Tolerance of Fragranced and Fragrance-Free Facial Cleansers in Adults With Clinically Sensitive Skin

Zoe D. Draelos, MD; Joseph Fowler, MD; Walter G. Larsen, MD; Sidney Hornby, MS; Russel M. Walters, PhD; Yohini Appa, PhD

PRACTICE **POINTS**

- Fragranced and fragrance-free versions of a gentle foaming cleanser with hydrophobically modified polymers (HMPs) were similarly well tolerated in participants with clinically diagnosed fragrance sensitivity.
- In a large population of female participants with sensitive skin, the fragranced gentle foaming cleanser with HMPs was as effective as a leading dermatologist-recommended, fragrance-free, gentle, nonfoaming cleanser.
- The gentle, HMP-containing, foaming cleanser with a fragrance offers a new cleansing option for adults with sensitive skin who may prefer to use a fragranced and foaming product.

Although mild, fragrance-free, nonfoaming cleansers generally are recommended for individuals with sensitive skin, many consumers choose fragranced foaming cleansers. The addition of hydrophobically modified polymers (HMPs) to mild facial cleansers has been shown to improve product tolerability in individuals with sensitive skin while facilitating foaming. The objective of the 2 studies reported here was to assess the tolerability of a mild, HMP-containing, foaming facial cleanser with a fragrance that was free of common allergens and irritating essential oils in patients with sensitive skin. In the first study, 8 participants with clinically diagnosed fragrance sensitivity used a gentle foaming HMP-containing facial cleanser with or without fragrance for 3 weeks. Both cleansers improved global disease severity, irritation, and erythema with similar cleansing effectiveness. The second study was a 3-week, prospective, double-blind, randomized, 2-center study of 153 participants with clinically diagnosed sensitive skin. In this study, the fragranced gentle foaming cleanser with HMP was as well tolerated as a benchmark gentle, fragrance-free, nonfoaming cleanser. Itching, irritation, and desquamation were most improved from baseline in both groups. The participant-rated effectiveness of the cleanser with HMP was similar or better than the benchmark cleanser after 3 weeks of use. In conclusion, the gentle facial cleanser with HMPs and a fragrance offers a new option for adults with sensitive skin who may prefer, and commonly use, a fragranced and foaming product.

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Dr. Draelos is from Dermatology Consulting Services, High Point, North Carolina. Dr. Fowler is from Dermatology Specialists, PSC, Louisville, Kentucky. Dr. Larsen is from Portland Dermatology Clinic, Oregon. Ms. Hornby, Dr. Walters, and Dr. Appa are from Johnson & Johnson Consumer Inc, Skillman, New Jersey.

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Correspondence: Sidney Hornby, MS, Johnson & Johnson Consumer Inc, 199 Grandview Rd, Skillman, NJ 08558 (shornby@its.jnj.com).

For thousands of years, humans have used fragrances to change or affect their mood and enhance an "aura of beauty."[1] Fragrance is a primary driver in consumer choice and purchasing decisions, especially when considering personal care products.[2] In addition to fragrance, consumers choose cleanser products based on compatibility with skin, cleansing properties, and sensory attributes such as viscosity and foaming.[3,4] However, fragrance sensitivity is among the most common causes of allergic contact dermatitis from cosmetics and personal care products,[5] and estimates of the prevalence of fragrance sensitivity range from 1.8% to 4.2%.[6]

A panel of 26 fragrance ingredients that frequently induce contact dermatitis in sensitive individuals has been identified.[7] Since 2003, regulatory authorities in the European Union require these compounds to be listed on the labels of consumer products to protect presensitized consumers.[7,8] However, manufacturers of cosmetics are not required to specify allergenic fragrance ingredients outside the European Union, and therefore it is difficult for consumers in the United States to avoid fragrance allergens.

Creation of a fragranced product for fragrance-sensitive individuals begins with careful selection of ingredients and extensive formulation testing and evaluation. This process usually is followed by testing in normal individuals to confirm that the fragranced product is well accepted and then evaluation is done in clinically confirmed fragrance-sensitive patients and those with a compromised skin barrier from atopic dermatitis, rosacea, or eczema.

Sensitive skin may be due to increased immune responsiveness, altered neurosensory input, and/or decreased skin barrier function, and presents a complex challenge for dermatologists.[9] Subjective perceptions of sensitive skin include stinging, burning, pruritus, and tightness following product application. Clinically sensitive skin is defined by the presence of erythema, stratum corneum desquamation, papules, pustules, wheals, vesicles, bullae, and/or erosions.[9] Although some of these symptoms may be observed immediately, others may be delayed by minutes, hours, or days following the use of an irritating product. Patients who present with subjective symptoms of sensitive skin may or may not show objective symptoms.

