

Effect of different moisturizers on SLS-irritated human skin

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Moisturizers are widely used to treat irritant contact dermatitis (ICD). Their use is, however, not well-documented and standardized models for testing skin care products are needed to acquire documentation of their efficacy. The present study was undertaken to evaluate the effect of 6 commonly-used moisturizers on the recovery of irritated human skin. No commercial interests were involved in the study. 36 healthy volunteers had patch tests with SLS 0.5% applied on their forearms/upper arms for 24 h. After irritation of the skin, all volunteers had a moisturizer applied on one forearm/upper arm, respectively, 3 × daily for the following 5 days. The other forearm/upper arm served as an untreated control. Each moisturizer was tested on 12 volunteers and each volunteer tested 2 moisturizers at the same time. Evaluation was done on days 1, 3 and 8 by transepidermal water loss, electrical capacitance, laser Doppler flowmetry, DermaSpectrometry and clinical scoring. All 6 moisturizers were found to accelerate regeneration of the skin barrier function when compared to irritated non-treated skin. The most lipid-rich moisturizers improved barrier restoration more rapidly than the less lipid-rich moisturizers. We suggest this experimental model for further moisturizer efficacy testing.

Key words: irritant contact dermatitis; skin barrier recovery; moisturizer efficacy testing; sodium lauryl sulfate; transepidermal water loss; laser Doppler flowmetry; electrical capacitance; DermaSpectrometer; bioengineering methods; skin-care products. © Munksgaard, 2001.

Accepted for publication 3 October 2000

Irritant contact dermatitis (ICD) is a major occupational disease in the industrialized world. Although moisturizers are often recommended in wet work occupations to prevent and treat ICD, documentation of their effect is still needed. Although most cases of ICD are localized to the hands, most studies have evaluated the effect of moisturizers on irritated human skin by using the forearm/upper arm or back. In a previous study by our group on moisturizer efficacy testing, we examined the correlation between a moisturizer tested on irritated human skin on the forearms compared with results obtained on the hands (1). The forearm model proved reliable and is used in the present set up to test 6 commonly used moisturizers. The aim of the present study was to test different moisturizers' ability to promote recovery of irritated human skin.

Materials and Methods

36 healthy volunteers (29 women, 7 men; mean age 40.4 years, range 18–58 years) participated in the study. Participants with a history of hand eczema

or atopic dermatitis were not included. The local ethics committee approved the study and all participants gave written informed consent.

Study procedure

The participants were randomized into 3 groups of 12 participants each (groups A, B, C). Each group tested 2 different moisturizers. The study period was 8 days. On day 1, all participants had 1 patch test applied on each volar forearm and on each volar upper arm for 24 h. Each patch contained 220 µl of an aqueous 0.5% sodium lauryl sulfate solution (SLS, >99% purity, Sigma Chemical Co., St. Louis, USA) on a filter disc (extra large Finn Chambers, diameter 18 mm, Epitest, Helsinki, Finland). A concentration of 0.5% of SLS was chosen according to the results from a previous study (1). The patch test chambers were placed symmetrically on each forearm/upper arm using a ruler to ensure the same distance from cubital fossa to the patch on each arm. The participants removed the patches themselves on day 2. After removal of the patches, the skin was rinsed with

lukewarm tap water and dried with a cotton towel. On day 3, evaluation of the irritant skin response was made by 4 non-invasive bioengineering measuring methods, and by clinical judgment. After evaluation, either the right or left arm was randomized to have 2 different moisturizers applied 3 × daily for the following 5 days (days 3–7). 1 moisturizer was tested on the forearm and another moisturizer was tested on the upper arm. The other arm served as untreated control. The randomization code was blinded to the investigator. The moisturizer treatment was initiated on day 3 shortly after measurements had been taken. All volunteers were instructed how to apply the moisturizer on the selected forearm/upper arm. Application was by using a plastic glove when applying the 1st moisturizer, to ensure no mixing of the 2 creams. Each moisturizer was applied in a thin layer on the entire forearm/upper arm: i.e., the moisturizer was applied on both normal and on SLS-irritated skin. Evaluations were made on day 8, after 5 days of treatment with the moisturizers. Selection of a 5-day treatment period was made according to a previous study (1). Measurements were taken more than 12 h after application of the moisturizers and all participants were told to shower in the morning on day 8 to ensure no residual cream was left on the skin.

