Dermal absorption of chemicals through normal and compromised skin
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Variation in barrier impairment and inflammation of human skin as determined by sodium lauryl sulphate penetration rate
C.M. de Jongh, I. Jakasa, M.M. Verberk, S. Kezic
Abstract

**Background** Skin irritability after a brief exposure to the model skin irritant, sodium lauryl sulphate (SLS), is known to vary considerably between individuals. A difference in the skin barrier to SLS may contribute to this variation. To date, no human *in vivo* data have been available on SLS penetration into the skin.

**Objectives** We studied whether the SLS penetration rate into the stratum corneum (SC) is related to impairment of the water barrier function and inflammation of the skin.

**Methods** The penetration of SLS into the SC was assessed using a noninvasive tape-stripping procedure in 20 volunteers after a 4-h exposure to 1% SLS. Additionally, the effect of a 24-h exposure to 1% SLS on the skin water barrier function was assessed by measuring the transepidermal water loss (TEWL). The accompanying inflammation was quantified by measuring erythema.

**Results** The mean ± SD diffusivity of SLS (*D*) and the SLS permeability coefficient (*K_p*) were $1.4 \pm 0.6 \times 10^{-8}$ cm$^2$ h$^{-1}$ and $1.5 \pm 0.7 \times 10^{-3}$ cm h$^{-1}$, respectively. A multiple regression analysis showed that the baseline TEWL, SC thickness and SLS penetration parameters *K* (SC/water partition coefficient) and *D* clearly influenced the increase in TEWL after the 24-h irritation test (explained variance: $r^2 = 0.80$). Change in erythema was mainly influenced by SC thickness.

**Conclusions** We found that variation in the barrier impairment and inflammation of human skin depends on the SLS penetration rate, which was mainly determined by SC thickness.
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Repeated cutaneous exposure to mild irritants is the leading cause of occupational contact dermatitis.\(^1\) High-risk occupations for developing chronic irritant contact dermatitis (ICD) include hairdressing\(^2,3\), healthcare\(^3\) and metalworking.\(^4\) For example, in a study of hairdressing apprentices, the incidence rate of ICD during the first year was 31.7 per 100 person-years.\(^2\) The mechanism of development of chronic ICD and the factors that determine an individual's susceptibility are not completely understood. The 'irritation threshold' to the model irritant sodium lauryl sulphate (SLS) has been suggested as a possible indicator of individual susceptibility to chronic ICD.\(^5-7\) The irritation threshold has been defined as the lowest SLS concentration that leads to visual skin inflammation, assessed in an acute 4-h patch test. The investigators used visual grading of the erythema reaction as a parameter of irritation. These studies revealed substantial interindividual differences in acute skin inflammation susceptibility: the irritation threshold ranged from $< 0.1\%$ to $> 20\%$ SLS.

We assumed that the irritant effect of SLS on the stratum corneum (SC)\(^8\) and the underlying viable tissues\(^9\) is related to the ability of SLS to penetrate into the SC. Thus, the differences in the skin barrier to SLS may be one of the factors contributing to the interindividual differences in skin irritability. In studies with healthy volunteers, interindividual differences of up to a factor of 4 were found in the skin penetration rate of several chemicals.\(^10\) In this regard, one important factor is the SC thickness, which varies between individuals by a factor of 2–3.\(^11\) As the penetration of chemicals into the skin is a diffusion process, the amount absorbed will be inversely proportional to the thickness of the SC membrane.

Several studies have been performed to obtain insight into SLS penetration into the skin. Most of these studies were \textit{in vitro}, using mammalian\(^9,12-14\) or human skin.\(^9,15-17\) In two studies, the ability of SLS to penetrate into the skin was investigated \textit{in vivo}, using rat models.\(^9,18\) None of these studies addressed the relationship between the SLS penetration and the skin inflammation reaction.

