Effectiveness of Barrier Creams against Irritant Contact Dermatitis

Christian Mostosi^a Thierry Simonart^b

^aCESI Prévention et Protection asbl., Charleroi, and ^bPrivate practice, Brussels, Belgium

Key Words

Barrier cream · Skin protection · Workplace · Irritant · Review

Abstract

Introduction: Skin tissue is frequently exposed to various irritant substances in the workplace, particularly in wet work, which can lead to the development of occupational contact dermatitis. 'Barrier' creams (BCs) are well known, and their applications are still the subject of many studies and controversies. **Methods:** We searched all controlled trials investigating BCs against cutaneous irritants in humans published between 1956 and December 2014 from MEDLINE, PubMed, reference lists and existing reviews. **Results:** Thirty-nine studies about the effects of BCs against skin irritants in humans were selected. Among these, 27 trials in healthy volunteers were found to show many differences with regard to BCs and irritants used, their quantities, test locations, procedures and assessment methods. Finally, 14 patch test trials assessed by clinical scoring and evaporimetry emerged. Although the findings were generally positive, only few findings could be cross-checked from all the data, and vehicles seem to be as effective as BCs. **Conclusion:** Although this review highlights the poor quality and the lack of standard-

ization of most studies, BCs seem to have protective effects against irritants. Further well-designed, adequately powered randomized controlled trials with clinical and biophysical assessments are required.

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Introduction

Occupational contact dermatitis (OCD) represents 90% of all occupational skin diseases, of which the annual incidence is 9.1–31.7 per 100,000 workers [1]. Change of job occurs in 29–72% of the cases [2]. The European OCD prevalence, during a defined 1-year period, is estimated to be between 6.7 and 10.6% [3].

Acute or chronic exposure to irritants can lead to *irritant contact dermatitis*, representing 80% of all OCDs [3]. Irritant contact dermatitis is caused by a non-immunological reaction which may be immediate or cumulative over time. It is found mainly in 'wet-work' occupations such as household-cleaning workers, dish washers, people who work in the food industry such as bakers, health care workers, hairdressers or metal workers [4, 5]. Some extraprofessional activities like gardening, do-

mestic work or do-it-yourself could be a confounding factor.

Damaged, dry and rough skin increases the penetration of substances in the stratum corneum, acting as a reservoir for the substances which have penetrated [6].

Among skin creams, two types of products for hand protection may be found: barrier protection creams or 'barrier' creams (BCs) and barrier repair creams [7]. BCs are used to prevent the irritant effect caused by occupational exposure and are recommended for application before and during work. Some authors call them prework creams [8–10]. They have also been called 'invisible gloves' but the term 'skin protective creams' is more appropriate [10]. The objective of the BCs is to inhibit or delay cutaneous penetration of substances which could have deleterious effects at the time of skin contact or induce systemic effects due to percutaneous absorption [11]. BCs are therefore used to reduce the irritant effect of substances, preventing irritant contact dermatitis. Barrier repair creams, also called 'regeneration creams', 'conditioning creams', 'emollients' or 'moisturizers' [10], are intended to enhance hydration by way of the hygroscopic action of humectants, such as amino acids, urea, glycerine, lactic acid (LA) or pyrrolidone carboxylic acid [12], and to restore the skin's natural barrier. They are especially recommended for use after work [13].

Despite controversies, the Cochrane database [14] showed that BCs and moisturizers may have a protective effect in some occupations including metal, printing and dye work, however without statistical significance reached from their 4 selected studies. Enlarging the focus on controlled trials investigating BCs against cutaneous irritants, we performed a systematic analysis in order to see if complementary data could be found on their effectiveness.

Materials and Methods

For further details, see the supplementary materials (for all online suppl. material, see www.karger.com/doi/10.1159/000444219) (fig. 1; tables 1–4).

Results

We identified 39 controlled trials (table 1) investigating the effect of BCs against skin irritants in a total of 929 volunteers (172 men, 279 women and 481 unspecified subjects) with healthy skin ($n = 28$), hand dermatitis ($n =$

Fig. 1. Flowchart.

