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Comparing the Influence of Five Patch Types on the Result of a 12-Day Cumulative Irritancy Patch Test

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Synopsis

A 12-day cumulative irritancy patch test is available for predicting skin irritation potential. This study is important to determine the ideal patch type to be used in the irritancy patch test. This study was conducted to determine the cumulative skin irritation potential of five different patch types using predictive patch test techniques. Five types of patches were tested in a 12 day repeated insult test. The patch types were Hill Top Chamber occlusive, Finn Chamber occlusive, Band-Aid semiocclusive, Webril® semiocclusive, and Webril® occlusive. The test materials applied to the patches were cream, lotion, 2% bath cream, and controls of 1% sodium lauryl sulfate (1% SLS), respectively. A dermatologist performed the grading. The test results revealed that with cream, the cumulative scores of Hill Top Chamber occlusive, Finn Chamber occlusive, Band-Aid semiocclusive, Webril® semiocclusive, and Webril® occlusive were 22, 27, 16, 9, and 21, respectively; with lotion, the cumulative scores were 192, 200, 192, 200, and 70, respectively; with 2% bath cream, the cumulative scores were 523, 306, 523, 306, and 506, respectively; with 1% sodium dodecyl sulfate solution, the cumulative scores were 792, 801, 753, 526, and 841, respectively. Comparison of the five different patch types revealed that Webril® semiocclusive had the lowest cumulative irritation scores and incidence of adverse reactions. Comparison of the three test materials revealed that cream was the mildest material with the lowest cumulative irritation scores.

INTRODUCTION

The cumulative irritation patch test is the industry standard and is used to determine and compare the dermal irritation potential and safety of test materials (1,2). Patch testing involves a patch test unit and patch test materials. The type of patch test system is one of the factors that influences patch test results (3,4). At present, various patch types are available for clinical tests. However, to our knowledge, comparison of the cumulative irritation potential of five patch types using a 12-d cumulative irritation study has not been reported in the literature. This study was performed to determine the cumulative irritation potential of three test materials and to compare the irritation potential of different patch types.

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MATERIALS AND METHODS

SUBJECTS

Twenty-five healthy subjects with Fitzpatrick skin types II–IV, aged 18–to 65 year, were recruited. The subjects agreed to avoid direct sun exposure to the test site area and avoid the use of tanning beds for the duration of the study. Volunteers who had shown an allergy in any previous patch test within the last 2 weeks, as determined by the initial paperwork, or who were currently participating in any other patch test, were excluded. Twenty-four subjects completed the study (aged 24–49 years; one male and 23 females), whereas one subject was rejected because of failure in adhering to the schedule. The subjects were informed of the nature of the test and possible adverse reactions. A written informed consent was obtained before participating in the study. The hospital's Ethics Committee (West China Hospital, Sichuan University) approved this study.