Moisturizers

6 moisturizers with different lipid contents were tested. All the moisturizers tested are commonly recommended by Danish dermatologists for the treatment of eczematous diseases.

1. **Ceridal lipogel**, Stiefel Laboratories Ltd.; contains petrolatum, cyclomethicone, ceto microcristallina; lipid content: 65%.

2. **Petrolatum**, white, made by the local hospital pharmacy, lipid content: 100%.

3. **Locobase repair**, Yamanouchi Pharma; contains petrolatum, aqua, paraffin, paraffinum liquidum, glycerin, sorbitan oleate, carnauba, cholesterol, ceramide 3, oleic acid, palmitic acid, carbomer, tromethamine; lipid content: 63%.

4. **Locobase**, Yamanouchi Pharma; contains paraffinum molle album, aqua, paraffinum liquidum, sodium citrate, citric acid, methylparaben, cetomacrogol 1000 and cetearyl alcohol; lipid content: 70%. Our group (1, 2) has used this moisturizer in other studies as a model moisturizer.

5. **Decubal**, Dumex-Alpha; contains aqua, isopropyl myristate, glycerin, sorbitan stearate, lanolin, dimethicone, cetyl alcohol, polysorbate 60, sorbic acid; lipid content: 38%.

6. **Essex**, Schering Plough; contains chlorocresol, cetomacrogol, cetearyl alcohol, vaselinum al-

bum, paraffinum liquidum, monosodium phosphate, phosphoric acid, aqua purificata; lipid content: 21%.

Moisturizers 1 and 2 were tested in group A, moisturizers 3 & 4 in group B, and moisturizers 5 & 6 in group C. Each moisturizer was tested in 6 volunteers on the forearm and in 6 volunteers on the upper arm. The participants were not allowed to use any other moisturizer on the arms 7 days prior to entering the study nor during the study period. Each participant was given a supply of the 2 moisturizers and a checklist for daily recording of the treatment. The moisturizer tubes were weighed before and after the study period.

Evaluation methods

Evaluations were made on days 1 (baseline), 3 (after irritation) and 8 (after moisturizer treatment). The following methods were used for evaluation.

Transepidermal water loss (TEWL), as an indicator of the skin barrier integrity, was measured by an Evaporimeter (Servo Med, Stockholm, Sweden). Measurements were taken according to the guidelines of the Standardization Group of the European Society of Contact Dermatitis (ESCDR) (3).

Electrical capacitance, indicating the hydration level of the skin, was measured by a Corneometer CM 820 (Courage and Khazaka, Köln, Germany) (4).

Laser Doppler flowmetry is a technique for measurement of blood flow and thereby an indicator of the inflammatory level of the skin. A laser Doppler blood flow monitor MBF3 (Moor Instruments, England) was used according to the guidelines of the ESCD Standardization Group (5).

Erythema index is an indicator for redness of the skin and was measured with a DermaSpectrometer (Cortex Technology, Hadsund, Denmark), according to the guidelines of the same group (6).

Recordings of measurements: 2 recordings for evaporimetry and 3 recordings of erythema index, laser Doppler flowmetry and corneometry on each test site were performed, and the median value was used.

Clinical score graded for erythema and scaling on the patch test sites was recorded according to the following scale: 0=no reaction, 0.5=very weak spotty erythema/scaling, 1=slight erythema/scaling, 2=moderate erythema/scaling, 3=intense erythema/scaling.

