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The influence of a cream containing 20% glycerin and its vehicle on skin barrier properties

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Synopsis

Glycerin is widely used in cosmetics and well as in pharmaceutical formulations, mainly as humectant. *In vitro* studies have shown glycerin to prevent crystallization of stratum corneum model lipid mixture at low room humidity. Whether this may affect the skin barrier function during repeated application of glycerin in a cream base to normal skin is not known. Therefore, the influence of a cream containing 20% glycerin was compared with its placebo cream in a bilateral, double-blind study on 17 healthy volunteers. The effect was evaluated as influence on hydration with a corneometer and on skin barrier function. Skin barrier function was assessed as permeability to water with an evaporimeter (transepidermal water loss; TEWL) and as sensitivity to an irritating surfactant by measuring the biological response (measured as TEWL and skin blood flow).

Ten days treatment of normal skin with 20% glycerin significantly increased skin corneometer values, indicating an increased hydration. However, our study failed to show an influence of glycerin on human skin, in terms of TEWL and skin sensitivity to SLS-induced irritation.

Résumé

La glycérine est largement utilisée dans les formulations cosmétiques aussi bien que pharmaceutiques, principalement en tant qu'humectant. Des tests *in vitro* ont montré que la glycérine empêche la cristallization de la structure lipidique du *Stratum Corneum* à humidité ambiante basse. La question de savoir si ceci peut affecter la fonction barrière de la peau durant des applications répetées d'une crème pour peau normale contenant de la glycérine n'a pas été demontrée. Par conséquent, une crème contenant 20% de glycérine a été comparée avec son placebo dans un test bilatéral en double aveugle sur 17 volontaires en bonne santé. L'effet hydratant de la glycérine a été évalué avec l'aide d'un cornéomètre, son influence sur la fonction barrière de la peau avec l'aide d'un évaporimètre (mesurant la Perte Trans-Epidermal en eau) et son effet protecteur après irritation á l'aide d'un agent de surface par la réponse biologique de la peau (mesure de la PTEL et du flux sanguin).

Dix jours de traitement sur une peau normale avec une crème contenant 20% de glycérine ont augmenté les mesures du cornéomètre de manière significative, indiquant une augmentation de l'hydration de la peau. Cependant notre étude n'a pas pu démontré l'influence de la glycérine sur la peau en terme de PTEL et la réduction du potentiel irritant du Sodium Lauryl Sulphate.

Introduction

The importance of glycerin in skin care products is well established and glycerin is widely used in cosmetics and well as in pharmaceutical formulations. To explain its benefits, studies have focused on its humectant and protecting properties. Glycerin diffuses into the stratum corneum [1], increases skin hydration [2–4] and relieves clinical signs of dryness [4–7]. One feature of dry skin is scaling, and studies show that glycerin increases the rate of corneocyte loss from the superficial surface of human skin, probably due to an enhanced desmosome degradation [8].

Glycerin might also influence the crystalline arrangement of the intercellular bilayer lipids. The

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bulk of the bilamellar sheets of the lipids has been proposed to be in crystalline/gel domains bordered by lipids in a fluid crystalline state [9]. In dry skin the proportion of lipids in the solid state may be elevated and glycerin may then help maintaining the lipids in a liquid crystalline state at low relative humidity [10].

The influence of glycerin on the skin barrier function is not well understood. After a single application to normal skin, glycerin reduces transepidermal water loss (TEWL) for some hours [7]. Furthermore, single application to tape-stripped and acetone-treated skin has been reported to decrease skin sensitivity to alkali, sodium lauryl sulphate (SLS) and dimethylsulfoxide, but increase bioavailability of hexyl nicotinate [11].

Whether glycerin can affect the skin barrier function during repeated application to normal skin has not been conclusively shown. Therefore, in the present study the influence of the glycerin-containing cream on skin barrier function in normal skin was compared with its placebo cream in a bilateral, double-blind study on healthy volunteers. Skin barrier function was evaluated as transepidermal water loss (TEWL) and as skin sensitivity to SLS-challenge [3, 12–14].

Materials and methods

Experimental design

In a double-blind, bilateral and randomised study, 17 healthy volunteers (14 females and three males) treated their forearms with a cream containing 20% glycerin and its placebo (glycerin replaced by water) for 10 days. Other ingredients in the cream were aqua, petrolatum, canola, mineral oil, cetearylalcohol, glycerylstearate, dimethicone, PEG-100 stearate, glyceryl polymethacrylate, cholesterol, propyleneglycol, methylparaben and propylparaben.

Informed consent was obtained from all volunteers and the study was approved by the local ethics committee. During the test period, the subjects were allowed to wash normally but not use any other skin care products on their arms. The study was carried out late September to October 1998. The test products were dispensed into white coded tubes and the volunteers were asked to apply the creams on the volar aspect of the forearms twice daily for 10 days. Before the first application and after 10 and 11 days the skin condition was measured using non-invasive biophysical instruments (see below). After the measurement on day 10 the skin was exposed to sodium lauryl sulphate (SLS) (see below). To ensure that no cream residue was left to influence the results, the subjects were asked to wash their forearms in the morning and not apply any product before the measurement.

