

Review Article

Moisturizer effect on Irritant Dermatitis: an overview

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Moisturizers are empirically used as prevention and treatment of surfactant and irritant dermatitis. Some products state they not only improve barrier function by providing moisturization but also create an environment optimal for healing. Yet, moisturizer clinical efficacy remains a topic of controversy. We reviewed publication from 1992 to 2006 that quantitatively examines moisturizer effectiveness, as an update of our prior overview, Zhai and Maibach in 1998 (2). We intuitively (in a testimonial sense) believe that moisturizers are sometimes effective for preventing and treating irritant dermatitis. However, moisturizer may not be broadly effective (8, 12) and may be relatively specific against certain acids, bases, hydrophilics, and lipophilics. We need to develop principles of what is formulated in moisturizers to improve efficacy; for this purpose, there is a need for experimental moisturizer models for comparative studies.

Key words: irritant dermatitis; irritation; man; moisturizer; prevention; treatment. © Blackwell Munksgaard, 2006.

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Healthy stratum corneum has 20–35% water content (1); insufficient water creates cracks, fissures and impaired water barrier function, leading to dermatitis and increased sensitivity to water, detergents and other irritants. Irritant contact dermatitis (ICD) is caused by acute/and/or cumulative exposure to irritants in home and work environments, leading to stratum corneum damage, skin barrier impairment and deeper alterations (2).

Detergents, one cause of irritant dermatitis, concentrate at oil/water interfaces, and provide cleansing as well as emulsifying properties. Anionic surfactants, used most frequently, represent between 43% and 67% of the active ingredients in personal care, cosmetics, household and industrial formulations (3). The mechanisms of surfactant-induced irritant dermatitis are inadequately understood (4). The effects of surfactants depend on concentration and surfactant–lipid molar ratios. At low concentrations, surfactants can disrupt membranes resulting in increased membrane permeability (5), whereas, at higher concentrations (above the critical micelle concentration) surfactants cause cell lysis (6). Thus, as already stated, two opposing events, namely, interaction with the membrane and the permeant with the micelle, may be responsible for the overall effect of the surfactant on membrane permeability (7).

Moisturizers are empirically used as prevention and treatment of surfactant and irritant dermatitis.

Some products state they do not only improve barrier function by providing skin moisturization, but also, create an environment optimal to healing, which maintains the skin barrier to prevent damage from recurring. Occlusives, humectants and hydrocolloids can be used to improve skin water barrier function by increasing moisturize. Occlusive moisturizers (e.g. petrolatum, lanolin, mineral oil, vegetable oil, cetyl alcohol, cholesterol, ceramides and silicones), are oily substances that retard transepidermal water loss (TEWL). Petrolatum, an effective occlusive agent, may reduce TEWL by 99% (1). Humectants (e.g. glycerin, propylene glycol, polysorbate 30, polyglyceryl-3, sorbitol, gelation, urea, sodium lactate, vitamins and proteins), are hygroscopic substances that draw water from the viable epidermis/dermis to the stratum corneum. Humectants can increase TEWL if they are not used with occlusives; hence, humectants are used in combination with occlusive moisturizing substance to create an artificial film until the defective barrier is repaired. Hydrocolloids (e.g. colloidal oatmeal, proteins in moisturizers and bath products), are large molecular weight substances that form an artificial membrane skin that physically inhibits TEWL from damaged skin. However, hydrocolloids are not an effective method of moisturizing the skin and usually are

used in combination with occlusives and humectants (1).

Moisturizer efficacy remains a topic of controversy.

We reviewed publication from 1992 to 2006 that quantitatively examines moisturizer effectiveness, as an update of our prior overview.

Materials and Methods

As a follow-up to Zhai and Maibach (2) in 1998, we searched Pub Med from 1992 to 2006, Science Citation Index from 1992 to 2006 and Embase® from 1992 to 2006. Search words were moisturizer, irritant dermatitis, prevention and treatment. We hand searched dermatitis journals in English, German and French and standard textbook in irritation, allergy, contact dermatitis, occupational dermatitis and moisturization in English, German, French and Spanish.