Gentle skin cleansing is particularly important for patients with compromised skin barrier integrity, such as those with acne, atopic dermatitis, eczema, or rosacea. Standard alkaline surfactants in skin cleansers help to remove dirt and oily soil and produce lather but can impair the skin barrier function and facilitate development of irritation.[10-13] The tolerability of a cleanser is influenced by its pH, the type and amount of surfactant ingredients, the presence of moisturizing agents, and the amount of residue left on the skin after washing.[11,12] Mild cleansers have been developed for patients with sensitive skin conditions and are expected to provide cleansing benefits without negatively affecting the hydration and viscoelastic properties of skin.[11] Mild cleansers interact minimally with skin proteins and lipids because they usually contain nonionic synthetic surfactant mixtures; they also have a pH value close to the slightly acidic pH of normal skin, contain moisturizing agents,[11,14,15] and usually produce less foam.[10,16] In patients with sensitive skin, mild and fragrance-free cleansers often are recommended.[17,18] Because fragrances often affect consumers' perception of product performance[19] and enhance the cleaning experience of the user, consumer compliance with clinical recommendations to use fragrance-free cleansers often is poor.

Low-molecular-weight, water-soluble, hydrophobically modified polymers (HMPs) have been used to create gentle foaming cleansers with reduced impact on the skin barrier.[12,16,20] In the presence of HMPs, surfactants assemble into larger, more stable polymer-surfactant structures that are less likely to penetrate the skin.[16] Hydrophobically modified polymers can potentially reduce skin irritation by lowering the concentration of free micelles in solution. Additionally, both HMPs and HMP-surfactant complexes stabilize newly formed air-water interfaces, leading to thicker, denser, and longer-lasting foams.[16] A gentle, fragrance-free, foaming liquid facial test cleanser with HMPs has been shown to be well tolerated in women with sensitive skin.[20]

This report describes 2 studies of a new mild, HMP-containing, foaming facial cleanser with a fragrance that was free of common allergens and irritating essential oils in patients with sensitive skin. Study 1 was designed to evaluate the tolerance and acceptability of 2 variations of the HMP-containing cleanser—one fragrance free and the other with fragrance—in a small sample of healthy adults with clinically diagnosed fragrance-sensitive skin. Study 2 was a large, 2-center study of the tolerability and effectiveness of the fragranced HMP-containing cleanser compared with a benchmark dermatologist-recommended, gentle, fragrance-free, nonfoaming cleanser in women with clinically diagnosed sensitive skin.

Methods

Study 1 Design—The primary objective of this prospective, randomized, single-center, crossover study was to evaluate the tolerability of fragranced versus fragrance-free formulations of a mild, HMP-containing liquid facial cleanser in healthy male and female adults with Fitzpatrick skin types I to IV who were clinically diagnosed as having fragrance sensitivity. Fragrance sensitivity was defined as a history of positive reactions

to a fragrance mixture of 8 components (fragrance mixture I) and/or a fragrance mixture of 14 fragrances (fragrance mixture II) that included balsam of Peru (*Myroxylon pereirae*), geraniol, jasmine oil, and oakmoss.[5] All participants provided written informed consent prior to enrolling in the study, and both the study protocol and informed consent agreement were approved by an institutional review board.

Participants were instructed to wash their face twice daily, noting the time of cleansing and providing commentary about their cleansing experience in a diary. The liquid facial test cleansers contained the HMP potassium acrylates copolymer, glycerin, and a surfactant system primarily containing cocamidopropyl betaine and lauryl glucoside prepared without added fragrance (as previously described[20]) or with a fragrance free of common allergens and irritating essential oils.

Half of the participants used the fragranced test cleanser and half used the fragrance-free test cleanser for a 3-week treatment period (weeks 1–3). Each treatment group subsequently switched to the other test cleanser for a second 3-week treatment period (weeks 4–6). Clinicians assessed global disease severity (an overall assessment of skin condition that was independent of other evaluation criteria), itching/burning, visible irritation, erythema, and desquamation at weekly time points throughout the study and graded each clinical tolerance attribute on a 5-point scale (0=none; 1=minimal; 2=mild; 3=moderate; 4=severe). Ordinal scores at baseline and at weeks 1 and 3 were used to calculate change from baseline.

