

What to consider when performing the follicular closure technique?

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For overcoming the skin barrier, there are three potential pathways: (1) the intercellular, (2) the transcellular and (3) the follicular penetration pathway. For many substances it is assumed that two or even all penetration routes are used in parallel.

When investigating the follicular penetration it is necessary to have two areas, which are optimally comparable to each other and do only differ that for one of the areas the follicular penetration pathway is excluded. For this purpose, the method of selective follicle closure was developed where a closure material is placed on each follicle [1]. Studies show that skin areas with available follicular pathway are able to deliver the model drug caffeine faster and in higher amount than a comparable area where this pathway is blocked [2].

Since further investigation of this pathway is desired, this study is concerned to verify that by performing the selective follicular closing technique no side effects like penetration enhancing are induced in the treated skin area. It also indicates which parameters in the protocol, like used closure material and application protocol, have an influence on the success or the failure of the follicular closure.

Two different closure materials (standard nail varnish, solvent free nail varnish) and four application protocols (spreading with pipette, careful finger massage, 5 Hz finger massage, 5 Hz automatic massage) were investigated. For all experiments ex vivo porcine ear skin was used. Penetration experiments were performed by covering the whole area of interest with the closure material and applying a caffeine gel. Also areas which were next to the covered area were investigated. Skin layers were separated using tape stripping and the heating technique for dermis and epidermis separation. Samples were homogenized and extracted with PBS by using a standardized extraction protocol. For analyzing the concentration of the extracted caffeine HPLC was used. To investigate the influence of the different application protocols the follicular closing was performed and a fluorescein gel was applied. Cryosections of the follicles were investigated using the confocal laser scanning microscopy. It could be determined whether the follicle got contaminated with the fluorescein gel.

It could be shown that using the standard nail varnish is leading to a secure follicular closure. The



solvent free nail varnish did not prevent substances from penetration. Not only the closure material but also the application protocol has an influence on the follicular closure. Only spreading the formulation with the tip of the pipette or applying a careful finger massage keeps the follicular closure intact. No penetration-enhancing effect attributable to the nail varnish could be observed.

[1] A. Teichmann et al., Follicular penetration: Development of a method to block the follicles selectively against the penetration of topically applied substances, *Skin Pharmacol Physiol.* 19 (2006) 216-223

[2] N. Otberg et al., The role of hair follicles in the percutaneous absorption of caffeine, *Br J Clin Pharmacol.* 65 (2008) 488-492