All measurements and clinical scorings were made blinded and under controlled environmental conditions. Relative humidity in the room varied between 25–45% and the room temperature was

Table 1. Data on baseline values (day 1) and after irritation with SLS (day 3) given for moisturizer-treated arms and untreated arms (all data are prior to initiation of treatment with moisturizer); results are given in medians and 25/75 percentiles; * $p < 0.05$

	Day 1		Day 3		Day 1 vs. day 3
	treated arm	control arm	treated arm	control arm	
TEWL (g/m ² /h)	5.3 (4.5–6.2)	5.5 (4.5–6.4)	41.4 (34.5–49.2)	40.5 (35.3–50.6)	$p < 0.0005^*$
electrical capacitance	67 (64–71)	68 (64–73)	84 (78–91.5)	84.5 (77–98.8)	$p < 0.0005^*$
laser Doppler	24 (19–29)	22 (17.3–28.4)	105 (75.3–150.5)	109.5 (77–155)	$p < 0.0005^*$
erythema index	7 (5–9)	7.5 (6–9)	12 (11–15)	12 (10–15)	$p < 0.0005^*$

20–22°C. The participants rested for at least 30 min before measurements. The study was carried out from November to January.

Statistics

The Wilcoxon test (non-invasive evaluation methods (continuous data)) and the marginal homogeneity test (clinical scoring (ordinal data)) for paired samples were used to compare moisturizer-treated with untreated symmetrical test sites. A Mann-Whitney test was used to compare the moisturizers. A significance level of $p < 0.05$ was chosen. All statistical calculations were made using the software program SPSS for Windows 10.0.

Results

Data on baseline values (day 1) and after irritation with SLS (day 3) are given in Table 1. After exposure to SLS, a statistically significant increase ($p < 0.0005$) was found in TEWL, erythema index, corneometry and laser Doppler flowmetry on day 3 compared to baseline values.

The following results are from evaluation on day 8 after 5 days of moisturizer treatment, where comparisons between moisturizer-treated arms and untreated controls were made for each of the 6 moisturizers.

TEWL For all moisturizers TEWL was statistically significantly reduced on moisturizer-treated arms compared to untreated controls (Fig. 1). When ranking the differences in TEWL (Δ TEWL = untreated control arm subtracted moisturizer-treated arm) the highest mean rank (total rank sum for each moisturizers divided by the number of volunteers, $n = 12$) was found for moisturizer 2, followed by 1, 4, 3, 6 and 5. High mean rank indicates that a large difference was found between moisturizer-treated arms compared to untreated arms. A statistically significant difference was found by using a Mann Whitney test between moisturizer 1 and 5 ($p = 0.045$) and between 2 and 5 ($p = 0.02$). The correlation between the lipid content of the moisturizer and the mean rank of Δ TEWL is shown in Fig. 2.

Electrical capacitance was statistically signifi-

cantly higher on moisturizer-treated arms compared to untreated arms for all moisturizers except for numbers 4 and 6 (Table 2).

Laser Doppler flowmetry was statistically significantly reduced on moisturizer-treated arms compared to untreated arms for moisturizers 1–5 but not for number 6 (Table 3).

Erythema index was statistically significantly reduced on moisturizer-treated arms compared to

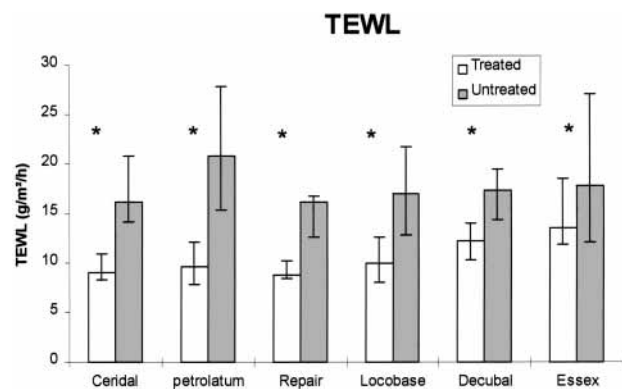


Fig. 1. Transepidermal water loss (TEWL) on day 8 for moisturizer-treated arms and untreated arms given for each moisturizer. Results are given in medians and 25/75 percentiles. * $p < 0.05$.

