

Effects of disinfectants and detergents on skin irritation

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We investigated the biological response of regular human skin to alcohol-based disinfectants and detergents in a repetitive test design. Using non-invasive diagnostic tools such as transepidermal water loss, laser-Doppler flowmetry and corneometry, we quantified the irritative effects of a propanol-based hand disinfectant (Sterillium[®]), its propanol mixture (2-propanol 45% w/w and 1-propanol 30% w/w), sodium lauryl sulfate (SLS) 0.5% and distilled water. The substances were applied in a 2-D patch test in a repetitive occlusive test design to the back. Additionally, we performed a wash test on the forearms that was supposed to mimic the skin affection in the normal daily routine of health care workers. In this controlled half-side test design, we included the single application of the hand rub, SLS 0.5% and water as well as a tandem application of the same substances. Patch test and wash test showed similar results. The alcohol-based test preparations showed minimal irritation rather comparable to the application of water. However, the detergent SLS produced stronger barrier disruption, erythema and dryness than the alcohol-based preparations. There was no additional irritation at the combined use of SLS and disinfectants. By contrary, there was even a decrease in barrier disruption and erythema induced by the tandem application of SLS followed by alcohol-based disinfection compared with the use of SLS alone. These findings show a less irritant effect of alcohol-based disinfectants on the skin than detergents. Our study shows that there is no summation of irritating effects of a common detergent and propanol and that the combination of washing and disinfection has a rather protective aspect compared with washing alone.

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Hand hygiene directly affects medical personnel and is vital for prevention of nosocomial infection. Single alcohols (1) and many alcohol-based formulations (2) are well tolerated by users but compliance in hand hygiene remains low, nonetheless (3). Key role in that problem is may be the combination of washing and disinfection. It has been shown that on average 45% of hand hygiene procedures are hand washes and the remaining 55% are hand disinfections (3). The harmful effect of sodium lauryl sulfate (SLS) has been proven in multiple studies (4–6) and is summarized by Lee and Maibach (7). The influence of alcohol – which is considered to be irritant by some users – seems to play rather a minor role in pathogenesis of skin irritation (1, 8) Onset of irritant contact dermatitis (ICD) is often induced by wet-work and detergents (9). It is insidious and mostly unnoticed. At the very beginning, an alcohol-

based disinfectant will sting on a skin, which is already disrupted. This is a well-known property of alcohols (10). Therefore, stinging on contact with an alcohol-based disinfectant can be an early sign for ICD and should set the focus on preventive skin care. Some studies illuminated already the combined use of detergent and disinfectant, showing that short-term exposure to SLS and *n*-propanol in an occlusive test does not lead to an enhanced skin irritation, when compared with single application of these substances (8, 11). Even a recent study using an open application of irritants indicates that disinfection with alcohol-based solutions containing emollients or alternate use of a disinfectant/detergent causes less skin irritation than only disinfection with a detergent (12).

What has not been addressed so far is the effect of alternate use of alcohol-based disinfection and detergent in a high-standardized patch test and in

a wash test representing the daily routine of health care workers.

Subjects and Methods

Study population

45 healthy volunteers, aged from 18 to 45 (median: 27 years, 25 women, 20 men), without acute dermatoses and without a history of atopic eczema participated in the study. Informed consent was obtained from all participants. The study was approved by the medical ethics committee of the University of Marburg on 5 July 2002.

Test substances

SLS was purchased as a highly purified powder (99%; Sigma Chemicals, Taufkirchen, Germany). Sterillium[®] is a formulated hand rub (subsequently called hand rub) and based on 2-propanol 45% w/w, 1-propanol 30% w/w and mecetronium etilsulfate (MES) 0.2% w/w. It is manufactured by Bode Chemie GmbH & Co. KG (Hamburg, Germany). We chose an SLS concentration of 0.5% because this is the concentration commonly referred to in literature to cause skin irritation in open and occlusive tests (8, 13).

