

# Raman spectroscopy detects dexpanthenol skin penetration depth depending on test set-up and mode of application

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## Background

Current global trends and increasing consumer needs demand superior cosmetic product efficacies, requiring a constant evolution of test designs for product evaluation. Dexpanthenol (DEX) is broadly used for decades as ingredient in various cosmetic applications and thereby known for several proven functions [1], like increasing skin hydration, supporting moisture retaining [2], and enhancing epidermal barrier recovery [3]. In contrast, data concerning DEX kinetic, and penetration are rare. Therefore, the present work focuses on the penetration of DEX.

## Methods and Materials

Three pilot study parts with Raman measurements (Model gen2-SCA Skin Analyzer) were conducted to evaluate DEX penetration and substantivity after topical application of a marketed and commercially available skin care lotion (o/w emulsion, Formula No. BKKM008): part I, II and III. The relevant test product characteristics: 2% Dexpanthenol, pH value  $4.91 \pm 0.1$ , viscosity [mPas] 2.500 and density (rel.) 0.989. For each of the three study parts, the subject panel, test site and area, application mode, and measurement set-up were differently defined (Table 1).

Table 1: Study design and schedule

Study	Part I	Part II	Part III
<b>objective</b>	penetration of DEX after single application of a cosmetic formulation in short term under open and occlusive condition	penetration and substantivity of DEX into skin after application of a cosmetic formulation in comparison to an untreated control area in different time points	penetration of DEX into the skin after application of a cosmetic formulation under different experimentally induced skin conditions and treatments: - treatment mode A: untreated - treatment mode B: 24h occlusive product application - treatment mode C: 1h product application on 24h "pre-hydrated" (occluded) skin site
<b>time points</b>	baseline measurement (before product application) measurement 1h after product application	day 1 to 5: product application day 6: baseline measurement (t1), after 2h product application further measurements were performed at 0h (t2), 2h (t3) and 4h (t4) after this last product impact	day 1: preparations for the treatment codes B occlusive product application and C (pre-hydration by occlusion) day 2: measurement after 30 min of acclimatization on the untreated site (treatment mode A) measurement after 24h of occlusive product application (treatment mode B) measurement 1h after product application on the "pre-hydrated" skin site (treatment mode C)
<b>test area</b>	two areas on volar forearms	lateral lower legs (random: right/left)	volar forearms (random: right/left)
<b>application</b>	area 1: occlusive application area 2: open application area 1: 200µl in an extra large Finn chamber area 2: 40µl on an area of 4cm x 5cm	the test product was applied twice daily in the morning and in the evening by the subjects at home. The application of day 6 was performed by a technician. application at home (day 1-5): four fingertips units were applied to the assigned test area (approx. 2g) application at study site (day 6): 40 µL on a test area of 4cm x 5cm	the test product and the patch materials were applied by a technician 250µl in the patch test system for the 24h occlusive application (treatment code B) 2mg/cm <sup>2</sup> on a 4cm x 5cm area, including the "pre-hydrated" skin site (treatment code C)
<b>subjects</b>	N=1 (age: 31 yrs, male)	N=6 (age: 48.0 ± 10.1 yrs, female)	N=6 (age: 56.7 ± 6.3 yrs, female)
<b>statistics</b>	not applied	comparison between treatments for substantivity comparison between assessment times for penetration	comparison between treatments

## Conclusion

Comparing the test results, DEX could be detected in the stratum corneum down to a skin depth of 5, 10, and 20µm, depending on the test set-up. Such investigations provide knowledge on the interaction between mode of application, measurement set-up, and active ingredient penetration. Finally, the present work helps to improve product development regarding active targeting activities and additionally provides insights to choose an appropriate test set-up for such product investigations.

[1] Proksch E, de Bony B, Trapp S, Boudon S (2017): Topical use of dexpanthenol: a 70th anniversary article. *J Dermatolog Treat* 28(8): 766-773.

[2] Gehring W, Gloor M (2000): Effect of topically applied dexpanthenol on epidermal barrier function and stratum corneum hydration. Results of a human in vivo study. *Arzneimittelforschung* 50(7):659-663.

[3] Proksch E, Nissen HP (2002): Dexpanthenol enhances skin barrier repair and reduces inflammation after sodium lauryl sulphate-induced irritation. *J Dermatolog Treat* 13(4):173-178.

## Results

**Study part I:** DEX was measured at the skin surface (0µm) and in the skin down to a depth of about 20µm, both after open product application as well as under occlusive product application.

