Characterization of Detergent-Induced Barrier Alterations – Effect of Barrier Cream on Irritation

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To gain a better understanding of the interaction of the model detergent sodium lauryl sulfate (SLS) with the stratum corneum, we investigated systematically the ultrastructural changes of the epidermal barrier and the nucleated parts of the epidermis after the occluded application of different concentrations of SLS in human. Different application models were investigated. Two of the three irritation procedures (long duration exposure and the repetitive exposure for 3 d) provoked damage of the nucleated parts of the epidermis and alterations of the lower parts of the stratum corneum. Here, the extrusion and transformation of lamellar body derived lipids into lamellar lipid bilayers were disturbed; however, the upper portions of stratum corneum displayed intact intercellular lipid layers that contradict the long-standing belief that surfactants damage the skin by delipidization. Furthermore, we investigated ultrastructurally and by measurement of transepidermal water loss the influence and protective capacity of a lipophilic barrier cream on acute irritant contact dermatitis. The irritant contact dermatitis was induced by the standardized cumulative short application model with two SLS concentrations (0.5% and 0.75%). The cumulative type of exposure simulates daily living more realistically. Because most of the previous tests have been performed on the human forearm or back, we analyzed whether the pattern of response was similar on both sites. The back showed a higher level of irritant reaction, but the pattern of irritant response proved to be similar to the forearm. Application of the barrier cream before and during irritation showed a decrease of transepidermal water loss enhancement with 0.5% SLS by 58% (back) and 49% (arm) and after irritation with 0.75% SLS by 56% (back) and 43% (arm). Because the experimental result correlated with the clinical experience, the development of the cumulative short exposure model might help to predict and to discriminate the efficacy of barrier creams. Key words: epidermal lipids/ SLS/TEWL/ultrastructure. Journal of Investigative Dermatology Symposium Proceedings 3:121–127, 1998

One of the most important functions of the stratum corneum (SC) is to serve as a barrier (Blank, 1965) that protects against the penetration of irritants and prevents transepidermal water loss (TEWL) through the skin. Irritation of the skin is accompanied by a complex array of epidermal and dermal metabolic responses. The role of the epidermal barrier and its repair seems to be especially crucial for the epidermal responses because recent studies have shown that the epidermal keratinocyte actively participates in the modulation of inflammatory reactions induced by the injuring agent (Wood et al., 1992; Nickoloff and Naidu, 1994; Tsai et al., 1994; von den Driesch et al., 1995) and the pathway of the irritant into the nucleated (viable) parts of the epidermis. Additionally, there seems to be a precise relationship between barrier function (after barrier disruption) and cytokine expression (Nickoloff and Naidu, 1994; Wilmer et al., 1994). The primary response to the irritation with the resulting barrier disruption is the attempt to restore the protective barrier so that penetration of environmental hazards and further alteration of the keratinocytes is prevented. The modulating and initiating effects of the keratinocytes are influenced by the reaction of the barrier and the pathway of the irritant into the nucleated (viable) parts of the epidermis. Furthermore, it has been shown that the mechanisms by which irritants impair the skin differ widely depending on the type of substance (Willis et al., 1991; Fartsch, 1993, 1997; Yang et al., 1995).

Sodium lauryl sulfate (SLS), an anionic surfactant, is frequently used in the induction of experimental irritant contact dermatitis in animals and humans (Tupker et al., 1997), and characteristically induces a dose-related increase in TEWL (Agner and Serup, 1990; Di Nardo et al., 1996). Also, it is known that the most sensitive parameter and best index to monitor barrier alterations induced by SLS is the measurement of TEWL (Frosch et al., 1993). SLS irritation has also been used to test efficacy and value of barrier creams, moisturizers (Hammelka and Kinnumen, 1992; Frosch and Kurte, 1994), and lipid mixtures (Yang et al., 1995).

Recently, it has been shown that the mechanism of SLS induced barrier disruption might be different from that of other irritants, especially from the solvent induced alteration (Yang et al., 1995). Yang et al. (1995) have shown that SLS induced barrier perturbation did not improve by the application of the optimal lipid mixtures.