A 7-item questionnaire also was administered to participants at each visit to assess skin condition, smoothness, softness, cleanliness, radiance, satisfaction with cleansing experience, and lathering. Each item was scored on a 5-point ordinal scale (0=none; 1=minimal; 2=good; 3=excellent; 4=superior). The scores for all parameters were statistically compared with baseline values using a paired *t* test with a significance level of $P \leq .05$.

Study 2 Design—This prospective, 3-week, double-blind, randomized, comparative, 2-center study to evaluate the tolerability of the fragranced, HMP-containing test cleanser from study 1 versus a benchmark gentle, fragrance-free, nonfoaming cleanser in a large population of otherwise healthy females who had been clinically diagnosed with sensitive skin (not limited to fragrance sensitivity). The study sponsor provided blinded test materials, and neither the examiner nor the recorder knew which investigational product was administered to which participants. Additionally, personnel who dispensed the test cleansers to participants or supervised their use did not participate in the evaluation to minimize potential bias. All participants provided written informed consent prior to enrolling in the study, and the study protocol and informed consent agreement were approved by an institutional review board.

Participants included women aged 18 to 65 years with mild to moderate clinical symptoms of atopic dermatitis, eczema, acne, or rosacea within the 90 days prior to the study period. They were randomized into 2 balanced treatment groups: group 1 received the mild, fragranced, HMP-containing liquid facial cleanser from study 1 and group 2 received a leading, dermatologist-recommended, gentle, fragrance-free, nonfoaming cleanser. Each treatment group used the test cleansers at least once daily for 3 weeks.

Clinicians evaluated facial skin for softness and smoothness, global disease severity (rated visually by the investigator as an overall assessment of skin condition that was independent of other evaluation criteria [as previously described[20]]), itching, irritation, erythema, and desquamation at baseline and at weeks 1 and 3. The effectiveness of each product to remove facial dirt, cosmetics, and sebum also was assessed; clinical grading was performed as described for study 1 using the same grading scale as in study 1 and percentage change from baseline (improvement) was calculated.

The study also included a self-assessment of skin irritation in which participants responded yes or no to the following question: Have you experienced irritation using this product? Participants also completed a questionnaire in which they were asked to select the most appropriate answer—agree strongly, agree somewhat, neither, disagree somewhat, and disagree strongly—to the following statements: the cleanser leaves no residue; cleanses deep to remove dirt, oil, and makeup; the cleanser effectively removes makeup; the cleanser leaves my skin smooth; the cleanser leaves my skin soft; the cleanser rinses completely clean; cleanser does not over dry my skin; and my skin is completely clean.

The statistical analysis was performed using a nonparametric, 2-tailed, paired Mann-Whitney *U* test, and statistical significance was set at $P \leq .05$.

Results

Study 1 Assessment—Eight female participants aged 22 to 60 years with clinically diagnosed fragrance sensitivity were enrolled in the study. After 3 weeks of use, clinician assessment showed that both the fragranced and fragrance-free test cleansers with HMPs improved several skin tolerance attributes, including global disease severity, irritation, and erythema (Figure 1). No notable differences in skin tolerance attributes were reported in the fragranced versus the fragrance-free formulations.

There were no reported differences in participant-reported cleanser effectiveness for the fragranced versus the fragrance-free cleanser either at baseline or weeks 1 or 3 (data not shown).

Study 2 Assessment—A total of 153 women aged 25 to 54 years with sensitive skin were enrolled in the study. Seventy-three participants were randomized to receive the fragranced test cleanser and 80 were randomized to receive the benchmark fragrance-free cleanser.

At week 3, there were no differences between the fragranced test cleanser and the benchmark cleanser in any of the clinician-assessed skin parameters (Figure 2). Of the parameters assessed, itching, irritation, and desquamation were the most improved from baseline in both treatment groups. Similar results were observed at week 1 (data not shown).

There were no apparent differences in subjective self-assessment of skin irritation between the test and benchmark cleansers at week 1 (15.7% vs 13.0%) or week 3 (24.3% vs 12.3%). When asked to respond to a series of 8 statements related to cleanser effectiveness, most participants either agreed strongly or agreed somewhat with the statements (Figure 3). There were no statistically significant differences between treatment groups, and responses to all statements indicated that participants were as satisfied with the test cleanser as they were with the benchmark cleanser.