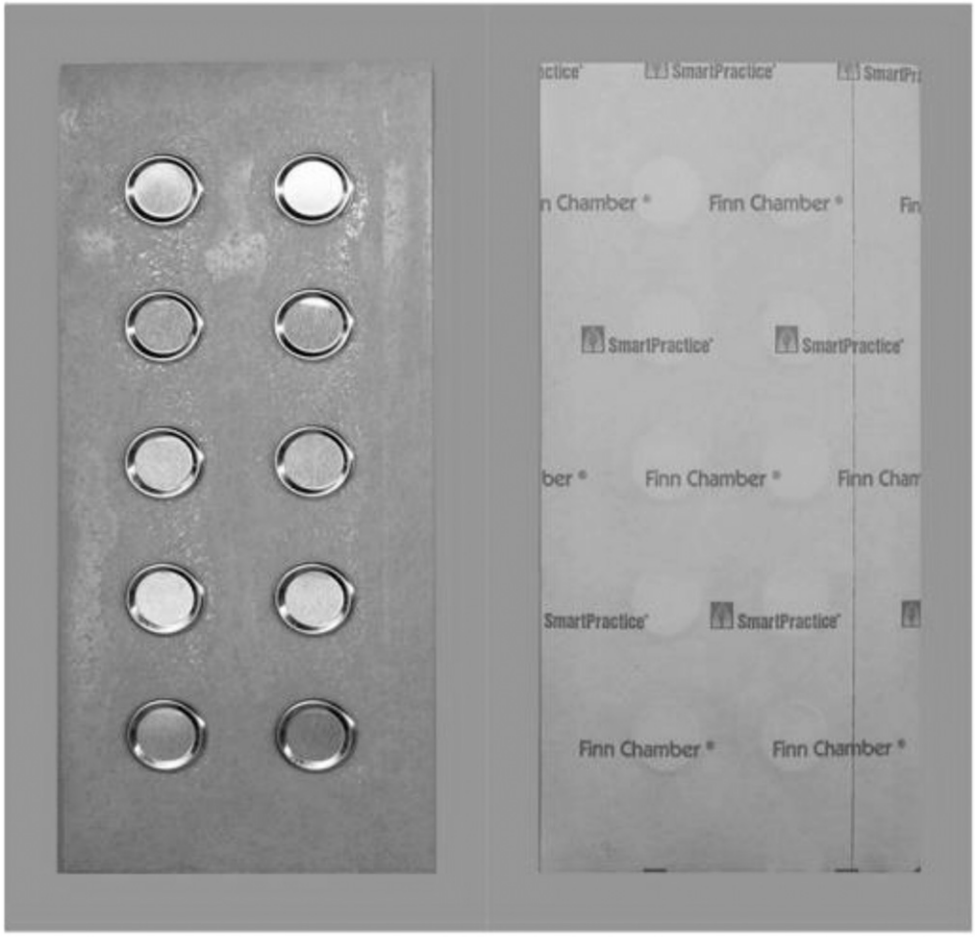

Figure 1. Finn Chamber.

PATCH TYPES AND TEST MATERIALS

Five types of patches were evaluated in this study:

- λ Finn Chamber Occlusive (Figure 1):

Finn Chamber occlusive (Epitest Oy, Tuusula, Finland) was made from two components: a chamber material and adhesive tape. The chamber material used was an alumina pad (diameter, 0.8 cm). The adhesive tape used was Scanpor tape (nonwoven microporous hypoallergenic tape; Norgesplaster A/S, Vennesla, Norway).

- λ Hill Top Chamber Occlusive (Figure 2):

Hill Top Chamber occlusive (Cliantha Research Limited, Mumbai, India) consisted of two components: a rubber pad and durapore tape (latex-free silklike hypoallergenic tape; 3M Co., Saint Paul, MN). Its side length was 1.9 cm, the outside diameter of the pad was 1.4 cm, and the inside diameter was 1.2 cm. The total patch area was approximately 1.13 cm^2.

- λ Band-Aid Semiocclusive (Figure 3):

Band-Aid semiocclusive (Johnson & Johnson Co., New Brunswick, NJ) consisted of two components: a cotton pad (1.8 cm × 1.8 cm) and adhesive tape (porous and hypoallergenic tape, 3.81 cm × 3.81 cm).

- λ Webril Occlusive (Figure 4):

Webril occlusive consisted of two components: a cotton pad (Webril occlusive; Kendall Co., Mansfield, MA) and durapore tape (latex-free silklike hypoallergenic tape; 3M Co., 3.5 cm × 3.5 cm). The cotton pads used for the patches were approximately 4 cm^2 in area.

- λ Webril Semiocclusive (Figure 5):

Webril semiocclusive consisted of two parts: a cotton pad (Webril occlusive; Kendall Co.) and micropore tape (latex-free hypoallergenic paper tape; 3M Co., 3.5 cm × 3.5 cm). The cotton pads used for the patches were approximately 4 cm^2 in area.