In spite of the fact that the use of purebred laboratory animals in current irritation test systems seems to ensure a uniformity of response (Paul et al., 1995) that cannot be expected in human subjects (Judge et al., 1996), the degree and the time course of irritation and barrier recovery for animals and humans seem to be different (Mortz et al., 1997). Therefore, we have performed studies on human skin in vivo. But the situation in humans is complicated by the fact that the factors governing individual responses to irritants are still poorly characterized. Thought also has to be given to the possibility of intrinsic variation in response to irritants (Basketter et al., 1996; Judge et al., 1996). It is likely

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Abbreviations: LB, lamellar body; SC, stratum corneum; SLS, sodium lauryl sulfate; TC, test cream; TEWL, transepidermal water loss.
that barrier function, which is mainly related to epidermal lipid composition, and one's genetically determined potential for epidermal cytokine release, both play an important role in an individual's susceptibility and response (Judge et al., 1996; York et al., 1996).

When studying the effect of a model irritant like SLS on human epidermal barrier in vivo, several variables have to be taken into account, such as the vehicle used in testing, the duration and number of applications, the type of occlusion, the site used, etc. Therefore, to understand the cellular mechanisms involved, we performed the following experiments:

(i) We first analyzed systematically the SLS-induced structural changes of the epidermal barrier and the nucleated parts of the epidermis reacting to different concentrations and different exposure times of SLS after a single application modus in human.

(ii) Because of the real-life exposure, where "cumulative" contacts with low concentrated irritants seem to induce contact dermatitis in most of the cases (Huenet et al., 1994), we finally chose a standardized test procedure with multiple short application times and low concentrations of the irritant (Kazdan, 1987) and a complete test system. It was important to choose a cumulative short exposure procedure that permits the development of a "positive," but not "severe," irritant response. This helps to avoid that too many subjects may have to discontinue the study due to a severe degree of reaction. Then we evaluated ultrastructurally and by measurement of TEWL, as a functional index for barrier alteration and repair, the irritating effect of the repeated short-term SLS exposure on the barrier and how the mechanisms and kinetics of the irritations were influenced by a model barrier cream.

(iii) Another aspect was to analyze the site of exposure (forearm or back). In most of the previous studies the forearm has been used as a convenient site for irritancy testing and the evaluation of barrier repair (Frosch et al., 1993; Mao–Qiang et al., 1996; Zhai and Maibach, 1996; Loden, 1997). Recently the back has been proposed because of the larger skin area (Frosch et al., 1994; Wigger-Alberti and Elsaer, 1997). Because it is known that different anatomical localizations have shown different susceptibility to irritation, it is crucial to prove that the pattern of response is identical in both localizations.

**MATERIALS AND METHODS**

**Biophysical noninvasive measurements** The quantitative measurements of TEWL were carried out using the Tewameter TM 210 (Courage and Khazaka, Cologne, Germany). The TEWL is calculated automatically and expressed in g per m² x h. The measurements were made according to the guidelines of Pinnagoda et al. (1990). Measurements were carried out in an air-conditioned room after a rest of 30 min for equilibration (room temperature 20–22°C, relative humidity between 30% and 45%). The Tewameter probe was used in a holding device to avoid heating of the probe. The probe was rested on the skin and TEWL was continuously recorded for a period of 3 min. Mean values were obtained from three successive recordings for every test site.

**Clinical examination** Visual scoring was performed according to the following scale: 0, no reaction; 0.5, slight scaling or very weak erythema, smooth surface; 1, weak erythema, possibly slight infiltration, slight roughness, slight scaling, mild edema, fine fissures; 2, erythema, more roughness, scaling and edema, fisses; 3, pronounced erythema, extensive scaling, pronounced edema, possibly vesicles, bullae, pustules, and/or pronounced crusting.

