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Investigations into octyldodecanol (Kollicream® OD) behavior in skin by spectroscopic methods

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PURPOSE

Octyldodecanol (OD), a lipophilic, Guerbet alcohol, has been widely use in cosmetics and topical pharmaceutical formulations over many decades. A few studies indicate that OD may enhance drug dermal penetration but the mechanism of action is unclear. Little is known about its skin penetration behavior. These studies were designed investigate the penetration of OD into skin and its influence on stratum corneum lipids.

OBJECTIVE(S)

1. Develop method to visualize OD presence and permeation into skin layers by ATR-FTIR imaging and Confocal Raman micro-spectroscopy.
2. Evaluate deposition, diffusion kinetics and permeation depth of Kollicream® OD (Octyldodecanol USP-NF, Ph. Eur.) on *ex vivo* human skin
3. Evaluate ability of OD to increase the disordering of stratum corneum lipid lamellar structure.

METHOD(S)

1. Samples of untreated human skin, Kollicream® OD and Kollicream® OD-treated skin were all scanned by FTIR and Raman. The spectra were evaluated (Figure 1) to define spectral markers for the OD.
2. The 1450, 1300 and 1080 peaks were associated with skin protein band which was used to normalize these Octyldodecanol peaks to the Phenylalanine peak.
In the spectroscopic images presented in this study, the higher is the ratio, then the redder is the image and the higher is the OD concentration inside the ex-vivo skin.
3. The surface of human skin samples, mounted on Franz Cells, were untreated or treated with OD. After 20 hours the skin was removed and interrogated by Confocal Raman microscopy. (Figure 2 shows results of analysis of 1450 cm^{-1} vs. Phenylalanine).
4. Analysis was repeated at 1080 and 1300 cm^{-1} vs. Phenylalanine. (See Figure 3).
5. For penetration kinetics analysis, confocal Raman images (down through the stratum corneum, into the epidermis) of human skin treated with OD were collected at approximately 5 minute intervals. Intensity of OD peaks at depth intervals and time intervals was mapped for 1080, 1300 and 1450 cm^{-1} peaks (Figure 4).
6. OD-treated skin cross-sections were scanned by ATR-FTIR imaging. Data (1465 and 2920 cm^{-1}) overlaid with images showed depth of OD permeation in outer layers of skin (Figures 5 and 6). Spectral images at 2850 cm^{-1} (CH_2 peak) evidenced lipid disordering (Figure 7).

RESULT(S)

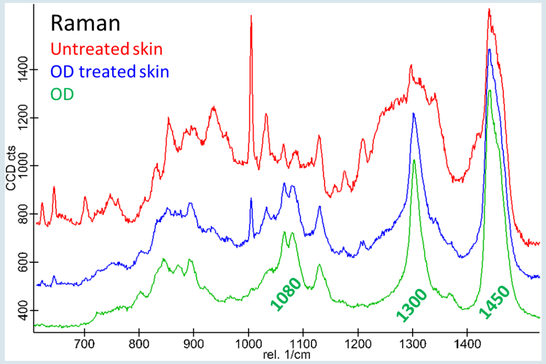

Figure 1. FTIR Spectra of OD, OD-treated skin and untreated skin with spectral range 600-1730 cm^{-1}, laser excitation = 532 nm, laser power = 30 mW and laser exposure = 20s. Three peaks were markers for OD: 1080, 1300 and 1450 cm^{-1}.

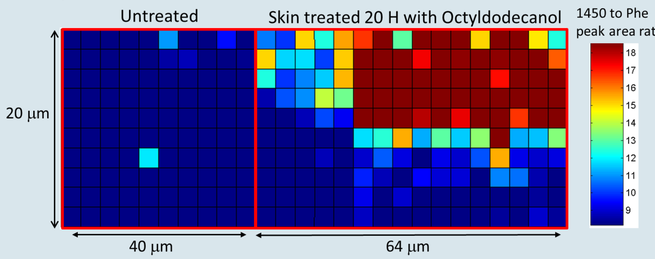

Figure 2. Spectral analysis (1450 to Phe peak area ratio) from Raman confocal microscopy of untreated and OD-treated skin. Samples were scanned along a single line (a total of 64 µm long) at 4 µm intervals and to a depth of 20 µm, at 2 µm intervals. The resulting scan graphically represented the relative Kollicream® OD levels in a grid where each square was 4 µm wide along the x-axis (surface of skin) and 2 µm high along the y-axis (depth into skin).