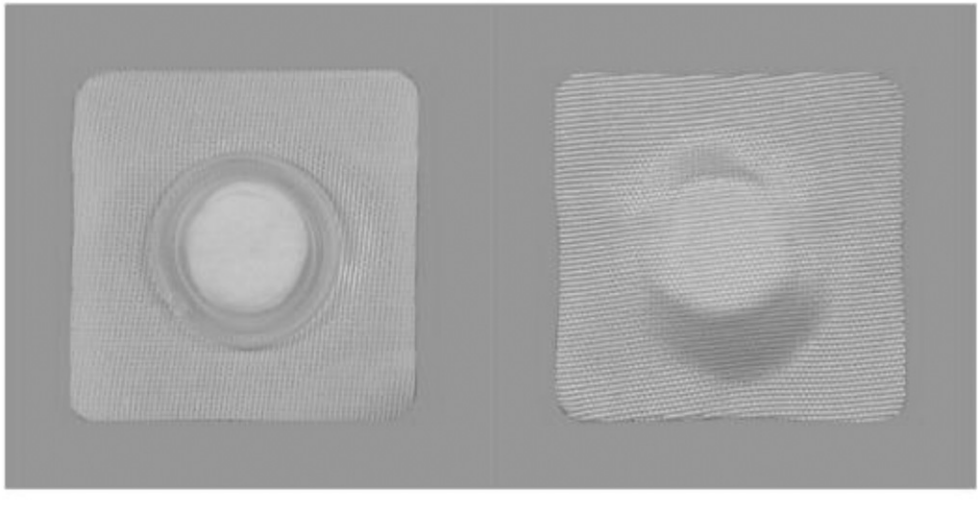

Figure 2. Hill Top Chamber.

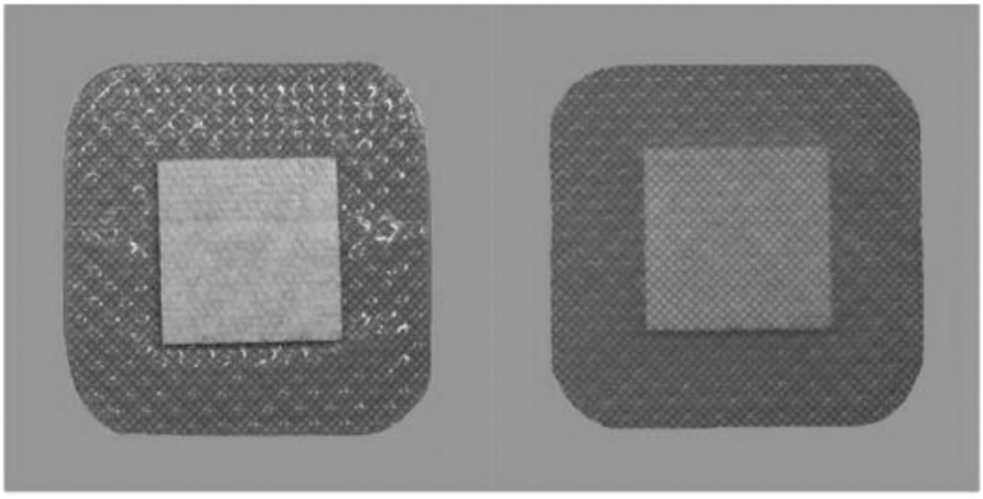

Figure 3. Band-Aid semiocclusive.

The test materials applied to the patches were cream, lotion, and 2% bath cream. The cream and lotion were similar in their main ingredients, but differed in dosage. The 2% bath cream was prepared using 2 g of the bath cream diluted with 98 g of distilled water. Main ingredients of the three test materials were shown in Table I.

Each patch had one positive control and one negative control. One percent sodium lauryl sulfate (SLS, purity > 99%, made by Sigma, St. Louis, MO) solution served as the positive control. Blank patches with a pad served as the negative control.

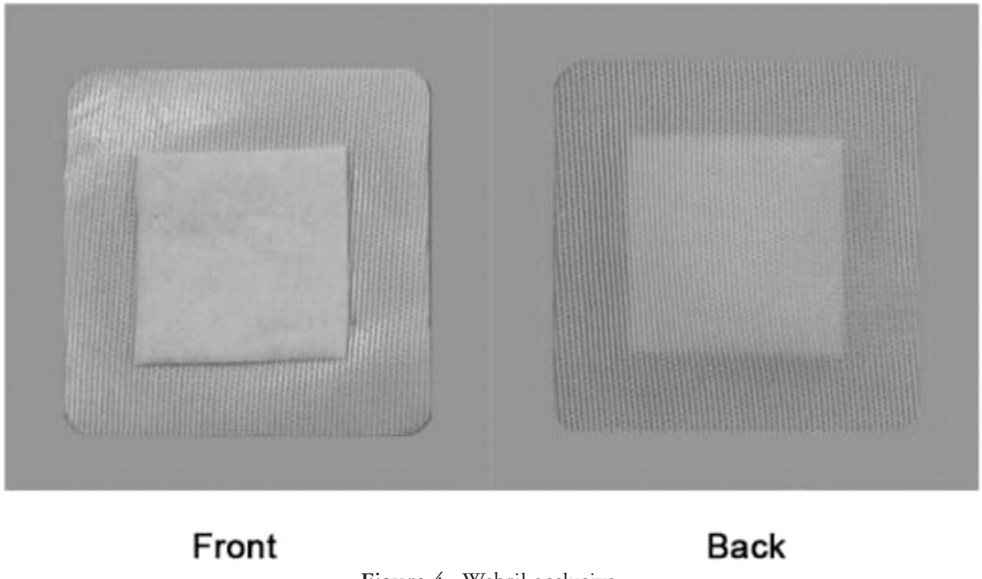

Figure 4. Webril occlusive.

