J. Cosmet. Sci., **62,** 361–369 (July/August 2011)

Skin moisturizing effects of panthenol-based formulations

FLÁVIO B. CAMARGO, Jr., LORENA R. GASPAR, and
PATRÍCIA M. B. G. MAIA CAMPOS, *Universidade de São Paulo, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Av. do Café s/n, Bairro Monte Alegre, Ribeirão Preto, SP, Brazil 14040-903.*

Accepted for publication April 16, 2011.

Synopsis

This study aims to evaluate the skin moisturizing efficacy of formulations containing different concentrations of panthenol. Formulations supplemented with or without 0.5%, 1.0%, or 5.0% panthenol were applied daily to the forearms of healthy subjects. Skin conditions in terms of moisture and transepidermal water loss (TEWL) were analyzed before and after 15- and 30-day periods of application. The formulations were also applied after skin washing with sodium laureth sulphate (SLES) to evaluate the immediate effects on TEWL and skin moisture. Panthenol-containing formulations (1.0% and 5.0%) produced significant decreases in TEWL after 30-day applications. In skin washed with SLES, significant reduction of TEWL was evident two hours after application of formulations loaded with panthenol when compared with control and vehicle. It is concluded that skin integrity is maintained by the improved protective effect of 1.0% panthenol added to the formulation.

INTRODUCTION

Moisturizing products are among the most important cosmetic types. Their use helps to prevent cutaneous early aging and may act as support in the treatment of several skin disorders (1–3).

Skin dryness or hydration, considered respectively as a sign of compromised skin or healthy skin, is the subject of many studies showing the importance of moisturizing active substances and products in different skin conditions (dry skin disorders, atopic skin, ichthyosis, and contact dermatitis) (4,5). The studies emphasize the influence of the careful choice of raw materials, which should have good sensorial and hydration properties.

Amino acids, lactic acid, silicones, vegetable and mineral oils, ceramides, and polymers are some of the several moisturizing agents used in cosmetic products. These agents act by different mechanisms, such as occlusion or water carried into the skin surface. Hydrophilic polymers have plasticizing and film-forming properties, which are able to suppress evaporation of water from the stratum corneum. Vitamins A, C, and E and panthenol are also moisturizing active substances, which play an important role in keeping skin in good condition; e.g., they can stimulate collagen production, act on epithelization in dry and rough skin, enhance skin hydration, and restore a healthy skin barrier (6–9).

Panthenol, the biologically active alcohol analogue of pantothenic acid is a pro-vitamin of the B-complex group that is a normal constituent of skin and hair. When applied topically, panthenol is converted to pantothenic acid, a component of coenzyme A and holo-fatty acid synthase that is essential to normal epithelial function (10).

Dermatologists have long been aware of the value of panthenol in the preservation of skin health. Clinical observations have reported that topically applied panthenol is an aid in superficial wound healing in burns, fissures, corneal lesions, and allergic dermatitis, and it is well tolerated, with minimal risks of skin irritancy (10,11). Indeed, it has been shown that panthenol has protective effects against skin irritation (12). In one irritation model, pretreatment with dexpanthenol cream resulted in significantly less damage to the stratum corneum barrier when compared with no pretreatment (13). However, its exact mechanism of action is not yet fully understood.

Moisturizers influence the skin barrier function of healthy skin, but the base formulation composition and the concentration of active substances may influence the hydration effect of the cosmetic product. The chemistry and function of dry skin and moisturizers is a challenging subject for the practicing dermatologist, as well as for those who develop these agents in the pharmaceutical/cosmetic industry (5). Consequently, more studies are needed to evaluate by objective noninvasive techniques the hydration effect of panthenol-containing cosmetic formulations on human skin.

New biochemical approaches and noninvasive instruments will increase our understanding of skin barrier disorders and facilitate optimized treatments. Among these methods are noninvasive validated skin biophysical techniques, which are widely used, as they allow evaluation of cosmetic products under actual conditions of use (1,14,15). They have been used to determine viscoelastic and moisturizing properties, and human skin barrier function, which is an important aspect of skin biology (16). However, alongside the development of anti-aging cosmetic products, it has become necessary to standardize the new methodologies employing noninvasive techniques, to evaluate benefits attributed to a given product (17–19).

