FACULTY OF PHARMACEUTICAL SCIENCES

Penetration enhancing effect of phytoceramides

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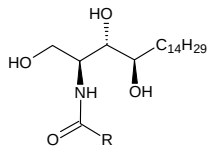
1. INTRODUCTION

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.



CER 1: phytosphingosine (-NH_2)
CER 2-8: R= $(CH_2)_nCH_3$ n=0, 2, 4, 6, 8, 10, 12
CER 9: R= Ph
CER 10: R= 2-OH-Ph

Figure 1: Structure of the investigated phytoceramides.

2. EXPERIMENTAL

- ✓ Dermatomed human skin (± 400 µm thick) using *in vitro* Franz diffusion cells (32°C)
- ✓ Dose formulation: testosterone, caffeine and ibuprofen (80% of S_{max}) in 50:50 (V/V) EtOH:H_2O ± 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

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.

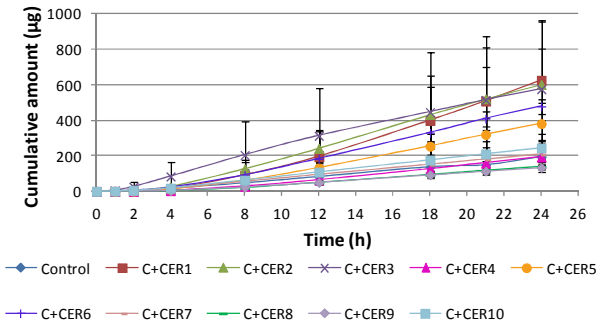


Figure 2: Flux curves for caffeine (error bars: SEM, n=2-4).

3. RESULTS (CONTINUED)

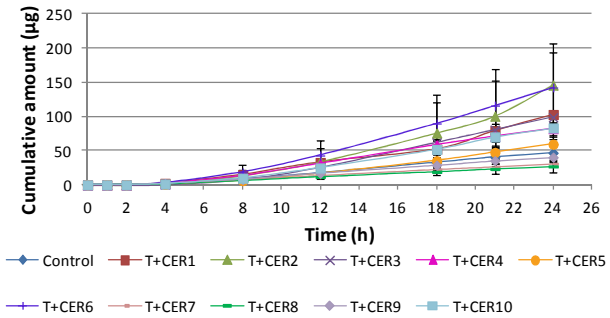


Figure 3: Flux curves for testosterone (error bars: SEM, n=1-4).

TRANSDERMAL PARAMETERS

Transdermal parameters were calculated and are presented for some phytoceramides in Table 1.

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

Penetration enhancer	Caffeine			Testosterone			Ibuprofen		
	K_p (10^{-4}.cm/h)	D_m (10^{-5}.cm²/h)	K_m	K_p (10^{-4}.cm/h)	D_m (10^{-5}.cm²/h)	K_m	K_p (10^{-4}.cm/h)	D_m (10^{-5}.cm²/h)	K_m
Control	2.68 ± 43.25	8.18 ± 45.25	0.13 ± 29.43	4.91 ± 46.31	5.12 ± 55.70	0.36 ± 10.50	20.53 ± 17.67	175.58 ± 130.78	0.12 ± 90.15
CER 2 (short chain)	6.37 ± 61.61	5.06 ± 68.01	0.49 ± 5.20	15.45 ± 48.90	3.32 ± 48.58	1.76 ± 13.61	20.00 ± 4.27	56.87 ± 127.91	0.65 ± 124.34
CER 6 (medium chain)	7.00 ± 1.93	6.16 ± 65.44	0.51 ± 54.42	17.64 ± 66.29	3.70 ± 32.33	1.69 ± 48.47	23.17 ± 6.64	94.74 ± 24.36	0.09 ± 6.44
CER 8 (long chain)	2.18 ± 32.38	4.49 ± 32.49	0.19 ± 51.98	2.86 ± 53.49	7.87 ± 72.97	0.20 ± 100.42	27.06 ± 24.86	158.20 ± 59.12	0.09 ± 85.87
CER 9 (aromatic chain)	2.05 ± 17.07	4.94 ± 25.64	0.16 ± 31.05	4.44 ± 9.11	6.25 ± 47.37	0.29 ± 45.22	-	-	-

ENHANCING RATIO (ER)

$$ER = \frac{K_p \text{ with penetration enhancer}}{K_p \text{ without penetration enhancer}}$$

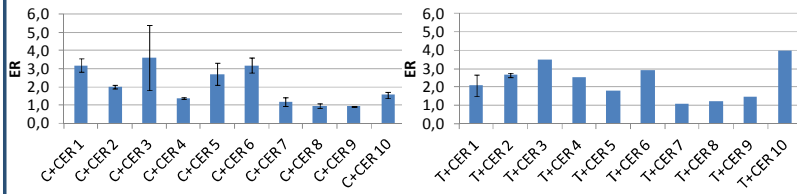


Figure 4: ER for caffeine (C) and testosterone (T) (error bars: SEM).

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

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