Penetration of topically applied substances into the SC \textit{in vivo} can be studied noninvasively, using a tape stripping procedure.\(^19,20\) In the present study, we investigated the relationship between SLS penetration into the SC and the impairment of the skin water barrier function and skin inflammation. To this end, we performed two exposures in volunteers. One exposure was a 24-h exposure to 1% SLS intended to evoke skin irritation: 24 h after patch removal, the effect of SLS on the skin water barrier function was measured by transepidermal water loss (TEWL), and the inflammation was assessed by measurement of erythema (skin redness). The second exposure was a 4-h application of 1% SLS to assess the rate of
penetration of SLS into the SC. The results presented here were part of a larger study designed to investigate individual susceptibility factors for developing chronic ICD (de Jongh et al., in preparation).

Subjects and methods

Study population
Twenty healthy volunteers with no visible skin abnormalities participated in the study (13 women, mean ± SD age 24 ± 3 years and seven men, mean ± SD age 25 ± 8 years). The study was approved by the ethics committee of the Academic Medical Centre, and all subjects gave their written, informed consent. The subjects were not allowed to use soap or moisturizers on the lower arms for 24 h prior to, and during the days of, the experiments. All participants filled in the Erlangen Atopy Questionnaire,\(^2^1\) which was used to derive an atopy score.

Single 24-h sodium lauryl sulphate irritation test
To evoke skin irritation, the dominant midvolar forearm was exposed over a 24-h period to a 1% w/v SLS solution (200 µL, ≥ 99% purity; Fluka, Buchs, Switzerland), using a patch test chamber (Finn chambers\(^\circledR\) of 18 mm diameter and filter paper discs; Epitest, Tuusula, Finland). Before application and 24 h after patch removal, TEWL and erythema were measured on the exposed site and on a control site on the dominant forearm. TEWL was measured with an Evaporimeter (VapoMeter SWL2g; Delfin Technologies Ltd, Kuopio, Finland). Nuutinen et al. describe this measurement device in detail.\(^2^2\) For at least 20 min prior to the measurements, the volunteers rested with their sleeves rolled up in the examination room, where the temperature was 20–22 °C and the relative humidity ranged between 50% and 60%. The erythema index was measured using an erythema meter (DermaSpectrometer; Cortex Technology, Hadsund, Denmark), as described by Clarys et al.\(^2^3\)

Sodium lauryl sulphate penetration test
In addition to the single 24-h irritation test site, two other sites on the dominant distal volar forearm were exposed for 4 h to 200 µL of a 1% SLS solution using patch test chambers to determine the SLS penetration rate. The chambers were separated by 15 mm and attached with adhesive tape (Scanpor\(^\circledR\) tape; Norgeplaster, Vennesla, Norway). A third, nonexposed site on this forearm served as a control.

Fifteen minutes after the chamber removal, the SC was sequentially removed using pieces of 19 × 25 mm adhesive tape (Diamond Ultra Clear Tape, 19 mm × 33 m;
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The Sellotape® Company, Eindhoven, the Netherlands). Templates of Scanpor® tape were fixed on the skin around each application spot to limit the tape stripping area (18 mm diameter). Pieces of tape were consecutively applied to the sites and homogeneously pressed on to the skin by moving a 1.0-kg stainless steel roller 10 times in two directions. The tapes were then slowly removed at an angle of 170° with the skin. The sites were multidirectionally stripped until it appeared that the SC was totally removed, as observed by the shininess and redness of the surface and a TEWL > 100 g m⁻² h⁻¹. Each tape strip was collected in a glass vial and stored at −20 °C. The tape stripping of the three sites (two SLS-exposed and one control, simultaneously) was completed after 20 min.

The amount of SLS on each strip was analysed using an adjusted method based on that of Rusconi et al.²⁵ The total amount of protein on each strip was analysed following a slightly modified procedure based on that of Dreher et al.²⁶ Blank tapes were processed and assayed as a negative control. To extract the SLS from the tape, 1 mL methanol (J.T. Baker, Deventer, the Netherlands) was added to each vial and the vials were shaken for 1 h (TPM-2; Sarstedt, Numbrecht, Germany). The methanol fraction was removed and stored at −20 °C for SLS analysis.