Result

Moisturizers efficacy data in preventing and treating ICD are in Table 1.

Prevention-1: normal skin

2 of 10 studies on normal skin, performed by Held and Agner (8) and Held et al. (9), suggest that using one moisturizer (Locobase®: Yamanouchi) on normal skin causes increasing susceptibility to experimental irritants. Ramsing and Agner (10) had the opposite experience with one of the products (Locobase®). Direct comparison is difficult as they utilize different anatomical sites and exposure duration.

Held and Agner (8) compared two moisturizers used on normal skin. 19 healthy volunteers applied them thrice daily for 5 days prior to 24 h patch testing with sodium lauryl sulfate (SLS). Evaluation, including TEWL, electrical capacitance, laser Doppler colorimetry and clinical scoring, concluded that skin response to SLS was increased on moisturizer-treated arms compared to controls for one moisturizer (Locobase®), while this was not statistically significant for the other (Decubal®: Dumex-Alpha). This difference is most likely because of lipid content. They suggest that increasing stratum corneum hydration enhances permeability to hydrophilic substances. A high level of hydration of the stratum corneum may facilitate transportation of a hydrophilic allergen, and this is likely to be positively related to lipid moisturizer content (11). Held et al. (9) observed 27 days treatment with

Locobase thrice daily before inducing irritation from a 24 h SLS patch testing. Evaluation by TEWL and electrical capacitance suggested that daily moisturizer use on normal skin may not necessarily offer protection against detergent irritation.

Broader selections on irritants of differing physical–chemical properties are needed before generalizing these conclusions.

Schliemann-Willers et al. (12), Zhai et al. (13), Wigger-Albert et al. (14) and Frosch and Kurte (15) studied several irritants. Schliemann-Willers et al. (12) examined the efficacy of perfluoropolyethers on 20 healthy volunteers. They tested 4 standard irritants (SLS of highest purity, sodium hydroxide, lactic acid and toluene) after 30 min treatment in an experimental study. Assessment was clinical and by the use of TEWL and chromametry. They observed difference in the protective efficacy against several irritants and dose-related efficacy of perfluoropolyether phosphate. Zhai et al. (13) observed the effectiveness of skin protective formulations in a previously described *in vivo* human model. Moisturizers were spread 30 min twice before 24 h irritant patch testing of some irritants (SLS, ammonium hydroxide + urea and rhus) and assessed by clinical scoring. Paraffin wax in cetyl alcohol (PW in CA) was the most effective formulation, but did not inhibit ammonium hydroxide (NH₄OH) and urea irritant dermatitis. Wigger-Albert et al. (14) evaluated the efficacy of protective creams on 20 healthy volunteers with assessments by visual scoring, TEWL and chromametry. In a 2 week irritation assay petrolatum had significant protective effect against irritation by SLS, sodium hydroxide (NaOH) and toluene. Less efficacy was observed against lactic acid. Frosch and Kurte (15) examined barrier cream efficacy. On 10 healthy volunteers, irritants were applied 30 min, 5 times during the first week and 4 times during the second week. Skin barrier creams were applied 30 min before contact with the irritants. Evaluation by erythema score, TEWL, blood flow volume (BFV) and capacitance showed that Taktosan Salbe® (Stockhausen, Krefeld, Germany) significantly suppressed irritation by SLS, NaOH and lactic acid (LA), which was apparent in most parameters. RAWI Sperrschutzcreme® (RAWI Ges.m.b.H., Linz, Austria) significantly inhibited SLS irritation, but only a positive trend against NaOH and LA. Both creams failed against toluene.

These results suggest these protective formulations provide some efficacy, but their applications remains chemical property specific.

