

## Abstract

Title of the master thesis: Optimization of reactions leading to the synthesis of labeled sphingoid bases

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The stratum corneum (SC) represents a key part of the skin barrier, located on the entire surface of the epidermis, which is subject to a constant renewal process. The SC is made up of corneocytes, lipids and desmosomes, with the lipid matrix being crucial for maintaining barrier function. The main components of these lipids are ceramides, cholesterol and free fatty acids. Ceramides play a vital role in skin protection and their basic components are sphingoid bases, aliphatic amino alcohols with a long chain, which together with fatty acids form the basic building blocks of sphingolipids. There are four basic sphingoid bases in the skin barrier: sphingosine, dihydrosphingosine, phytosphingosine and 6-hydroxysphingosine. These compounds differ in the presence of double bonds and hydroxyl groups, each contributing to the function and structure of ceramides in the skin.

Mass spectrometry is very often used to quantify lipids from human SC. However, in order to reliably and accurately quantify substances using this method, it is necessary to use suitable internal standards, very often in the form of isotopically labeled physiological molecules.

The aim of this project was to optimize the individual steps of the synthesis of sphingosine, which in the future would contain part of the chain with isotopic labeling. The first sub-goal was to check whether the planned reactions actually work, and the second sub-goal was to achieve the highest possible yields of individual reactions. The project focused on the synthesis of physiological sphingosine into which it would be possible to insert a six carbon chain with appropriate labeling. Physiological sphingosine was prepared in ten steps using hexanal as a starting material with a total yield of approximately 2 %. The resulting isotopically labeled product will be used for a detailed study of the behavior of sphingolipids in the SC using mass spectrometry. This optimized

synthetic procedure was developed to provide a valuable tool for further research in the field of the skin barrier and lipid metabolism.