The concentration of SLS was determined spectrophotometrically, using a dye (Stains-All®; Sigma-Aldrich Chemie GmbH, Schnelldorf, Germany). Standards of SLS for the calibration curve were prepared in methanol (2.3–50 μg mL⁻¹) and 20 μL from each standard and sample was pipetted into a 96-well plate. After evaporation of the methanol, 200 μL of Stains-All® working solution was added to each well and absorbance was read at 450 nm (Model 680 Microplate reader; Bio-Rad Laboratories, Hercules, CA, U.S.A.).

The remaining methanol in the vials containing tape strips was evaporated, using nitrogen. Subsequently, 1 mL of 1 mol L⁻¹ NaOH was added. The vials were then shaken for 2 h and left at room temperature overnight. After addition of 1 mL of 1 mol L⁻¹ HCl, the sample was ready for the protein assay. The total protein on each strip was determined with the Bio-Rad DC protein assay kit (Bio-Rad Laboratories), using the supplied bovine serum albumin as the standard. Standards and samples were pipetted into a 96-well plate and assayed following the kit instructions. The concentration of SLS on each strip was expressed as μg SLS μg⁻¹ protein. Assuming an SC density¹¹ of 1 g cm⁻³ and a uniform distribution of SC on the tape strips (stripped skin area: 2-54 cm²), the protein mass removed was converted to a volume enabling estimation of the thickness of SC on each strip and the cumulative SC thickness.
Data analysis

After the 4-h SLS penetration test, analysis of the sequentially tape-stripped SC yielded values of the SLS concentration as a function of the relative depth \((x/L)\) into the SC. The SLS concentration profile is given by a solution to Fick's Second Law of Diffusion (Fig 1),\(^{19,20}\) where \(C(x)\) is the SLS concentration \((\mu g \text{ cm}^{-3})\) at depth \(x\) in the SC, \(K\) is the SC/water partition coefficient of SLS, \(C_{veh}\) is the applied SLS concentration \((\mu g \text{ mL}^{-1})\) in the vehicle (water), \(L\) is the total thickness of the SC (cm), \(D\) is the diffusivity of SLS in the membrane \((\text{cm}^2 \text{ h}^{-1})\), and \(t\) is the exposure duration \((\text{h})\).

The rate constant for diffusion across the SC \((D/L^2)\) is obtained by fitting this nonsteady-state diffusion equation to the data of the SLS concentration profile. \(KC_{veh}\) equals the intercept at \(x = 0\). The SLS permeability coefficient \((K_p)\) across the SC layer is calculated by \(K_p = KD/L\). The calculation of penetration parameters from the concentration vs. depth curve has been described in detail elsewhere.\(^{19,20}\)

Data of duplicate SLS penetration tests were pooled to obtain one regression curve for each subject. The first strip was not included in the regression analysis, as it contained some SLS that remained on the surface of the skin. Prism 4 (GraphPad, San Diego, CA, U.S.A.) was used for curve fitting.

Statistics

For our statistical analysis, we used Student's two-sample \(t\)-test to compare subgroups, and the Pearson correlation coefficient. For the effect of SLS penetration rate on skin water barrier function, we used a multiple linear regression analysis with the change in TEWL as the dependent parameter, and the baseline TEWL, \(K\), \(L\) and \(D\) as the independent parameters. For the effect on skin inflammation, we used the change in erythema as the dependent parameter, and \(K\), \(L\) and \(D\) as the independent parameters. \(P \leq 0.05\) was considered significant.

