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Profile of irritant patch testing with detergents: sodium lauryl sulfate, sodium laureth sulfate and alkyl polyglucoside

H. LÖFFLER AND R. HAPPLE
Department of Dermatology, University of Marburg, Germany

The cutaneous reaction to detergents follows distinct kinetic rules: the duration of application and the irritant concentration are of major importance. The aim of this study was to evaluate the differences in kinetics of skin reaction between the standard irritant sodium lauryl sulfate (SLS), and 2 modern detergents: sodium laureth sulfate (SLES) and alkyl polyglucoside (APG). We performed patch testing with SLS and SLES (or APG) at different concentrations (0.125, 0.25, 0.5, 1.0 and 2.0%) and with different exposure times (6, 12 and 24h). Evaluation was conducted by measurement of transepidermal water loss (TEWL) and laser Doppler flowmetry (LD) 24h, 7 and 10days after patch removal. We found a pronounced reaction to SLS, and a far milder one to SLES. Even at the highest concentration the skin reaction to APG was hard to detect. During the regeneration period (day 3–10) SLS showed even at day 10 an increased TEWL at all concentrations tested. The irritation due to SLES was convincingly detectable only up to day 7, whereas the APG-tested skin areas showed no significant reaction even at day 3. These results demonstrate the improvement in reduction of skin irritation achieved by development of novel detergents.

Key words: irritant contact dermatitis; laser Doppler flowmetry; patch test; skin recovery; transepidermal water loss.

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In a recent study, the kinetics of irritant skin reaction to the model irritant sodium lauryl sulfate (SLS) were described (1, 2). However, SLS is usually not a major irritant in daily practice. Modern detergents have replaced SLS in many fields, because they seem to be less irritating. Because SLS is still a standard model irritant for patch testing of detergents (3–5), the diminished irritant potential of newer detergents should be defined in comparison to SLS. In this study, the kinetics of irritant skin reaction to the modern detergents sodium laureth sulfate (SLES) and alkyl polyglucoside (APG) is compared to those of SLS, following the test protocol of the above-mentioned study (2). Moreover, the regeneration phase of the irritated skin will be observed over 10days, to investigate possible differences between the irritants tested.

Patients and Methods

Study population

20 healthy volunteers (12 women and 8 men, aged between 18 and 60years) participated in this study. They were recruited from the out-patient clinic and in-patient ward of the Department of Dermatology, University of Marburg (e.g. patients with phlebological problems or for venom immunotherapy). Informed consent was obtained from all participants, and the study was approved by the ethical committee of the University of Marburg. Atopic individuals and patients with dermatitis of any kind were excluded. No patient received any systemic immunosuppressive medication.

Test procedure

On the back of each volunteer 6 rows of test plaster were applied, each containing 5 Large Finn Chambers® (inner diameter 12mm, Epitest Ltd, Hyrlä, Finnland) on Scanpor® tape. The 5 chambers (each containing a filter paper) of the first 3 rows were filled with 60μL SLS (Sigma, Germany, 99% purity) 0.125%, 0.25%, 0.5%, 1.0% and 2.0% in water. The other 3 rows were filled with either SLES or APG (Cognis Deutschland GmbH & Co. KG, Düsseldorf, Germany) in the

Table 1. TEWL and LD values (Δ-value = difference to the basal value) on patch testing with different SLS concentrations and exposure times. Results are displayed as median values, TEWL in g/m²/h

%	6 h		12 h		24 h		3 days		7 days		10 days	
	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD
0.125	3.2	4.4	6.3	16.4	6.5	6.2	7.8	9.6	3.7	5.2	4.5	4.5
0.25	3.7	5.7	9.4	22.5	10.5	13.6	9.9	11.1	6.5	6.7	4.5	7.8
0.5	10.8	10.6	18.1	35.6	22.2	25.4	13.2	13.6	10.1	8.2	6.8	8.2
1.0	15.0	22.8	27.0	42.4	32.6	46.7	19.1	29.6	12.2	16.4	7.4	12.8
2.0	18.9	48.9	35.9	68.9	40.2	55.2	25.7	33.2	14.5	25.8	9.3	16.2