**Morphologic methods** Punch biopsies were divided in half for transmission electron microscopy and processed for visualization of routine morphology and for epidermal lipids characterization. For routine electron microscopy, tissue was double fixed with 2.5% glutaraldehyde and OsO₄ and embedded in Epon 812. To study the epidermal lipids, the other half was fixed in acrolein vapor and 2.5% glutaraldehyde for 2 h, rinsed in buffer for 3 h, postfixed with 0.5% RuO₄ (PolyScience, Warrington, PA) with 0.25% potassium ferrocyanide (pH 6.2) for 1 h in darkness at 4°C, and embedded in Spurr's resin (Fartasch et al., 1993; Fartasch and Ponec, 1994). All tissues were sectioned and viewed on a Jeol 100 CX transmission electron microscopy. Thin sections were examined before and after double staining with uranyl acetate and lead citrate. Semi-thin sections were partly examined unstained by light microscopy to control penetration of RuO₄ (dark staining). Serial sections were stained with 1% methylene blue.

**Statistical analyses** Data of clinical scoring are presented as means ± SEM. The distribution of ΔT EWL (equal to difference between the individual's baseline TEWL and increased TEWL after irritation) are presented as box plots. Box plots show the median, the twenty-fifth and seventy-fifth percentile, and values that are removed from the test. The lower boundary of the box is the twenty-fifth percentile, the upper boundary the seventy-fifth percentile; the line inside the box represents the median. Lines are drawn from the ends of the box to the largest and smallest observed values that are not outliers. Cases with values that are between 1.5 and 3 box lengths from the upper or lower edge of the box are called outliers (designated by the letter o). Cases with values that are more than three box lengths from the upper or lower edge of the box are called extreme values (designated by *).

The Wilcoxon test was used for statistical analysis. The correlation between the reaction pattern of the arm and the forearm was analyzed by the Spearman correlation coefficient (R). All the analyses were conducted with SPSS/PC+ Version 5.0 statistical software. All statistical tests were two-tailed, and a p value of less than 0.05 was considered to indicate statistical significance.

**Ultrastructural studies on SLS irritation** To ascertain the structural basis and cellular mechanism responsible for barrier disruption by SLS and the influence of test creams on the process of irritation and recovery, we studied the effect of different SLS exposures on human skin.

**Experimental protocols Long-term exposure (24 h):** nine human volunteers with no history of skin disease were tested after having given informed consent. SLS, minimum purity (Merck, Darmstadt), were used at dilutions of 0.5% and 1% (wt/vol). Patch tests (Large Fink Chambers (inner diameter 12 mm) with filter paper discs, fixed on Scanpor tape (Scapone tape; Herzal, Reinbeck, Germany)) were saturated with 50 µl of the SLS solution.

Each SLS-treated subject had five test areas on the volar aspects of both forearms (left arm: 0.5% SLS, 1.0% SLS, control with water; right arm: 0.5%, 1% SLS). In three of the seven subjects, biopsies of two test sites (0.5% and 1% SLS) were performed 30 min after the 24 h patch test. In the other six subjects the biopsies were performed after the maximum TEWL had been reached upon application of both concentrations (enhancement of TEWL as sign of an impaired barrier function; 24–48 h after the patches have been removed).

The TEWL measurements in the recovery phase were performed 2 h after the removal of patches and then every 6 h for the first 3 d. After the 3 d measurements were performed daily until baseline TEWL values were achieved. The experiments were performed simultaneously on both volar forearms and biopsies were only taken from the test sites of the left arm.

**Short-term exposure (application times: 0.5 h, 2 h):** four human volunteers were patch tested with 0.5% SLS for 0.5 h and 2 h on the forearms. The biopsies were performed 24 h after the removal of the patch tests. TEWL measurements were performed 30 min, 2 h, 6 h, 12 h, and 24 h after the removal of the patches. No measurable changes in TEWL values were detectable.

**Short-term cumulative exposure (2 × 0.5% SLS) with and without test cream (TC):** in two volunteers, SLS 0.5% (dissolved in water) was applied with large Finn chambers (12 mm, filling volume 0.05 ml) on two areas of the forearms. One test site was pretreated with the TC 10 min before each irritation. The chambers were removed after 30 min of exposure. A second exposure and pretreatment were performed at the same day after 3.5 h. Using this application scheme, the volunteers were treated for 3 d. To compare the morphologic changes of the irritated but with TC pretreated versus irritated skin alone, two 3 mm punch biopsies were performed in each panelist on day 3, 2 h after the last exposure.