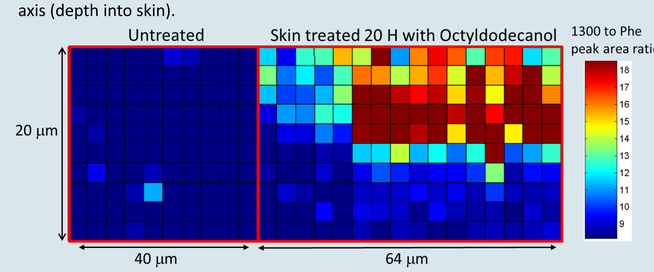

Figure 3. Spectral analysis (1300 to Phe peak area ratio) from Raman confocal microscopy of untreated and OD-treated skin. Same scanning parameters as in Figure 2. The last marker of OD 1080 cm^{-1} yielded similar results (not shown here)

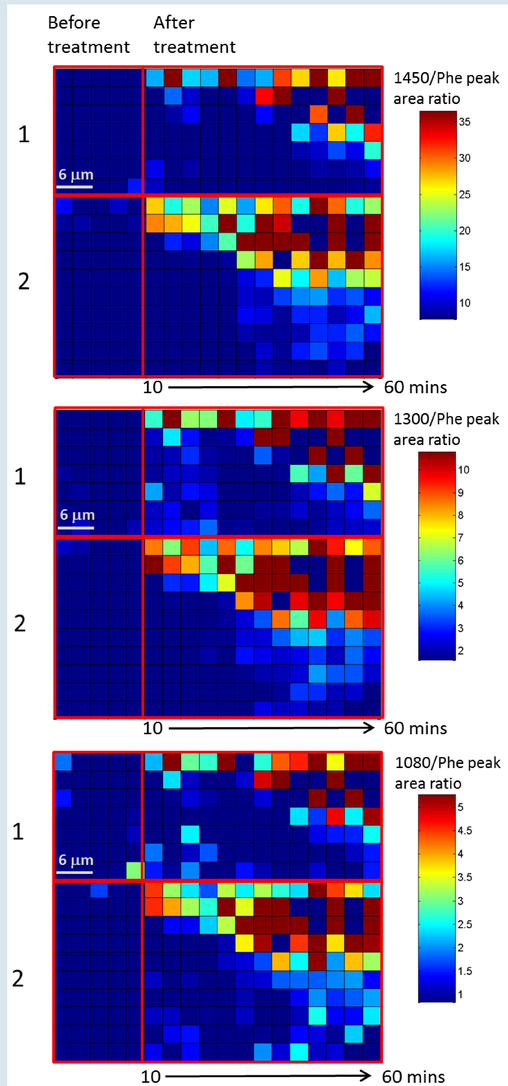

Figure 4. Raman images of duplicate kinetics studies showing the OD penetration inside the skin using three markers of the OD. The peak area of each marker was normalized to the Phenylalanine band. Pixels along x-axis were recorded with time intervals (~5 min each). Pixels along y-axis were recorded at specific skin depth (2-3 µm per pixel). In total 20 µm were investigate over 1 hour period.

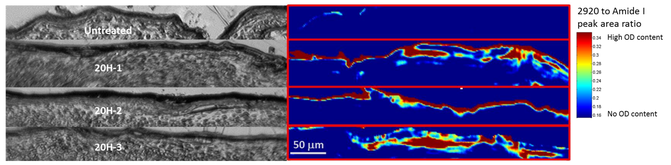

Figure 5. ATR-FTIR images showing the 2920 (octyldodecanol) to 1644 (Amide I) area peak ratio for four skin samples, 20 hours after OD application.

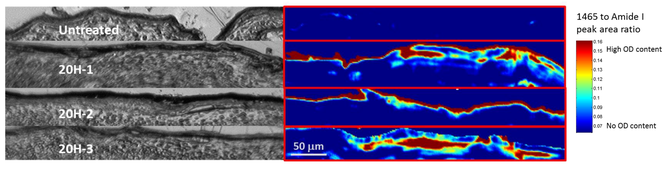

Figure 6. ATR-FTIR images showing the 1465 (octyldodecanol) to 1644 (Amide I) area peak ratio for four skin samples, 20 hours after OD application.

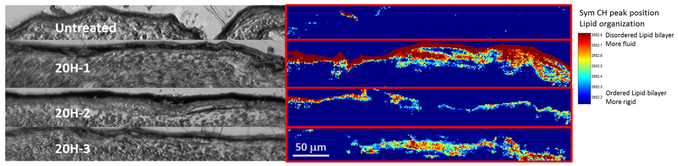

Figure 7. ATR-FTIR images showing the CH_2 (~2850 cm^{-1}) peak position in 4 skin samples , 20 hours after OD treatment. Color indicates intensity of SC lipid disordering.

CONCLUSION(S)

1. FTIR and confocal Raman micro-spectroscopy were used to semi-quantitatively evaluate the presence of octyldodecanol (Kollicream® OD) after topical application on the surface of human skin and in layers of the stratum corneum and epidermis.
2. By capturing Raman data at different depths in the skin and at time intervals it was possible to visualize penetration kinetics of OD.
3. Spectral analysis was successfully used to observe the presence and depth of OD in cross-sections of skin samples using ATR-FTIR imaging method.
4. Spectral analytical methods (of skin cross-sections) that can detect disruptions in lipid lamellar ordering, demonstrated that OD can increase lipid disordering (and this could impact API permeability).

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