

Abstract

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Title of the thesis: Synthesis of fluorinated serine derivatives and study of their effect on skin barrier function

The human skin serves as a barrier against physical, chemical and microbial injury. When the skin barrier is perturbed, there is a possibility of microbial infiltration and biochemical damage. Ceramides, as essential components of the skin lipid layer, help to maintain the barrier integrity. Decreased content of skin ceramides in epidermis is connected with skin diseases such as atopic dermatitis and psoriasis. Previous findings of our research group proved that a ceramide analogue with similar steric and hydrophobic parameters to skin ceramides could selectively supplement the recovery of perturbed human skin barrier.

The goal of this study was to design a convenient synthesis of ceramide analogues derived from L-serine with two long aliphatic chains. The first chain is amidically bound lignoceric acid and the second chain is either a 10 or a 14 carbon polyfluorinated chain conjugated with the rest of the molecule by an ester bond. Furthermore, the aim of this study was to test the potential ability of synthesized compounds to recover a controllably perturbed human skin barrier in comparison with their non-fluorinated analogues.

Permeation experiments with the newly synthesized polyfluorinated ceramide analogues have shown a slight improvement in skin barrier properties of previously damaged human stratum corneum. However, both 10 and 14 carbon fluorinated derivatives have shown worse results than their non-fluorinated analogues, with the former having much better permeation profile than the latter.

From the results, the first idea is that polyfluorination did not improve the skin repairing ability of the molecules. However, it is vital to mention the struggles with low solubility of polyfluorinated compounds in common solvents. This could lead to insufficient impact on the damaged stratum corneum. Therefore, the future approach is to find an alternative application

conditions for these compounds in order to observe the influence of the polyfluorination more reliably.