Table 2. TEWL and LD values (Δ-value = difference to the basal value) on patch testing with different SLES concentrations and exposure times. Results are displayed as median values, TEWL in g/m²/h

%	6 h		12 h		24 h		3 days		7 days		10 days	
	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD
0.125	3.2	2.8	4.6	11.7	6.5	7.4	4.5	3.8	4.6	2.7	3.2	0.2
0.25	3.1	3.8	6.3	10.5	6.8	14.3	5.9	5.1	5.5	3.6	3.6	3.4
0.5	5.2	4.4	12.0	12.7	12.7	24.8	9.4	9.9	5.1	8.3	3.0	1.1
1.0	9.6	13.0	13.6	20.7	17.3	30.1	10.5	7.8	6.8	2.4	2.6	5.2
2.0	13.3	19.7	17.7	32.1	24.0	41.2	11.1	10.5	5.9	5.3	4.1	2.8

same way as SLS. The first row of each detergent was removed after 6 h and the skin reaction of each SLS concentration was measured. The remaining test rows were removed after 12 and 24 h and the skin reaction was measured in the same way. For the regeneration measurements at day 3, 7 and 10, only those chambers that had been applied on the skin for 24 h, were evaluated. Testing was performed according to the guidelines for sodium lauryl sulfate exposure tests of the Standardization Group of the European Society of Contact Dermatitis (6).

During measurements the patient was lying face down on a bed. Skin reactions were evaluated by measurement of TEWL with a Tewameter TM210 (Courage & Khazaka, Cologne, Germany) and by measurement of cutaneous blood flow with a Laser Doppler (LD) Flowmeter (Peri Flux System 5000, Perimed, Sweden) by use of an integrating probe. Measurements were performed prior to application of test chambers (basal values) and 24 h after patch removal, because the effect of occlusion lasts several hours after removal of the patch (7). During the TEWL measurements, the probe was hand-held by use of an insulating glove until a stable TEWL value was established (~1 min). Air convection was prevented by a protective measuring-chamber and by reducing movement and speech in the testroom. The test results were evaluated by 2 experienced persons according to the guidelines for transepidermal water loss measurement of the Standardization Group of the European Society of Contact Dermatitis (8). Each TEWL test value was the average of 3 single measurements. Prior to measurement the volunteers rested for at least 0.5 h in the testroom, a fully air-conditioned compartment [climatization without air movement by Thermotexx® (MET AG, Chemnitz, Germany)] with a stable temperature between 20 and 22°C and a relative humidity of 35–62%. The tests were performed within a period of 12 weeks during winter and spring 2000/2001.

Statistical methods

Data were calculated with SPSS for Windows®. After calculation with the Kolmogorov–Smirnov test, TEWL and LD values were shown as medians. As there was no symmetrical contribution it is not possible to calculate mean or standard deviation values. Correlation between SLS concentration and skin reaction as evaluated by TEWL and LD was calculated by the Pearson correlation coefficient. Differences between the detergents were calculated by means of the Wilcoxon test.

Results

As the Kolmogorov–Smirnov test showed no symmetrical distribution, descriptive statistics were appropriate for the calculation. The basal values were 6.5 g/m²/h for TEWL and 14.5 for LD.

Acute irritation

TEWL and LD values are listed in Tables 1–3 as delta values (Δ = difference to the basal value). TEWL test results are visualized in Figs 1–3. There was a clear-cut correlation between skin reaction (evaluated by measurement of TEWL as well as of

Table 3. TEWL and LD values (Δ-value = difference to the basal value) on patch testing with different APG concentrations and exposure times. Results are displayed as median values, TEWL in g/m²/h