Results

Atopy score

The subjects' Erlangen Atopy Scores ranged from 3 to 16 (the maximum for the questionnaire is 34), and the mean ± SD score was 7.9 ± 3.9. Six subjects had a score ≥ 10 points, which is considered as having atopy.\(^{21}\)
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\[ C(x) = KC_{\text{reh}} \left( 1 - \frac{x}{L} \right) - \sum_{n=1}^{\infty} \frac{2}{n\pi} KC_{\text{reh}} \sin \left( \frac{n\pi x}{L} \right) \exp \left( -\frac{Dn^2 \pi^2 t}{L^2} \right) \]

**Fig 1**: Fick's Second Law of Diffusion.

**Single 24-h sodium lauryl sulphate irritation test**

One day after the 24-h irritation test with 1% SLS, the mean ± SD TEWL had increased from 9.0 ± 3.0 g m\(^{-2}\) h\(^{-1}\) (baseline) to 81 ± 42 g m\(^{-2}\) h\(^{-1}\), and the degree of erythema from 7.8 ± 2.1 arbitrary units (AU) to 12.2 ± 3.2 AU.

**Sodium lauryl sulphate penetration test**

On average, 13 ± 4 tape strips were removed from each SLS test site and 20 ± 4 strips from the control site. The mean ± SD total amount of protein removed from one site was 2140 ± 570 µg, corresponding to a SC thickness of 8.6 ± 2.4 µm.

Acceptable curve fitting was obtained for 19 volunteers. The data on two volunteers had to be excluded from the analysis. This was because a linear relationship was found between the SLS concentration and SC depth, indicating a steady-state absorption to which Fick's Second Law of Diffusion is not applicable. Figure 2 shows the SLS concentration profiles across the SC for two selected subjects. Nonlinear regression was used to obtain the best fit of the equation given in Figure 1 (dashed lines).

The SLS penetration results are summarized in Table 1. We observed fairly high interindividual variation in all penetration parameters: the coefficients of variation (CV) ranged from 24% to 51%. The mean values were also calculated separately for the subjects with \((n = 6)\) and without \((n = 11)\) atopy. No difference in \(K\) was found between these two groups. In the atopy group, the SC tended to be thinner, and \(D/L^2\) and \(K_p\) were almost doubled \((P = 0.002)\) and \(P = 0.001\), respectively.

Table 1 shows that changes in TEWL (ΔTEWL) and erythema (Δerythema) were higher in atopics than in nonatopics \((P = 0.04)\) and \(P = 0.06\), respectively) after the 24-h irritation test. Baseline TEWL did not clearly differ between subjects with and without atopy (Table 1).
Table 2 shows the relationship between $\Delta$TEWL and $\Delta$erythema after the 24-h irritation test, and the obtained penetration parameters $K$, $L$, $D$ and $D/L^2$. A good relationship was found between the effect parameters, $\Delta$TEWL and $\Delta$erythema, and $D/L^2$ ($r = 0.74$, Fig 3, and $r = 0.58$, respectively). Moreover, $L$ had a clear influence on $\Delta$TEWL ($r = -0.64$) and $\Delta$erythema ($r = -0.63$), as well as an influence on the baseline TEWL ($r = -0.43$). No clear relationship was found between $K$ and $D$ and the skin irritation parameters. As regards the baseline TEWL, subjects with a higher baseline value also had a higher $\Delta$TEWL ($r = 0.62$). As the lag time to reach steady state is defined as $L^2/6D$, it appeared that the lag time in our subjects would be $10.5 \pm 6.0$ h.

