

Percutaneous penetration of topical corticosteroids: effect of skin occlusion

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Introduction

Background

- Occlusion by covering the skin with an impermeable wrap enhances skin hydration, affects drug penetration and can induce a drug reservoir within the stratum corneum.¹ This is desired in local therapy with topical corticosteroids: the longer the local effect, the better.
- Tape stripping is adequate to investigate the phenomenon of drug accumulation in stratum corneum, which has especially been investigated in the context of corticosteroid-therapy.²
- Triamcinolone acetonide (TACA) is a medium potency topical glucocorticoid often used in dermatology.

Aim

- The aim of the present study was to investigate the effect of:
 - » occlusion before application (pre-occlusion) (experiment 1)
 - » occlusion after application (post-occlusion) (experiment 2)
- on the penetration of triamcinolone acetonide into stratum corneum.

Methods

1 Application of the formulation

Experiment 1: Pre-Occlusion

Investigation of the effect of skin pre-occlusion on the TACA-penetration into stratum corneum.

- Forearms of 5 healthy volunteers
- Occlusion of one forearm for 16h with plastic foil (pre-occlusion)
- Application of 100 µg/cm² TACA in acetone on 3 sites per arm
- Skin sampling after:
 - » 0.5 h
 - » 4 h
 - » 24 h

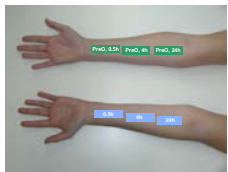


Fig. 1 Treatment pattern of experiment 1 (PreO = Pre-occlusion).

Experiment 2: Post-Occlusion

Investigation of the effect of occlusion after application on the TACA-penetration into stratum corneum.

- Forearms of 5 healthy volunteers
- Application of 100 µg/cm² TACA in acetone on 2 sites per arm
- Occlusion of one arm for 4 h or 24 h until skin sampling (post-occlusion)
- Skin sampling after:
 - » 4 h
 - » 24 h

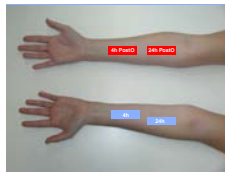


Fig. 2 Treatment pattern of experiment 2 (PostO = Post-Occlusion).

2 Skin sampling by tape stripping

- Stratum corneum was completely removed by standardized tape stripping³
- This is the prerequisite to determine the thickness of stratum corneum of the individual volunteers

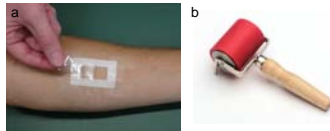


Fig. 3 The tape stripping area (5.6 cm²) was defined by a template (a). Tapes were uniformly pressed on the skin by a roller (pressure 140 g/cm²) (b) and removed from the skin.

- Adhering on the tapes we found: corneocytes and TACA

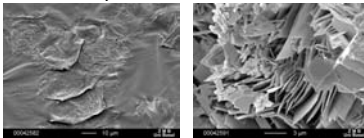


Fig. 4 Corneocytes on tape 20 (raster-electron-microscopic view).

Fig. 5 TACA-crystal on tape 1 (raster-electron-microscopic view).

3 Analytics

Quantification of corneocytes by VIS-Spectroscopy

- Corneocytes were quantified directly on the tapes
- Pseudo-absorption of the corneocytes at 430 nm was measured against a blank tape⁴

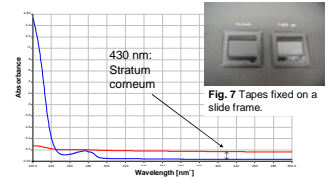


Fig. 6 UV/VIS-spectra of a blank tape (Tesa Multi-Film Crystal-Clear 19 mm) (blue line) and of a stripped tape (red line). The spectrophotometer was modified to produce a beam of 1 cm².

Quantification of TACA by HPLC

- TACA was quantified at 240 nm after extraction of the tapes
- HPLC was performed with a RP-18 column and 60% methanol as eluent
- The method was validated according to ICH



Fig. 8 Each tape was extracted with 1.5 ml Methanol. The extract was injected into the HPLC-system, and the chromatograms at 240 nm were evaluated.

Results

Penetration Profiles

- The whole stratum corneum was removed to compare individual penetration profiles
- A total of 28-70 tapes were stripped off each skin site
- TACA accumulated on the skin surface: about 50% of the applied dose remained on tapes 1 to 3
- TACA permeated through the stratum corneum and reached deeper tissues

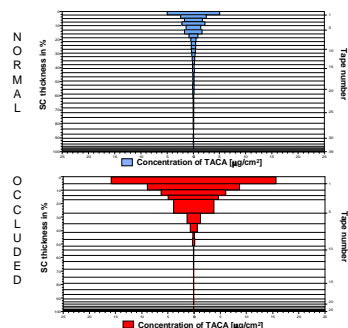
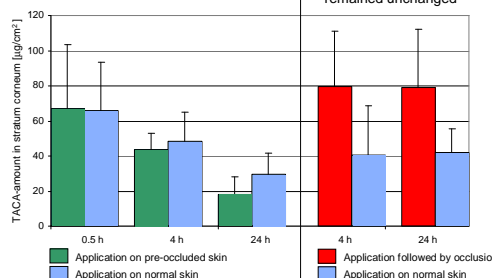


Fig. 9 Penetration profile of TACA into the stratum corneum 24 h after normal application and after application followed by occlusion.

Experiment 1: Pre-Occlusion

- For statistical evaluation, the total TACA-amount penetrated into the stratum corneum was calculated for each skin site
- The TACA-amounts were evaluated in a multifactor ANOVA

- TACA-amounts with and without pre-occlusion showed no significant difference
- The TACA-amount within stratum corneum significantly decreased with time ($p < 0.0001$)



Experiment 2: Post-Occlusion

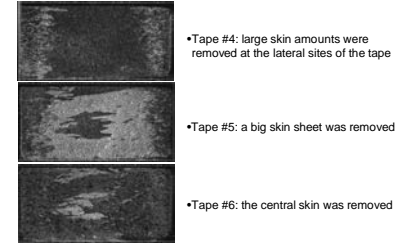
- Occlusion after application produced a marked accumulation of TACA in stratum corneum
- TACA-amounts with and without occlusion showed a highly significant difference ($p < 0.01$)
- The TACA-amount between 4h and 24h remained unchanged

Curiosity

Occlusion hydrated the stratum corneum and loosened its structure:

- » larger amounts of skin were removed on single tapes as skin "sheets": less tapes were required to remove the entire stratum corneum
- » this happened after 5-10 tapes

„Special“ tapes after 24 h occlusion:



„Normal“ tape:

- Tape #23: no skin occlusion, no skin "sheets"

Conclusions

- Occlusion before application shows no effect on the TACA-penetration into stratum corneum.
- Occlusion after application enhances TACA-penetration into stratum corneum by a factor of 2, favoring the development of a desired drug reservoir.
- Occlusion causes an enhanced hydration of the stratum corneum and a loosening of its structure.

References

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