%	6h		12h		24h		3days		7days		10days	
	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD	TEWL	LD
0.125	3.2	3.5	3.5	6.4	0.2	2.1	0.4	0.3	5.2	5.2	2.5	1.9
0.25	3.6	2.5	2.8	3.4	3.6	0.1	5.2	−0.1	2.9	2.5	3.6	1.1
0.5	4.1	6.2	3.8	1.9	3.9	2.7	3.7	2.5	4.3	4.1	3.2	2.4
1.0	3.0	3.2	4.1	4.2	0.1	0.3	4.5	3.2	0.5	2.9	4.3	2.7
2.0	3.1	1.6	4.5	4.1	4.4	1.3	4.1	0.6	2.4	6.4	4.1	3.1

LD) and detergent concentration and exposure time ($P<0.01$) for SLS and SLES. However, SLES produced at all concentrations a significantly lower irritation than the corresponding concentration of SLS. The severity of irritation caused by 2.0% SLS is nearly as strong as that induced by 0.5% SLES. APG showed no correlation between skin reaction and detergent concentration, because it failed to produce a significant concentration-dependent irritation. The TEWL values after APG irritation were for all concentrations only slightly higher than the basal values (Fig. 3). Any dependency of APG-induced irritation on the application time was also not observed.

Regeneration time

TEWL and LD values measured after 3, 7 and 10 days are listed as delta values (Δ = difference to the basal value) in Tables 1–3. TEWL results are visualized in Figs 4–6. We found distinct differences between the 3 detergents tested in the regeneration time: SLS showed the longest-lasting irritation. The strongest irritation was evaluated 24 h after removal of the patch and a continuous decrease in TEWL and cutaneous blood flow was observed over the following days. Detectable irritation by SLS lasted at least 10 days, because even at day 10 an increase in TEWL (which was even slightly concentration-dependent) was observed. After testing with SLES, the irritation could be detected by measurement of TEWL up to 3 days only. After 7 days no significant irritation was noted, even at the highest concentration (2.0%). Because we saw no substantial irritation after application of APG, no regeneration could be seen either.

Discussion

SLS is one of the most irritant detergents and has led to severe problems in occupational dermatology (9). In recent years several detergents with lower irritancy have been developed. In this study, 2 of these detergents (SLES and APG) were compared with SLS.

When the results of the 6–24 h patch test were analyzed, we found in comparison to SLS significantly less damage of the epidermal barrier caused by SLES. However, the kinetics of the irritation were similar: the greatest increase in irritation was

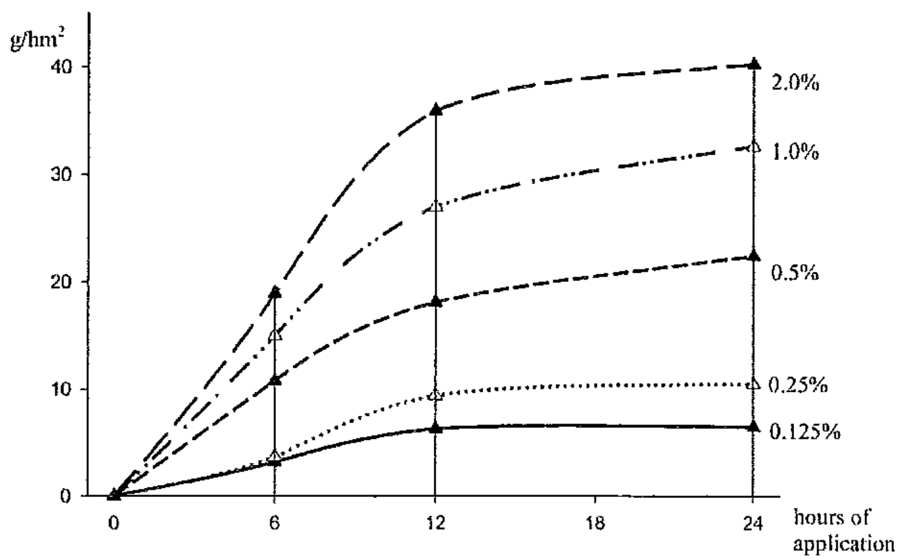

Fig. 1. Kinetics of SLS-induced ΔTEWL 24 h after patch removal.