**Development of a repetitive irritation test in humans: determination of the threshold tolerance** In assessing the appropriate test concentration in an occluded patch and repetitive test system, a continuous approach to testing was adopted.

In the first experiment (n = 8) we have chosen different concentrations of SLS (0.1%, 0.2%, 0.3%; 0.5%, 0.75%) for the above-mentioned cumulative exposure. In a preliminary study we had also included the concentration 1% of SLS in another four volunteers; but this concentration had to be canceled due to the strong clinical reactions in three of them.

**Subjects** Eight healthy subjects (three female, five male, mean age 30.1 y, range 26–53 y) with no history of atopic eczema or other skin diseases participated in the study. Informed consent was obtained from all of them.

**Application of SLS** The different concentrations of SLS (0.1%, 0.2%, 0.3%; 0.5%, 0.75% SLS dissolved in water) were applied with large Finn chambers (12 mm, filling volume 0.05 ml) and fixed with an overlapping sheet of Fixomull stretch tape (Beiersdorf, Hamburg, Germany). The chambers were removed after 30 min of exposure. A second exposure was performed at the
same day after 3.5 h. Using this scheme of application, the volunteers were treated for 3 d.

Comparison of anatomic sites The forearm and the back were used as sites for testing the efficacy of TC. As there can be intra-individual variation between different sites in their threshold tolerance of irritants (Judge et al, 1996), we compared the pattern of response in the forearm (A) and the back (B) in all of our subjects.

Site A: The volar side of the right forearm. Because of the instability of TEWL at the wrist and the enhancement of irritancy on proximal parts of the arm (Van der Valk and Maibach, 1989; Panisset et al, 1992), the five areas were located in the middle part of the forearms, 1 cm above the wrist skinfold. Two further test sites served as controls (treated with water or remaining untreated).

Site B: The paravertebral skins of the mid-back, and the test fields (two vertical rows with four chambers each) were randomized. The designation of SLS concentrations and controls to the test sites was randomized among the panelists.

Studying the effect of TC on irritation in a cumulative model (n = 13) In 13 volunteers (six female, seven males) the test fields on the forearm and the back were pretreated with the above-mentioned TC 10 min before the two different concentrations of SLS (0.75% and 0.5% SLS) were applied. Two further test sites on the back and forearm remained only exposed to the irritant. Water served as control. Regarding the pretreatment a standardized amount (0.05 ml) of the TC was subsequently applied to the allotted areas of 2 cm² on the forearms and back for 1 min with a gloved finger. In the case of remnants of the product being on the skin surface they were removed with absorbent paper tissue before irritation via different SLS concentrations was performed.

The chambers were removed after 30 min of exposure. A second exposure and pretreatment were performed at the same day after 3.5 h. Using this scheme of application (see above), the volunteers were treated for 3 d. TEWL measurements were performed at day 1 before the first application and at day 3 2 h after the last application. In six of the volunteers the TEWL was additionally recorded 2 h after the second exposure on day 2 (Fig 7). TEWL measurements were continued daily until baseline values of TEWL were reached by the test field irritated with 0.5% SLS and pretreated with the TC.

Test cream: Lindesa (Faweco, Darmstadt, Germany) with beeswax. Further constituents: water, glyceryl stearate SE, paraffinum liquidum, stearic acid, fragrance, methyl paraben, and allantoine.

The above-mentioned barrier cream had been selected due to clinical experience and observations in a population of hairdressers and metal workers, where it has been proven to reduce the frequency of irritant contact dermatitis.

Because there were no scientific data on the optimal timing of the application of barrier creams regarding the contact with the irritant, we have chosen an application time of 10 min before exposure to the irritant.

