

Barrier recovery and influence of irritant stimuli in skin treated with a moisturizing cream

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Moisturizers are used daily by many people to alleviate symptoms of clinically and subjectively dry skin. Recent studies suggest that certain ingredients in creams may accelerate the recovery of a disrupted barrier and decrease the skin susceptibility to irritant stimuli. In the present single-blind study, a moisturizing cream was tested for its influence both on barrier recovery in surfactant-damaged skin and on the susceptibility of normal skin to exposure to the irritant sodium lauryl sulphate (SLS). Parameters measured were transepidermal water loss (TEWL) and skin corneometer values, indicating degree of hydration. Treatment of surfactant-damaged skin with the test cream for 14 days promoted barrier recovery, as observed as a decrease in TEWL. Skin corneometer values also normalized more rapidly during the treatment. In normal skin, use of the test cream significantly reduced TEWL after 14 days of treatment, and irritant reactions to SLS were significantly decreased. Skin corneometer values increased after only 1 application and remained elevated after 14 days. In conclusion, the accelerated rate of recovery of surfactant-damaged skin and the lower degree of SLS-induced irritation in normal skin treated with the test cream may be of clinical relevance in attempts to reduce contact dermatitis due to irritant stimuli.

Key words: sodium lauryl sulfate; irritant contact dermatitis; bioengineering methods; transepidermal water loss; skin lipids; barrier function; moisturizers; emollients. © Munksgaard, 1997.

Accepted for publication 4 February 1997

Moisturizing creams are used daily by many people to alleviate symptoms of clinically and subjectively dry skin. Often they contain low molecular weight humectants, such as urea, glycerine, lactic acid, pyrrolidone carboxylic acid (PCA) and salts. It is assumed that these substances are absorbed into the stratum corneum and there, by attracting water, increase the degree of hydration. In a recent study, it was also found that some moisturizers improve the barrier properties of normal skin (1). The commonly used humectant urea was shown to influence both the transepidermal water loss (TEWL) and the apparent susceptibility to irritation caused by sodium lauryl sulphate (SLS). The irritant response diminished significantly after applications of urea-containing moisturizers.

Besides humectants, moisturizers may also contain lipids. Lipids in moisturizers have traditionally been considered to be inactive and have been incorporated into formulations on the basis of their technical and sensory properties rather than on any possible effect on the epidermis. However, moisturizers or ointment bases that do not contain

any ingredients that are known to be pharmacologically active often assist in the improvement of skin diseases, such as irritant contact dermatitis (2). The mechanisms of the beneficial effects are not yet fully understood. Surfactant-induced skin irritation has been found to be reduced by application of canola oil and its sterol-enriched fraction (3). The effect of the latter fraction was especially pronounced and was similar to that of a hydrocortisone cream. Canola oil has a relatively high content of sterols, which might possibly influence the structure of the epidermal membrane lipids. A mixture of sterols, free fatty acids and sphingolipids forms the intercellular membrane bilayers of the stratum corneum, and it is presumed that this mixture regulates the epidermal barrier function (4, 5).

In the present study, the influence of a cream containing both urea and canola oil on some skin properties was investigated. The aims were to evaluate the influence of the cream on (i) the barrier recovery of surfactant-damaged skin and (ii) the susceptibility of normal skin to irritation

caused by SLS. Skin corneometer values (which might reflect skin hydration) and TEWL were measured objectively and the degree of irritation was assessed visually.

Materials and Methods

Volunteers

13 healthy individuals, aged 24 to 58 years, 10 women and 3 men, with no visible signs of skin disease, participated in the study. During the test period, the subjects were allowed to wash normally, but not to use any other skin care products on their arms. Informed consent was obtained from all volunteers and the study was approved by the local ethics committee. The study was carried out in the months October–November.

Test product

The tested cream contained 5% urea and 5% hydrogenated canola oil. Other ingredients were water, caprylic / capric triglyceride, cetearyl alcohol, propylene glycol, glyceryl polymethacrylate, lactic acid, dimethicone, paraffin, acetylated lanolin alcohol, cetyl acetate, carbomer, PEG-20 stearate, glyceryl stearate, PEG-100 stearate, methylparaben, propylparaben, and perfume.