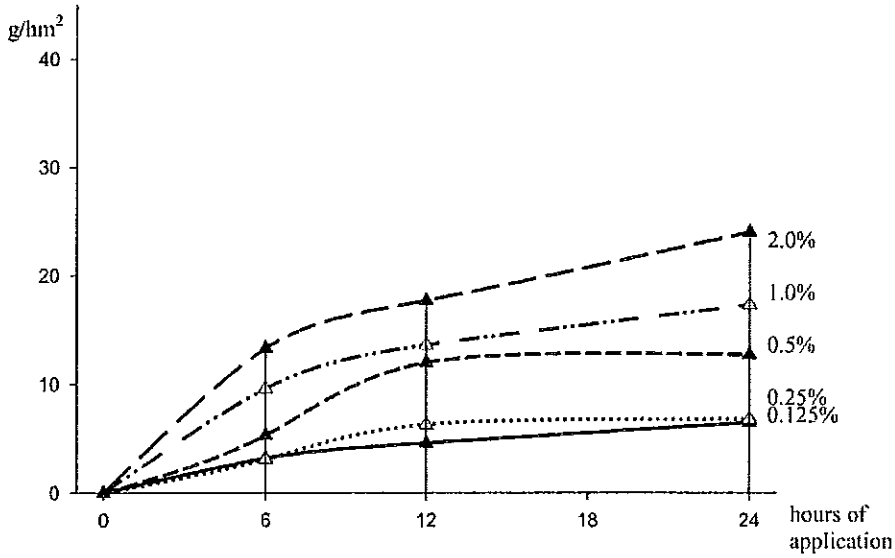

Fig. 2. Kinetics of SLES-induced ΔTEWL 24 h after patch removal.

observed with both detergents after the first 6h. Subsequently, the irritation increased to a lesser degree. This may relate to the penetration of these detergents into the epidermis, which takes place mainly during the first few hours after patch application (10–13). The irritation caused by APG was hardly detectable. We saw an increase in TEWL (and a minimal one in LD values), which was not dependent on the concentration of APG or the application time. Therefore, we think that this minimal irritation was not caused by the substance. More likely it was the occlusion (and the water as vehicle) itself which caused this minimal irritation, as the irritant effect of both occlusion and water is well-known (14–17). Therefore, it can be stated that even 2.0% APG applied over 24 h does not produce any substantial irritation.

During the regeneration time of SLS, a continuous decrease in the irritation can be observed. However, even 10days after patch testing a concentration-dependent increase in TEWL can be observed. This was described in a similar way for 0.5% SLS in a study by Wilhelm *et al.* (18). Regeneration of barrier disruption caused by SLS can clearly not be achieved within a short period of time. In a further study, regeneration times of up to 4weeks have been described for SLS-irritated skin (19). This long period may be due to the severe irritation induced, as simple disruption of the barrier (e.g. by tape-stripping) led to much faster

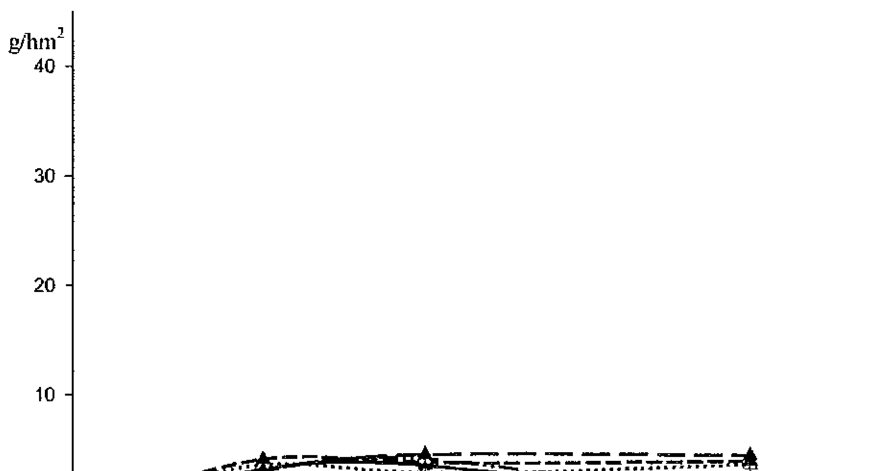

Fig. 3. Kinetics of APG-induced ΔTEWL 24 h after patch removal.

