

Putative skin-protective formulations in preventing and/or inhibiting experimentally-produced irritant and allergic contact dermatitis

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The effectiveness of skin protective formulations was evaluated in a previously-described in vivo human model. All formulations failed to inhibit ammonium hydroxide and urea irritation. Only paraffin wax in cetyl alcohol statistically ($p < 0.01$) reduced *Rhus* allergic contact dermatitis. 3 commercial formulations markedly ($p < 0.001$) suppressed sodium lauryl sulfate irritation. Paraffin wax in cetyl alcohol was quantitatively the most effective formulation. These results suggest that some formulations may provide protective effects against certain, but not all, irritants or allergens.

Key words: barrier creams; irritation; sodium lauryl sulfate (SLS); urea; *Rhus*; ammonium hydroxide (NH₄OH); irritant contact dermatitis; allergic contact dermatitis; prevention. © Munksgaard, 1999.

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Previously, we described an in vivo human model for screening the effect of potential protective materials against 2 acute irritants: sodium lauryl sulfate (SLS) and ammonium hydroxide (NH₄OH) plus urea, and 1 allergen (*Rhus*) (1). This study evaluated the efficacy of several protective formulations utilizing this model.

Materials and Methods

Subjects

10 healthy, male Caucasian volunteers (mean age 40.5 ± 14.6 years) participated after providing informed consent. The study was approved by the University of California, San Francisco, Human Research Committee.

Irritants

Group 1. 10.0% sodium lauryl sulfate (SLS) (99% purity, Sigma Chemical Co., St. Louis, MO) in water.

Group 2. 22.9% ammonium hydroxide (Fisher Scientific, Fair Lawn, NJ) and 2.0% urea (Ashland Chemical Co., Columbus, OH) in water.

Group 3. 3.0% *Rhus* allergen (Hollister-Stier, Spokane, WA) in acetone.

Test materials and preparations

All test products and materials were purchased commercially. The propylene glycol vehicle (PGV) was an o/w (oil in water) emulsion that included propylene glycol, isopropyl adipate, stearic acid, glycol monostearate, triethanolamine, methylparaben, propylparaben, and deionized water. The experimental materials were formulated at 4% in PGV. The experimental preparations and test sites were designated as below:

- (a) PGV;
- (b) PW+CA: paraffin wax (PW) in cetyl alcohol (CA);
- (c) P+PGV: perfluorophosphate (P) in PGV;
- (d) PA+PGV: perfluorosalicic acid (PA) in PGV;
- (e) formulation A: Kerodex 51[®] (Medtech, Inc., Jackson, WY) (Dry Work); bentonite, calcium carbonate, cellulose gum, cetearyl alcohol, chloroxylenol, glycerin, iron oxide, isopropyl alcohol, kaolin, methylparaben, petrolatum, propylparaben, sodium hy-

- droxide, sodium lauryl sulfate, zinc oxide, spermaceti, stearic acid, water;
- (f) formulation B: Kerodex 71[®] (Medtech, Inc., Jackson, WY) (Wet Work): calcium carbonate, cetearyl alcohol, cetrimonium bromide, cetyl alcohol, iron oxide, isopropyl alcohol, kaolin, methylparaben, mineral oil, paraffin, petrolatum, propylparaben, sodium hexametaphosphate, sodium lauryl sulfate, zinc oxide, water;
- (g) formulation C: PGV plus Lad-Fos (LF) (3M Company, St. Paul, MN). Lad-Fox is the half ester of N-methyl, N-2 hydroxyethyl perfluorooctane sulfamide and linoleic acid dimer and its salts;
- (h) U: Untreated skin

Methods

Details of the method have previously been described (1). Briefly, each test formulation (0.05 ml) was spread over a 2.0 cm² area, massaged in, allowed to dry for 30 min, and reapplied with another 30-min drying period. The experimental irritants or allergen was then applied (0.025 ml) to an A1-test (IMECO AB, Södertälje, Sweden) occlusive patch which, in turn, was placed over the designated site. The patches were removed after 24 h. Inflammation was scored, according to an expanded scale, 72 h post application. This 10-point expanded scale provides greater test discrimination than smaller scales. The lower the clinical score, the more effective the treatment.

The Wilcoxon signed rank test was performed for the non-parametric score. Friedman test was performed for analysis of variance by ranks of all test sites.

