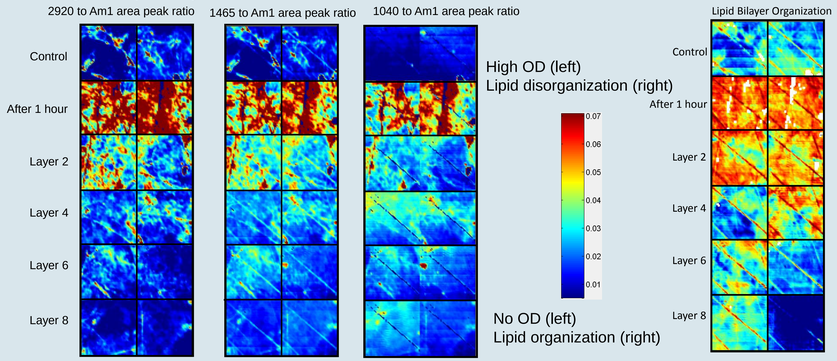
RESULTS

The flow behavior and penetration of Kollicream® OD (octyldodecanol), on and through the layers of the SC was evaluated using ATR-FTIR imaging spectroscopy coupled with tape stripping methodology. As shown in the spectra below, octyldodecanol can be measured by tracking different IR markers, specifically noting peaks that are not significantly influenced by the peak presence of the untreated skin.



ATR-FTIR spectra of human untreated skin (Black), skin treated with Kollicream® OD (Blue), difference spectrum of treated and untreated skin (red) and neat Kollicream® OD (grey)

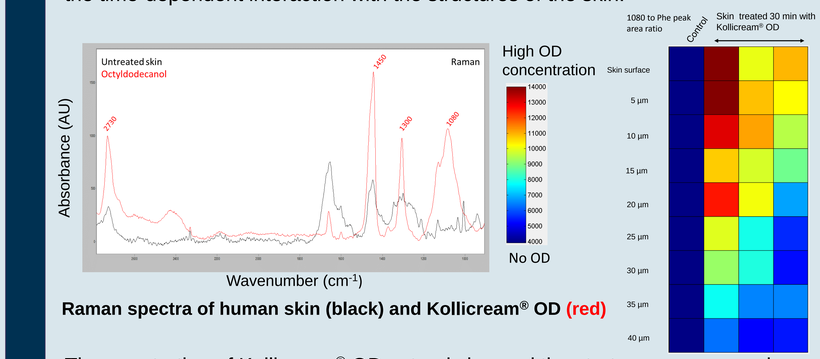
It was necessary to first establish an approximate depth to which Kollicream® OD penetrates prior to completing more advanced spectroscopic techniques (Raman spectroscopy). The confirmation of Kollicream® OD penetration may be observed from the FTIR-ATR spectroscopic imaging results below. It is clear from the scans of the tape stripped layers of ex-vivo human skin that the Kollicream® OD penetration has reached, to a degree, up to layer 8 of the stratum corneum.



The mechanism of penetration and flow of Kollicream® OD on human skin is evidenced by the concentration variation in the x, y and z direction. The features of the skin surface contribute to these patterns, and thus additional methodologies were employed to further explore the behavior of Kollicream® OD on and through the skin. ATR-FTIR spectroscopic techniques support the proposal that the presence of Kollicream® OD promotes the temporary disordering of the lipid bilayers. This is shown in the ATR-FTIR spectroscopic image (above right) as an increase in lipid bilayer disordering as compared to the control.

RESULTS

Additionally, 2D images of the penetration of octyldodecanol beyond the SC, inside the epidermis, was evaluated by Confocal Raman Spectroscopy. Using this method, it is also possible to provide kinetic information concerning the delivery of neat Kollicream® OD in the different skin layers to better understand the time-dependent interaction with the structures of the skin.



Raman spectra of human skin (black) and Kollicream® OD (red)

The penetration of Kollicream® OD extends beyond the stratum corneum and into the epidermis as shown by the Raman spectrum above. The vertical blocks indicate Kollicream ® OD concentrations at increasing depth into the epidermis and horizontal blocks differentiate multiple data collections.

CONCLUSIONS

Through ATR-FTIR imaging and Confocal Raman Spectroscopy we have investigated and visualized the behavior of the lipidic fluid, Kollicream® OD (octyldodecanol) on and through the skin. This data ultimately provides insight into the interaction between the structures of the skin and the simplistic chemistry of long chain alcohols. Many lipidic fluids, when applied to the skin surface alter the lipid organization and in consequence, the skin barrier function. As a result, there is an effect on the penetration of the vehicle and potentially the active through the stratum corneum and epidermis. The results of ATR-FTIR spectroscopic imaging and Raman spectroscopy indicate that Kollicream® OD is interacting with the lipid bilayers of human skin; resulting in penetration through the stratum corneum to a depth of 40 microns into the skin layers. These findings are significant in the selection and determination of excipient selection for effective formulation of semi-solids.

This work was jointly completed by BASF Pharma Solutions, Skin Delivery Lab and TRI Princeton

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