We produced a 0.5% w/v solution of SLS in water. The propanol solution containing 2-propanol 45% w/w and 1-propanol 30% w/w (subsequently called propanol solution) was delivered by Bode Chemie GmbH & Co. KG. We used this propanol solution because it is the same combination of alcohols as in Sterillium[®], which was tested also.

Test procedure

Patch test. The patch test procedure was used basically to reproduce an acute irritancy. The test substances were applied epicutaneously using Finn Chamber[®] patch test technique (12-mm inner diameter; Epitest Ltd., Oy, Finland). The Finn Chambers[®] were equipped with matching filter paper before 60 µl of the substances was added, and they were attached to the skin on the test person's back. SLS 0.5%, hand rub, propanol solution and water were added in separate fields. One field was left empty as a control.

The substances were left in place for 1 D on the skin. Using tandem application, the inflammatory reaction on a combined application of two substances as well as the reaction on repetitive application of the same test substance was measured. The first application was made at $t = 0$ and the second application at $t = 1$ D. After 2 D, the chambers were removed without further treatment of the skin. Measurement was taken 3 D

after the first application. The placement of the chambers were randomized and blinded to the test person.

Wash test. Additionally, we used a wash test procedure to provoke and reproduce cumulative irritancy. The test persons were randomized into three different groups: A, B, and C. Those groups underwent different wash test procedures during a 7-day period as shown in Table 1.

Individuals in group A, bathed one forearm (randomized) in a suspension of SLS 0.5% and washed it with a foam roller using a standardized procedure for 5 min (altogether 50 times up and down). After removing the SLS with clear water, the skin was swabbed off the water with a paper towel. This was followed by the application of the alcohol-based hand rub with another foam roller on the previous treated skin. The procedure was identical but the hand rub was not swabbed off. During each procedure, about 50 ml of hand rub was applied. Afterwards, the contralateral side was treated with hand rub alone in the same fashion.

Individuals in group B were treated with the combination of SLS and hand rub on one forearm as described in group A. The test persons treated the contralateral side with SLS only, as described above.

Individuals in group C were treated with hand rub on one forearm and the with clear water in contralateral side in the same fashion as described above.

The test persons were not allowed to use any additional emollients or detergent on the test areas during the entire study.

Measurements

Evaluation was performed using the TEWA-METER TM 210 (Courage and Khazaka, Cologne, Germany) as a marker of barrier disruption (14), the Laser-Doppler flowmetry as a marker for cutaneous blood flow (15) (PERI-FLUX 5010; Perimed, Stockholm, Sweden), and the CORNEOMETER CM 820 (Courage and Khazaka) additionally in the wash test as a marker for the intraepidermal water content. The basal values were taken on D0, the final measurements were performed 1 D after patch test removal and

Table 1. Application protocol wash test

	Forearm 1	Forearm 2
Group A	SLS + hand rub	Hand rub
Group B	SLS + hand rub	SLS
Group C	Hand rub	Tap water

SLS, sodium lauryl sulfate.

1 D after the test persons finished the wash test, respectively. All measurements were conducted at controlled ambient conditions (40–50% relative humidity, 20–22° celsius). The volunteers rested at least 30 min in the evaluation room before the measurements were conducted.

Statistical analysis

Data were calculated with SPSS 11.0 for Windows® (SPSS Inc., Chicago, IL, USA). Before statistical analysis, the values were tested for normative distribution by use of the Kolmogorov–Smirnov test. Because no normal distribution was found, we used Wilcoxon signed rank test, a nonparametric alternative to the paired *t*-test, for checking the significance among the delta values for all measurement methods.

Results

Patch test

Transepidermal water loss. The patch test showed significant higher transepidermal water loss (TEWL) values of SLS 0.5% compared with the hand rub ($P < 0.001$) as well as compared with the propanol solution ($P < 0.001$; Table 2). Furthermore, we found a significantly higher transepidermal water loss of the hand rub in comparison with the propanol solution ($P = 0.015$). The combined patch tests SLS/hand rub and SLS/propanol

solution compared with SLS/SLS showed a highly significant stronger water loss in the SLS/SLS application ($P < 0.001$).