RESULTS

Structural basis of SLS irritation

SLS-treated skin after 24 h exposure Visual scoring: clinical grading of the 0.5% SLS test sites showed scaling (1+) in five of seven subjects. One additional subject also showed erythema (1+). With 1% SLS, five of seven subjects showed intense redness with scaling (2+) and one with edema, fissures, and vesicles (3+). Monitoring of the nonbiopsied test areas showed a normalization of TEWL after 10–12 d.

In the subjects exhibiting dry skin (a scaly surface) induced by 0.5% SLS, a one layered transit-cell zone, a sign of premature keratinization, and lipid droplets (L) were found in the matrix of horny cells (Fig 1a). The epidermal lipids showed a lamellar arrangement (Fig 1b). With 1% SLS, and to lesser degree with 0.5% SLS, the intercellular spaces showed focal intercellular edema. Disturbance of the rearrangement of lamellar body (LB) sheets into parallel lipid layers appeared in the lower SC (stratum compactum) as demonstrated by routine fixation of the 1% SLS-irritated tissue. The cornified envelope displayed broadening of its electron-dense margin as a sign of structural alteration of the horny cell as demonstrated by routine fixation (Fig 2). In some areas, especially in the stratum granulosum and the upper stratum spinosum of the epidermis, paranuclear vacuoles (V), indenting one side of the nuclei of the keratinocytes, were present. Simultaneously, widening of epidermal intercellular spaces partially filled with a homogenous grey granular substance was present (Fig 3).

After short-term exposure Biopsies that were performed a few hours after short-term exposure did not show parakeratosis. There were no

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Figure 1. SC alterations induced by SLS. (a) Lipid droplets (L) in the matrix of the corneocytes and a transit cell (T) can be seen (RuO₄; scale bar, 10 µm). (b) Regular lamellar arrangement of epidermal lipids (white arrows) in the upper regions of SC in spite of SLS exposure. (D, desmosome; RuO₄; scale bar, 0.1 µm.)

Figure 2. SC—stratum granulosum interface: the intercellular spaces showed widening. Instead of regular lamellar body-lipids (sheets), the intercellular spaces of the lower SC (stratum compactum) revealed granular material (*). The cornified envelope displayed broadening of its electron-dense margin (arrow) as a sign of structural alteration of the horny cell. (SG, stratum granulosum; OsO₄; scale bar, 1 µm.)
signs of alteration regarding the barrier structures or the nucleated parts of the epidermis.

**Cumulative short-term exposure with and without TC** The observed changes were comparable with the long-term exposure and showed lipid droplets located in the cornocytes. Marked intercellular edema was seen in the nucleated parts of the epidermis. Influx of the granular substance into the intercellular spaces of the epidermis appeared in all regions of the epidermis. With RuO₄ staining a disturbance of LB lipid transformation into regular arranged epidermal lipids was seen, whereas the upper regions of stratum disjunctum still showed regular lamellar lipid structures. The pretreated areas showed similar alterations but the observed changes where less pronounced, with only a few vacuoles in the nucleated parts of the epidermis. There were only focal areas with alterations of LB sheet formation, and in most of the parts of the stratum compactum lamellar arrangement of epidermal lipids could be found.

**SLS susceptibility of the back compared with the forearm** Determination of the threshold tolerance to irritants: the back showed significantly higher clinical scorings than the forearm (Fig 4a, b). On the forearm clinical signs of irritation were not visible on day 1. Only a moderate response was seen on day 3. On the back clinical responses were already visible on the first day, and stronger reactions on day 2 and 3.

The increase of TEWL values (ΔTEWL), the difference between an individual's baseline TEWL (pre-exposure on day 1) and increased TEWL after irritation (on day 3), was more pronounced with higher concentrations of SLS (Fig 5a, b). The distributions of ΔTEWL are shown as box plots. There was a statistically significant difference between the applied SLS concentrations and the control sites (p < 0.02).

But the irritation with 0.1% SLS showed no statistical difference compared with the water control. The variability of ΔTEWL values increased with increasing SLS concentrations (see length of box and of whiskers).

The back showed higher TEWL values than the forearm. Additionally, the ΔTEWL of the back showed a higher interindividual variability of values. There was a statistically significant correlation between the reaction pattern of the arm compared with the forearm (Spearman correlation coefficient R > 0.7).