Fig 2: Sodium lauryl sulphate (SLS) concentration obtained by tape stripping in two subjects as a function of stratum corneum (SC) depth ($x/L$) after a 4-h exposure to 1% SLS. Experimental data were fitted to the equation given in Figure 1, using a nonlinear regression analysis (dashed lines; $r = 0.95-0.97$)* $K_p$ = SLS permeability coefficient.
Table I. SLS penetration parameters (mean ± SD) and skin irritation parameters for subjects with and without atopy.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>All subjects</th>
<th>Atopy</th>
<th>No atopy</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC/water partition coefficient (K)</td>
<td>n = 17</td>
<td>n = 6</td>
<td>n = 11</td>
<td>+/- atopy</td>
<td></td>
</tr>
<tr>
<td>SC thickness (L)</td>
<td>µm</td>
<td>93 ± 22</td>
<td>95 ± 12</td>
<td>91 ± 27</td>
<td>n.s.</td>
</tr>
<tr>
<td>Diffusion coefficient (D)</td>
<td>x10^8 cm² h⁻¹</td>
<td>1.4 ± 0.6</td>
<td>1.8 ± 0.5</td>
<td>1.2 ± 0.5</td>
<td>0.05</td>
</tr>
<tr>
<td>Rate constant for SLS diffusion (D/L²)</td>
<td>x10⁻² h⁻¹</td>
<td>2.1 ± 1.1</td>
<td>3.1 ± 0.8</td>
<td>1.6 ± 0.7</td>
<td>0.002</td>
</tr>
<tr>
<td>Permeability coefficient (Kₚ)</td>
<td>x10⁻³ cm h⁻¹</td>
<td>1.5 ± 0.7</td>
<td>2.2 ± 0.5</td>
<td>1.2 ± 0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline TEWL</td>
<td>g m⁻² h⁻¹</td>
<td>8.6 ± 3.0</td>
<td>9.2 ± 3.9</td>
<td>8.3 ± 2.5</td>
<td>n.s.</td>
</tr>
<tr>
<td>ΔTEWL</td>
<td>g m⁻² h⁻¹</td>
<td>66 ± 40</td>
<td>93 ± 45</td>
<td>52 ± 30</td>
<td>0.04</td>
</tr>
<tr>
<td>Δerythema</td>
<td>AU</td>
<td>4.1 ± 2.9</td>
<td>5.9 ± 2.5</td>
<td>3.2 ± 2.7</td>
<td>0.06</td>
</tr>
</tbody>
</table>

SC, stratum corneum; TEWL, transepidermal water loss; NS, not significant; AU, arbitrary units. *Independent sample t-test (two-sided)

To estimate the contribution of individual skin properties on the skin irritation parameters, we performed a multiple linear regression analysis. The following relationship was obtained [estimated coefficients (SE)]: ΔTEWL = 23 (38) + 5.3 (1.9) baseline TEWL + 0.63 (0.24)K - 1.1 (0.25) × 10⁵L + 2.8 (0.91) × 10⁹D with an explained variance of r² = 0.80 (P = 0.001). In a model with only the baseline TEWL and L as the independent parameters, the explained variance was 0.55. For Δerythema, we obtained: Δerythema = 11 (3.0) - 1.2 (2.6) × 10⁻²K - 8.8 (2.6) × 10³L + 1.6 (1.0) × 10⁶D with an explained variance of r² = 0.50 (P = 0.024). Regarding ΔTEWL, all independent factors showed a significant contribution. By contrast, only L contributed significantly for Δerythema.
Fig 3: Increase in transepidermal water loss (DTEWL) after a 24-h irritation test as a function of the rate constant (D/L²) for diffusion of sodium lauryl sulphate across the stratum corneum.

Table II. Relationships between SLS penetration parameters and skin irritation parameters in volunteers.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SC/water partition coefficient (K)</th>
<th>SC thickness (L)</th>
<th>Diffusivity of SLS (D)</th>
<th>Rate constant for SLS diffusion (D/L²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline TEWL</td>
<td>-0.26</td>
<td>-0.43*</td>
<td>0.02</td>
<td>0.43*</td>
</tr>
<tr>
<td>ΔTEWL</td>
<td>0.10</td>
<td>-0.64**</td>
<td>0.22</td>
<td>0.74***</td>
</tr>
<tr>
<td>Δerythema</td>
<td>-0.25</td>
<td>-0.63**</td>
<td>0.09</td>
<td>0.58**</td>
</tr>
</tbody>
</table>

r = Pearson correlation coefficient, n = 17, * P < 0.05, ** P < 0.01, *** P < 0.001 (one-sided)
Discussion