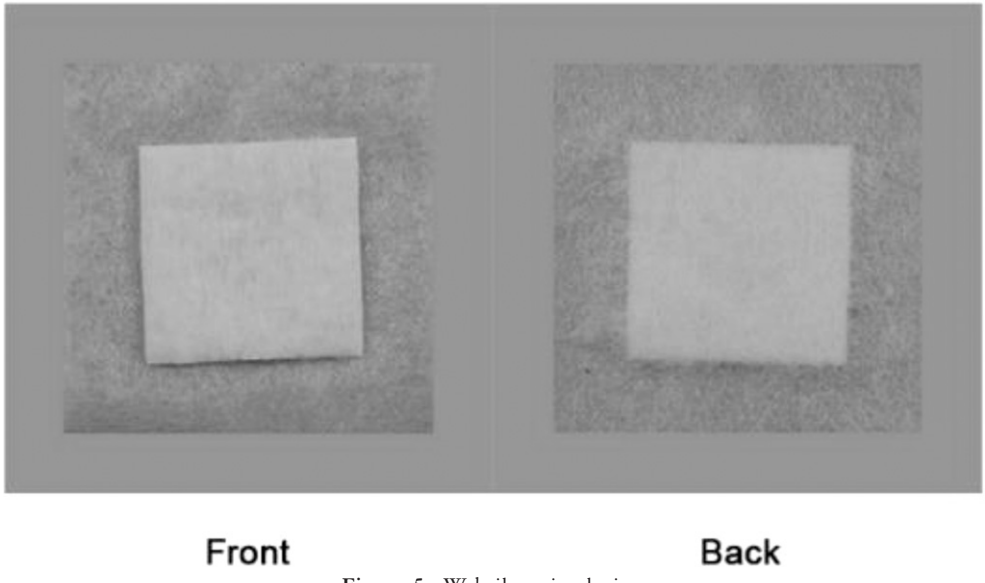

Figure 5. Webril semiocclusive.

METHOD

Patches dosed with test materials were applied laterally between the shoulder blades on the upper back, but not directly over the spine. Each type of patch was placed in a separate row. Test samples were added in the same sequence according to Figure 6.

Test and control materials were applied to each patch in 20 µl. Patches were applied for approximately a 24-h period, then removed and discarded by the dermatologist approximately 2 h before grading. After an evaluation, materials were reapplied to their assigned sites. These procedures were performed daily for 11 d, with final evaluations performed after the final patch removal on day 12.

All induction patches were applied to the same sites, unless the cumulative grade of reaction was more than three or the adhesive necessitated removal.

Table I
Main Ingredients of the Three Test Materials

Cream	Lotion	Bath cream
Water	Water	Water
Glycerine	Glycerine	Sodium benzoate
Cetyl alcohol	Cetyl alcohol	Cocamidopropyl betaine
Cocoglycerides	*Glycine soja* oil	Sodium laureth sulfate
Glycine soja oil	*Helianthus annuus* seed oil	Sodium lauroamphoacetate
Helianthus annuus seed oil	*Zea mays* starch	Polysorbate 20
Dimethicone	Dimethicone	Polyethylene glycol-150 distearate
Zea mays starch	Phenoxyethanol	Citric acid
Potassium cetyl phosphate	Ethylhexylglycerin	
Hydrogenated palm glycerides	Potassium cetyl phosphate	