Because concentrations of 0.1%, 0.2%, and 0.3% of SLS in some of the volunteers induced only a small increase in TEWL regardless of the test sites, 0.5% and 0.75% SLS have been chosen for the efficacy studies.

The **irritant response in a cumulative model diminished significantly after the application of the TC**. The study suggested that irritation of the skin with 0.5% and 0.75% SLS would show sufficient positive reaction in the panelists. The intensity of irritation was diminished by the pretreatment with a cream. This was shown by clinical scoring and by the decrease of TEWL (Fig 6a, b). Comparison with the untreated but irritant exposed sites (0.5% SLS) showed a decrease of TEWL enhancement by 58% (back) and 49% (forearm) (Table 1). After irritation with 0.75% SLS the TEWL was diminished by 56% (back) and 43% (forearm). Monitoring of TEWL showed an increase of ΔTEWL regardless of the fact that there has been a pretreatment on day 1. On day 2 a plateau was reached due to the treatment with TC (see, for example, Fig 7a, b, where in six volunteers TEWL had been measured on day 2 as well).

**DISCUSSION**

To study the reaction of the skin barrier to detergents, subjects have been exposed to different concentrations of the anionic surfactant SLS. In "every day" life the contact is usually cumulative and of short

![Figure 3. Paranuclear vacuoles (V), indenting one side of the nuclei of the keratinocytes, were present especially in the stratum granulosum and the upper stratum spinosum of the epidermis. Widening of epidermal intercellular rooms (ICR) partially filled with a homogeneous gray granular substance was present (OsO₄; scale bar, 1 μm).](image)

![Figure 4. Clinical score (mean ± SEM) after irritation with different concentrations of SLS at the back (a) and forearm (b). The back showed significantly higher clinical scorings than the forearm. On day 1, clinical signs of irritation were not visible on the forearm, but were on the back.](image)
duration. This was the reason why a cumulative model was chosen for our studies on humans.

Studying the irritation by SLS ultrastructurally and functionally, we could show that the topical treatment with an anionic detergent such as SLS seems to alter the permeability barrier by mechanisms that were different from the process induced by an organic solvent. Whereas with acetone the extraction of SC lipids seems to be the main cause of barrier disruption (Yang et al, 1995; Fartasch, 1997) and barrier recovery seems to improve very quickly, the situation with detergents appears to be more complex (Yang et al, 1995). It has been suggested that detergents, such as SLS, may possibly cause more extensive damage, e.g., the denaturation of proteins, which would result in alterations that cannot be ameliorated by providing externally applied lipid mixtures alone. It has been suggested that SLS might penetrate and damage the deeper nucleated layers of the epidermis (Yang et al, 1995).

Our ultrastructural studies have shown that SLS at the concentration applied did not extract lipids like has been shown after application of acetone (Fartasch, 1995, 1997), but rather caused extensive damage to the deeper nucleated layers of the epidermis. A predominant feature of cutaneous response to the detergent was parakeratosis, the retention of nuclei within the SC and lipid droplets (Willis et al, 1989). Such an appearance may have a number of causes, including increased epidermal cell proliferation, accelerated keratinization, or direct cytotoxic injuries (Willis et al, 1991). In some areas the epidermal intercellular spaces were filled with a granular substance similar to that described by Tovell et al (1974), and probably representing serum influx into the epidermis.

The supposition that surfactants degrease the skin (e.g., a selective depletion of the lipids from the intercellular spaces; Proksch et al, 1991) has persisted in the literature (Imokawa et al, 1989). In this study, the upper SC showed regular lamellar arrangements of lipids after exposure to SLS for 24 h. This corroborates biochemical studies that have shown that in experimentally SLS treated skin the amount of ceramides did not differ from that in healthy control skin, with only a 4–7% removal of lipids (Froeb et al, 1990). This contradicts the long-standing belief that surfactants damage the skin by delipidization (Froeb et al, 1990).