Exposure to 1% SLS over 24 h led to a decrease in the skin water barrier function and to skin inflammation. The mean increase in TEWL and erythema was 72 g m⁻² h⁻¹ and 4.4 AU, respectively, with considerable interindividual variation. These findings are in agreement with those of other studies.²⁷-²⁹

In the present study, we aimed to investigate the influence of the skin penetration rate of SLS on skin irritation effects. The differences in the SLS penetration rate have been suggested as one of the possible sources of high interindividual differences in SLS irritability.⁵

In this study, we determined the penetration of SLS into the SC by means of an SC tape-stripping method. This noninvasive method is increasingly being used to determine the penetration parameters of compounds with various physicochemical properties, e.g. naphthalene,³⁰ 4-cyanophenol¹⁹,³¹ and cimetidine.³¹ The advantage to this method is that it enables measurement of the local SLS concentration, close to the effect site. The individual penetration parameters, \( K \) and \( D \), were deduced from the SLS concentration in subsequent tape strips based on Fick's Second Law of Diffusion. The SLS permeability coefficient \( (K_p) \) calculated from these penetration parameters was \( 1.5 \pm 0.7 \times 10^{-3} \text{ cm h}^{-1} \).

To date, no human in vivo data have been available on SLS penetration. However, some data has been published on in vitro experiments.⁹,¹²,¹⁵-¹⁸ In vitro assays showed that after a 24-h dermal application, only 2-3% of the applied SLS penetrated through the skin into the receptor fluid.¹⁶,¹⁷ Due to this low permeability, the blood concentrations of SLS will be too low to assess in vivo permeation of SLS. The experimental conditions in the mentioned in vitro studies differed from those used in our study. For example, the in vitro SLS exposure was longer (> 24 h), which makes changes in the barrier due to SLS effects more likely.⁶,³²,³³ Furthermore, the types of skin and methods of sampling in those studies were different. It is difficult therefore to compare the results obtained in our study with the in vitro values reported in the literature. As an alternative to experimentally determined data, for practical purposes the \( K_p \) of a compound can be predicted by skin permeation models. The Environmental Protection Agency has proposed an empirical model, which is based on the molecular weight and the octanol/water partition coefficient.³⁴ This model estimates a \( K_p \) for SLS of \( 4.5 \times 10^{-4} \text{ cm h}^{-1} \). Considering the SC as the major rate-limiting barrier to SLS penetration, this \( K_p \) is only a factor of 3 lower than our result: \( 1.5 \times 10^{-3} \text{ cm h}^{-1} \).
In general, $K_p$ describes the diffusion of a compound through a membrane under steady-state conditions. For our 24-h irritation test, the lag time to reach steady state ($L^2/6D$) can be estimated roughly at 10.5 ± 6.0 h. So, for the purpose of predicting the increase of TEWL and erythema, $K_p$ has limited value, because it reflects only the steady-state flux. The sooner the steady state is reached, the higher the time-weighted concentration of SLS in the SC of a subject will be, and the more intense the effect on TEWL and erythema. So the finding that the rate constant for diffusion ($D/L^2$) appeared to be a good predictor of the irritation effects was according to expectations.

With respect to $K$, the estimation of this parameter from the curve of the SLS concentration vs. SC depth depends very much on the quality of the first data points. To improve the reliability of this estimation Reddy et al. suggested conducting two exposure experiments: one experiment in the nonsteady-state condition to determine $D$ and another experiment with a longer exposure to determine $K$. As the curve of the SLS concentration vs. SC depth becomes a straight line at the steady state, the estimation of $K$ depends less on the error in the superficial strips. However, longer exposure could lead to alteration of the skin barrier to SLS.