Experimental design

The study was designed as single-blind. Damaged skin was produced by exposure of an area (D 12 mm) on the volar aspect of each forearm to an aqueous solution of 14% SLS (for details, see below). The volar aspect of one of the forearms was then treated 2× daily for 14 days with the cream, which was applied both to the surfactant-damaged area and to the surrounding normal skin, while the other forearm was left untreated. The arm to be treated was chosen randomly. Comparisons could then be made between the cream surfactant-damaged area on the cream-treated arm and that on the contralateral arm. The normal skin treated with the cream and the untreated normal skin on the contralateral arm were also compared. Measurements of TEWL and skin hydration were performed with an Evaporimeter EP1 and a Corneometer, respectively, on days 1, 4, 7, 10 and 14 after exposure to SLS. The degree of irritation on the damaged areas was also scored visually (see below).

TEWL and skin hydration were measured about 15 h after the last application of the cream, i.e., the product was applied in the evening and the measurements were made on the following day. To ensure that no cream residue on the surface of the skin influenced the measurements (6), the subjects

were asked to wash their arms and not to apply any product on the morning of the measurements.

After 14 days, the normal skin which had been treated with the cream and the corresponding untreated skin were exposed to 14% SLS for 7 h (see below) and the resultant irritant reaction was assessed. The SLS-exposure was begun between 35 and 40 h after the last cream application and the degree of irritation was evaluated the day after the SLS exposure.

SLS exposure

50 µl of the aqueous solution of 14% SLS (Ph. Eur.) was pipetted onto a layer of filter paper placed in each of several aluminium chambers (D 12 mm, Finn Chambers, Epitest Oy, Finland). The chamber was fixed to the skin for 7 h with adhesive tape (Scanpor, Norgeplaster, Oslo, Norway). Upon removal of the patch, the skin was gently rinsed with water and allowed to dry. 24 h after the patch removal, each site was examined both visually and with an Evaporimeter EP1 (see below).

Visual evaluation

The subjective assessment of the degree of irritation was made before the instrumental readings. The volunteers were asked not to reveal which arm they had treated. 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, either spotty or diffuse
- 2 = moderate erythema
- 3 = intense erythema, infiltration, possible vesicles.

Instrumental evaluation

All measurements were performed without knowledge of prior treatment. First TEWL was measured, then skin capacitance. Noise in the room and talking during the recordings were restricted.

TEWL was quantified using an Evaporimeter EP1 (Servomed, Kinna, Sweden) (7). The probe for the measurement was equipped with a screen and grid to reduce air convection. The output signal was 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 corneometer values, indicating degree of skin hydration (8, 9) was measured with a Corneometer CM-820 (Kourage and Khazaka GmbH, Cologne, Germany).

Table 1. Visual scoring of the degree of irritation on days 1–14 after exposure to SLS and treatment with the test cream; $n=13$

Day	Treated		Untreated	
	score, % of possible maximum	no. people showing visible irritation	score, % of possible maximum	no. people showing visible irritation
1	17.9	9	14.1	8
4	0	0	0	0
7	0	0	0	0
10	0	0	0	0
14	0	0	0	0

Data treatment and statistics

Data from the instrumental recordings are presented as mean $\pm$ SD. The results from the visual scoring are given in % of the total possible score. Total possible score is the number of subjects multiplied by 3. The Wilcoxon signed rank test was used when comparing the results of the treated and the control areas. $p < 0.05$ was adopted as the level of significance.

Results

Exposure of normal skin to SLS induced barely perceptible or slight erythema in 10 of the 13 exposed subjects and caused a significant increase in TEWL (Fig. 1). Within 4 days, the visible signs of redness had disappeared (Table 1), although in some subjects scaly skin was observed (not scored). The area treated with the cream showed significantly higher TEWL than the untreated area on the 1st day after the SLS exposure, but no difference in the degree of visible irritation was observed (Fig. 1, Table 1). During the next 2 weeks, TEWL reached normal values and it appeared that application of the cream increased the rate of recovery, since the area treated with the cream showed significantly lower values on days 10 and 14 (Fig. 1).