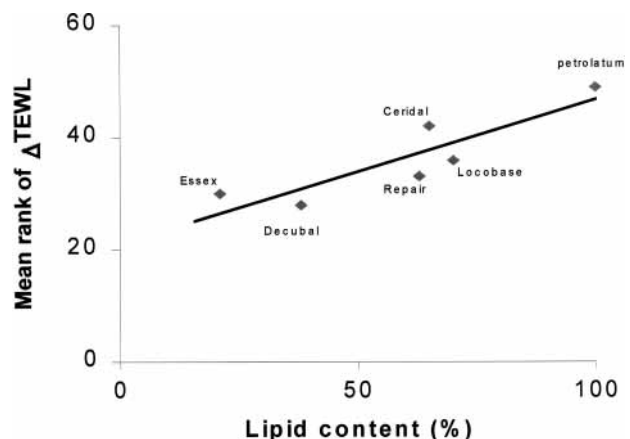


Fig. 2. Correlation between percentage of lipid content of the moisturizer and the mean rank of Δ TEWL.

Table 2. Electrical capacitance (arbitrary units) for moisturizer-treated arms and untreated arms on day 8. Results are given in medians and 25/75 percentiles; * $p < 0.05$

	Treated arm	Control arm	Level of significance
Ceridal Lipogel	47 (41.5–53.8)	33 (31.5–36.5)	0.004*
petrolatum	43 (38–63)	33 (26–41)	0.002*
Locobase Repair	66 (55–71)	39 (32–45)	0.005*
Locobase®	38 (33–44)	36 (31–40)	0.064
Decubal	74 (62–78)	38 (33–40)	0.003*
Essex	41 (31–47)	41 (33–45)	0.970

Table 3. Laser Doppler flowmetry (arbitrary units) for moisturizer-treated arms and untreated arms on day 8. Results are given in medians and 25/75 percentiles; * $p < 0.05$

	Treated arm	Control arm	Level of significance
Ceridal Lipogel	26 (23–33)	55 (34–73)	0.003*
petrolatum	31 (25–37)	74 (32–105)	0.009*
Locobase Repair	26 (21–44)	49 (31–75)	0.021*
Locobase®	32 (23–37)	50 (43–62)	0.003*
Decubal	29 (25–38)	42 (33–69)	0.021*
Essex	40 (27–58)	61 (24–80)	0.213

Table 4. Erythema indices (arbitrary units) for moisturizer-treated arms and untreated arms on day 8. Results are given in medians and 25/75 percentiles; * $p < 0.05$

	Treated arm	Control arm	Level of significance
Ceridal Lipogel	9 (8.5–10.3)	10 (8–12.3)	0.088
petrolatum	9 (8–11.3)	10.5 (8–12.3)	0.017*
Locobase Repair	10 (8–10.3)	11 (8.8–13.5)	0.005*
Locobase®	10 (9.5–11)	12 (9.5–13)	0.325
Decubal	10 (9–11)	11 (9–12.3)	0.196
Essex	10.5 (10–13.3)	12 (10.5–13.5)	0.237

Table 5. Clinical scoring (erythema) for moisturizer-treated arms and untreated arms on day 8; results are given in medians and 25/75 percentiles; * $p < 0.05$

	Treated arm	Control arm	Level of significance
Ceridal Lipogel	0.5 (0.5–0.63)	1 (1–2)	0.004*
petrolatum	0.8 (0.5–1)	1.5 (0.9–2.1)	0.016*
Locobase Repair	0.5 (0.4–1)	1.5 (1–2.1)	0.004*
Locobase®	1 (1–1.3)	1 (0.9–1.5)	0.854
Decubal	0.5 (0.4–1)	1 (0.5–1.1)	0.072
Essex	1 (0.9–1.5)	1 (0.9–1.5)	0.414

Table 6. Clinical scoring (scaling) for moisturizer-treated arms and untreated arms on day 8. Results are given in medians and 25/75 percentiles; * $p < 0.05$

	Treated arm	Control arm	Level of significance
Ceridal Lipogel	0.4 (0–0.5)	1.5 (1–1.6)	0.005*
petrolatum	0.5 (0–1)	1 (0.8–1.5)	0.019*
Locobase Repair	0 (0–0.5)	1 (0.5–2)	0.007*
Locobase®	0.5 (0.2–1)	0.8 (0.5–1.6)	0.093
Decubal	0.5 (0.3–1)	1 (0.9–2)	0.012*
Essex	1 (0.5–1.1)	1.4 (1–2)	0.010*

untreated arms for moisturizers 2 and 3 but not for 1, 4, 5 and 6 (Table 4).