SLS exposure

The skin on the volar aspect of both forearms was exposed to 15% aqueous solutions of SLS. A 50-µl aliquote of the solution was pipetted onto one layer of filter paper placed in aluminium chambers (Ø = 12 mm, Finn chambers, Epitest OY, Finland). The chambers were fixed to the skin for 7 h with adhesive tape (Scanpore, Norgeplaster, Oslo, Norway). Upon removal of the patches, the skin was gently rinsed with water and allowed to dry, and 17 h later each site was examined visually and TEWL, skin capacitance and blood flow were measured. A high concentration of SLS and short exposure time are considered to facilitate detection of differences in skin barrier function [3, 12, 13]

Visual examination

The subjective assessment of the degree of irritation on day 11 was made before the instrumental readings. The degree of irritation was evaluated by visual scoring according to the following scale: 0 = no reaction; 0.5 = barely perceptible very weak spotty erythema; 1 = slight erythema; 2 = moderate erythema; 3 = intense erythema, infiltration, possible vesicles. The assessments were made by one observer (C.W.).

Instrumental evaluation

All measurements were performed without knowledge of prior treatments. First TEWL was measured, then skin blood flow followed by skin capacitance. TEWL was quantified using an evaporimeter EP1 (Servomed, Kinna, Sweden) [15]. After application of the probe onto the skin, TEWL values were automatically transferred into a computer during the next 70 s. The mean values from the last 30 s were recorded and used for further calculations. The cutaneous blood flow was measured with a laser Doppler flowmeter (Periflux Pf1, Perimed, Stockholm, Sweden) [16] equipped with a special multifibre probe which had seven fibre triplets instead of one, one being in the middle and six

around, forming a circle 8 mm in diameter (PF 113 integrating probe, Perimed). Thus, each blood flow value is the mean of the seven spots, which reduces variation due to spotty erythema. The probe was attached to the skin with a standard probe holder without pressure and using double-sided adhesive tape. The output signals were recorded on a chart strip recorder until equilibrium was reached, usually within 1–2 min. The value at equilibrium was used for the calculations. The electrical capacitance, indicating the degree of skin hydration, was measured with a Corneometer CM-820 (Courage and Khazaka, Cologne, Germany).

Statistics

The results are presented using box plots. The bottom line of the box is the first quartile (Q1), and the top is at the third quartile (Q3) value. A line is drawn across the box at the median. The whiskers are the line that extends from the top and bottom of the box to the lowest and highest observations that are still inside the region defined by the following limits:

Lower limit: Q1–1.5 (Q3–Q1)

Upper limit: Q3 + 1.5 (Q3–Q1)

Outliers are points outside of the lower and upper limits and are plotted with asterisks.

Wilcoxon signed rank test on paired data was used to test the differences between the Miniderm and its placebo at days 0, 10 and 11. $P < 0.05$ was considered significant. Minitab® statistical software, Release 12 (PA, U.S.A.) for Windows was used for calculations and plots.

Results

No differences in TEWL or in skin blood flow were found between the glycerin cream and its placebo at the start of the study or after 10 days (Figs 1 and 2), but 20% glycerin induced a significantly higher corneometer value than placebo at day 10 (Fig. 3).

Challenge of the skin with SLS did not induce a different response in the glycerin-treated area compared to the placebo treated area (Table I, Figs 1 and 2).

Discussion

Ten days treatment of normal skin with 20% glycerin significantly increased skin corneometer values, indicating an increased hydration. However, no influence on TEWL was observed following treatment with glycerin and no difference in skin sensitivity to SLS-induced irritation was obtained between the areas treated with the active and the placebo cream.

Increased hydration [17] and changes in skin plasticity [18] have been found in previous studies on glycerin. Aqueous solutions also reduce TEWL for some hours after application [7–8] and decrease skin sensitivity to alkali, SLS and DMSO, but increase bioavailability of hexyl nicotinate [11]. In the present study, no reduction in TEWL or skin sensitivity to SLS were observed. Our results might be explained by the repeated use of the cream or the passage of time after last application and the skin measurements (> 8 h). It is also possible that other ingredients in the cream affected the results.