**Study part II:** After 5 days of product application a significant detection of DEX substantivity was measured on the treated surface of the skin ( $p=0.002$ ), as well as in 5µm skin depth ( $p=0.002$ ). As shown in Figure 1, in deeper layers of the stratum corneum DEX was still observed with a level of significance at 25µm ( $p=0.015$ ). However, further significant DEX enrichment after a renewed 2-hours product application on day 6 was not detected at the defined time points: immediately, 2h and 4h (not shown).

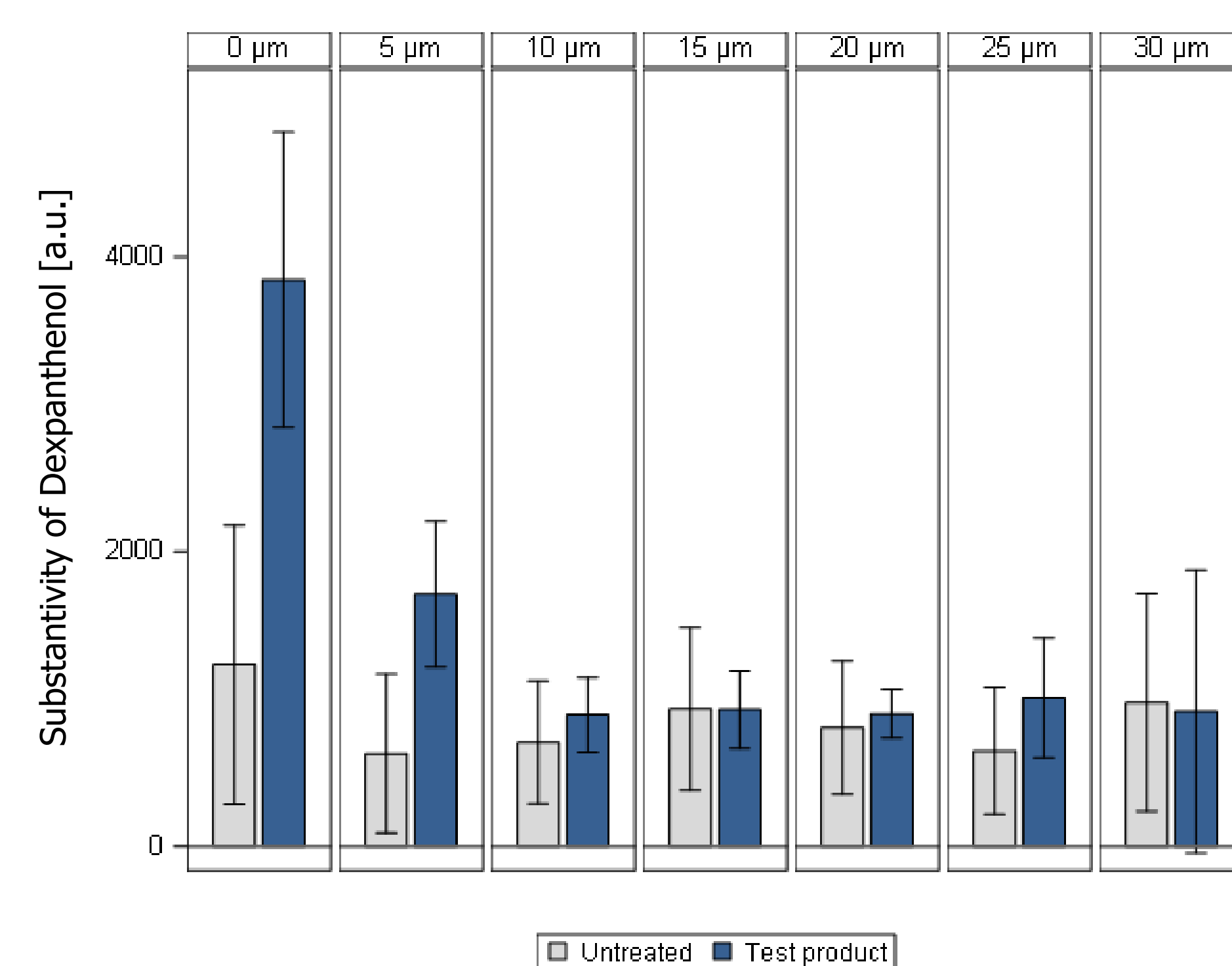


Fig. 1: Substantivity of DEX by Raman spectroscopy [a.u.] after 5 days of product application. Mean values and 95% confidence intervals for t1 (N=6). Untreated (offset, to be subtracted from DEX data) versus test product with 2% DEX.

**Study part III:** At skin surface ( $p<0.001$ ;  $p<0.001$ ) and 5µm ( $p=0.004$ ;  $p<0.001$ ), for both areas (treatment mode B and C, Table 1) significantly higher DEX signals were found in comparison to the untreated area (mode A). On the occlusive treatment area (mode B) a significant ( $p=0.046$ ) detection of DEX also was shown at 10µm in comparison to untreated skin site (Figure 2).

