Abstract

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Title of diploma thesis: Synthesis of modified and labeled acylceramides

Upper most layer of skin, stratum corneum is providing effective barrier which protects us from impact of environment. Extracellular lipids of stratum corneum are mostly composed of ceramides, free atty acids and cholesterol. Earlier it was suggested that these lipids are highly rigid, which enables sufficient barrier function. But presently, it is known that some structural parts of these lipids are more fluid. So far, ultralong ceramides (also known as acylceramides), lipids which are necessary for correct barrier function still remain partly unexplored. Mobility of sphingosine part and linoleic ester have already been studied, but mobility of the ultralong chain is speculative.

Obtaining information about mobility of particular parts of acylceramides is difficult because of their unavailability with required labelling. Our aim was to prepare acylceramides with deuterium-labelled half of their ultralong chain between carbons $C_{17} – C_{32}$ from commercially available perdeuterated compounds.

From available options we chose 1,12-dibromodocecane and γ-butyrolactone, which will after their condensation provide 16 carbon chain. That is exactly half of the ultralong chain in acylceramides. These precursors were converted to phosphonium salt and aldehyde in multiple steps to contribute as partners in Wittig reaction which provided 16 carbon chain labelled with deuterium. This labelled chain was used in another Wittig reaction together with 16 carbon unlabelled chain which resulted in 32 carbon chain with selective labelling in required positions of this molecule. Final molecule of acylceramide was prepared by esterification of the ω-hydroxyl group with linoleic acid and subsequential connection of this precursor to the molecule of sphingosine.