Hannikselä and Kinnunen (16) modelled an almost real work situation: regular use of emollients and detergents, in a washing test. The participants washed with a liquid detergent and

Table 1. Moisturizers efficacy data in preventing and treating irritant contact dermatitis

Irritant		%	Vehicle	Body site	Moisturizer	Duration	Result	Reference
A: Prevention								
1. Normal skin	SLS	0.25	Water	Upper arm Forearm	Locobase [®] (A) (Yamanouchi) Decubal [®] (B) (Dumex-Alpha)	Thrice daily for 5 days before 24-h patch test	Ineffective	Held & Agner 2001 (8)
	SLS	5	Water	Mid-back	Fomblin [®] (HC/P2)	30 min treatment, before occlusive irritation (30 min exposure) for 9 days (from D1 to D5 and from D8 to D11)	Effective	Schliemann-Willers et al. 2001 (12)
	NaOH	0.5	Water		^a B: gel base 1		Dose-related efficacy (data table not provided)	
	Lactic acid (LA)	20	Water		^b C: gel base 2			
	Toluene	100			^c D: gel base 1			
					^d E: gel base 2			
					^e F: gel base 2			
	SLS	0.5	Water	Forearm	Dimethicone (2%)	30 min pretreated before 24-h patch test	Effective	Zhai et al. 2000 (34)
	SLS	10	Water	Forearm	^f PGV	Spread 30 min twice before 24-h patch test	Effective	Zhai et al. 1999 (13)
	NH ₄ OH + UA	22.9 + 2.0	Water		^g PW + CA		PW + CA: most effective (not inhibit to NH ₄ OH + UA) PW + CA > B > C	
	Rhus	3.0	Acetone		^h P + PGV		> A > PGV > PA + PGV > P + PGV > untreated	
					ⁱ PA + PGV			
					^j Kerodex51 [®] (A) (Medtech, Inc, Jackson, wY)			
					(Dry Work)			
					^k Kerodex71 [®] (B) (Medtech, Inc, Jackson, wY)			
					(Wet Work)			
					^l PGV + Lad-Fos(C) (#M Company, St.Paul, MN)			
	SLS	0.3	Water	Forearm	Locobase [®] (Yamanouchi)	Thrice daily for 27 days before 24-h patch test	Ineffective	Held et al. 1999 (9)
	SLS	5	Water	Forearm	Petrolatum	30 min treatment before irritation (applied for 30 min under occlusion) for 9 days (from D1 to D5 and from D8 to D11)	Effective	Wigger-Albert et al. 1999 (14)
	NaOH	0.5					Significant protective effect against irritation by SLS, NaOH and toluene	
	LA	1					Less efficacy observed against lactic acid	
	Toluene	30					Effective (data table is not provided)	
	SLS	20					Effective	Ramsing & Agner 1997 (10)
	SLS	100					Both effective against irritation by SLS, NaOH, and LA	Frosch & Kurtz 1994 (15)
							Both failed toluene	

Table 1. Continued

Irritant		%	Vehicle	Body site	Moisturizer	Duration	Result	Reference
2. Damaged skin	Liquid detergent (Fairy [®] ; Procter & Gamble Ltd)			Upper arm	(Water content %) 1: o/w cream (70) 2: o/w cream (70) 3: o/w cream (65) 4: double emulsion (50) 5: skin oil (—) 6: double emulsion (67) 7: double emulsion (48) 8: double emulsion (61)	First week: after each wash Second week: twice daily without wash	Effective	Hannikselä & Kinnunen 1992 (16)
	Water & detergent			Hands	^a Barrier cream control (same preparation without aluminium chlorohydrate)	Frequently during their work day and especially before contact with skin irritants for 1 month	Effective (no difference from control)	Berndt et al. 2000 (17)
	Water & detergent			Hands Arms	Locobase [®] (Yamanouchi)	2 weeks treated. Next 2 weeks untreated	Effective	Halkier-Sorensen & Thesterup-Pedersen 1993 (18)
3. Normal and damaged skin	Hand rubs; based on Propan-2-ol	45		Cubital Fossa	P ₀ 81% emollient (contain in one rub)	Twice daily over 2 weeks	Effective	Kampf et al. 2005 (19)
	Propan-1-ol	30						
	Mecetronium etilsulfate	0.2						
B: Treatment								
1. Normal skin	Liquid detergent (Fairy [®] ; Procter & Gamble Ltd)			Upper arm	(Water content %) 1: o/w cream (70) 2: o/w cream (70) 3: o/w cream (65) 4: double emulsion (50) 5: skin oil (—) 6: double emulsion (67) 7: double emulsion (48) 8: double emulsion (61)	First week: not treated Second week: treated Twice daily without wash	Effective	Hannikselä & Kinnunen 1992 (16)
2. Damaged skin	SLS	0.5	Water	Upper arm Forearm	1: Ceidal lipogel [®] (Stiefel Laboratories Ltd) 2: Petrolatum 3: Locobase repair [®] (Yamanouchi) 4: Locobase [®] (Yamanouchi) 5: Decubal [®] (Dumex-Alpha) 6: Essex [®] (Schering Plough)	After 24-h patch test Three times daily for 5 days	Effective	Held et al. 2001 (20)