1), skin sensitized to a specific allergen ($n = 4$) and 1 study on latex glove allergens [6, 15–52]. From these 39 papers, studies on excised skin [18, 24, 40, 41, 43, 46] have been discarded, and only trials on subjects with healthy and non-sensitized skin were retained, reducing the list to 27 papers detailed in table 1. Untreated skin was used in each trial as a control. The skin localizations in subjects were the forearms ($n = 15$), back ($n = 8$), hands ($n = 3$), forearms and back ($n = 1$). Stokoderm® ($n = 3$), Taktosan® ($n = 3$), Kerodex 71® ($n = 2$) and Arretil® ($n = 2$) are the 4 most frequently investigated creams. Several articles mention only the composition of the creams studied with no commercial name. The amounts of BC used range

Table 1. Details of the selected studies

First author [Ref.], year	Study design	Subjects, n	Tested creams	Site	Quantity of BC	Control	Irritants	Methods	Assessment	Efficiency
Guillemin [15], 1974	Controlled	10 men								
Lauwerys [16], 1978	Controlled	13 (11 men, 2 women)								
Fischer [17], 1983	Controlled	30 confirmed of 47 patch test positive to cobalt (gender NS)								
Lodén [18], 1986	Controlled	Human female breast skin from 2 or 3 donors								
Blanken [19], 1987	Controlled	11 (gender NS)								
Marks [20], 1989	Controlled	1st method: 15 (3 men, 12 women); 3 groups of 5 subjects testing separate dye 2nd method: 8 men								
Nouaigui [21], 1989 ^{a,b}	Controlled	First assay: 8 (gender NS) 2nd assay: 5 (gender NS)	Anthydro (silicone 5%)	Forearms	0.005 ml/cm ²	Untreated skin	30 µl SLS 5%	Treated site without irritant, irritant on treated and untreated sites Patch tests, 24 h Vehicle with irritant, irritant on treated and untreated sites Patch tests, 24 h	Scoring, corneometry, evaporimetry, Doppler laser	Yes but incomplete (increased irritation on untreated sites); no differences between cream and vehicle
Frosch [22], 1993 ^b	Controlled	20 (6 men, 14 women)	(1) Taktosan cream (n = 10) (2) Marly Skin (n = 10)	Forearms	0.007 ml/cm ²	Untreated skin	1 ml SLS 1.5–10%	Glass cylinders, 30 min RIT: 5× the 1st week, 4× the 2nd week	Scoring, evaporimetry, Doppler laser, colorimetry	(1) Yes (2) No
Frosch [23], 1994 ^b	Controlled	10 (1 man, 9 women)	(1) Taktosan cream (2) Ravi Sperrschutzcreme	Paravertebral skin of the mid-back	0.02 ml/cm ²	Untreated skin	SLS 10%, NaOH 1%, LA 30%, TOL 99.5%	Patch tests, 30 min RIT: 5× the 1st week, 4× the 2nd week	Scoring, evaporimetry, Doppler laser, corneometry	(1) Yes except against TOL (2) Yes against SLS, no for TOL, poor against LA and NaOH
Treffel [24], 1994	Controlled	Human female breast skin from 3 Caucasian donors								
Marks [25], 1995	Controlled, randomized, single-blind, multicentre	211 men and women (NS)								
Schlütter-Wigger [26], 1996 ^b	Controlled	20 (6 men, 14 women)	(1) Reinol Aqueguard (2) Reinol-B (3) Reinol-F (4) Reinol Dryguard	Paravertebral skin of the mid-back	0.02 ml/cm ²	Untreated skin	SLS 10%, NaOH 1%, LA 30%, TOL 99.5%	Patch tests, 30 min RIT: 5× the 1st week, 4× the 2nd week	Scoring, evaporimetry, colorimetry	No against TOL (Reinol-B increase irritation) Yes against others
Zhai [27], 1996	Controlled, randomized	6 Caucasians (3 men, 3 women)								
De Fine Olivarius [28], 1996	Controlled	12 Caucasians (9 men, 3 women)								
Baur [29], 1998	Controlled, randomized	109 (gender NS)								
Fartasch [30], 1998 ^b	Controlled	13 (7 men, 6 women)	Lindesa	Forearms and back	0.025 ml/cm ²	Untreated skin	SLS 0.5–0.75%	Patch tests, 30 min RIT: 2×/day during 3 days	Scoring, evaporimetry	Yes