Subpapillary dermal blood flow. The patch test showed significantly higher laser-Doppler flowmetry values of SLS compared with the hand rub ($P < 0.001$) as well as compared with the propanol solution ($P < 0.001$). We also found a significantly stronger increased subpapillary dermal blood flow with the hand rub in comparison with the propanol solution ($P < 0.001$). The combined application of SLS/hand rub and SLS/propanol solution, respectively showed a lower blood flow compared with the SLS/SLS application.

To sum up, there was a significantly higher blood flow and transepidermal water loss using the detergent than using the alcohol-based preparations. Moreover, there was a lower blood flow and lower transepidermal water loss in the combination of the detergent and the alcohol-based preparations compared with the detergent alone (Table 2 and Figs. 1 and 2).

Wash test

Transepidermal water loss. The wash test produced similar results. The combined application of SLS/hand rub led to a significant lower TEWL increase than single SLS application ($P = 0.003$). The use of SLS/hand rub showed significant stronger increase in TEWL than the single hand rub application ($P = 0.001$). We also observed a significantly higher transepidermal water loss with the hand rub compared with tap water ($P = 0.031$).

Table 2. Repetitive patch test values measured by TEWL and laser-Doppler flowmetry 1 D after patch removal

Test substances	<i>n</i>	Minimum	Maximum	Median	25th/75th percentile
Δ TEWL					
SLS/SLS	45	17.5	65.7	36.9	29.8/46.0
ST/ST	45	−1.6	9.9	3.2	1.8/4.4
Pro/Pro	45	−2.3	11.5	1.7	0.2/4.4
Aq./Aq.	45	−0.8	10.1	1.7	0.3/3.1
SLS/ST	45	3.1	69.4	18.6	13.4/31.1
ST/SLS	45	3.7	48.5	17.9	13.2/25.1
SLS/Pro	45	0.5	58.3	21.7	16.5/32.6
Pro/SLS	45	0.1	42.3	17.5	10.1/23.7
Empty/empty	45	−3.2	9.6	1.7	0.2/2.8
Δ Laser-Doppler flowmetry					
SLS/SLS	45	4.6	27.3	60.8	37.4/86.7
ST/ST	45	−2.9	33.8	6.8	2.4/15.1
Pro/Pro	45	−3.8	57.7	2.0	−0.3/5.7
Aq./Aq.	45	−3.2	31.2	2.4	−0.4/6.8
SLS/ST	45	1.0	121.3	28.3	15.2/62.8
ST/SLS	45	0.4	85.8	21.1	13.2/44.2
SLS/Pro	45	−2.5	89.0	20.7	8.4/51.1
Pro/SLS	45	−0.20	136.5	18.7	8.1/32.0
Empty/empty	45	−5.6	15.7	1.5	−0.2/4.0

Aq., tap water; Δ, delta values differences; HR, hand rub; Pro, propanol solution (2-propanol 45% w/w and 1-propanol 30% w/w); SLS, sodium lauryl sulfate 0.5%.

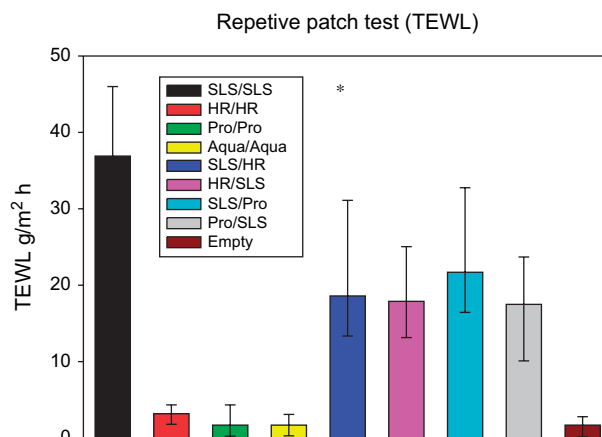


Fig. 1. Comparison of transepidermal water loss response between control site, the test preparations and their combinations, measured after 3 D (median values and 25th/75th percentile). Aqua, tap water; HR, hand rub; Pro, propanol solution (2-propanol 45% w/w and 1-propanol 30% w/w); SLS, sodium lauryl sulfate 0.5%. * $P < 0.05$.

