ABSTRACT

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Title of diploma thesis: Synthesis and study of *O*- and *N*-modified ceramides

Ceramides which are composed of fatty acid and basic alcohol, naturally occur in the human body and play a role in many physiological processes. They are known like molecules participating in the cell signaling, they take part in differentiation, proliferation and apoptosis of the cell but they are also structural elements of cell membrane. Last but not least, they are included in extracellular matrix of stratum corneum where they participate in the barrier function of the skin.

In addition to research of naturally occurring ceramides, of course it is necessary to study various modifications of these substances and to find connections between structure of ceramides and their ability to keep the barrier function.

1-deoxy, 3-deoxy a *N*-methyl analogues of ceramides, that I investigate in my diploma thesis, have not been examined yet in terms of their barrier function. Before the measuring of the properties of model membranes consisting of these analogues, it was necessary to synthesize these analogues.

Synthesis was performed in two ways. The first procedure consisted of the preparation of the acylating agent in the form of succinimid-*N*-ylester of lignoceric acid and acylation of the corresponding sphingosine analogue. The second way of preparation was the reaction of lignoceric acid with *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide and after it the reaction of the product with the corresponding sphingosine analogue.

Before permeation experiments the model ceramide membranes were prepared. They should be simplified models of lipid layer in the stratum corneum. The lipid layer contains equimolar amount of cholesterol, ceramides and fatty acids with the addition

five percent of cholesteryl sulfate.

The electrical impedance, the relative water loss throught the membrane and the flux of drugs (theophylline and indomethacin) were measured on the prepared model membranes to define their barrier characteristics. These characteristics were compared with standard (physiological ceramide instead of the analogues) and they demonstrate the ability of analogues to maintain the barrier function of the skin.

From the results it is evident that all prepared analogues have worse barrier properties than the standard ceramide. We can therefore assume that the change of ceramide molecules, such as the elimination of the hydroxyl function in position 1 or 3 or the methylation of the nitrogen leads to a distortion of ceramide bilayers in the stratum corneum and so to disruption of the protective function of the skin.