Table 1 (continued)

First author [Ref.], year	Study design	Subjects, n	Tested creams	Site	Quantity of BC	Control	Irritants	Methods	Assessment	Efficiency
Elsner [31], 1998 ^{a,b}	Controlled, randomized	10 (7 men, 3 women)	PPPE 0.5-1.2-4%	Paravertebral skin of the mid-back	0.016 ml/cm ²	Vehicle, untreated skin	SLS 10%, NaOH 0.5%, LA 15%, TOL 99.5%	Patch tests, 30 min RIT: 5× the 1st week, 4× the 2nd week	Scoring, evaporation, colorimetry	Yes against SLS and NaOH for all preparations No against LA and TOL (but 4% PPPE cream showed a significant protective effect on day 5) No difference between vehicle and creams
Wigger-Alberti [32], 1998 ^b	Controlled, randomized	15 Caucasians (6 men, 9 women)	3 BCs (A-B-C; given compositions)	Paravertebral skin of the mid-back	0.016 ml/cm ²	Untreated skin, petrolatum	SLS 10%, NaOH 0.5%, LA 15%, TOL 99.5%	Patch tests, 30 min RIT: 5× the 1st week, 4× the 2nd week	Scoring, evaporation, colorimetry	SLS: yes, but B is more effective NaOH: A and C are more effective LA: B more effective, A effective during 5 days TOL: C no, B increases irritation
Zhai [33], 1998 ^c	Controlled, randomized	10 Caucasian men								
Patterson [34], 1999	Controlled, randomized, double-blind	20 with sensitivity to poison ivy								
Zhai [35], 2000 ^{a,b}	Controlled	12 Caucasians (5 men, 7 women)	Protège International	Forearms	0.025 ml/cm ²	Vehicle, untreated skin	0.2 ml SLS 0.5%	Patch tests, 24 h	Scoring, evaporation, Doppler laser and colorimetry for 5 days	Yes Vehicle: worse than cream with scoring and evaporation assessment; no difference with Doppler laser Cream 1 > 2 > 3
Schnetz [36], 2000 ^{b,c}	Controlled, multicentre	Phase 1: 20 (6 men, 14 women) Phase 2: 33 (11 men, 22 women)	(1) Cremor basalis (2) Lanae alcoholium unguentum aquosum (3) Petrolatum	Forearms	0.025 ml/cm ²	Untreated skin	50 µl SLS 0.5%, 50 µl TOL >99%	Patch tests, 30 min RIT: 2×/day, during 2 weeks (phase 1) and 5 days (phase 2)	Scoring, evaporation, colorimetry	
Sun [37], 2000	Controlled	6 (5 men, 1 woman)								
Schliemann-Willers [38], 2001 ^a	Controlled, randomized, double-blind	20 Caucasians (7 men, 13 women)	PPPE (Fomblin HC/P2) 2-5%	Paravertebral skin of the mid-back	0.016 ml/cm ²	Vehicle, untreated skin	0.05 ml SLS 5%, 0.05 ml NaOH 0.5%, 0.05 ml LA 20%, 0.05 ml TOL	Patch tests, 30 min RIT: 5× the 1st week, 4× the 2nd week	Scoring, evaporation, colorimetry	Yes against SLS, NaOH and LA at 5% No against TOL Vehicle: no significant benefit
Wöhr [39], 2001 ^a	Controlled, randomized, double-blind	45 (4 men, 41 women) with positive patch tests to metals								
Chilcott [40], 2002	Controlled	Human breast skin								
Van der Bijl [41], 2002	Controlled	Human breast Caucasian skin								
Wigger-Alberti [42], 2002 ^b	Controlled, randomized	20 Caucasians (3 men, 17 women)	Stokoderm	Forearms	0.016 ml/cm ²	Untreated skin	SLS 0.5%, TOL	Patch tests, 30 min TRIT: mixtures SLS/SLS, TOL/TOL, SLS/TOL, 2×/day during 4 days	Scoring, evaporation, colorimetry, corneometry	Yes