Water & detergent		Hand	^a Hand Sense [®] (North American Safety Products Inc, Orange, Calif) [†] Lubriderm [®] (Schering Plough)	At least 4 times daily for 4 weeks	Effective	McCormick et al. 2000 (21)
SLS	0.125 0.25 0.5	Water	Hand Forearm	After irritation (hand: 10 min of immersion twice daily for 2 days. Forearm: 24-h closed patch test) applied thrice daily for 9 days	Effective	Held & Agner 1999 (22)
SLS	0.375	Water	Hand	Locobase [®] (Yamanouchi)	Effective	Ramsing & Agner 1997 (10)
SLS	14	Water	Forearm	Locobase [®] (Yamanouchi)	Effective	Loden 1997 (11)
Water & detergent		Fingers Hands Arms	Locobase [®] (Yamanouchi)	After 7-h patch test twice daily for 14 days 2 weeks untreated; next 2 weeks treated.	Effective	Halkier-Sorensen & Thestrup-Pedersen 1993 (18)

^aB: gel base 1 (Xanthan Gum) (base preparation/placebo).

^bC: gel base 2 (Xanthan Gum) containing 2% HC/P2 1000 (molecular weight 1000).

^cD: gel base 1 (Xanthan Gum) containing 5% HC/P2 1000 (molecular weight 1000).

^dE: gel base 2 (Carbomer) containing 5% HC/P2 1000 (molecular weight 1000).

^eF: gel base 2 (Xanthan Gum) containing 5% HC/P2 2000 (molecular weight 2000).

^fPGV: propylene glycol vehicle.

^gPW + CA: paraffin wax in cetyl alcohol.

^hP + PGV: perfluorophosphate in PGV.

ⁱPA + PGV: perfluorosalicylic acid in PGV.

^jKerodex51(A): benetonite, calcium carbonate, cellulose gum, cetearyl alcohol, chloroxyleneol, glycerin, iron oxide, isopropyl alcohol, kaolin, methylparaben, petrolatum, propylparaben, sodium hydroxide, sodium lauryl sulfate, zinc oxide, spermaceti, stearic acid, and water.

^kKerodex71(B): calcium, carbonate, cetearyl alcohol, cetrimonium bromide, cetyl alcohol, iron oxide, isopropyl alcohol, kaolin, methylparaben, sodium hexametaphosphate, sodium lauryl sulfate, zinc oxide, and water.

^lPGV + Lad-Fos(C): Lad-Fox is the half ester of *N*-methyl, *N*-2 hydroxyethyl perfluorooctane sulfamide, and linoleic acid dimer and its salts.

^mTaktosan Salbe: water-in-oil emulsion with Eucorinol.

ⁿRAWI: oil-in-water emulsion with triethanolamine monoester of stearic acid and acid amide of C₁₇H₃₅ with a stearyl radical (CONHCH₂CH₂OCH₂CH₂OH) as active ingredients.

^oBarrier cream: ingredients: aqua, paraffinum liquidum, behenyl alcohol, glycerin, aluminium chlorohydrate, octyl palmitate, buxus chinensis, ceteth-10, steareth-20, dimethicone).