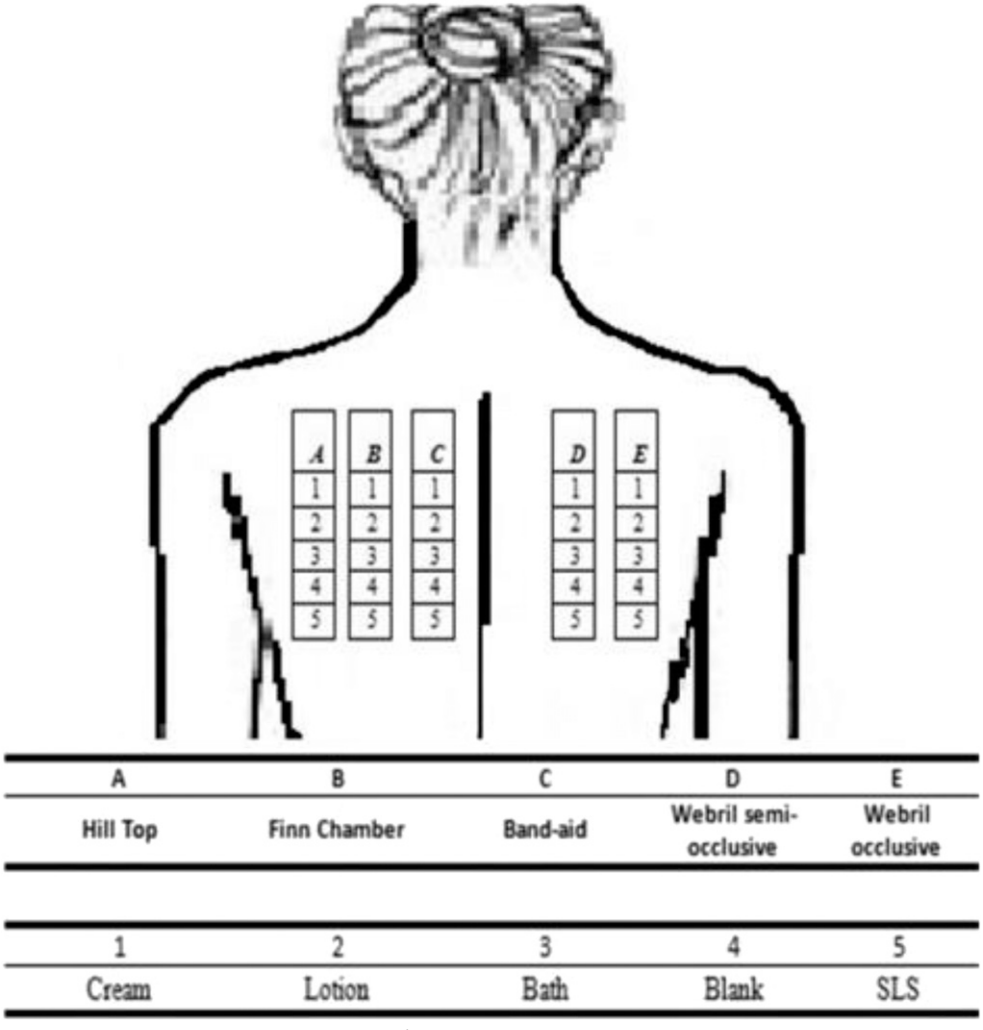

Figure 6. Sample adding sequence.

Reactions to the test materials were scored using a combination of the grading scales (Tables II and III).

The actual patch test scores were the combination of a numerical and/or letter score consistent with the definitions given in the scoring scale. Scores containing letter grades were converted into numerical equivalents as follows: A = 0, B = 1, C = 2, and D, E, and F = 3. These equivalents were considered comparable with any numerical score.

STATISTICS

To obtain classifications of the test materials, subject scores were added for each test site. Berger and Bowman established a standardized interpretation system for base (n = 10) irritation scores during induction at 14 d (5). This system was adjusted proportionally for

Table II
Erythema and Elevated Responses

Grade	Description
0	No evidence of irritation
1	Minimal erythema, barely perceptible
2	Definite erythema, readily visible; or minimal edema; or minimal papular
3	Erythema and papules
4	Definite edema
5	Erythema, edema, and papules
6	Vesicular eruption
7	Strong reaction spreading beyond test site

12 d of induction, and for base ($n = 24$) as shown in Table IV. Categories were based on percentages of the maximum possible score for each test site. For the calculation of a total score, an upper limit of three was used because the intent of this test would be to compare material treatments that are relatively mild; it would be meaningless in this context to evaluate test materials that cause extreme irritation. For cumulative scoring purposes, any score of three or higher was considered to be a three overall for the remainder of the test and patching was discontinued.

The following classification system was used for the interpretation of results.

RESULTS

One subject had site discontinuation during testing; thus, data from 24 of the 25 subjects tested were analyzed. As shown in Table V, the total cumulative irritation score resulting from exposure to each test material on each test day was calculated and scores were ranked orderly.

