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Irritancy testing of sodium laurate and other anionic detergents using an open exposure model

R. A. Tupker¹, K. Vermeulen¹, V. Fidler² and P. J. Coenraads¹

¹Department of Dermatology, University Hospital, Groningen and ²Department of Medical Statistics, University of Groningen, The Netherlands

Background/aims: The irritant potency of soap (sodium laurate, LAU) as opposed to other anionic detergents is not uniformly agreed upon. The aim of the study was to compare the irritancy of sodium laurate with that of sodium laurylsulphate (SLS), sodium cocoyl isethionate and disodium lauryl 3-ethoxysulphosuccinate by means of a 4-day repeated open exposure model in order to achieve a more realistic mimicry of daily practice.

Methods: The effects of the exposures were evaluated by: a) number of fulfilled exposures, b) visual score after exposures, and c) transepidermal water loss (TEWL) after exposures.

Results: In the majority of subjects, exposure to LAU had to be stopped because of burning sensations, erythema and/or scaling. The number of fulfilled exposures to LAU was lower than that of SLS. The other agents were tolerated very well. These less irritative agents had much lower visual scores and TEWL

values after the repeated exposures compared with LAU and SLS.

Conclusions: The explanation for the irritant nature of LAU in the present study might be the type of alkyl chain length distribution. Its 12-carbon chain content was $\leq 99\%$, and this agent can therefore be designated as pure sodium laurate. The same holds true for SLS. In daily practice, however, soap is a mixture of different – less irritant – chain lengths. Therefore, these findings cannot be extrapolated to commercially available soap bars.

Key words: irritancy – open exposure – transepidermal water loss – sodium laurate – sodium laurylsulphate

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THE OUTCOME of irritancy testing is dependent on the type of exposure model used. Several exposure models have been developed in order to test the irritant potency of detergents, namely, one-time occlusive (24-h patch test), repeated short-time occlusive, repeated open and immersion tests (1). The irritant potency of soap (sodium laurate) as opposed to other anionic detergents is not uniformly agreed upon. Based on old literature in which the high pH value of soap was blamed (2), many manufacturers make 'pH-neutral' products. In more recent literature, however, soap has been ranked, using a one-time occlusive model (3, 4) and a multiple repeated occlusive model (5), in the group of detergents with low irritant potency. Smeenk, using an arm immersion model, has also classified soap together with the low irritancy detergents, whereas in the same study soap was found to be highly irritative in a one-time occlusive test (6). The one-time occlusive test does not mimic the real-life development of chronic irritant contact dermatitis (1). The aim of the present study was to compare the irritancy of sodium laurate with that of other anionic detergents by means of an open exposure model in order to achieve a more realistic mimicry of daily

practice. These detergents were sodium cocoyl isethionate, sodium laurylsulphate and disodium lauryl 3-ethoxysulphosuccinate.

Material and Methods

A well-informed group of 22 healthy volunteers (13 women, 9 men) participated in the study. The age ranged from 19 to 47 years. None had a history of atopic dermatitis and none had manifest skin ailments. The study was performed from February to April, 1995.

The following agents were tested: sodium cocoyl isethionate (ISE) (Elfan AT84, Akzo Nobel, Amersfoort, The Netherlands), sodium laurate (LAU) (Fluka 61715, Buchs, Switzerland), sodium laurylsulphate (SLS) (Merck 13760, USA) and disodium lauryl 3-ethoxysulphosuccinate (SUL) (Elfanol 616, Akzo Nobel). All agents were tested in an aqueous solution of 70 mM. For ISE and SUL a correction was made for the % active mass. Table 1 shows the concentration, pH and alkyl chain length distribution of the detergent solutions tested. Analysis of alkyl chain length distribution was performed semiquantitatively by gas

TABLE 1. Characteristics of the detergent solutions used: concentration and pH of the solution, and alkyl chain length distribution

Agent	Concentration ^a	pH	Chain length distribution ^b					
			C8	C10	C12	C14	C16	C18
ISE ^c	2.9	5.5	5	6	52	19	9	9
LAU	1.5	9.1	0	0.3	99	0.4	0.2	0
SLS	2.0	8.2	0	0	100	0	0	0
SUL	12.0	6.1	0	0	58	42	0	0

^a Figures given are% (g/100 ml); ^b Chain length distribution in%; ^c ISE, sodium cocoyl isethionate; LAU, sodium laurate; SLS, sodium lauryl sulphate; SUL, disodium lauryl 3-ethoxysulphosuccinate.

chromatography of the methylated fatty acids. The fatty acids were isolated from the detergents by hydrolysis with 6 N HCl and extracted with ethyl acetate. The chain length distribution was calculated by normalisation. As a result, the distribution percentage is a relative figure instead of a mass percentage.