Visual scoring for assessment of *redness* was statistically significantly reduced on moisturizer-

treated arms compared to untreated arms for moisturizers 1–3 but not for 4–6 (Table 5). *Scaling* was statistically significantly reduced on moisturizer-treated arms compared to untreated arms for

moisturizers number 1–3 and 5–6 but not for number 4 (Table 6).

Total amount in grams of moisturizer used (mean, range), moisturizer 1: 5.8 (2.0–9.5), 2: 6.5 (3.5–10.5), 3: 4.5 (2–7.5), 4: 7.5 (2.5–15.5), 5: 5.3 (3.0–13) and 6: 4.7 (1.5–11), was not related to outcome of data (data not shown).

Discussion

In the present study, all moisturizers accelerated barrier regeneration after 5 days of treatment. The study shows that barrier recovery was related to the total amount of lipids in the moisturizer (Fig. 2). In the present study non-physiological lipids, such as petrolatum, ranked the highest in ability to promote recovery of irritated skin. Animal studies (hairless mice) indicate that barrier recovery depends on the composition of lipids, requiring physiological lipid mixtures (7, 8). This was not confirmed in the present study design in humans. Moisturizer 3 (Locobase Repair), which contains physiological lipids (cholesterol, ceramide 3, oleic acid, palmitic acid), was of no advantage compared to moisturizer 4 (Locobase) with respect to promotion of barrier recovery. Moisturizers based on few ingredients and with a high lipid content (moisturizer 1 and 2) improved barrier regeneration best and were significantly better than moisturizer 5. While this is probably due to high lipid content, it should be conceded that moisturizers 3–6 have several ingredients and that some of these may possibly have slight irritant potential. An experimental study showed that emulsifiers incorporated in moisturizers may influence skin barrier function and cause an increase in TEWL values (9).

In acetone-treated skin in hairless mice, topically applied non-physiologic lipids (petrolatum) were found to penetrate all levels of the stratum corneum (10) whereas physiologic lipids (cholesterol, ceramides, linoleate and palmitate) were found to enter the nucleated layers of epidermis and even become incorporated into lamellar bodies (11). It is doubtful whether results from such studies can be applied to humans. It is a key question if topically added lipids are incorporated in stratum corneum and thereby support or replace the endogenous lipids in humans. The accelerated recovery of irritated skin seen when treated with a moisturizer could also be due to a protective and semi-occlusive effect of the moisturizer, which restricts water evaporation from the skin thereby allowing the skin to recover undisturbed. Data on occlusion of human skin are conflicting. Occlusion of normal and irritated skin with protective gloves was re-

ported to impair skin barrier function (12–14). However, occlusive treatments of irritated human skin were, in another study, reported not to delay barrier recovery (15) or even to promote healing of the skin (after laser resurfacing) (16).

The hydration level of the skin was significantly increased after use of all but 2 moisturizers. However, even these 2 moisturizers significantly improved barrier recovery as compared to the untreated symmetrical controls. Different bioengineering instruments measure different parameters (hydration, barrier function, inflammation, erythema, etc.) and the results obtained with different instruments are not always expected to correlate. Overall, moisturizer 2 was superior in most of the parameters as judged by bioengineering methods as well as by clinical judgement, followed closely by moisturizer 1 (Fig. 2 and Tables 2–6). When comparing evaporimetry, laser Doppler flowmetry, ultrasound A-scan and measurement of skin color, evaporimetry was found to be the best suited method overall for evaluation of SLS-induced skin damage (17). For moisturizer testing in SLS-damaged skin, evaporimetry is probably the most important evaluation method but it should be supported as a minimum by clinical scoring of redness and scaling.

In the present study, the moisturizers were also used on normal skin and not only on SLS-irritated skin, which the differences in the amount of cream used may reflect. Further, the viscosity of the creams varied, which may also have had an impact on how much cream was used.

Few studies have focused solely on the effect of a moisturizer on the recovery phase of diseased skin. A moisturizer containing urea and canola oil was able to accelerate the recovery of surfactant-damaged skin when used 2 $\times$ daily for 14 days on the forearms (18). Another moisturizer was found to accelerate recovery of SLS-irritated skin on the hands after 5 days of treatment (2).

