Abstract

Ceramides that are present in stratum corneum (SC), the uppermost layer of the skin, are responsible for skin barrier function and thus for its permeability for drugs. Their role in the formation of skin barrier has been widely described; however, up to now, their structure-activity relationships have not been fully revealed. Previous studies suggested, that the ceramide acyl chain length is a key factor for the permeability of the skin barrier.

The aim of this work was to study the influence of the length of ceramide acyl chain on the permeability of the skin barrier using short ceramides, sphingosine, phytoshingosine and ceramide 2 (NS). Short ceramide analogues contained sphingosine with 18 carbon atoms and the acyl chain ranging from 2 to 18 carbon atoms. Their influence on skin permeability was tested *in vitro* in Franz diffusion cells on dermatomed porcine skin using two model drugs – theophylline (TH) and indomethacin (IND). Donor samples were prepared as 5% (w/v) suspension of TH and 2.5% (w/v) suspension of IND with addition of 1% (w/v) ceramide in 60% (v/v) propylene glycol. Negative samples for the comparison of the fluxes and the drug concentrations contained 5% (w/v) suspension of TH and 2.5% (w/v) suspension of IND propylene glycol without the addition of ceramide. Phosphate buffer saline (PBS) was used as an acceptor phase.

The results of this study showed that short ceramides with 2-8C acyl chain lost their barrier function, hence increased the skin permeability. The highest permeability was observed in ceramide analogue C4, which increased the flux of TH 3.8-times and that of IND 2.7-times. Similar pattern was obtained for the skin concentration, with the highest value in ceramide analogue C6. This ceramide increased the concentration of TH and IND in the skin 2.6 and 2.1-times respectively. Pretreatment application of the ceramide analogues confirmed the previous results and proved that the obtained results do not come from an interaction of the tested substances with the model drugs in the sample but from a direct interaction with the skin barrier. These results were also verified by electrical resistance of the skin. The presence of the ceramides did not significantly influence the solubility of TH and IND in donor sample.

The results of this thesis confirmed the previous suggestion that the ceramide chain length plays a key role in skin permeability and that the ceramides with short acyl chain do not have the barrier properties of physiological ceramides.