Despite the fact that panthenol is often used in topical formulations in order to improve or maintain good skin conditions and the rate of wound healing, its optimal concentration and the correct choice of vehicle in terms of sensorial and stability properties have not been sufficiently studied. This study constitutes a clinical objective evaluation of the hydration and protection effects of cosmetic formulations containing panthenol in different concentrations by noninvasive biophysical methods. The results contribute to the elucidation of the effects of panthenol on skin barrier function and may also be helpful in maintaining homeostasis in healthy skin that is frequently compromised by continuous UV radiation and pollution.

MATERIAL AND METHODS

FORMULATIONS STUDIED

Experimental formulations, (Table I), containing 2.0% (w/w) of *sclerotium* gum (Amigel®, Alban Muller International, Vincennes, France) and 2.0% (w/w) of methylphenyl polysiloxane (Net FS®, Nikko Chemicals, Tokyo, Japan) were prepared in a Heidolph

Table I
Formulation Composition

Components	Percentage (w/w)
Sclerotium gum	2.0
Methylphenyl polysiloxane	2.0
Propyleneglycol	2.5
Glycerin 86%	2.5
Phenoxyethanol and parabens	0.8
Hydrogenated and ethoxylated castor oil 40 OE	2.0
Deionized water	100.0

RZR 2021 shaker at approximately 650 rpm, and supplemented or not (vehicle/placebo) with 0.5%, 1.0%, or 5.0% (w/w) panthenol (D-panthenol, DSM Nutricional Products, Basel, Switzerland).

DETERMINATION OF CLINICAL EFFICACY

Study design. The one-sided blind, placebo-controlled study was approved by the Faculty of Pharmaceutical Sciences Ethics Committee (CEP/FCFRP 40/2005) and complied with the Declaration of Helsinki. A total of 40 healthy female subjects, 20–35 years old and having Fitzpatrick (20) skin types II and III, participated in this study after having given their written informed consent. The exclusion criteria were (a) the presence of any dermatitis and/or other skin or allergic diseases and (b) a smoking habit. Volunteers were instructed not to apply any topical products such as moisturizers, sunscreens, and anti-aging formulations on the test sites for two weeks before and during the study.

During the test period the subjects were allowed to wash normally, but did not use any other skin care products on their arms. Formulations were applied daily on the volunteers' forearm skin, and prior to all measurements they stayed in the testing room for at least 30 min in order to allow temperature (20° ± 2°C) and humidity (45-60%) adaptation. An analysis of skin conditions, according to a standardized study protocol, was conducted before and after 15- and 30-day periods of daily application (six to ten hours after the last application). It consisted of measurements of skin moisture (capacitance method), transepidermal water loss (TEWL), and viscoelasticity (skin deformation in response to suction).

Study of long-term efficacy. After the baseline measurements, all subjects were instructed to apply 0.2 grams of two of the formulations (one on each forearm—in an area of approximately 100 cm^2), twice daily, in the morning and in the evening. The applications sites of the four formulations studied (placebo and formulations containing 0.5%, 1.0%, and 5.0% of panthenol) were randomized between groups and between subjects' left-right forearms (parallel-group, investigator-blinded randomization) in order to guarantee that the four formulations under study were applied to an equal number of participants and to an equal number of right and left forearms. As an example, the first volunteer applied the vehicle to the right forearm and the formulation containing 0.5% of panthenol to the left one; the second volunteer applied formulations containing 1.0% and 5.0% of panthenol to the left and right forearms, respectively; the third one applied the formulation containing 5.0% of panthenol and the vehicle to the left and right forearms, respectively; and the

fourth volunteer applied formulations containing 0.5% and 1.0% of panthenol to the left and right forearms, respectively, and so on. Another group of 20 volunteers (control group) did not receive any formulation and were exposed to the same conditions as the 40 experimental volunteers.

