Topical bioavailability of sunscreen agents in stratum corneum: effect of vehicle and time

T. Tassopoulos[1,3], H. Vuong[3], C. Pellanda[1,3], G. Imanidis[3] , V. Figueiredo[1], T. Rufli[2], E.W. Smith[4], C. Surber[1,2,3]

[1] *Institut für Spital-Pharmazie, Universitätskliniken, Kantonsspital Basel, Basel, Switzerland*
[2] *Department of Dermatology, University Clinics, Kantonsspital Basel, Basel, Switzerland*
[3] *Institute of Pharmaceutical Technology, University of Basel, Basel, Switzerland*
[4] *College of Pharmacy, University of South Carolina, Columbia, SC, USA*

Introduction

- The ability of UV-filters to act on the skin surface and within the stratum corneum was demonstrated by Treffel et al.[1] For maximal sun protection and minimal UV-filter permeation the penetrated amount must remain in the outer layers of the stratum corneum.
- The vehicle has an important effect on skin penetration and retention properties, and even on the sun protection factor (Treffel et al.[1]).
- 3-(4-methylbenzyliden)-camphor (MBC) is a UVB-filter with high absorptivity approved in the EU and suitable for use in all major types of sunscreen products.

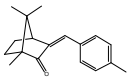

Fig 1 3-(4-methylbenzyliden)-camphor (MBC)

- The purpose of the present study was to investigate the effect of:
  - » vehicle
  - » penetration enhancer
  - » application-duration

  on the topical *in vivo* bioavailability of MBC.
- Following methods were used:
  - » standardized tape stripping as a sampling method
  - » UV/VIS spectrometry for the quantification of stratum corneum and MBC on the tapes (method validated previously[2]).

Methods

1 Application of the formulations: Experiment 1

- Investigation of the effect of the following factors on the MBC-penetration into stratum corneum from saturated solutions (thermodynamic activity = 1):
  - » vehicle: Mineral Oil (MO) vs. Propyleneglycole (PG)
  - » application duration: 1h, 3h, 6h.
- Application on the forearm of 5 healthy volunteers.
- After removal of the solutions, stratum corneum samples were immediately collected by standardized tape stripping an area of 2.99 cm².

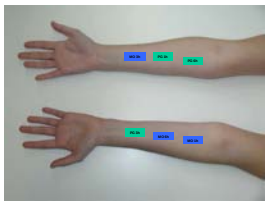

Fig. 2 Treatment pattern of experiment 1. The different application sites (area 13 cm²) were randomized.
PG = Propyleneglycole, MO = Mineral Oil

Experiment 2

- Investigation of the effect of penetration enhancer Transcutol® CG on substantivity of MBC in stratum corneum.
- The applied formulation consisted of saturated (thermodynamic activity = 1) MBC-solutions in Macrogol 400 containing:
  - » 0% Transcutol® CG (applied to each volunteer as a reference)
  - » 10% Transcutol® CG
  - » 50% Transcutol® CG.
- Application on the forearm of 10 healthy volunteers during 1 hour.
- After removal of the solutions, tape stripping followed immediately or after 6h at the different sites.

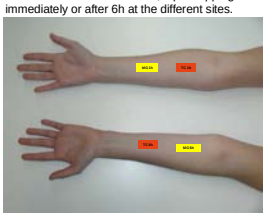

Fig. 3 Treatment pattern of experiment 2. The different application sites (area 13 cm²) were randomized.
MG = Macrogol 400 formulation (n=10),
TC = Macrogol 400 formulation with 10% (n=5) or 50% (n=5) Transcutol® CG.

2 Sampling method: Tape Stripping

- Stratum corneum was completely removed by tape stripping, which is a prerequisite to determine the thickness of stratum corneum of the individual volunteers.
- The first stripped tape was discarded due to potential drug remaining on the skin surface.

Tab. 1 Parameters and defined values for tape stripping standardization.

Parameter	Defined value
Environmental conditions	20 ± 1℃ (temperature) 38 ± 5% (rel. humidity)
Skin washing	distilled water
Tape characteristics	Tesa 57315 Beiersdorf (1.5 cm)
Template	1.3 cm x 3.3 cm
Pressure applied	140 g/cm²
Time interval between tape stripping and measurement	24 hours

Fig. 4 The tape stripping area of the skin is defined by a template. Tapes are pressed on the skin by a roller (pressure of 140 g/cm²) and fixed on a slide frame.