It is possible that the SLS penetration rate into the skin may have been altered during the 4-h exposure, leading to a higher SLS diffusion. To minimize this risk, we opted for a relatively short exposure time and a low concentration. Moreover, in a pilot study, we observed no differences in penetration between a 1% SLS solution and a 0.1% solution. In the light of that, we assume that during a 4-h exposure SLS has a minimal effect on alterations in the barrier to SLS.

In the present study, we obtained substantial interindividual variation in all the measured penetration parameters (CV ranged from 24% to 51%). Fullerton et al. also found considerable interindividual variation (CV = 44%) in the in vitro penetrated amount of SLS in the epidermis of five different donors. We found higher penetration of SLS in atopics than in nonatopics.

The main objective of this study was to investigate the relationship between SLS penetration rate and the impairment of the skin water barrier function and skin inflammation. Several mechanisms are involved in skin irritation after exposure to SLS. In the SC, SLS interacts with the protein components of the SC and causes disorganization of the lipid bilayers. Both of these processes lead to barrier perturbation, resulting in an increased TEWL. In the epidermis, SLS has a direct toxic effect on the keratinocytes. As a consequence of epidermal cell
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damage, primary cytokines such as interleukin-1α are released from the keratinocytes, triggering the production of secondary cytokines and other inflammatory mediators by epidermal cells. Subsequently, these mediators induce an inflammatory reaction with cellular infiltrate in the epidermis and vasodilation in the dermis. \(^{39,41}\)

The effect of SLS on the skin water barrier function is known to vary considerably between subjects.\(^{24,42}\) The permeability of the SC to SLS will contribute to those interindividual differences, as it determines the concentration of SLS in the SC and, by consequence, the extent of barrier perturbation and increase in TEWL. The permeability of the SC depends on the composition and structure of the SC, reflected in the parameters \(K\) and \(D\). The partition coefficient of SLS between water and SC, \(K\), will determine the amount of SLS that enters the SC. The diffusion coefficient, \(D\), will dictate the rate by which the SLS moves through the SC. Both parameters and the SC thickness will determine the actual concentration in the SC. Taken alone, the baseline TEWL and SC thickness had a fair predictive value \((r^2 = 0.55)\) in predicting the impairment of the skin water barrier function after a 24-h SLS irritation test. This predictive value increased to \(r^2 = 0.80\) when the SLS penetration parameters were added. The positive relationship between the baseline TEWL and the increase in TEWL after SLS exposure fell in line with the findings of other SLS susceptibility studies.\(^{7,43,44}\)

In skin inflammation, as assessed by erythema, considerable interindividual differences were found after SLS exposure.\(^{5,7,24}\) In our study, the SC thickness seemed to be the most important factor influencing the extent of erythema after a 24-h SLS irritation test.

The observed interindividual variation in SLS penetration only partly explains the considerable variation in the SLS irritation effects. In our study, the range \((P_{5}-P_{95},\) data not shown) of SLS penetration between subjects was about a factor of 4 (3.6 for \(K_p\) and 4.4 for \(D/L^2\)). However, the SLS irritation threshold in acute exposure was found to differ by a factor of 200 between individuals \(< 0.1\% \text{ to } > 20\%).\(^{5-7}\) It is likely therefore that factors other than permeability play a role in individual susceptibility to SLS irritation. Aside from differences in skin barrier properties, one important factor may be the cytokine profile after exposure to SLS, which will affect the inflammatory response. Allen et al. showed an association between the individual irritant threshold for SLS and the presence of the polymorphism at position -308 in the \(TNFA\) gene.\(^{45}\)
We expect that individuals who have a higher SLS permeability also have a higher permeability for other substances, which makes them more susceptible to skin damage, e.g. in occupational exposure. This emphasizes that such individuals at risk have a greater need for skin protection in order to achieve a sufficient barrier to environmental chemicals. In conclusion, we have shown that the variation in barrier impairment and inflammation of human skin depends on the SLS penetration rate.

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