Table 1 (continued)

First author [Ref.], year	Study design	Subjects, n	Tested creams	Site	Quantity of BC	Control	Irritants	Methods	Assessment	Efficiency
Lati [43], 2004	Controlled	Human abdominal male skin								
Teichmann [6], 2006 ^a	Controlled	6 (men and women)								
Elsner [44], 2007	Controlled, randomized	20 (gender NS)								
Rieger [45], 2007 ^a	Controlled	6 men								
Korinth [46], 2008	Controlled	Human abdominal female skin (2 white, 1 black)								
Slade [47], 2008	(1) Controlled, single-blind (2) Controlled, double-blind	(1) 36 sensitized men and women (2) 15 sensitized females + 25 additional participants								
Lembo [48], 2010	Controlled	19 women with hand dermatitis								
Roure [49], 2012	Controlled	14 Caucasian women								
Schliemann [50], 2013 ^b	Controlled, randomized, double-blind	35 Caucasians (12 men, 23 women)	6 BCs (given composition)	Paravertebral skin of the mid-back	0.008 ml/cm ²	Untreated skin with SLS 0.5%	240 µl <i>n</i> -octane 99.2%, 240 µl cumene 99%	Patch tests, 10 min RIT: 2×/day, during 11 consecutive days	Evaporimetry, corneometry, scoring	No; 2 BCs enhanced the irritation
Schliemann [51], 2014 ^b	Controlled, randomized, single-blind	20 Caucasians (5 men, 15 women)	3 BCs (A-B-C; given composition)	Back	2 mg/cm ² (5 µl) and 20 mg/cm ² (50 µl)	Untreated, untreated with SLS 0.5%, untreated with NaOH 0.5%	50 µl SLS 0.5%, 50 µl NaOH 0.5%	Patch tests, 30 min, twice daily (1) 5 µl A + SLS (2) 50 µl A + SLS (3) 5 µl A + NaOH (4) 50 µl A + NaOH (5) 5 µl B + SLS (6) 50 µl B + SLS (7) 5 µl C + SLS (8) 50 µl C + SLS (9) 5 µl C + NaOH (10) 50 µl C + NaOH	Evaporimetry, colorimetry, corneometry, scoring	Methods 2-4-6-8-10: yes Methods 1-3-7: decreased irritation Method 5: no
Sadhra [52], 2014 ^b	Controlled	21 men	BC (given composition)	Forearms	NS	Untreated skin and unexposed	SLS 5%	Patch tests, 1 h SLS only, BC only, BC + SLS	Colorimetry, evaporimetry, scoring	Reduced skin damage compared with SLS alone but does not prevent ICD

Only studies including patch tests and assessment by scoring and evaporimetry are detailed. NS = Not specified; PPPE = perfluoroalkylpolyether; RIT = repetitive irritation test; ROIT = repetitive occlusive irritation test; TOI = toluene; TRIT = tandem repeated irritation test; ICD = irritant contact dermatitis.

^a Studies using vehicles.

^b Patch test studies assessed by evaporimetry and scoring.

^c Study using only vehicles.

Table 2. Protective effect of the 4 most tested BCs

	Epoxy resins 1% [19]	Crystal violet 0.5% [28]	SLS 0.5% [42, 44]	Toluene [42, 44]	SLS 1-5-10% [22]	SLS 10% [23]	Oil red O 5% [27]	<i>m</i> -Xylene [16]
Stokoderm	–	–	<i>Yes</i>	<i>Yes</i>	–	–	<i>Yes</i>	–
Taktosan	–	–	–	–	<i>Yes</i>	<i>Yes</i>	<i>Yes</i>	–
Kerodex	<i>Yes</i>	<i>Yes</i>	–	–	–	–	–	–
Arretil	No	–	–	–	–	–	–	No

Reproducible results are in italics.