^p0.81% emollient (contain in one rub): yristyl alcohol, glycerol, dexpanthenol, levomenol and lanolin alcohol.

^qHand sense: novel barrier skin cream (glycerin, isopropyl myristate, triethanolamine, 1,3 diol, acrylates C-10/C-30 and alkyl acrylate cross polymer, with the preservative methylparaben in water, and is marketed for use in States as a cosmetic skin care product).

^rLubriderm:mineral oil, petrolatum, lanolin sorbitol, stearic acid, cetyl alcohol, glycerolstearate, polyethylene glycol-100 stearate, triethanolamine, dimethicone, propylene glycol, disodium ethylenediamine tetraacetic acid and parabens in water.

applied 8 moisturizers after each wash in the 1st week, and twice daily without wash in the 2nd week. Evaluation skin blood flow and TEWL concluded regular use of emollients prevented irritant dermatitis from this detergent.

Prevention-2: damaged skin and prevention-3: normal and damaged skin

Berndt et al. (17) compared barrier cream with its vehicle. 50 hospital nurses with mild signs of compromised skin on their hands were followed over 1 month in a field study. They applied cream frequently during their work day and especially before contact with skin irritants. Evaluation by TEWL, visual score, skin colour and stratum corneum hydration demonstrated no significant differences. Halkier-Sorensen and Thestrup-Pedersen (18) utilized Locobase for 2 weeks treated followed by 2 weeks untreated on 111 cleaners and kitchen workers in a field study measuring skin surface temperature, electrical capacitance and TEWL. Locobase was effective among cleaners and kitchen assistants during everyday exposure to water and detergents.

Kampf et al. (19) studied emollient (0.81% w/w) twice daily over 2 weeks on 35 subjects, half of them having an atopic predisposition. Assessed by visual inspection for erythema and dryness according to a standard scale showed that the addition of emollients to a propanol-based hand rub can significantly decrease irritant contact dermatitis under frequent-use conditions.

They are not pure prevention studies as they utilized moisturizers for prevention and treatment.

Treatment

These combined studies showed that their moisturizers decreased irritation and enhanced repair.

Held et al. (20) examined moisturizers on SLS-irritated human skin. 36 healthy volunteers had a SLS 24 h patch test. After irritation, volunteers applied a moisturizer thrice daily for 5 days. Evaluation with TEWL, electrical capacitance, laser Doppler flowmetry, DermaSpectrometry and clinical scoring showed that the most lipid-rich moisturizers improved barrier restoration more rapidly than less lipid-rich moisturizers.

McCormick et al. (21) examined 54 health care workers with severe hand irritation (74% with one or more full-thickness cracks or other integumentary breaks) and examined chronic ICD in a field study. The volunteers used cream at least 4 times daily for 4 weeks and were scored for

scaling, cracking, weeping, bleeding, and pain. They concluded that an oil-containing lotion or a barrier cream can protect against drying and chemical irritation.

Held and Agner (22) compared 2 test models (hand and volar forearm) in evaluating the effect of a moisturizer, Locobase. 12 healthy volunteers had their hands immersed in SLS 10 min twice daily for 2 days, and at the same time the volunteers were patch tested with SLS on their forearms for 24 h. After irritation, the volunteers had a moisturizer applied on one arm/hand thrice daily for the following 9 days. Evaluation was by TEWL, electrical capacitance, laser Doppler flowmetry, and DermaSpectrometry. Both models were useful; the moisturizer accelerated regeneration of the skin barrier function in both hands and volar forearms. The proposed forearm model seemed more sensitive than the more realistic but cumbersome hand immersion model.