Immediate effects—SLES wash test. The volar forearms of 20 new volunteers were divided into three areas (six areas for each person); after the baseline measurements each area was submitted to a 1% SLES (sodium laureth sulphate - 3EO), (~ 3.7%, Genapol ZRO Liq, Clariant) wash test once a day for five days. The standardized wash test was performed on the forearm as follows: a foam roller was soaked in 1.0% SLES (test solution) and moved up and down ten times on the volar forearm within one minute. Then, another foam roller was soaked with test solution and the whole procedure was repeated altogether five times. Finally, the forearm was rinsed with clear tap water and dried carefully with a paper towel (21). For each washing procedure 50 ml of test solution was used. In two groups tap water was used instead of SLES. At the end of the fifth day, new measurements were carried out. After this, 0.1 grams of the four different formulations under study (containing 0.5%, 1.0%, and 5.0% of panthenol and the vehicle) were applied to the areas previously established (in an area of approximately 40 cm^2) and new measurements were carried out after two hours to evaluate their influence on TEWL. A control site was submitted to the SLES wash test but did not receive the application of any formulation. The four formulations studied and the control sites were randomized over the areas in the volar forearm.

INSTRUMENTATION

Corneometer® measurements. The stratum corneum moisture content was determined with a noninvasive, skin capacitance meter (Corneometer® CM 825, Courage + Khazaka, Cologne, Germany), which makes use of the relatively high dielectric constant of water (22). This device determines the water content of the superficial epidermal layers down to a depth of about 0.1 mm and expresses the values obtained in arbitrary units. The averaged values of twenty measurements were used for subsequent calculations. (2).

Tewameter® measurements. Transepidermal water loss was determined by an evaporimeter (Tewameter® CM 210, Courage + Khazaka, Cologne, Germany). TEWL values were registered for two minutes following a 30-second period of equilibration of the probe on the skin (2, 21).

The Tewameter® is based on Fick's diffusion law, indicating the quantity being transported per a defined area and period of time. By using the data obtained from thermo- and hydro-sensors, and after processing the information by an inbuilt microprocessor, a numerical value of the TEWL is obtained, commonly shown in $g/m^2/h$ (14,23).

Cutometer® measurements. Viscoelastic properties of the skin were determined using a noninvasive, *in vivo* suction skin-elasticity meter (Cutometer® SEM 575, Courage + Khazaka, Cologne, Germany). The instrument consists of a microprocessor-regulated pneumatic system that applies suction via a 2-mm circular opening in the handheld probe. Evaluation of skin viscoelasticity is based on the measurement of skin deformation in response to suction. Each measurement consisted of five consecutive cycles of a two-second suction application period followed by a two-second relaxation period. The suction load was 450 mbars. The ratio of viscoelastic to elastic distension, Uv/Ue (related to viscoelastic properties) was analyzed (19).

STATISTICAL ANALYSIS

Parametric tests were selected for statistical analysis of the experimental data points, since they showed a Gaussian distribution. The ANOVA test was used for comparison of multiple measured data points using the statistical software, MINITAB. Differences were accepted as statistically significant at $p < 0.05$.

RESULTS AND DISCUSSION

DETERMINATION OF CLINICAL EFFICACY

Long-term study. Biophysical measurements before and after daily applications for 15- and 30-day periods are reported in Figures 1 and 2.

All the formulations studied produced a significant increase in stratum corneum moisture ($p < 0.001$) 15 and 30 days after daily application, when compared with the baseline values and with the control group (Figure 1). The effect was more evident with the use of formulations supplemented with panthenol.

After long-period treatments, all formulations produced a significant increase in stratum corneum moisture, including the ones without panthenol. Other raw materials in this cosmetic formulation (i.e., *sclerotium* gum and hydrogenated and ethoxylated castor oil) could also act on the epidermis, causing improved skin hydration (24). No significant alterations were observed in skin viscoelastic properties in the long-term studies ($p < 0.05$) when compared with baseline values.