Our study corroborates the findings of Fulmer and Kramer (1986), who observed changes in lipid composition that did not reflect the immediate consequences of surfactant exposure. Ultrastructurally, the surfactant in low concentration did not seem to alter the existing lipid structure, but rather the processing into new epidermal lipids by: (i)
the direct alteration of the LB-secretory system of the stratum granulo-
sum cells; (ii) disturbing the processing of LB-derived sheets (glycylceramides) into bilayer structures in the intercellular spaces of the SC; and (iii) indirectly inducing a disturbed differentiation by altering the viable epidermis (intracellular vacuoles, cytoplasmic edema, and widening of intercellular spaces). All these changes might explain the lasting TEWL enhancement since normalization of barrier function first occurred after 10–12 d.

The short-term exposure in the above-mentioned cumulative model showed similar ultrastructural changes after the 3 d (but to a lesser degree with the TC). This can be explained by the tendency of SLS to accumulate in the epidermis. Studies on rat skin have shown that traces of SLS persist in tissues 7 d after a single 24 h exposure of 1% SLS — with higher levels in epidermis than in dermis (Patil et al., 1995; Skoalar-Platzer et al., 1996). Therefore, it is possible that accumulation of SLS in the epidermis after and during the cumulative exposure with low concentrations which normally would not have evoked irritative reactions in single exposure finally induces irritation.

Results of animal experiments may not be valid for humans, particularly when dealing with irritants, in view of their complex action mechanisms and the high interindividual variability in susceptibility of human skin (Zhai and Maibach, 1996). In vivo methods (the biophysical techniques, like TEWL measurement) in human are based on the assessment of the reduction in the induced irritant and inflammatory changes in the skin when a barrier cream is used before application of an irritant. To study the efficacy of barrier creams to prevent irritation by SLS and whether the barrier recovery is influenced by TC, we had first to determine the degree of irritation. The concentrations of 0.5% and 0.75% SLS seemed to be optimal for our model. As expected, the clinical tissue response to SLS exposure was quite varied in the different volunteers (Judge et al., 1996). The back proved to be much more susceptible to irritation than the forearm, especially when concentrations of 0.75% were applied; however, the back showed the same pattern of response, with a retarded response to SLS than the forearm. This difference was also visible when the TC had been applied.

Pretreatment and treatment during the cumulative irritant exposure influenced the barrier properties of surfactant-damaged skin. The irritant response to SLS became significantly less pronounced after treatment of normal skin with the cream. The effect was more pronounced after the second and third day. The mechanism of these beneficial effects is not yet fully understood. The benefit of barrier creams in SLS-damaged skin seems not to be in reestablishing extracted lipids, as has been shown in previous studies (Yang et al., 1995; Mao-Qiang et al., 1996). Also, the internal structures of the lamellar bodies seemed not to be influenced by the TC, as it has been shown when applying so-called physiologic lipid mixtures.

But lipophilic barrier creams, like our TC, might alter the penetration of substances into the skin by interaction between the barrier cream and the substance or interaction between the barrier cream and SC (De Fine Olivarius et al., 1996). An important aspect might be that the lipophilic TC acts comparably with petrolatum (Ghadially et al., 1992; Mao-Qiang et al., 1995; Wigger-Alberti and Elsner, 1997), where repair of the barrier occurs by forming a bulk hydrophobic phase in the SC interstices (Mao-Qiang et al., 1996). The interaction of the cream with components of the barrier might influence and stabilize barrier function so that cytokine expression and the resulting induction of dermal inflammatory reaction are diminished.

We have to take into account, however, that the data of the cumulative test were generated with a model surfactant; it remains to be determined whether similar responses will be noted with chemicals of different physicochemical properties.

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REFERENCES

Di Nardo TA, Sugino TK, Wette TP, Ademola TJJ, Maibach TJJ: Sodium laurel sulfate (SLS) induced irritant contact dermatitis: a correlation study between ceramides and in vivo parameters of irritation. Contact Dermatitis 35:58–61, 1996
Pauwels TF, Trefil T, Pulten TB, Brunert Lecomte TP, Agache TP: Transepidermal water loss related to volar forearm sites in humans. Acta Derm Venereol (Stockh) 72:4–5, 1992