Penetration enhancing effect of phytoceramides
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1. INTRODUCTION
Ceramides are essential components in the stratum corneum barrier function. Different classes of ceramides are present in human skin, differing in the nature of sphingosine and acyl moieties with respect to chain length, degree of saturation and the presence of an OH group [1]. Ceramides with a saturated sphingosine base containing a hydroxyl function at C4 are known as phytoceramides. A few studies demonstrated the penetration enhancing properties of ceramides [2-5], however, systematic studies using phytoceramides are lacking. This led us to assess the penetration enhancing effect of phytosphingosine and a series of nine phytoceramides via transdermal experiments.

2. EXPERIMENTAL
✓ Dermatomed human skin (± 400 µm thick) using in vitro Franz diffusion cells (32°C)
✓ Dose formulation: testosterone, caffeine and ibuprofen (80% of Smax) in 50:50 (V/V) EtOH: H2O ± penetration enhancer (1% m/v) [6]
✓ Receptor fluid:
  • 0.01 M PBS (pH 7.4) for caffeine and ibuprofen
  • 0.01 M PBS (pH 7.4) + 5% BSA (m/v) for testosterone
✓ Analyses were done using validated high-throughput HPLC-UV methods

3. RESULTS

3.1. RESULTS (CONTINUED)

FLUX CURVES
The penetration enhancing effect of a phytosphingosine (CER 1) and phytoceramides (CER 2-10) was evaluated. The cumulative amounts of caffeine (C) and testosterone (T) permeated across the skin were plotted against the time and are given in Figures 2 and 3, respectively. No significant differences between the ibuprofen flux curves were seen.

Table 1: Apparent primary transdermal parameters: permeability K, diffusion D, and partition coefficient Kp (mean ± RSD (%), n=2-4).

<table>
<thead>
<tr>
<th>Penetration enhancer</th>
<th>Kp (10-5 cm/s)</th>
<th>Dp (10-5 cm²/h)</th>
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<th>Dp (10-5 cm²/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>20.3 ± 3.27</td>
<td>1.23 ± 0.45</td>
<td>13.5 ± 0.57</td>
<td>0.36 ± 0.10</td>
<td>17.8 ± 0.93</td>
<td>0.80 ± 0.20</td>
<td>20.4 ± 3.86</td>
<td>1.00 ± 0.35</td>
</tr>
<tr>
<td>CER 2 (short chain)</td>
<td>6.37 ± 0.61</td>
<td>0.06 ± 0.05</td>
<td>5.43 ± 0.06</td>
<td>0.30 ± 0.05</td>
<td>5.67 ± 0.70</td>
<td>0.10 ± 0.05</td>
<td>6.68 ± 0.80</td>
<td>0.12 ± 0.04</td>
</tr>
<tr>
<td>CER 3 (medium chain)</td>
<td>7.00 ± 0.50</td>
<td>0.16 ± 0.05</td>
<td>10.77 ± 0.04</td>
<td>0.06 ± 0.03</td>
<td>10.69 ± 0.04</td>
<td>0.08 ± 0.03</td>
<td>11.84 ± 0.04</td>
<td>0.08 ± 0.03</td>
</tr>
<tr>
<td>CER 8 (long chain)</td>
<td>21.38 ± 0.32</td>
<td>0.44 ± 0.05</td>
<td>10.72 ± 0.04</td>
<td>0.16 ± 0.03</td>
<td>10.69 ± 0.04</td>
<td>0.08 ± 0.03</td>
<td>11.84 ± 0.04</td>
<td>0.08 ± 0.03</td>
</tr>
<tr>
<td>CER 9 (aromatic chain)</td>
<td>2.05 ± 0.17</td>
<td>2.94 ± 0.24</td>
<td>1.86 ± 0.15</td>
<td>0.20 ± 0.05</td>
<td>1.94 ± 0.15</td>
<td>0.21 ± 0.05</td>
<td>2.03 ± 0.15</td>
<td>0.23 ± 0.05</td>
</tr>
</tbody>
</table>

4. CONCLUSIONS
Results showed that the penetration enhancing effect of the phytoceramides depends on the used model compound. Phytoceramides have no pharmaceutically relevant penetrating enhancing effect on ibuprofen (ER < 2), while selected phytoceramides exhibited a penetration enhancing ratio of more than two in the presence of caffeine or testosterone.

5. REFERENCES