The viscoelastic-to-elastic ratio (Uv/Ue) is a parameter obtained by cutometer analysis, which can be used not only to evaluate skin elasticity properties but also hydration of the

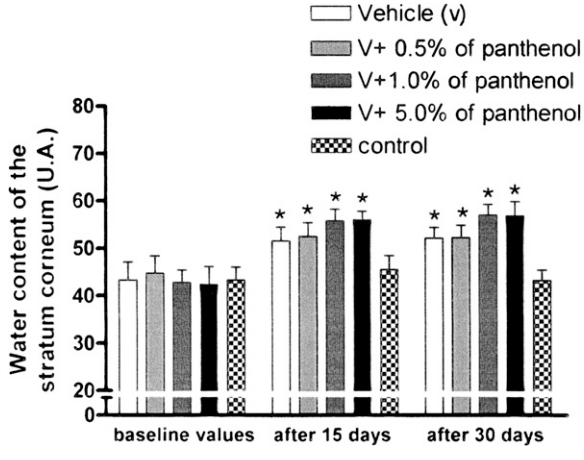

Figure 1. Water content of the stratum corneum before (baseline values) and 15 and 30 days after daily application of the formulations: vehicle (V), V+0.5%, V+1.0%, and V+5.0% of panthenol and control site (ANOVA test, n = 20 subjects, mean ± SEM). *Significantly different from the base values and control site ($p < 0.001$).

deeper layers of the epidermis (19). Results suggest that the formulations under study did not present any of the above-mentioned effects on the epidermis. They seem to have not only a moisturizing effect on stratum corneum but they also reduce TEWL due to filmogen and protective properties.

Moisturizers may act by an occlusive mechanism. They impair evaporation of skin moisture by forming an epicutaneous greasy film that prevents water loss, as is the case with the oils, lipids, and hydrogenated and ethoxylated castor oil used in the formulation under study. A humectant activity by glycerin and urea may attract water from the environment to the stratum corneum (2,25,26). Studies with moisturizing products should evaluate the increase in water content of the stratum corneum and also the decrease in transepidermal water loss, in order to determine their mechanism of action. Thus, multiple assessments to evaluate barrier function and the raising of questions about the effects of cumulative repeated application of cosmetic formulations on stratum corneum function are necessary.

Evaluation of transepidermal water loss (TEWL) showed that formulations supplemented with 1.0% and 5.0% of panthenol improved the skin barrier function, resulting in a significant decrease ($p < 0.001$) in TEWL values 15 and 30 days after daily application of these formulations (Figure 2).

This result showed that to have significant long-term effects on skin barrier function, the formulation must be supplemented with higher concentrations of panthenol, such as 1.0% and 5.0%. In addition, the concentration of panthenol also influenced the improvement of skin hydration since 1.0% of panthenol was enough to show efficacy in the reduction of TEWL.

Thus, it is suggested that daily use of formulations containing panthenol is important to protect the skin barrier function by reducing TEWL, to keep the skin in good condition, and to maintain skin homeostasis.

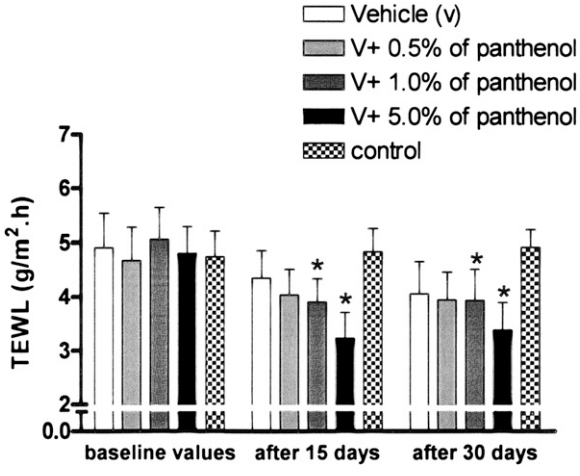

Figure 2. Transepidermal water loss before (baseline values) and 15 and 30 weeks after the application of the formulations: vehicle (V), V+0.5%, V+1.0%, and V+5.0% of panthenol and control site (ANOVA test, n = 20 subjects, mean ± SEM). *Significantly different from the base values and control site ($p < 0.001$).