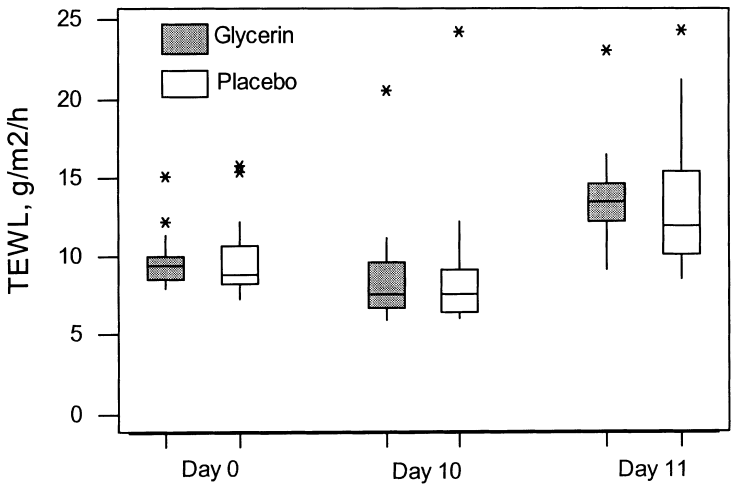

Figure 1 Transepidermal water loss (TEWL, g m^{-2} h^{-1}) at the start of the study and after 10 days treatment with 20% glycerin and its placebo. The values at day 11 represent the result following the SLS-challenge at day 10. The results are presented as box plots with the median value as a line across the box and the first quartile value at the bottom and the third at the top. The whiskers are the line that extend from the top and bottom of the box to the lowest and highest observation within a defined region, with outliers plotted as asterisks outside this region. $n = 17$.

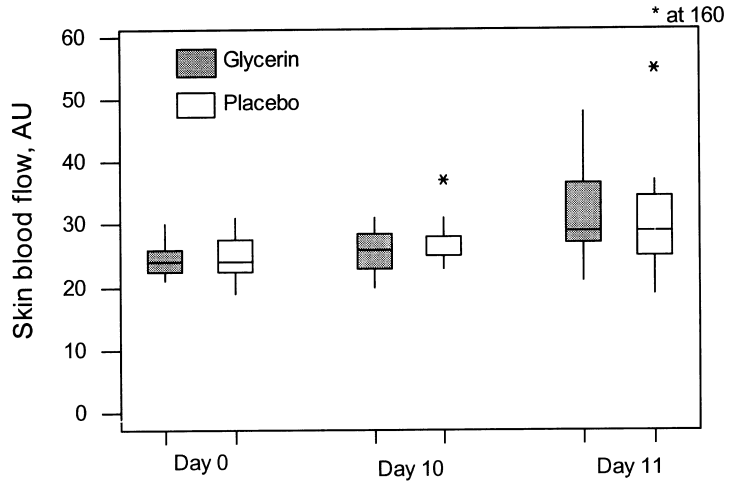

Figure 2 The skin blood flow at the start of the study and after 10 days treatment with 20% glycerin and its placebo. The values at day 11 represent the result following the SLS-challenge at day 10. For explanation of box plots, see Fig. 1. $n = 17$.

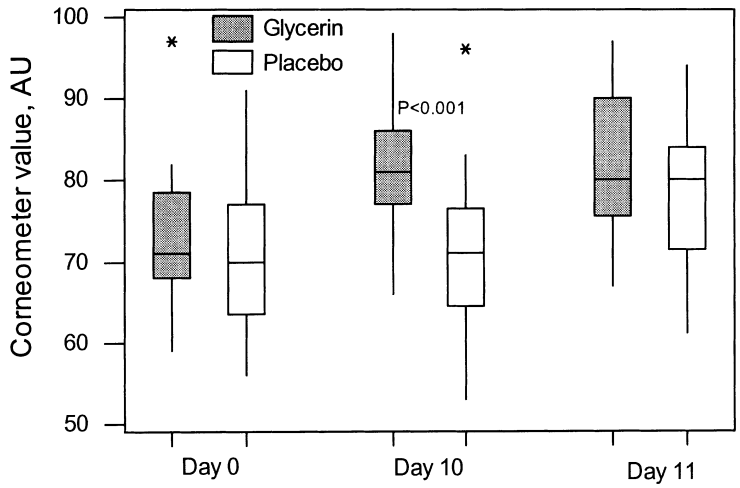

Figure 3 The skin corneometer value at the start of the study and after 10 days treatment with 20% glycerin and its placebo. The values at day 11 represent the result following the SLS-challenge at day 10. For explanation of box plots, see Fig. 1. $n = 17$.

Table I Distribution of number of skin reactions to 15% SLS after treatment with 20% glycerin or its placebo ($n = 17$)

	0	0.5	1	2	3
Glycerin	6	8	3	0	0
Placebo	7	4	6	0	0

0 = no reaction; 0.5 = barely perceptible very weak spotty erythema; 1 = slight erythema 2 = moderate erythema 3 = intense erythema, infiltration, possible vesicles.

However, the results in the present study are in accordance with a previous study on a cream containing 7% glycerin [3]. In that study no change in TEWL was noted after repeated application for some weeks and no change in SLS-induced irritation compared to untreated skin was found. However, another humectant; urea, has been found to decrease TEWL and to decrease skin sensitivity to SLS-induced irritation in a similar type of experiment [3, 13].

In conclusion, our study failed to show any influence of repeated application of 20% glycerin to human skin on skin barrier function, in terms of TEWL or skin sensitivity to SLS-induced irritation.

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