The skin corneometer values, indicating the degree of hydration, decreased during the 1st week after SLS exposure, but increased during week 2 (Fig. 2). Cream treatment both of the surfactant-damaged skin and of normal skin resulted in higher values than on the corresponding untreated areas (Figs. 2, 3).

After 14 days of treatment of normal skin with the cream, TEWL was significantly lower than in untreated skin (Table 2). The corneometer value was increased after only 1 application and was still elevated after 14 days (Fig. 3). Application of SLS resulted in a significantly lower degree of irritation on the cream-treated area than on the corresponding untreated area. Both TEWL and the visual signs of irritation were significantly reduced by the cream (Table 3).

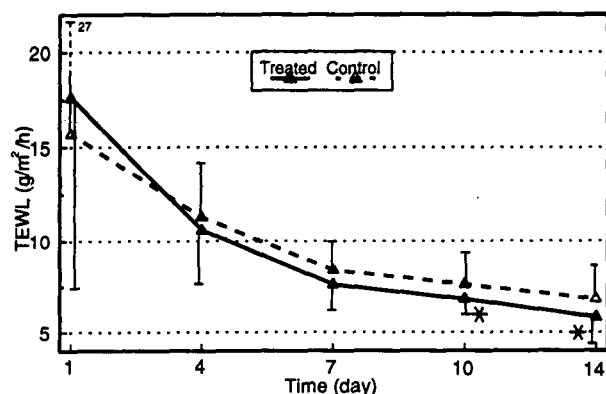


Fig. 1. Transepidermal water loss (TEWL) on days 1–14 after exposure to SLS in areas treated with the cream after exposure and in those left untreated (control). The bars represent SD and the asterisks indicate values significantly different from those in the untreated area. $n=13$.

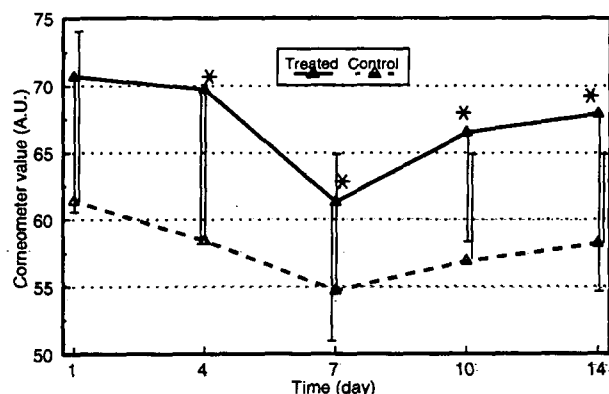


Fig. 2. Skin corneometer values (A.U.) on days 1–14 after exposure to SLS in areas treated with the cream after exposure and in those left untreated after exposure (control). The bars represent SD and the asterisks indicate values significantly different from those in the untreated control area. $n=13$.

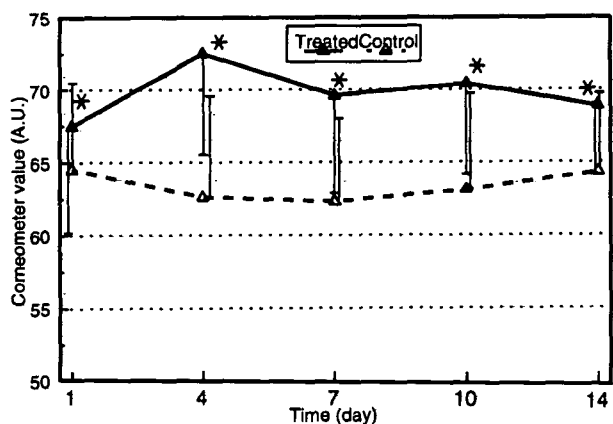


Fig. 3. The influence of the test cream on the corneometer values in normal skin. The bars indicate SD and the asterisks values different from the untreated control. $n=13$.