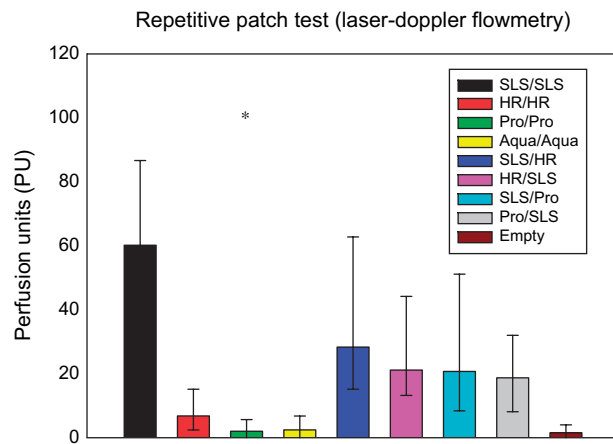


Fig. 2. Comparison of laser-Doppler flowmetry between control site, the test preparations, and their combinations, measured after 3 D (median values and 25th/75th percentile). Aqua, tap water; HR, hand rub; Pro, propanol solution (2-propanol 45% w/w and 1-propanol 30% w/w; SLS, sodium lauryl sulfate 0.5%. * $P < 0.05$.

Subpapillary dermal blood flow. The SLS/hand rub application induced a significantly ($P = 0.008$) lower dermal blood flow than the SLS application alone. The combination SLS/hand rub compared with hand rub alone showed a significantly ($P = 0.009$) higher blood flow of the tandem application.

Considering the dermal blood flow, there was no statistically significant difference between application of the hand rub and tap water ($P = 0.427$).

Corneometry in wash test. Considering the epidermal water content, there was no significant ($P = 0.513$) difference between the application of water and the hand rub. The combination of SLS/hand rub compared with SLS alone showed no significantly stronger epidermal hydration of the tandem application ($P = 0.052$). The SLS/hand rub combination induced a significantly lower epidermal water content than the hand rub alone ($P = 0.022$).

To sum up, there were no differences in blood flow and epidermal hydration between the application of water and the hand rub. Moreover, the combination of the hand rub and the detergent showed a higher epidermal hydration, a lower dermal blood flow and a lower epidermal water loss than the detergent alone (Figs. 3–5).

Discussion

The mechanism of irritant dermatitis produced by combined exposure with clinical or subclinical dosages of irritants is well known (16–18). Recently, a review of these tandem mechanisms is published by Kartono and Maibach (19).

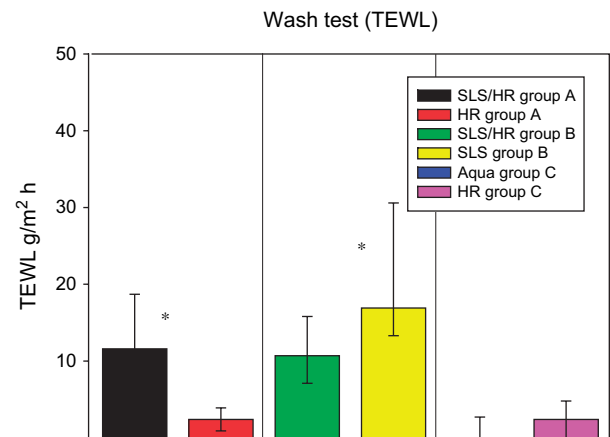


Fig. 3. Pair-wise comparison of transepidermal water loss response between the test preparations and their combinations after 7 days of wash test, measured at D8 (median values and 25th/75th percentile). Aqua, tap water; HR, hand rub; SLS, sodium lauryl sulfate 0.5%. * $P < 0.05$.

