Abstract

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Title of diploma thesis: Synthesis of acylceramides modified on their linoleate part

Acylceramides (ceramides ω-*O*-acylated with linoleic acid) are a group of lipids present in the *stratum corneum* of the skin, where they play an important role in barrier formation. They can be found either in a free form, where they play an important role in forming intercellular lipid lamellae, or covalently attached to the surface of corneocytes providing a structure called corneocyte lipid envelope (CLE). The CLE biosynthesis is based on the oxidation of linoleate moiety to an epoxy enon, which then reacts with the protein coat of corneocytes, probably by a mechanism of Michael reaction, but the exact mechanism remains unclear.

The goal of this thesis was to synthesize a model epoxidized acylceramide using a method based on an acylceramide precursor, that could be selectively ω-acylated by any fatty acid. The model epoxidized acylceramide will be used to study the mechanism of CLE formation.

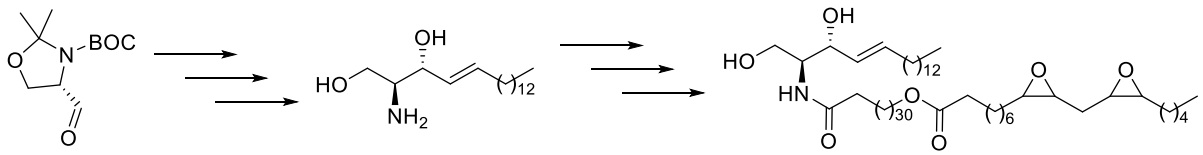

Diagram: Synthesis of oxidized acylceramide

In the first step of the process, sphingosine was synthesized from Garner's aldehyde in a two-step reaction. Next, a ceramide was prepared by an *N*-acylation reaction of sphingosine with the activated fatty acid, whose OH-group was protected. OH-groups of the sphingosine were protected by a different protective group and the OH-group of the fatty acid was deprotected, to allow for the ceramide to be acylated with either linoleic acid or its oxidized form. In the last

step, all the remaining protective groups were removed to provide the desired molecule of a specifically oxidized acylceramide [diagram].

Keyywords: acylceramides, corneocyte lipid envelope, epoxidized linoleic acid