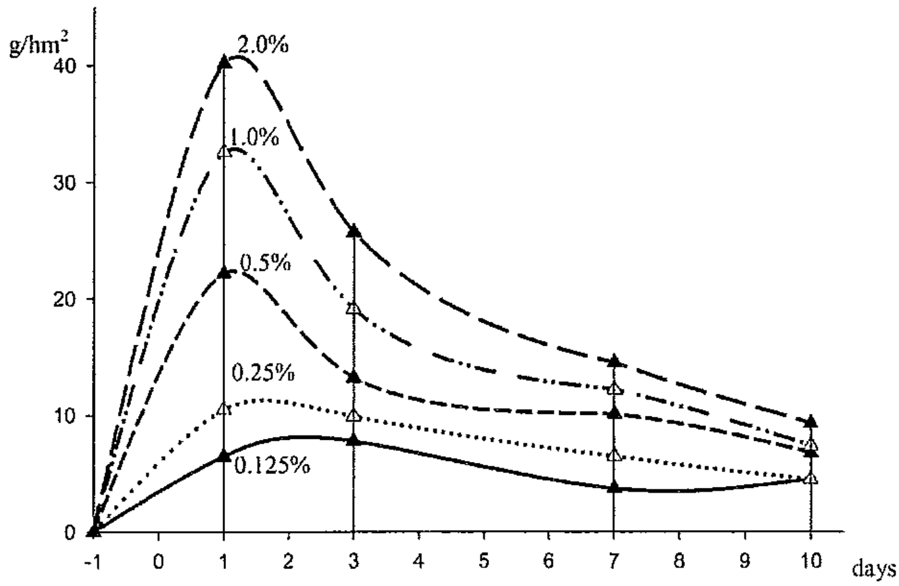

Fig. 4. Regeneration of ΔTEWL induced by 24 h application of SLS (application on day −1, removal on day 0, measurement on days 1, 3, 7 and 10).

regeneration. Hence, it must be detergent-specific processes which are responsible for these long periods of regeneration. A likely explanation may be detergent remaining within the stratum corneum for long periods after removal of the test patch (20).

Regeneration after skin irritation caused by SLES takes place much faster than that induced by SLS at the same concentration. 7 days after removal of the patch no increase in TEWL or LD values as compared to basal values was observed. These results document the distinctive characteristic of SLES as an anionic detergent with lesser irritancy, confirming previous findings (21). The LD values support these results. Because cutaneous blood flow is a parameter for more severe irritation, it is understandable that even after 3 days only slight SLES-induced irritation could be observed. Therefore, for regeneration studies TEWL measurement seems to represent a more reliable method.

Because we saw no irritation caused by APG, no regeneration could be expected either. The substantial advantage of APG as a low-irritant