An immersion test more faithfully mimics dish-washing liquids in a realistic exposure (23). Ramsing and Agner (10) examined the effect of a moisturizer with on immersion test; 12 volunteers were treated with Locobase thrice daily for 5 days after the last SLS immersion (D3). Skin barrier function was evaluated by TEWL, blood flow by laser Doppler flowmetry and skin hydration by electrical capacitance. They concluded the moisturizer could accelerate regeneration of the barrier function of irritant skin. Berndt et al. (17), McCormick et al. (21), and Halkier-Sorensen and Thestrup-Pedersen (18) examined hospital nurses, health care workers, and cleaner and kitchen workers under actual work situation. Their treatment results demonstrated efficacy, but Berndt et al. (17) compared barrier cream with its vehicle and McCormick et al. (21) compared an oil-containing lotion with a novel barrier cream but did not include a control group. Berndt et al. (17) found no difference from vehicle.

Discussion

We identified 14 efficacy publications from 1992 to 2006.

Data limitations include lack of formula quantitative composition, making direct comparisons problematic. Note that proprietary registered, trade names often remain constant (brand identity), but the chemical formulation may change; hence comparison, by trade name, in the quoted publications does not document sameness. Thus we need the principles of what is formulated in moisturizers to ascertain efficacy. and for this purpose, there is a need for experimental model moisturizers for comparative studies. The benchmark

sunscreen used in Skin Protection Factor assays represents such an approach. The same can be said for validating relevancy of patch test occlusive models as these systems differ from typical open applications industrial use.

Examination of some points might aid interpretation of future investigations.

First, we note anatomical site specificity. The hand and forearm are commonly studied. The volar forearm was a more discriminating site than the dorsal hand (24). Marked regional variations of skin reactivity attributed to differences in keratinization and in the density of epidermal shunts such as hair follicles and sweat duct exist (25). Additional comparisons of anatomical site reactivity might aid generalization from the data at one site.

Secondly, when exposure inducing acute irritant dermatitis is repeated, the dermatitis tends to persist and becomes chronic (more than 6 weeks has been suggested as an arbitrary threshold period). In chronic ICD, the most common type of ICD, the frequency of exposure exceeds the skin recovery time (26). Chronic ICD may differ biologically from acute ICD. Hence, the value of examining is the relation between the acute and chronic irritant model.

Thirdly, we note physical–chemical properties and proclivity to moisturizer efficacy.

SLS, an anionic surface active agent used as an emulsifier in many pharmaceutical vehicles, cosmetics, foaming dentifrices, and even foods (27), is a widely utilized irritation model (3). However we should extend our model studies to a broader range of chemical of varying characteristics.

Many studies utilize a 24 h patch application. But in real life, surfactant exposure is usually of short duration, open application, and cumulative. In recent years, assay methods resembling usage situations have been developed; such methods as repeated short duration chamber test, repeated open application test, plastic occlusion stress test and soak or wash tests (28). Validation based on actual work situation or home environment will, in the end, prove or disprove the relevance of these models. Much remains to be done; these model systems should accelerate our knowledge growth curve.

We intuitively (in a testimonial sense) believe that moisturizers are sometimes effective for preventing and treating for irritant dermatitis. However, moisturizer may not be broadly effective (8, 9) and may be relatively specific against certain acids, bases, hydrophilics, and lipophilics.

Increasing the hydration level of the stratum corneum may facilitate transportation of a

hydrophilic allergen and it may relate to lipid moisturizer content (29).

Hyperhydration occurs in wet work and with prolonged glove wearing. Water and occlusion may irritate. Zhai and Maibach (30) and Tsai and Maibach (31) overviewed this complex biology. Much definitive experimented work on the effect of both on irritant and allergens remains to be done.

New rapid throughput percutaneous penetration models may aid moisturizer development and provide insights; Karande et al. (32) reports transdermal penetration enhancers mixtures *in vitro* that increase skin permeability to macromolecules (approximately 1–10 kDa) by up to approximately 100-fold without inducing skin irritation. Should this model be appropriately validated, formulation development would be accelerated. When efficacy techniques are appropriately validated, product labelling based on a specific efficacy test (like a Sun Protection Factor; SPF) would aid the health care professional and the consumer.

Taken together we are impressed with recent quantitative data that provide the basis for future investigation. Because of ubiquitous nature of the chemical problem, the extension of the excellent work summarized here justifies priority. For an updated summary of other aspects of moisturizer science, see Loden and Maibach (33).

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