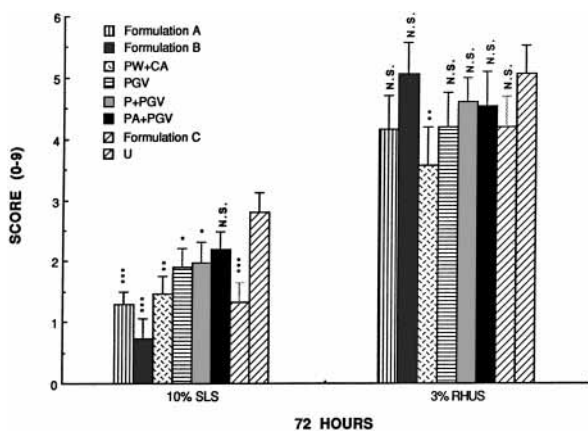


Fig. 1. Efficacy of protective formulations (see *Materials and Methods* for additional details). Results expressed as the means $\pm$ SE. Statistical differences in comparison with untreated skin site. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; N.S. = not significant.

Table 1. Rankings of materials by effectiveness for groups 1 and 3

Protective Formulations	Average rank	Group 1 (SLS)	Group 3 (Rhus)
paraffin wax in cetyl alcohol	3.89	4.2**	3.53**
formulation B	4.19	2.88***	5.62 (NS)
formulation C	4.21	3.68***	3.98 (NS)
formulation A	4.37	4.15***	4.35 (NS)
propylene glycol vehicle	4.48	4.75*	4.02 (NS)
perfluorosalicic acid in propylene glycol vehicle	4.80	5.45 (NS)	4.8 (NS)
perfluorophosphate in propylene glycol vehicle	4.82	4.92*	4.57 (NS)
untreated skin	5.23	5.97	5.13

Statistical differences in comparison with untreated skin site.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; NS = not significant.

Results

Group 1. SLS

All test formulations, except PA in PGV, showed a statistically significant decrease in SLS irritation, in comparison with the untreated control site (Fig. 1); formulation A, formulation B, and formulation C markedly ($p < 0.001$) suppressed irritation.

Group 2. Ammonium hydroxide (NH₄OH) plus urea

Although there were minor differences in comparison with the untreated control site, no formulation significantly decreased irritation (data not given).

Group 3. Rhus

Only paraffin wax in cetyl alcohol statistically ($p < 0.01$) suppressed the allergic reaction to *Rhus*.

Ranking of effectiveness

Table 1 shows the rank of effectiveness for each formulation. Separate rankings were made by each group. Based on average ranks, PW in CA was the most effective. The sequence of effectiveness was PW in CA; >formulation B; >formulation C; >formulation A; >PGV; >PA in PGV; >P in PGV; >untreated control site.

Discussion

Formulation B, marketed as a protectant against water-soluble irritants, and formulation A, an oleophobe, were chosen as marketed controls. PW in CA was selected because of high efficacy in previous evaluations (1). The emulsion vehicle (oil in water) was chosen due to the widely applied in protective products.

P is a completely hydrogen-replaced, fluorine-saturated hexafluorophosphate molecule. PA is a completely hydrogen-replaced, fluorine-saturated salicylic acid molecule. Lad-Fos is the half ester of N-methyl, N-2 hydroxyethyl perfluorooctane sulfanide and linoleic acid dimer and its salts.

PW in CA was the most effective formulation, but did not inhibit irritant contact dermatitis due to NH_4OH and urea. The results suggest that these protective formulations may provide efficacy, but their applications remain limited to certain environments. In other words, some formulations protect against certain, but not all, irritants or allergens.

Development of barrier creams, as well as protective ointments or emulsions, etc., may be divided into 3 major steps: screening potential materials, optimizing formulations, and finalizing the products. Comparing the protective effects of potential formulations with marketed products is an important step for formulation optimization. Recently, bioengineering techniques, with their accuracy and objectivity, have been widely used in evaluating their efficacy (2–9). Bioengineering techniques may mandate a constant environment for maximum efficacy, and various factors may modify the results (10–12). The current model is simple, rapid, and economic, and can be used as a reference system and to optimize qualitative and quantitative formulation chemistry. In the end, only the more time-consuming field studies will provide the key standard.

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