But what is known about the widely used alcohol-based disinfectants and detergents? These substances are used each day by millions of health care workers in a repetitive way. Some studies show that standard alcohols are well tolerated on the volar forearm of human skin (1, 2, 20, 21). In an extensive investigation, Löffler et al. showed that various alcohols have a minor irritative potential to human skin on the back and on forearms (8). Even on preirritated skin, 60% *n*-propanol causes low irritation, which was evaluated by TEWL and skin surface capacitance (22). We could confirm these findings showing only small irritative potential of a propanol mixture (2-propanol 45% w/w and 1-propanol 30% w/w).

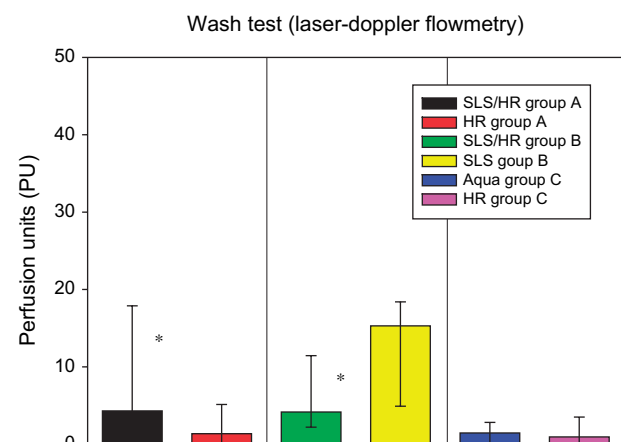


Fig. 4. Pair-wise comparison of laser-Doppler flowmetry response between the test preparations and their combinations after 7 days of wash test, measured at D8 (median values and 25th/75th percentile). Aqua, tap water; HR, hand rub; SLS, sodium lauryl sulfate 0.5%. * $P < 0.05$.

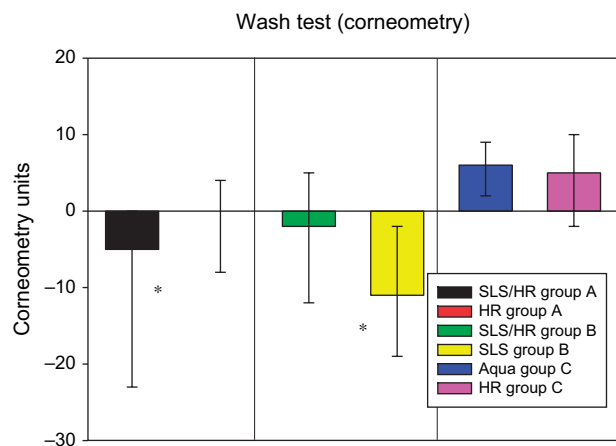


Fig. 5. Pair-wise comparison of intraepidermal water content response between the test substances and their combinations after 7 days of wash test, measured at D8 (median values and 25th/75th percentile). Aqua, tap water; HR, hand rub; SLS, sodium lauryl sulfate 0.5%. * $P < 0.05$.

in the patch test that was in the same range with water.

Additionally in our patch test series, we could show that the irritative effect of SLS on the skin is reduced, when used in a tandem application with the propanol solution or the hand rub. Our test confirmed the assumption of Kappes et al. that tandem applications of propanol to a detergent do not lead to a summation of the irritative potentials (11). We could also confirm the results of Pedersen et al. that the alternate use of detergents/alcohol-based disinfectants causes less skin irritations than hand treatment with a detergent (12). Pedersen et al. evaluated the short-term effects of detergents and disinfectants on the skin. It was shown that detergent affect the skin to a higher degree than a combination of alcohol/disinfectant and alcohol separately. Our study could prove these short-term effects as shown in the patch test.

