Penetration ability of caffeine and propylene glycol in the skin

The stratum corneum (SC) is the uppermost layer of the skin, which provides an efficient barrier function. This barrier is always an obstacle for cosmetic formulations or medical ointments applied to the skin. The permeation through the SC barrier is successful when penetration enhancers are added into the formulation.

Propylene glycol is a known penetration enhancer and widely used in dermatology. Caffeine is an active component, which is employed in many applications to stimulate the hair growth, to inhibit the effect of UVB-radiation and to promote wound healing. The penetration of caffeine through the SC has been controversially discussed in the literature.

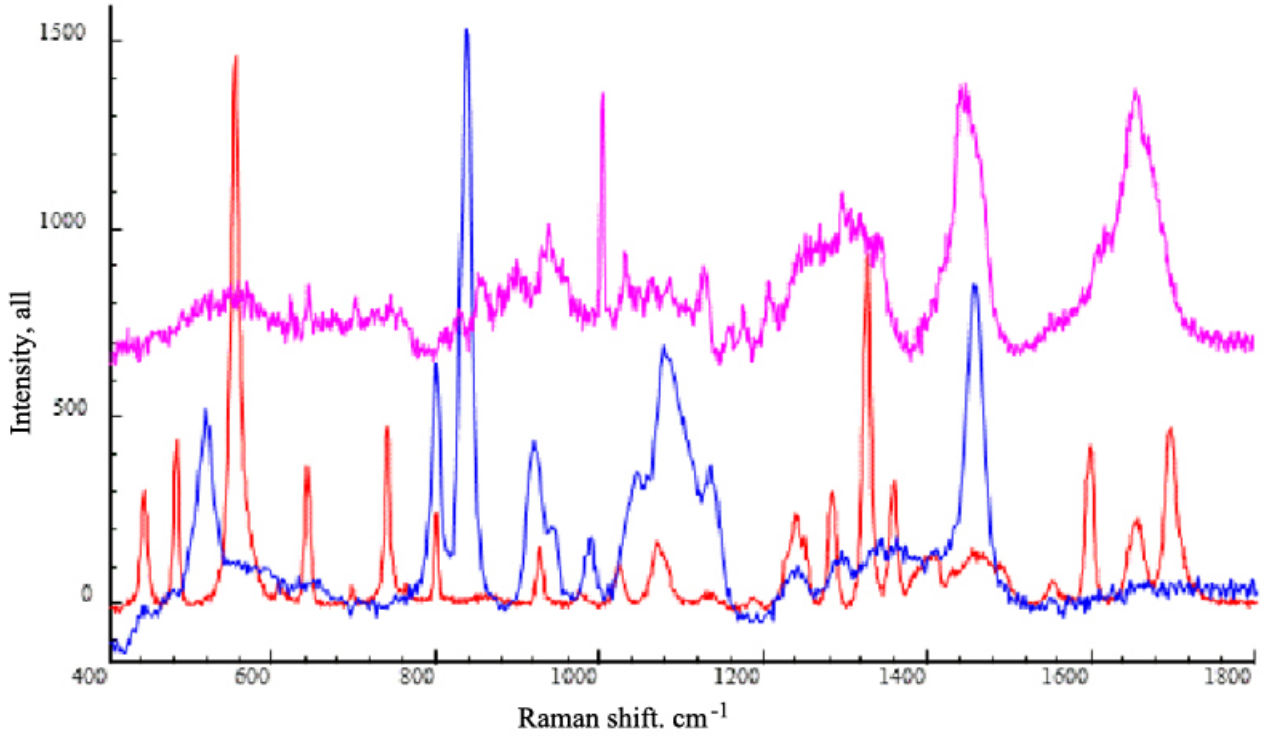

Fig. 1. Molecular information (Raman spectra) of porcine skin (purple line), caffeine (red line) and propylene glycol (blue line). Excitation wavelength: 633nm.