For exposure, use was made of a plastic strip with five holes (diameter, 20 mm) in which 0.8 ml of the solutions was applied. The strip was fixed to the volar side of the right forearm with nonadhesive bandages. The distance between the most distal exposure site and the wrist joint was kept at 60 mm. In each subject, this most distal site was exposed to distilled water (WAT). The other solutions were exposed to the remaining sites in a sequence that changed cyclically from one subject to the next. Two applications lasting 30 min each were made on 4 consecutive days. The minimal time interval between these 2 applications was 3 h. After their removal the skin was cleaned with running water and gently dried with a cotton towel.

On each day the sites were graded visually for erythema, scaling and fissures, according to Frosch and Kligman (3). Total scores for these signs were recorded. TEWL measurements were performed at all sites on day 1 and day 5, using a Tewameter TM210 (Courage & Khazaka, Cologne, Germany). The meas-

urements were performed in an air-conditioned room at a temperature of 19–21°C and a relative humidity of 40–50%, following the guidelines of the standardization group of the European Society of Contact Dermatitis on this topic (7). When a subject experienced severe burning or stinging during or after exposure to a particular solution, further exposure to that solution was stopped. The number of fulfilled exposures to each solution was recorded.

The effects of the four detergents were compared with respect to: a) number of fulfilled exposures; b) total visual score on day 5; c) TEWL on day 5. For comparison the Wilcoxon signed-rank test and its generalization (8) were used. A p -value ≤ 0.05 was considered as significant.

Results

In the majority of subjects exposure to LAU had to be stopped because of burning or stinging sensations during and shortly after the exposures. This was accompanied by some degree of erythema and/or scaling, in some cases followed by fissuring. Discontinuation of exposure to soap occurred even earlier than to the known 'standard' irritant, SLS. The two other anionic detergents tested in this study turned out to be far less provocative (Table 2). Figure 1 shows the box plots of TEWL on day 5, for all agents.

Statistical analysis of the medians of the tested variables yielded the following results. Number of exposures: LAU < SLS < ISE \leq SUL \leq WAT ('</>', significant difference; ' \leq/\geq ', no significant difference); total visual score on day 5: SLS \geq LAU > ISE \geq SUL \geq WAT; TEWL on day 5: SLS > LAU > ISE > SUL \geq WAT.

Discussion

The irritative effect of LAU in the present study seems surprising in view of the more recent litera-

TABLE 2. Mean values and standard deviations for number of fulfilled exposures, visual score on day 5 and transepidermal water loss (TEWL) value on day 5, in a 4-day repeated open exposure model using anionic detergents and water

Agent	Exposure number		Visual score		TEWL	
	Mean	SD ^a	Mean	SD	Mean	SD
ISE ^b	7.95	0.21	0.27	0.55	15.8	9.8
LAU	5.95	1.84	2.0	2.25	24.0	11.2
SLS	6.64	1.68	2.23	1.80	31.6	13.6
SUL	8.0	0	0.05	0.21	9.9	4.3
WAT	8.0	0	0	0	8.3	3.6

^a SD, standard deviation; ^b For explanation of the abbreviations, see Table 1; WAT, water.