Moreover, we could highlight that the prolonged use of a combination of alcohol-based disinfectant and synthetic soap can decrease the risk of developing and exacerbating irritation compared with single use of SLS, as it is shown in the wash test, which took 7 days. Recently, Pedersen et al. proved our results in a 10-day study (23).

When comparing the acute versus the cumulative irritancy in this study, it is important to mind the application site of the irritant. An uncritical comparison of results on the skin of different body sites should be avoided (24, 25).

Furthermore, our study showed that under repetitive occlusive test conditions, apparently a combination of propanols (2-propanol 45% w/w

and 1-propanol 30% w/w), which is used in tested hand rub, has a slightly better skin compatibility compared with the hand rub itself, although it contains glycerin that has been described to increase skin hydration (26) by retention of water in the stratum corneum (27) and the detergent MES that has been described as having substantial skin care effects (28). Our finding is in contrast to the previously reported data. It has been shown before in a repetitive occlusive patch test with 55 subjects that even 9 repetitive applications of the hand rub are well tolerated by the skin (2). In an open test with up to 20 applications per day on hands, the same hand rub did not show any significant change in TEWL, skin hydration, or sebum content and was well tolerated by the subjects (28). Even more, it was the one hand product that was tolerated the best by users in comparison of 6 alcohol-based hand products (28). This achievement was interpreted, *inter alia*, as the emollient effect of MES and glycerol, which are added in the hand rub. Recent data suggest that even the skin of subjects with an atopic predisposition tolerates the hand rub very well (2).

The benefits of adding emollients to a propanol-based hand rub have been described recently (2). Each alcohol-based hand rub can induce burning sensations on irritated skin, familiar to everyone who has used a alcohol-based substance on fissured skin (22). Because of that sensation, health care workers seem to avoid the application of alcohols for the benefit of hand washing with a detergent. A vicious circle is about to start. As the use of detergents provides the development of irritation and disruption of the epidermal barrier, alcohol hand disinfectants will be more and more avoided because of increasing burning sensations. Additionally, damaged skin shows a higher bacterial count. Therefore, the use of detergents instead of alcohol-based hand rubs causes even a hygienic problem (29–32). It is described that a 1-min simple hand wash reduces artificial bacterial contamination of hands by a log(10) reduction factor of 2.8 and a 1-min reference disinfection with 2-propanol (60%, v/v) by a factor of 4.6 steps (2). This shows the advantages of alcohol-based hand rubs not even in matters of the dermal tolerance but also in the efforts of preventing transmission of nosocomial pathogens.

The hand rub that was tested in our study has been described to have a significantly better subjective perception of the emollient effect compared with 5 other hand rubs in a blinded design (28). This may well be an important factor to stimulate high compliance rates in hand hygiene (2). Increasing the compliance in hand hygiene can reduce nosocomial infections; therefore, hand

hygiene is a key to infection control (3). But nowadays, compliance in hand hygiene on average of 50% is still considered to be far too low (33).

In a current study, Creedon et al. point out that the implementation of a multifaceted interventional behavioural hand hygiene programme resulted in an overall improvement of compliance in all features of current hand hygiene guidelines. Furthermore, health care workers believed that their skin condition improved. They state that alcohol-based hand rubs (with emollients) need to be provided at each patient's bedside and issues surrounding health care workers' skin irritation need to be addressed urgently (34). Therefore, it is feasible to add substances with positive effects regarding comfortable feeling by using skin disinfectants. Moisturizers, like glycerol, seem to have at least this property (2).

Of course, if the hands of health care workers are visibly soiled, soap and water have to be used instead of or before hand disinfection. However, it must be emphasized that the combined use of a detergent and a propanol-based hand disinfectant, whether it contains a moisturizer or not, is significantly better tolerated by skin than the single use of a detergent. The switch from hand wash to alcohol-based hand rub may improve health care workers skin if mistakes are avoided and hand rinses are used correctly.

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