Tolerance Profile of a Sterile Moisturizer and Moisturizing Cleanser in Irritated and Sensitive Skin

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Background: This study evaluates the tolerance of preservative free sterile cleanser and sterile moisturizer in irritated and sensitive face skin.

Materials and Methods: An exploratory, open-label study using the cleanser and the moisturizer in combination was performed with 98 patients with a documented history of allergic contact dermatitis. The 2 products could each be used once or twice daily for 28 days. The assessment parameters at baseline and end of treatment (day 28) included the intensity of erythema, dryness/scaling by the investigator and subjective signs (burning, pruritus and stinging), according to a defined 4-point scale (absent to severe). In addition, a global assessment of the change from baseline and the overall tolerance of the products were performed by the investigator at the end of treatment.

Results: Ninety-four patients were included for the efficacy analysis and 96 patients for the safety analysis. At baseline, a majority of patients expressed some degree of erythema (63%), and dryness/scaling (56%). Fewer patients experienced subjective signs at baseline (44%). At the end of treatment, the results showed a statistically significant improvement of all the objective signs of irritated skin ($P < 0.0001$, Mac Nemar test), as well as the subjective signs of sensitive skin ($P < 0.02$). This was confirmed by the overall investigator assessment, showing an excellent or good response in 90% of the patients. In the safety analysis, 1 patient developed contact allergy to 1 ingredient of the test products (carbomer), and 3 patients exacerbated their dermatitis.

Conclusion: Taken together, these results suggest that adequately formulated cosmetics might reduce both irritated and sensitive skin, with clinical improvement of dryness, erythema and stinging.

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Numerous consumers suffer from adverse reactions to cosmetics. These adverse reactions include contact allergy to common ingredients (e.g., perfumes and preservatives), cutaneous irritation (e.g., emulsifiers) and sensory irritation (stinging). Moreover, these signs are frequently associated. For instance, on one hand, patients with multiple contact allergies also frequently express signs of sensitive and/or irritated skin. On the other hand, patients with irritated skin increase their risk of developing contact allergic reactions. This pilot clinical study investigates in patients with a history of contact allergy the tolerance profile of a sterile cleanser and a sterile moisturizer, with the following characteristics: no emulsifier, preservative, or fragrance.

Materials and Methods

The study was conducted as a multicenter, open-label, exploratory clinical trial. The trial was performed in 4 centers in the United States (CA and NY), and 8 centers in Europe (France and Belgium), during winter. Patients, aged 18 and over, with a documented history of allergic contact dermatitis were selected. Patients who were known to have positive reactions to one of the test formulations were excluded. Patients with an unstable skin condition, and patients who received oral or topical treatments that might have preclude test evaluation within 4 weeks before study entry also were excluded. Those who were unable to follow the study directive, or sign the informed consent form were not selected.
A sterile cleanser and a sterile moisturizer were to be applied according to the patients normal routine (i.e., once or twice daily during 28 days). The test products comprised a minimal number of the following ingredients: glycerin, mineral oil, squalane, hybrid safflower oil, cyclomethicone, glyceryl stearate, titanium dioxide, carbomer, sodium hydroxide, and thermal spring water (Ave`ne). Because these products were formulated and stored (5 mL tubes for the moisturizer and 10 mL tubes for the cleanser) under strict sterile condition, no preservative, emulsifier or fragrance, were included. After opening, each tube was guaranteed to be usable for 3 days, and then had to be discarded. Other moisturizers and cleansers than the test products, topical corticosteroids, and any medication that, in the opinion of the investigators, might interfere with the assessment of the study parameters were prohibited. Usual shampoos and facial makeup were permitted.

Study parameters were evaluated at baseline and at the end of the study (day 28). Erythema, dryness/scaling, and subjective signs (burning, pruritus, and stinging) were recorded by the investigator according to a 4-point defined scale (absent, mild, moderate, severe). At the end of treatment, a global assessment of the patient evolution also was performed by the investigator, using the following 5-point scale: excellent, good, fair, unchanged, worsening. In addition, the overall tolerance of the 2 test products was assessed at the end of treatment, with the following 4-point scale: excellent, good, bad, and very bad. The patient questionnaire allowed the assessment of the cosmetic features of the 2 products. Changes from baseline of the study parameters were analyzed using the Mac Nemar test.

Results

98 patients were enrolled; 2 patients dropped out for reasons unrelated to the study treatment. Two patients were prematurely withdrawn from the study for a reason that was not judged by the investigator as related to the 2 test products. Accordingly, the population comprised 94 patients for the efficacy analysis, and 96 patients for the safety analysis. Demographic data as well as the distribution of the efficacy analysis population according to the contact allergens and the presence of erythema, dryness/scaling, and subjective signs at baseline are given in Table 1. Globally, 77% of patients displayed some signs of irritated and/or sensitive skin at baseline.