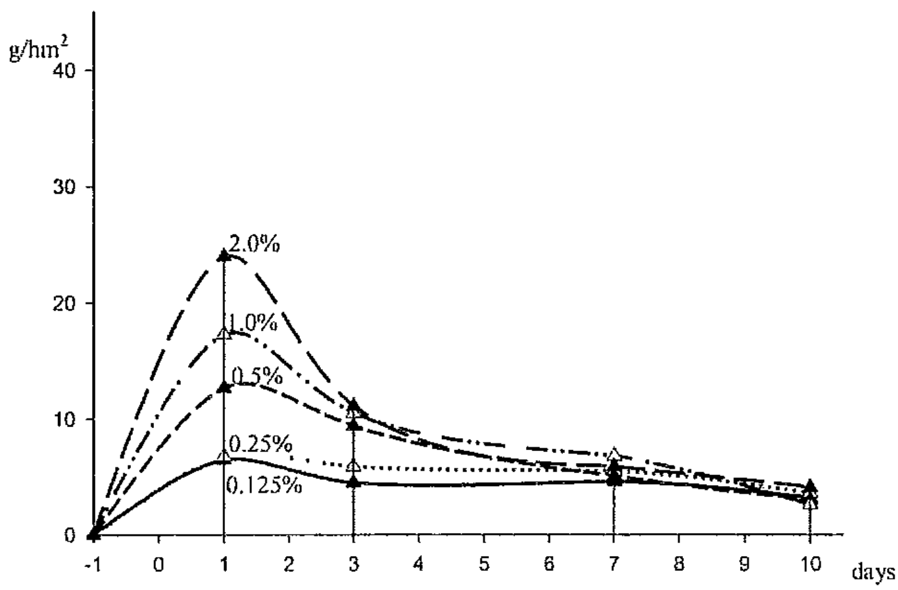

Fig. 5. Regeneration of ΔTEWL induced by 24 h application of SLES (application on day −1, removal on day 0, measurement on days 1, 3, 7 and 10).

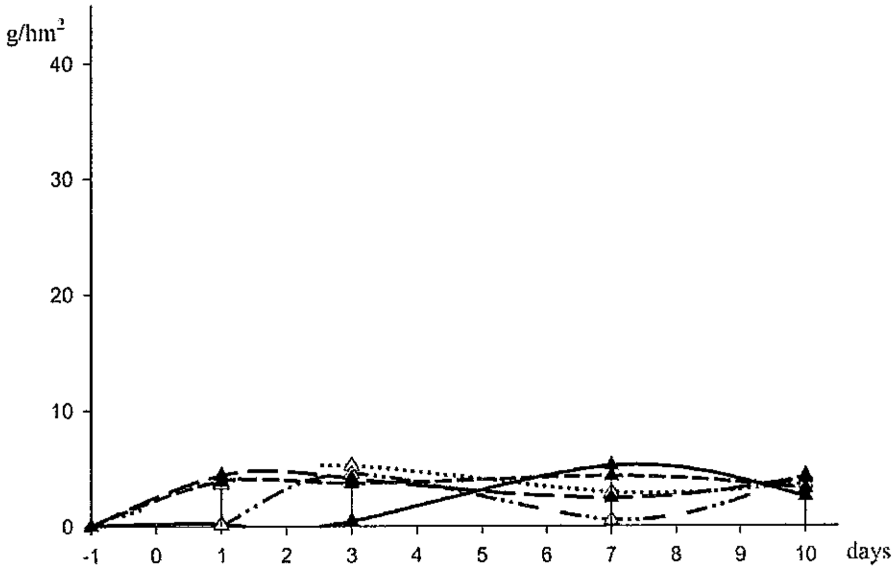

Fig. 6. Regeneration of ΔTEWL induced by 24 h application of APG (application on day −1, removal on day 0, measurement on days 1, 3, 7 and 10).

detergent is emphasized. However, the claim that non-detectable irritation is proof of nonexistent irritation should be rejected. It has been shown that even after a regeneration period of 10 weeks clinically normal skin still reacts significantly more to further irritation, when compared to non-pre-irritated skin. Therefore, a mild irritant is still an irritant. But because we know very well the effect of cumulative irritation, for daily work these mildly irritating detergents should be used. Even in combination with stronger irritants, these mild irritants can reduce the irritant effect of a detergent-containing product, which may lead to a decrease in clinically relevant irritation (20, 22). This effect may be of the greatest relevance, especially for the many patients with occupational dermatitis on the hands (23–25).

For the first investigation of an irritation profile, the demonstrated test procedure should be used. With this test procedure it is possible to investigate the different irritant potential of detergents in detail, both during the early acute irritant skin reaction period and during the regeneration period. After demonstration of a similar profile of irritation between 2 detergents, a single 24 h patch test may be sufficient for further evaluation. Because SLS is the best-known standard irritant (3, 5, 6, 26), we still recommend assessing the irritant potential of other detergents by comparison with SLS.

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Address:
Dr H. Löffler
Department of Dermatology
University of Marburg
Deutschhausstr. 9
D-35033 Marburg
Germany
Tel: +49 6421 2862321
Fax: +49 6421 2862324
e-mail: Harald.Loeffler@mailer.uni-marburg.de