Table VI summarized the mean cumulative irritation data with statistical comparisons of the responses observed for each patch for a given test material. Table VII detailed the mean total cumulative scores with statistical comparisons of the responses observed for each test material for a given patch.

Comparing cumulative irritation scores of the three test materials, cream elicited the lowest cumulative irritation score. Based on Table IV, the cream was less irritating than the other materials across all patch types. We can draw a conclusion that cream is a mild

Table III
Effects on Superficial Layers of the Skin

Grade	Description
A	Slight glazed appearance
B	Marked glazing
C	Glazing with peeling and cracking
D	Glazing with fissures
E	Film of dried serous exudate covering all or portion of the patch site
F	Small petechial erosions and/or scab

Table IV
Classification System Used for the Interpretation of Cumulative Scores of Test Materials

Rank	Score	Indications from test	Description of observed response
1	0 to 70.71	Mild material—no experimental irritation	Essentially no evidence of cumulative irritation under the conditions of test (i.e., continuous at concentration specified)
2	>70.71 to 285	Probably mild in normal use	Evidence of slight potential for very mild cumulative irritation under conditions of test
3	>285 to 640.71	Possibly mild in normal use	Evidence of moderate potential for mild cumulative irritation under conditions of test
4	>640.71 to 829.29	Experimental cumulative irritant	Evidence of strong potential for mild to moderate cumulative irritation under conditions of test
5	>829.29 to 900	Experimental primary irritant	Evidence of potential for primary irritation under conditions of test

material. Lotion was revealed to be "probably mild in normal use" in most patch types, except for Webril semiocclusive. Bath cream was revealed to be "mild material—no experimental irritation" in patch type of Webril semiocclusive, "probably mild in normal use" in patch type of Band-Aid semiocclusive, "possibly mild in normal use" in patch type of Hill Top Chamber occlusive, Finn Chamber occlusive, and Webril occlusive.

Comparing cumulative irritation scores of the five patch types, we found that among all patch types (i) the Finn Chamber occlusive showed the highest cumulative irritation scores for cream and lotion. (ii) The Webril occlusive showed the highest cumulative irritation scores for 2% bath cream and 1% SLS. (iii) The Webril semiocclusive showed the lowest cumulative irritation scores for all test materials.

DISCUSSION

There were two purposes for our study: (i) to determine the cumulative irritation potential of the three test materials by the use of predictive patch test techniques and (ii) to compare the five patch types in terms of their irritancy.

Table V
Total Cumulative Scores of Test Materials in Various Types (Standardized Cumulative Score Based on $n = 24/25$)

	Cream		Lotion		2% bath cream		1% SLS		Blank
Patch type	Score	Rank	Score	Rank	Score	Rank	Score	Rank	Score
Hill Top Chamber occlusive	21.12	1	184.32	2	502.08	3	817.92	4	83.52
Finn Chamber occlusive	25.92	1	192	2	293.76	3	768.96	4	61.44
Band-Aid semiocclusive	15.36	1	56.64	1	245.76	2	722.88	4	61.44
Webril semiocclusive	8.64	1	20.16	1	16.32	1	504.96	3	7.68
Webril occlusive	20.16	1	67.2	1	485.76	3	807.36	4	22.08

Table VI
Comparison of Mean Total Cumulative Scores of Each Patch Type by Test Material

	Total cumulative irritation[a]				
Test material	Hill Top Chamber occlusive	Finn Chamber occlusive	Band-Aid semiocclusive	Webril semiocclusive	Webril occlusive
Cream	0.92 ± 2.08	1.13 ± 1.75	0.67 ± 2.01	0.38 ± 0.82[b]	0.88 ± 3.08
Lotion	8.00 ± 8.75	8.33 ± 7.22	2.46 ± 6.10[b,c]	0.88 ± 2.13[b,c]	2.92 ± 5.52[b,c,d]
2% Bath cream	21.79 ± 5.21	12.75 ± 8.01[c]	10.67 ± 7.27[c]	0.71 ± 1.30[b,c,e]	21.08 ± 8.21[b,d,e]
1% SLS	35.50 ± 1.06	33.38 ± 2.20[c]	31.38 ± 2.90[b,c]	21.92 ± 8.13[b,c,e]	35.04 ± 1.00[b,c,d,e]
Blank	3.63 ± 2.81	2.67 ± 5.14[c]	2.67 ± 3.64	0.33 ± 1.09[b,c,e]	0.96 ± 1.37[c,d,e]

[a]Numbers represent the mean ± standard deviation total cumulative irritation score ($n = 24$ subjects).
[b]Significant difference versus Finn Chamber occlusive ($p < 0.05$).
[c]Significant difference versus Hill Top Chamber occlusive ($p < 0.05$).
[d]Significant difference versus Webril semiocclusive ($p < 0.05$).
[e]Significant difference versus Band-Aid semiocclusive ($p < 0.05$).