Table 3. Number of named BCs showing a protective or no protective effect on the 4 most used irritants

Irritants	Number of BCs reported	
	protective effect	no protective effect
SLS	13	1
Toluene	1	8
NaOH	8	–
LA	7	1

from 0.25 to 20 mg/cm² and from 2 to 25 µl/cm². The most used irritants are sodium lauryl sulphate (SLS, hydrophilic model, n = 16) and toluene (lipophilic model, n = 9). Sodium hydroxide (NaOH, n = 7) and LA (n = 5) are other common irritants tested. Their concentrations range, according to the authors, from 0.5 to 10% for SLS, from 0.5 to 4% for NaOH and from 15 to 30% for LA, whereas toluene was used pure (>99%). The quantity of irritants used is often not specified. However, a range from 0.03 to 1 ml of SLS was applied (specified in 6 trials) and from 0.05 to 0.1 ml for NaOH (specified in 3 studies). The contact time of irritants ranges from 5 s to 24 h but the most frequent contact time is 30 min (n = 11) and 24 h (n = 4). Repetitive irritation tests, including repetitive occlusive irritation tests and tandem repetitive irritation tests, were performed in 11 studies [22, 23, 26, 30–32, 36, 38, 42, 44, 50]. The assessment methods often consist of clinical scoring of irritation after cutaneous patch tests (n = 17) and bioengineering methods which are habitually evaporimetry (n = 17), colorimetry (n = 12), corneometry (n = 7), flow velocimetry by Doppler laser (n = 6), spectrometry (n = 3) or other more infrequently used methods. Two studies showed an increased penetration

of the irritant [27, 45], and the irritation increased in 3 trials [26, 32, 50]. Table 2 displays the protective effects of the 4 most used BCs. It shows that Stokoderm was effective against SLS 0.5% and toluene in 2 studies [42, 44]. The efficiency of this same BC against Oil red O (a staining dye) was confirmed by only 1 study [27]. Taktosan was found to be effective against SLS 10% in 2 different studies from the same author [22, 23]. Fourteen patch test studies assessed by scoring and evaporimetry (table 1) were selected to better compare the results in tables 3 and 4. In table 3, which reports the presence or absence of efficiency of the named BCs on the 4 most used irritants, we can see that BCs seem to have protective effects against SLS, NaOH and LA, but not against toluene. Four studies [21, 31, 35, 38] compared BCs with vehicles. The results displayed in table 4 show no difference (n = 3) [21, 31, 38] and a worse effect for scoring and evaporimetry in the last study [35].

Discussion

Our table 1 highlights that the selected studies have not been conducted under the same conditions: study design, creams, irritants used and assessment methods. One must also take into account skin temperature, pH, the thickness of the layer of cream, the number of applications, drying time before exposure, time required for application, time in contact with the irritant, concentrations and quantities of the irritant agents, areas of the body studied (back, hands or forearms), subjects studied (gender and ethnicity), presence or absence of occlusion and the length of the study [4, 28, 41, 53]. Human skin is also characterized by an interindividual variability [22]. In the workplace, irritants are often a mixture of various substances, yet the trials selected in this study were carried out with isolated

Table 4. Effects of vehicles compared to BCs

Studies using vehicles	BC	Irritants	BC effect	Vehicle effect
Nouaigui et al. [21], 1989	Anthydro (silicone 5%)	SLS 5%	+	=
Elsner et al. [31], 1998	PFPE (0.5-1-2-4%)	SLS 10%	+	=
		NaOH 0.5%		
		LA 15%	-	
		Toluene 99.5%		
Zhai et al. [35], 2000	Protèque International	SLS 0.5%	+	- (for scoring and evaporimetry) = (for Doppler laser)
Schliemann-Willers et al. [38], 2001	PFPE (2-5%)	SLS 5%	+ (at 5%)	=
		NaOH 0.5%		
		LA 20%	+	
		Toluene	-	

PFPE = Perfluoroalkylpolyether; + = protective (or better for vehicle) effect; - = no protective (or worst for vehicle) effect; = = no difference.

irritants. Duration of exposure, frequency of exposure and concentration of the irritant are 3 factors affecting occupational exposure. Because OCD is often the outcome of chronic exposure, the repetitive irritation test procedure could reproduce conditions closer to occupational exposure than studies with single contact. Concerning the application of BCs, an efficient layer and an efficient drying time are needed [18, 54]. It has also been shown in the study of Wigger-Alberti et al. [55] about self-application of a protection cream that certain areas of the hands were not sufficiently protected.