Comment

Consumers value cleansing, fragrance, viscosity, and foaming attributes in skin care products very highly.[3,4,10] Fragrances are added to personal care products to positively affect consumers' perception of product performance and to add emotional benefits by implying social or economic prestige to the use of a product.[19] In one study, shampoo formulations that varied only in the added fragrance received different consumer evaluations for cleansing effectiveness and foaming.[4]

Although mild nonfoaming cleansers can be effective, adult consumers generally use cleansers that foam[10,16] and often judge the performance of a cleansing product based on its foaming properties.[3,10] Mild cleansers with HMPs maintain the ability to foam while also reducing the likelihood of skin irritation.[16] One study showed that a mild, fragrance-free, foaming cleanser containing HMPs was as effective, well tolerated, and nonirritating in patients with sensitive skin as a benchmark nonfoaming gentle cleanser.[20]

Results from study 1 presented here show that fragranced and fragrance-free formulations of a mild, HMP-containing cleanser are equally efficacious and well tolerated in a small sample of participants with clinically diagnosed fragrance sensitivity. Skin tolerance attributes improved with both cleansers over a 3-week period, particularly global disease severity, irritation, and erythema. These results suggest that a fragrance free of common allergens and irritating essential oils could be introduced into a mild foaming cleanser

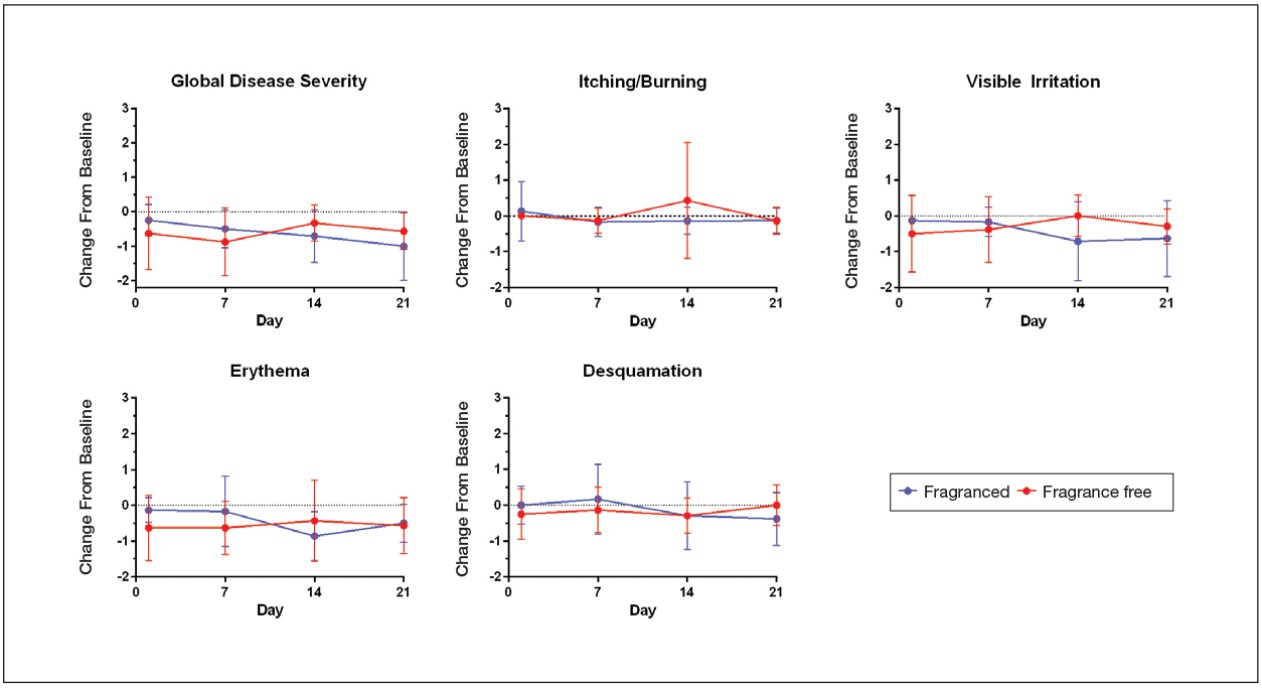

Figure 1. Investigator evaluation of skin tolerance to fragranced and fragrance-free cleansers containing hydrophobically modified polymers after 3 weeks of treatment. Mean reduction from pretreatment baseline score signifies improvement. Error bars indicate standard deviation. Tolerance attributes were scored on a 5-point scale (0=none; 1=minimal; 2=mild; 3=moderate; 4=severe).