In contrast with other test materials, cream was a mild material that had the lowest cumulative irritation test scores in our studies. This was probably because cream has a lower level of surfactant compared with the other materials. It had been reported that the initial interaction of surfactant with the intercellular lipids of the stratum corneum leads to penetration of the surfactant into the viable epidermal cell layer underneath. The surfactant can then cause cell damage or even cell lysis with the development of a clinically obvious irritant reaction (6).

In addition, we found different results between Webril occlusive patch and Webril semiocclusive patch. Although the same test materials having the same concentrations were applied for the same duration in both patches, the semiocclusive patch showed lower cumulative irritation test scores than the occlusive patch for all test materials. The only difference between the two patches was the adhesive tape; one was latex-free hypoallergenic paper tape, whereas the other was latex-free silklike hypoallergenic tape. The latex-free silklike hypoallergenic tape has worse air permeability. When silklike hypoallergenic

Table VII
Comparison of Mean Total Cumulative Scores of Each Test Material by Patch Type

	Total cumulative irritation[a]				
Patch type	Cream	Lotion	2% bath cream	1% SLS	Blank
Hill Top Chamber occlusive	0.92 ± 2.08	8.00 ± 8.75[b]	21.79 ± 5.21[b,c]	35.50 ± 1.06[b,c,d]	3.63 ± 2.81[b,c,d,e]
Finn Chamber occlusive	1.13 ± 1.75	8.33 ± 7.22[b]	12.75 ± 8.01[b,c]	33.38 ± 2.20[b,c,d]	2.67 ± 5.14[c,d,e]
Band-Aid semiocclusive	0.67 ± 2.01	2.46 ± 6.10[b]	10.67 ± 7.27[b,c]	31.38 ± 2.90[b,c,d]	2.67 ± 3.64[b,d,e]
Webril semiocclusive	0.38 ± 0.82	0.88 ± 2.13	0.71 ± 1.30	21.92 ± 8.13[b,c,d]	0.33 ± 1.09[e]
Webril occlusive	0.88 ± 3.08	2.92 ± 5.52[b]	21.08 ± 8.21[b,c]	35.04 ± 1.00[b,c,d]	0.96 ± 1.37[d,e]

[a]Numbers represent the mean ± standard deviation total cumulative irritation score ($n = 24$ subjects).
[b]Significant difference versus cream ($p < 0.05$).
[c]Significant difference versus lotion ($p < 0.05$).
[d]Significant difference versus 2% bath cream ($p < 0.05$).
[e]Significant difference versus 1% SLS ($p < 0.05$).

tape sticks on the skin, it forms an airtight skin area, which causes sweat as a source of irritant (7). Moreover, occlusion of the skin may cause an increased transepidermal water loss (TEWL) and the increase in TEWL may be interpreted as damage to the skin barrier (8).

We also compared the respective impacts on the patch test between the chamber and tape in this study. Among the five patch types, Finn Chamber occlusive showed the highest cumulative irritation scores for cream and lotion. This was because the alumina used was more irritating than rubber and cotton, even though the tape of the Finn Chamber occlusive was a microporous paper tape. Considering that cream and lotion were mild and probably acted as a slight irritant to the skin, the type of chamber induced bigger effects on cumulative irritation than type of tape for low irritating material. Hill Top Chamber occlusive revealed the highest cumulative irritation scores, Webril occlusive showed the second highest, and Finn Chamber occlusive showed the third highest for the positive control SLS. This is mainly because the three types of patches have different types of tapes. The tape of Hill Top Chamber occlusive and Webril occlusive was latex-free silklike hypoallergenic tape, the tape of Finn Chamber occlusive was nonwoven microporous hypoallergenic tape, and the air permeability of latex-free silklike hypoallergenic tape was worse than that of paper tape. This result reveals that the influence of the permeability of tape to cumulative irritation may be greater than the type of chamber for highly irritating material, which encourages us to design further studies to test the idea.

ACKNOWLEDGMENTS

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