The degrees of severity of erythema, dryness/scaling, and subjective signs at baseline and end of treatment (day 28) are illustrated in Figure 1. Erythema was significantly decreased at the end of treatment, with an improvement of at least 1 grade in 60% of the patients ($P < .0001$; Fig 1A). Dryness/scaling also improved dramatically, with disappearance of this sign in 82% of the patients ($P = .0001$, Fig 1B). Similarly, a significant reduction of at least 1 grade of the subjective signs was observed in 68% of the patients ($P < .02$, Fig 1C). These results were confirmed by the overall investigator assessment, as follows: an excellent response in 57 patients (61%), a good response in 28 patients (30%), a fair change in 1 patient (1%), an unchanged status in 5 patients (5%) and a worsening in 3 patients (3%).

For the safety analysis, 2 patients experienced an exacerbation of their dermatitis. After repeated patch and challenge tests, these adverse events were considered by the investigator as not related to the test products. One patient developed during treatment a verified contact allergy to 1 ingredient (carbomer) included in the 2 test products. Another patient had an aggravated erythema after application of the cleanser, and 2 patients had a flare-up of their dermatitis, but challenge tests

\begin{table}
\centering
\caption{Demographic Data, Contact Allergens, and Distribution of Patients According to the Presence of Erythema, Dryness/Scaling and Subjective Signs in the Efficacy Analysis Population (n = 94) at Baseline}
\begin{tabular}{ll}
\hline
Age (Mean ± SEM) & 43 ± 1.5 \\
Sex (n): & \\
Male & 4 \\
Female & 90 \\
Documented Contact Allergens (n): & \\
Fragrance mix & 51 \\
Preservatives (formaldehyde, methylisothiazolinone, quaternium-15,methyldibromo glutaronitrile, phenoxyethanol, and so on) & 48 \\
Balsam of Peru & 21 \\
Wool Alcohol & 16 \\
Objective Parameters (n): & \\
Erythema & 59 \\
Dryness/scaling & 53 \\
Subjective parameters (n): & 42 \\
\hline
\end{tabular}
\end{table}

\textbf{Abbreviation: SEM, standard error of mean.}
could not be performed in these patients. Accordingly, the 4 latter adverse events were considered to be test product-related. The overall tolerance of the 2 combined products was judged by the investigator as excellent in 71 patients (74%), good in 19 patients (20%), bad in 4 patients (4%), and very bad in 2 patients (2%). Finally, the cosmetic acceptability of the test products was good, with an overall agreement in 79 patients (84%) for both products.

**Discussion**

The use of cosmetics is increasing in economically advantaged countries. Cosmetics are complex products including multiple ingredients such as preser-
vatives, perfumes, emulsifiers, and plant extracts. Their frequent use implies an enhanced risk of adverse local reactions dependent on the number and the nature of the ingredients applied. For instance, perfumes and preservatives are well known for provoking contact allergy.\textsuperscript{8} Emulsifiers induce an alteration of the barrier function, which results in enhanced penetration of associated ingredients and skin irritation.\textsuperscript{9} Other adverse reactions without necessarily objective signs of dermatitis (i.e., sensory irritation) also occur. The affected individuals explain that they experience adverse perceptions such as stinging, burning, or itching when they apply cosmetics on their faces.\textsuperscript{10} Sensory irritation might either be caused by cosmetics alone, or associated with skin disorders and environmental factors (sun, cold, pollution, and so on).\textsuperscript{5} More importantly, 25% of the patients who were allergic to cosmetics also had objective signs of skin irritation.\textsuperscript{1} This indicates that patients with history of contact allergy to cosmetics might be prone to have a more irritated and sensory irritation.\textsuperscript{3,5} Our findings support these observations, because a majority of our study population combined an history of allergic contact dermatitis with signs of chronic irritant facial erythema (63%) and dryness/scaling (56%) at baseline. Subjective signs of local intolerance also appeared to be associated, but to a lesser extent (44%).

The interpretation of our findings entails an obvious limitation. Indeed, the absence of a placebo-controlled, double-blind design, which was here technically difficult with regards to the nature of the test products (no active ingredient, no vehicle), suggests that conclusions should be drawn with caution. However, one probable explanation of the results is that the use of sterile preservative, emulsifier and perfume-free cosmetics amends damaged skin condition. Therefore, the avoidance of these ingredients appears to be possibly crucial to restore normal skin barrier function, possibly by reducing penetration of compounds with high irritant and allergenic potential. In conclusion, this pilot study suggests that patients intolerant to classic cosmetics require adequately formulated cosmetics that might assist them with improvement of their irritated and/or sensitive skin.

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