3 Analytics: UV/VIS Spectrometry

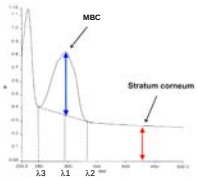

Fig. 5 UV/VIS spectrum of a tape strip removed from skin treated with MBC formulation. The spectrophotometer was modified to monitor a rectangular beam of 1 cm².

- Amount of stratum corneum and MBC adhering to the tape is determined simultaneously:
  - » 430 nm: stratum corneum
  - » 297 nm: MBC

$$A_{MBC} = A(\lambda 1) - \frac{[A(\lambda 2) - A(\lambda 3)](\lambda 1 - \lambda 3)}{(\lambda 2 - \lambda 3)} - A(\lambda 3)$$

- Penetration profiles of MBC in stratum corneum were assessed.
- The area of the penetration profile (without tape 1) was used to calculate $AUC_{conc\text{-}sc}$ as a parameter for quantitative comparison of penetration experiments.
- A variance analysis (ANOVA) was conducted with the logarithmic values of $AUC_{conc\text{-}sc}$.
- The impact of the test factors: formulation, time and volunteer, as well as their interactions, was determined.

Results

Experiment 1

- Saturation solubility (w/w) of 4-MBC at 33℃:
  - » 2.4 ± 0.1% in Propyleneglycole
  - » 8.8 ± 0.7% in Mineral Oil
- Significant differences in 4-MBC-penetration were found between Mineral Oil and Propyleneglycole formulations ($p<0.05$).
- The factors time, volunteer, as well as their interaction showed no significant influence on MBC-penetration in both vehicles.

→ **More MBC penetrates the skin from Propylenglycole (concentration 2.4%) than from Mineral Oil (concentration 8.8%) vehicle.**

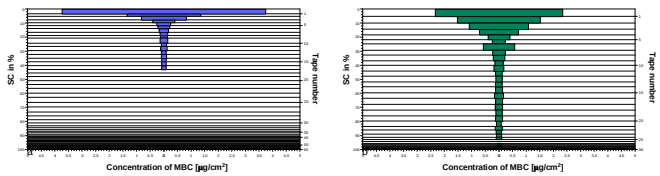

Fig. 6 a. Penetration profile of MBC from a saturated Mineral Oil formulation (MBC concentration: 8.8%) after 1 hour of application.
b. Penetration profile of MBC from a saturated Propylenglycole formulation (MBC concentration: 2.4%) after 1 hour of application.

Experiment 2

- Saturation solubility (w/w) of 4-MBC at 33℃:
  - » 7.7 ± 0.3% in Macrogol 400 (reference)
  - » 9.4 ± 0.4% in 10% Transcutol® CG in Macrogol 400
  - » 19.6 ± 0.6% in 50% Transcutol® CG in Macrogol 400
- 10% Transcutol® CG in Macrogol compared to Macrogol reference: no significant influence of the formulation, time and volunteer and their interactions was found.
- 50% Transcutol® CG in Macrogol compared to Macrogol reference: significant influence of formulation, time and volunteer was found ($p<0.05$).

→ **Significant influence of formulation, time and volunteer on the MBC-penetration was observed comparing 50% Transcutol® vehicle to Macrogol reference, but not comparing 10% Transcutol® vehicle to the reference.**

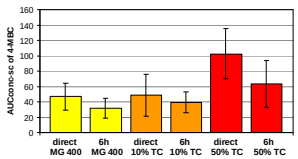

Fig. 8 AUC-values of MBC after skin treatment with Macrogol 400 (n=10), Macrogol 400 with 10% Transcutol® (n=5) and Macrogol 400 with 50% Transcutol® (n=5). MG = Macrogol, TC = Transcutol®

Conclusions

- MBC-penetration into stratum corneum was influenced by different vehicle, penetration enhancer and application-duration parameters.
- Propyleneglycole had much more impact on MBC-penetration than Mineral Oil, even though MBC-concentration in the Mineral Oil vehicle was four times higher.
- Increasing concentration of penetration enhancer Transcutol® CG enhanced MBC-penetration into the stratum corneum.

References

[1] Treffel, P., Gabard, B. Skin penetration and sun protection factor of ultra-violet filters from two vehicles. Pharm Res. 1996; 13(5): 770-774.

[2] Weigmann, H.-J., Lademann, J., Meffert, H., Schaefer, H., Sterry, W. Determination of the horny layer profile by tape stripping in combination with optical spectroscopy in visible range as a prerequisite to quantify percutaneous absorption. Skin Pharmacol Appl Skin Physiol. 1999; 12(1-2): 34-35.