The range of quantities of cream applied found in our review is very wide. Schliemann et al. [56] pointed out that the quantities of BCs per skin surface area used in experiments might be far from those used in real conditions, leading to an overestimation of their efficacy.

While occupational skin diseases involve hands in more than 90% of cases [7], the most frequent application sites, in our selected studies, are the forearms and back. Overall, the studies have not taken into account friction movements which occur in realistic situations nor do they consider perspiration, resulting in an overestimation of the efficacy of BCs [28, 57].

Kütting et al. [58] published a prospective 4-armed randomized controlled trial on 1,020 metal workers regularly exposed to cutting fluids, followed during 12 months. The volunteers were assessed only by skin score. They showed that the skin protection programme (using BCs and skin care creams) is effective as well as the use of BCs

alone, contrary to moisturizers alone, but the best protective effect was obtained by combining BCs and moisturizers. Kütting et al. [59] underline the contrast with the results of an Austrian prospective 4-armed randomized controlled trial on 485 of 1,006 workers coming from building (n = 198) and timber (n = 287) industries, followed over 1 year, in which each subject was assessed by clinical hand dermatitis categorization, transepidermal water loss and subjective perception. None of the 4 groups showed a protective effect on dermatitis. We must note that Kütting et al. assessed their subjects only by clinical scoring while, according to the recent paper of Sadhra et al. [52], it seems that clinical assessment is not sufficient without bioengineering. For the latter, it is also suggested that biophysical studies may provide information on changes in the skin condition before any visible dermatological changes occur [52] while other authors believe that clinical scoring is more appropriate at work [36, 60]. According to several authors, the measure of transepidermal water loss is the best parameter of the barrier's alteration, even if some substances alter this parameter only slightly [22, 35, 36, 61, 62].

There is a considerable lack of standardization in the selected studies, with more than 20 named commercial BCs tested in different ways against several different irritants (table 1), meaning that pooling of the results was not possible. The results were generally positive against 3 of the 4 more frequent irritants used (table 3). It seems that vehicles are as efficient as BCs (table 4). Our results

stand in contrast with the Cochrane database conclusion. In their double-blind randomized controlled trial on 50 nurses comparing a BC and its vehicle, Berndt et al. [63] found an improvement in skin condition when using creams without any significant differences between the two groups, underlining however a lack of placebo-controlled, randomized clinical studies. Although the composition of BCs is sometimes very similar to that of simple emollients, we decided to differentiate between the two to focus only on studies investigating the BCs' efficiency. As explained in the Introduction, emollients are recommended after work. A larger comparison, including BCs and emollients, should be evaluated because they could be considered vehicles. We must note that the BCs cited in tables 2 and 4 are still available on the online market except for Protèque International.

By contrast to Wang et al. [64], some authors suggest that BCs should only be used for exposure to mild irritants (water, detergents, organic solvents or cutting oils) because they cannot neutralize a high dose of irritant [13, 61]. Indeed, after saturation, the agents sequestered in the layer of cream continue to penetrate the skin [18, 28] if the substances are not inactivated by BCs. This explains the potential of some BCs to induce contact dermatitis [4] and to increase the skin's susceptibility to irritants [61]. As may be seen in table 3, protection against toluene is very low and must be improved in the future. Only primary protection of as yet uncompromised skin can be of optimal efficacy in the prevention of OCD [63].

Conclusion

The comparability of trials evaluating the efficiency of BCs is affected by the lack of standardization even if a trend toward some degree of protection seems to be suggested, although vehicles appear to be just as efficient. The repetitive irritation test procedure is closer to the reality and could be used to assess exposures to one or more irritants.

However, the prevention of OCD goes beyond the pure application of BCs. Efforts should focus on field randomized controlled studies of skin protection programmes with standardized clinical and biophysical assessments.

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The authors have no conflicts of interest to disclose.

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