Table 2. The influence of the test cream on transepidermal water loss (TEWL; g/m²/h, mean $\pm$ SD) in normal skin on days 1–14 of cream treatment; $n=13$; NS: not significant

Day	Cream treated skin	Untreated skin	<i>p</i>
1	6.6 $\pm$ 2.4	6.4 $\pm$ 2.4	NS
4	7.6 $\pm$ 1.9	7.4 $\pm$ 2.2	NS
7	7.1 $\pm$ 1.2	6.7 $\pm$ 1.2	NS
10	6.5 $\pm$ 1.2	6.6 $\pm$ 1.2	NS
14	5.5 $\pm$ 0.8	6.3 $\pm$ 1.4	<0.01

Table 3. The influence of 14 days treatment with the test cream on the skin susceptibility to SLS-induced irritation, evaluated as TEWL and visual scoring of the degree of irritation; $n=13$

Assessments	Cream-treated skin	Untreated skin	<i>p</i>
TEWL (g/m ² /h)	12.4 $\pm$ 4.1	19.7 $\pm$ 11.2	<0.01
Score (% of possible maximum)	11.1	26.4	<0.05

Discussion

Detergents and water are external substances contributing to the development of irritant contact dermatitis. For studying acute and cumulative irritation, the use of non-invasive biophysical methods and the model substance SLS has proved highly informative (10, 11). In the present study, a 7-h patch application of SLS was used to produce irritation and the effects of treatment with a moisturizer were evaluated. It was concluded from the results that the test cream influenced the barrier properties of both surfactant-damaged skin and normal skin. Application of the cream to surfactant-damaged skin resulted in higher TEWL the 1st day after SLS exposure. A similar increase in TEWL after a few applications of urea-containing moisturizers to normal skin has been observed previously (1). The reason for the initially elevated TEWL is unclear, but it may be due to a temporary disorganization of the lipid bilayers and/or hyperhydration of the stratum corneum.

Skin corneometer values showed a decrease during the 1st week after the SLS exposure, followed by a rise during the following week. In an earlier study, a similar time course in the changes in corneometer values was noted and this also paralleled the clinical appearance of dryness (12). Skin corneometer values are claimed to reflect the degree of skin hydration, but appear to be sensitive to materials other than water, such as cream residues and body hair (6, 8, 9, 13). To reduce the influence of non-absorbed cream components on the readings (6), the skin was cleaned well in advance prior to the measurements. However, it was noted that the cream-treated surfactant-damaged

skin showed higher values than the normal skin. Whether this reflects a greater degree of hydration in this SLS-exposed skin, or is due to cream components in the skin, is not known.

During the late phase of the barrier repair, the cream-treatment accelerated the recovery in TEWL. Recent reports have pointed out the possibility that application of lipid mixtures might influence barrier repair (14–16). In acetone-treated murine skin, petrolatum appears to be internalized within the stratum corneum and promote early barrier repair, whereas physiological lipid mixtures (cholesterol, free fatty acids, and ceramides) accelerate late barrier recovery after incorporation into nascent lamellar bodies (14–16).

Treatment of normal skin for 14 days with the test cream decreased TEWL and increased skin capacitance. This is in accordance with previous observations of lower TEWL and increasing corneometer values after treatment with urea-containing moisturizers (1). Decreased susceptibility to irritation from SLS was also noted, both in the present study and in the study last-mentioned (1).

In summary, the test cream influenced the barrier properties of surfactant-damaged and normal skin. The cream promoted late barrier recovery in both surfactant-damaged skin and the irritant response to SLS became significantly less pronounced after treatment of normal skin with the cream. These results emphasize that future dermatological products may have an even better defined field of action than the products of today.

Acknowledgement

I am grateful to Dr. Magnus Lindberg for valuable criticism of the manuscript.

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