It is well known that the skin plays an important role in the prevention of transepidermal water loss by protecting the skin barrier function, which in turn maintains cutaneous homeostasis and prevents skin disorders and physical, chemical, and bacteriological injuries (26). Vitamins A, C, and E and panthenol are widely used in dermatological and cosmetic formulations to improve skin conditions, but not many studies address the effects of panthenol on healthy skin, as observed for other entities such as vitamin A (8,27,28). Consequently, the results obtained in this study contribute to a better understanding of the effects of cosmetic products containing panthenol on healthy skin, when evaluated by clinical studies under actual conditions of use.

Immediate effects—SLES wash test. The results obtained in the SLES wash test showed that panthenol has good protection properties for skin barrier function. Formulations containing 1.0% and 5.0% of panthenol significantly reduced TEWL values, when compared with the control site (with SLES washing and without the application of the formulations) and also with the vehicle (formulation without panthenol) (Figure 3B). Considering that skin biophysical techniques may evaluate skin conditions by more than one parameter, the analysis of corneometer and tewameter results may suggest that panthenol acts on skin by protecting its barrier function, since TEWL values were significantly reduced when compared with the vehicle and control areas (Figure 3A). Thus, the SLES wash test showed that when skin barrier function was altered, the formulations containing 1.0% and 5.0% of panthenol significantly reduced TEWL.

In summary, this study emphasizes the importance of adequate panthenol concentrations required in effective formulations for skin protection as evaluated by clinical objective studies.

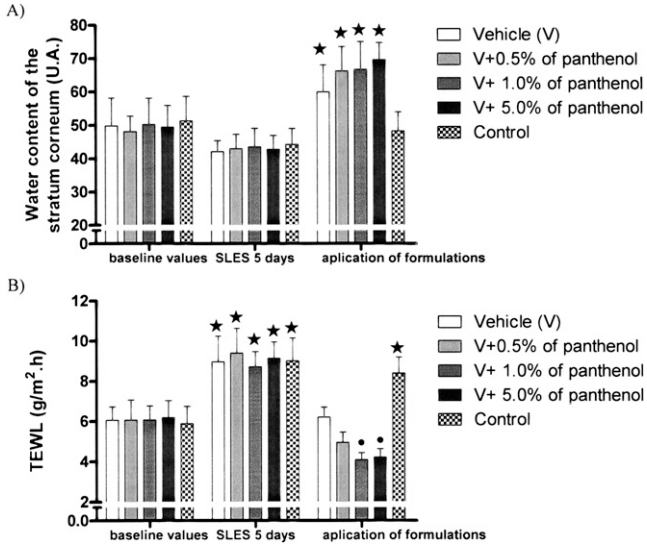

Figure 3. Water content of the stratum corneum (A) and transepidermal water loss (B) before (baseline values) and after repetitive skin washing with SLES solution for five days (SLES five days) and two hours after a single application of the formulations: vehicle (V), V+0.5%, V+1.0%, and V+5.0% of panthenol and the control site (with SLES washing and without the application of the formulations) (ANOVA test, n = 20 subjects, mean ± SEM). ★ Statistically significantly higher compared to baseline values ($p < 0.001$); • Statistically significantly lower compared to baseline values ($p < 0.001$).

CONCLUSION

This clinical study showed that panthenol-based formulations increased skin moisture and had a significant effect on skin barrier function by decreasing TEWL values. In addition, concentrations of pro-vitamin also influenced the improvement of skin barrier function. One percent panthenol added to the basic formulation tested was sufficient to show efficacy in this parameter. It seems that the moisturizing effects of panthenol can be attributed mainly to the protection of skin barrier function, and thus it may be used in cosmetic products to maintain physiological skin conditions and to prevent dry skin alterations, since loss of water may adversely impact skin appearance and lead to skin disorders.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the financial support of Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

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