

# Abstract

Charles University, Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Technology

Supervisor: PharmDr. Anna Paraskevopoulou, Ph.D.

Author: Kateřina Žofková

Title of the thesis: Interaction of PAMAM dendrimers with human *stratum corneum*

Dendrimers are highly branched, monodisperse macromolecules. On the basis of the degree of branching, can be distinguished different generations of dendrimers that arise as the dendrimers expand. Higher generations of dendrimers form spherical structures with an internal cavity, where molecules such as a drug can be encapsulated. Due to their structure, which can be specifically and controllably modified, dendrimers are investigated for their use in biomedicine. One of the most widely used groups of dendrimers are polyamidoamine (PAMAM) dendrimers, based on an ethylenediamine core, branched amide and amine units, and terminal functional groups. PAMAM dendrimers with amine groups have proven useful in the past as skin penetration enhancers of different drugs. However, the mechanism how these molecules affect skin barrier function is not yet known.

Therefore, in this work was investigated the mechanism of interaction of PAMAM dendrimers with lipids of *stratum corneum* (SC), the uppermost skin layer where the skin barrier is found. Second, third and fourth generation of PAMAM dendrimers with surface-bound primary amine groups were used in the experiment. First, 1mM and 10mM solutions of dendrimers from each generation were prepared. These dendrimer solutions were then applied to the hydrated isolated SC. Two measurement methods were used to evaluate the effect of PAMAM dendrimers. The first method was infrared spectroscopy (IR). The second method was differential scanning calorimetry (DSC).

Obtained results showed that during the interaction of PAMAM dendrimers with SC a change in the skin lipid arrangement occurred. This fact suggests that dendrimers could allow transportation of a drug through the skin by the intercellular route. Moreover, the dependence on the dendrimers generation was found. Significant changes in the skin lipids arrangement occurred after the application of PAMAM dendrimers of the fourth generation. This effect was not dependent on the concentration of dendrimers in the applied solution.