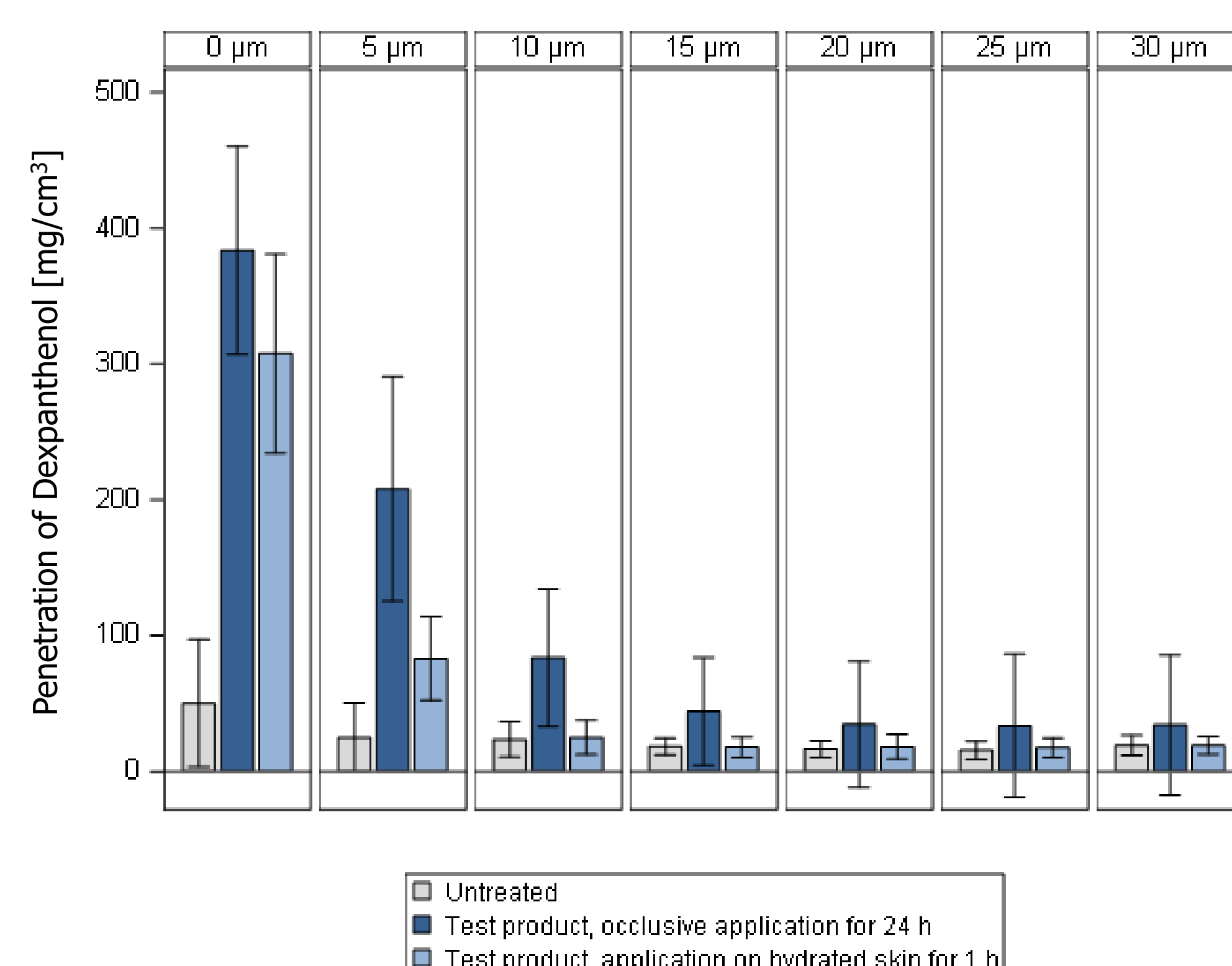


Fig. 2: Penetration of DEX by Raman spectroscopy [mg/cm<sup>3</sup>] in treatment mode A (untreated), B (24h application under occlusion) and C (application on pre-hydrated skin for 1h). Untreated area (offset). Bar chart with mean values and 95% confidence intervals of raw data (N=6).

Summarizing, DEX is well detectable on the skin surface and down to a depth of 10 up to 20µm. Occlusive conditions led to DEX penetration into stratum disjunctum and into stratum compactum. On pre-hydrated skin DEX penetrates into stratum disjunctum at measurable amounts. After 5 days open product application DEX is measurable even 12-16 hours after the last application and was significantly enriched in the upper layer of the stratum corneum.