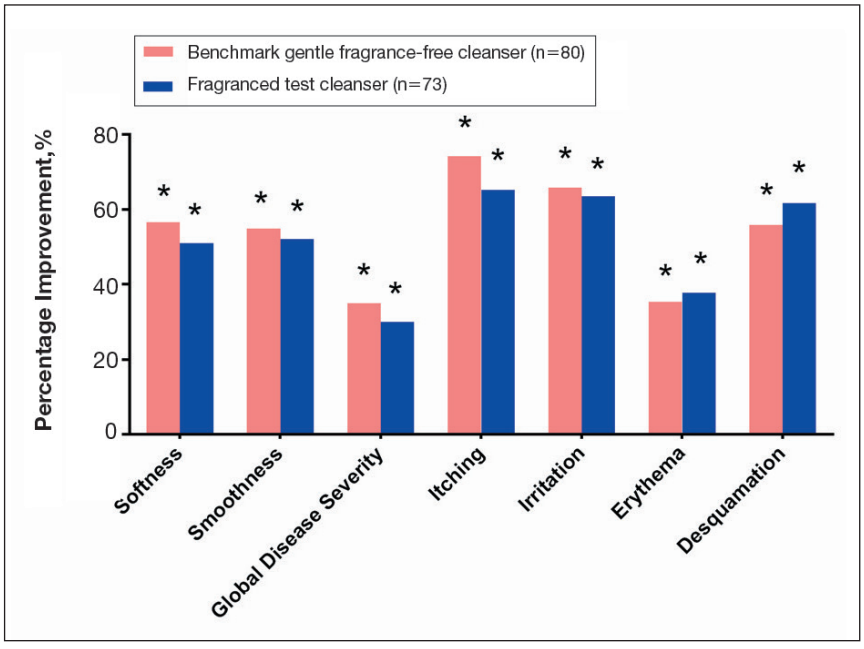

Figure 2. Percentage improvement from baseline based on clinician assessment of skin parameters after 3 weeks of using either the fragranced test cleanser or the benchmark gentle fragrance-free cleanser. Asterisk indicates $P<.001$ vs baseline.

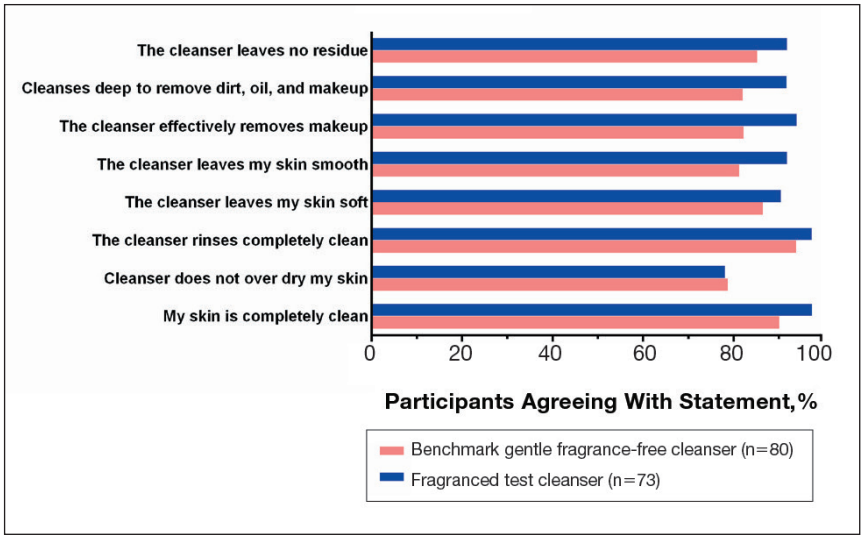

Figure 3. Self-assessment of cleanser effectiveness after 3 weeks. Participants selected from the following responses: agree strongly, agree somewhat, neither, disagree somewhat, and disagree strongly. Percentage of participants agreeing with statement indicates those who responded agree strongly and agree somewhat.

containing HMPs without causing adverse reactions, even in patients who are fragrance sensitive.

Although the populations of studies 1 and 2 both included female participants with sensitive skin, they were not identical. While study 1 assessed a limited number of participants with clinically diagnosed fragrance sensitivity, study 2 was larger and included a broader range of participants with clinically diagnosed skin sensitivity, which could include fragrance sensitivity. The well-chosen fragrance of the test cleanser containing HMPs was well tolerated; however, this does not imply that any other fragrances added to this cleanser formulation would be as well tolerated.

Conclusion

The current studies indicate that a gentle fragranced foaming cleanser with HMPs was well tolerated in a small population of participants with clinically diagnosed fragrance sensitivity. In a larger population of female participants with sensitive skin, the gentle fragranced foaming cleanser with HMPs was as effective as a leading dermatologist-recommended, fragrance-free, gentle, nonfoaming cleanser. The gentle, HMP-containing, foaming cleanser with a fragrance that does not contain common allergens and irritating essential oils offers a new cleansing option for adults with sensitive skin who may prefer to use a fragranced and foaming product.

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