Abstract

Acylceramides, subgroup of ceramides with ultralong chains, are essential component of extracellular lipid matrix in the uppermost skin layer, stratum corneum. They have crucial role in mammalian survival on dry land. Deeper understanding of their function in physiology of pathophysiology of the skin and their therapeutic potential are hampered by their limited availability.

Analysis of the skin surface lipids of the ass (*E. asinus*) has shown, that these lipids contain up to 56% of unbranched ω-lactones (equolides), from which 51.2% is mono-unsaturated dotriacontanolide and 41.3% is mono-unsaturated triacontanolide. Carbon chain length of these lactones match the most common length of carbon chain in acylceramides (30 and 32 carbon atoms) therefore they could be used in their total synthesis.

Aim of this thesis was to isolate mono-unsaturated ω-lactone with 32 carbon chain (dotriacontanolide) from the mixture of donkey skin surface lipids, followed by hydrogenation and transformation to the suitable precursor (succinmidyl ester) in order to find the easiest synthetic path in its conversion to acylceramides.

We have tried many synthetic pathways. From direct aminolysis of lactone, through reaction with N-hydroxysuccinimide in various reaction conditions to opening of the lactone to the potassium salt of ω-hydroxyacid, followed by reaction with dissucinimidyl carbonate. However, all synthetic pathways are complicated by low solubility of these compounds and their very low reactivity. Opening of the lactone to the methylester of ω-hydroxyacid, followed by protection of ω-hydroxy group, methylester hydrolysis and activation to the N-succinimidyl ester, which is precursor that can be directly used in acylceramide synthesis seems as the most suitable pathway.