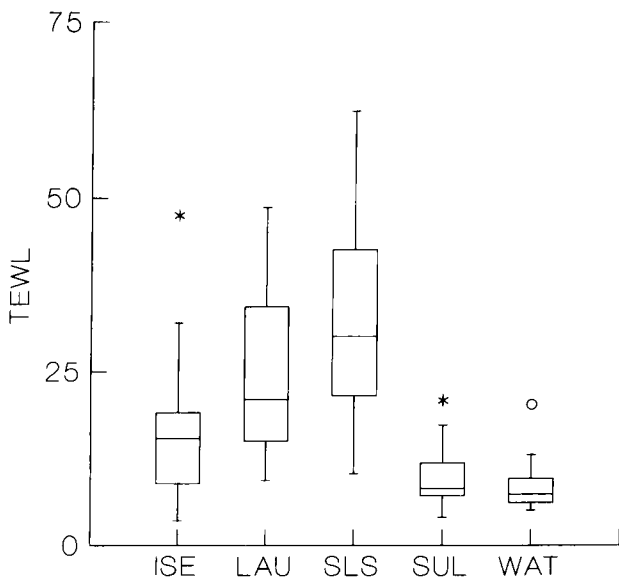


Fig 1. Box plots of transepidermal water loss (TEWL) values on day 5, after repeated open exposures to anionic detergents and water. (ISE, sodium cocoyl isethionate; LAU, sodium laurate; SLS, sodium lauryl sulphate; SUL, disodium lauryl 3-ethoxysulphosuccinate; WAT, water). The box plots according to Tukey (12) are defined as follows: the lower boundary of the box is the 25th percentile and the upper boundary is the 75th percentile. The horizontal line inside the box represents the median. Cases with values that are more than 3 box-lengths from the upper or lower edge of the box are designated with empty circles, and cases with values that are within 1.5 and 3 box-lengths from the edges are designated with an asterisk. The largest and smallest observed values that are less than 1.5 box lengths from the lower and upper box edges.

ture on this agent. Generally, the irritative effect of a detergent is dependent on many factors, including chemical characteristics of the detergent, concentration, quantity and pH of the solution, surface area of contact, and type of exposure method (1). An explanation for the irritant nature of LAU in the present study might be the type of alkyl chain length distribution. It has been found that soap with a chain length of 12 carbon atoms had the most pronounced clinical effects and the highest percutaneous penetration rate (9). The same phenomenon has been demonstrated for SLS. Brands with a very high content ($\geq 99\%$) of 12-carbon chains were far more irritative than those having additional fractions of longer alkyl chains (10). In the present study, soap had a 12-carbon chain content of $\geq 99\%$, and can therefore be considered as pure sodium laurate. In the previous literature, the tested soap was probably supplied by soap manufacturers who make this product by saponification of the naturally occurring tallow and cocoyl fatty acids (3–6). Saponification of these fatty acids result in a 'broad' alkyl chain length distribution, including sodium caprate (C10), laurate

(C12), myristate (C14), palmitate (C16) and stearate (C18), which may render these soaps less irritative because of the reduced amount of sodium laurate. It must be stressed that commercially available soap bars are based on these tallow and cocoyl fatty acids, and not on pure sodium laurate (11).

Another factor explaining the highly irritative influence of LAU in the present study may be the large quantity (0.8 ml) of the solution used, and large surface area of contact (diameter, 20 mm). In the previous studies smaller quantities and exposure areas were used, but the concentrations in these studies were higher (3,4). The type of exposure method may also play a significant role, as in our open exposure test a large proportion of the volume is in direct contact with the skin, whereas in the previous studies the skin was exposed to pieces of Whatmann paper or cotton, in which the detergent solution was absorbed. In the study by Smeenk, soap tested in the patch test was more irritating than in the open test, but the concentration in the open test was only 0.1% (6). The high pH value of LAU solution in the current study (pH, 9.1) cannot be a contributory factor, as the pH of the soap solutions in the other studies was stated to be at least as high (3–5).

LAU and SLS, tested in the present study, were of very high purity in terms of 12-carbon chain content, whereas ISE and SUL had broad alkyl chain lengths. Therefore, the irritancy of LAU may be compared only with that of SLS. LAU turned out to be more irritating than SLS, as determined by the number of fulfilled exposures. This lower number of exposures to LAU has probably influenced the fact that the mean TEWL value on day 5 at the SLS site was higher than at the LAU exposed site.

In conclusion, in the open exposure model of the current study it was found that sodium laurate has a highly irritative effect. However, caution must be paid to extrapolate findings of this study to commercially available soap bars in the practical daily situation, since these soap bars are not only based on sodium laurate but also on less irritative tallow and cocoyl fatty acid derived alkyl chains.

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Address:

R. A. Tupker
Department of Dermatology
University Hospital
PO Box 30.001
NL-9700 RB Groningen
The Netherlands

Tel.: ++31503616161
Fax: ++31503612624