In conclusion, all the moisturizers tested in the present study were found to improve barrier regeneration when compared to untreated symmetrical test sites. We do not know if this is true for all moisturizers. Theoretically, a moisturizer could also delay barrier recovery, which has been shown in hairless mice (7). According to results from the present study, the ideal moisturizer for treating irritant contact dermatitis should have a high lipid content and may contain physiological as well as non-physiological lipids.

According to the new cosmetic legislation in Europe claims for moisturizers must be supported (19). We recommend that the present test design should be used more widely for documentation of the effect of moisturizers. The model is realistic,

easy to handle and suitable for testing moisturizers in humans.

References

- Held E, Agner T. Comparison between 2 test models in evaluating the effect of a moisturizer on irritated human skin. *Contact Dermatitis* 1999; 40: 261–268.
- Ramsing D W, Agner T. Preventive and therapeutic effects of a moisturizer. An experimental study of human skin. *Acta Dermato-venereologica* 1997; 77: 335–337.
- Pinnagoda J, Tupker RA, Agner T, Serup J. Guidelines for transepidermal water loss (TEWL) measurement. *Contact Dermatitis* 1990; 22: 164–178.
- Barel AO, Clarys P. *Measurement of epidermal capacitance. Non-invasive methods and the skin*. Boca Raton, Florida: CRC, 1995.
- Bircher A, De Boer E M, Agner T, Wahlberg J E, Serup J. Guidelines for measurement of cutaneous blood flow by laser Doppler flowmetry. A report from the Standardization Group of the European Society of Contact Dermatitis. *Contact Dermatitis* 1994; 30: 65–72.
- Fullerton A, Fischer T, Lahti A, Wilhelm K P, Takiwaki H, Serup J. Guidelines for measurement of skin colour and erythema. A report from the Standardization Group of the European Society of Contact Dermatitis. *Contact Dermatitis* 1996; 35: 1–10.
- Man M Q, Feingold K R, Elias P M. Exogenous lipids influence permeability barrier recovery in acetone-treated murine skin. *Arch Dermatol* 1993; 129: 728–738.
- Man M Q, Feingold K R, Thornfeldt C R, Elias P M. Optimization of physiological lipid mixtures for barrier repair. *J Invest Dermatol* 1996; 106: 1096–1101.
- Barany E, Lindberg M, Loden M. Unexpected skin barrier influence from nonionic emulsifiers. *Int J Pharm* 2000; 195: 189–195.
- Ghadially R, Halkier-Sorensen L, Elias P M. Effects of petrolatum on stratum corneum structure and function. *J Am Acad Dermatol* 1992; 26: 387–396.
- Mao-Qiang M, Brown B E, Wu-Pong S, Feingold KR, Elias P M. Exogenous nonphysiologic versus physiologic lipids. Divergent mechanisms for correction of permeability barrier dysfunction. *Arch Dermatol* 1995; 131: 809–816.
- Graves C J, Edwards C, Marks R. The effects of protective occlusive gloves on stratum corneum barrier properties. *Contact Dermatitis* 1995; 3: 183–187.
- Ramsing D W, Agner T. Effect of glove occlusion on human skin (I). Short-term experimental exposure. *Contact Dermatitis* 1996; 34: 1–5.
- Ramsing D W, Agner T. Effect of glove occlusion on human skin (II). Long-term experimental exposure. *Contact Dermatitis* 1996; 34: 258–262.
- Welzel J, Wilhelm K P, Wolff H H. Skin permeability barrier and occlusion: no delay of repair in irritated human skin. *Contact Dermatitis* 1996; 35: 163–168.
- Collawn S S. Occlusion following laser resurfacing promotes reepithelialization and wound healing. *Plast Reconstr Surg* 2000; 105: 2180–2190.
- Agner T. Noninvasive measuring methods for the investigation of irritant patch test reactions. Thesis, University of Copenhagen 1992. *Acta Dermato-venereologica* 1992 (suppl 173).
- Lodén M. Barrier recovery and influence of irritant stimuli in skin treated with a moisturizing cream. *Contact Dermatitis* 1997; 36: 256–260.
- European directive 93/95/EEC amending for the sixth time Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products. *EC Official J* 1993; L 151: 32–36.

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