The aim of this study was to investigate the penetration of a gel containing caffeine and propylene glycol into the porcine skin *ex vivo*. The porcine skin was chosen due to its morphological similarity with human skin. The skin has been topically treated with the gel at an amount of 2mg/cm^2. After one hour of passive penetration, the remaining gel was removed from the skin surface with filter

paper. The skin samples were analyzed by a confocal Raman microscope (CRM), which is able to extract the molecular information of the gel components (caffeine and propylene glycol) in different depths of the skin. Figure 1 shows the molecular information known as Raman spectrum of porcine skin, caffeine and propylene glycol.

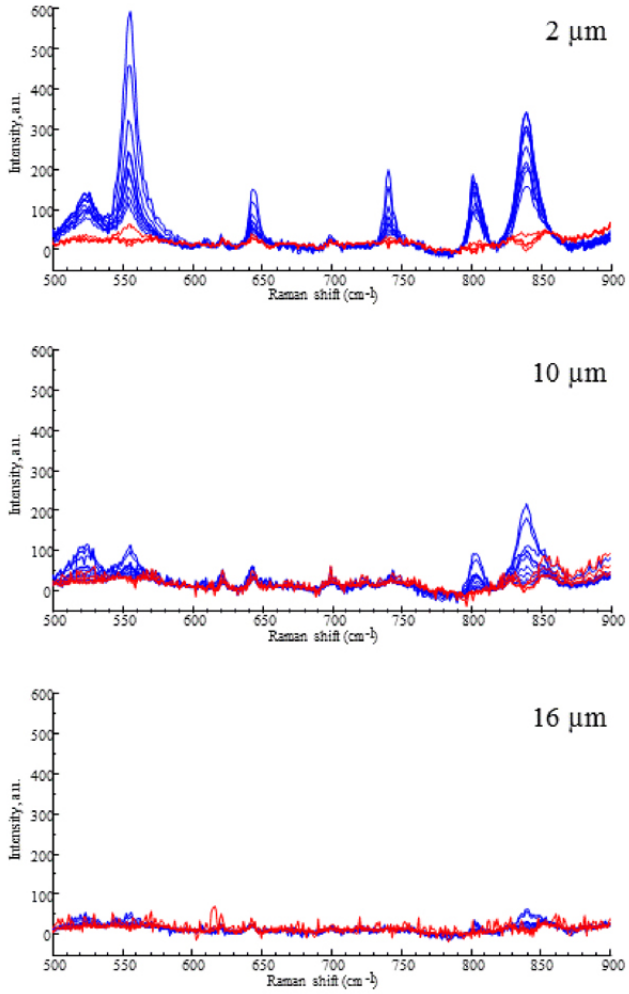

Fig. 2. Comparison between intact skin (red lines) and gel-treated skin (blue lines) showing caffeine- and propylene glycol-related Raman peaks in the depths of 2 µm, 10 µm and 16 µm.

The peaks in the Raman spectra of caffeine and propylene glycol at 555cm^{-1} and 840cm^{-1}, respectively, were chosen for analysis due to the minor overlapping with the skin spectrum. Figure 2 shows the caffeine- and propylene glycol-related Raman peaks measured in different depths. The presence of caffeine and propylene glycol is visually defined near the skin surface (see depths 2µm and 10 µm), but in the deeper SC layers it is difficult to visually recognize whether the components can be detected or not. In order to evaluate the maximum penetration depth of

caffeine and propylene glycol, a multivariate statistical analysis (PCA-LDA) is employed to distinguish the presence of these gel components in the skin. This complex statistical method compares the corresponding spectral ranges for the gel-treated (blue lines) and intact skin (red lines) in every skin depth and estimates a mean value for caffeine, propylene glycol and for intact skin. The comparison of the mean value of each component with the value of intact skin answers the question if the corresponding component is detectable or not in a certain depth.

The results of the study show that caffeine and propylene glycol can reach different depths inside the skin. Propylene glycol penetrates until the depth of 20.7-22.0 µm, while caffeine penetrates until the depth of 12.3-13.0 µm. Considering that the SC has a thickness of 18.1±1.0 µm, only propylene glycol can permeate through the skin barrier, while the caffeine cannot.

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