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ORIGINAL CONTRIBUTION

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Cutaneous acceptability of a moisturizing cream in subjects with sensitive skin

Jane Snatchfold RGN

GSK Consumer Healthcare, Weybridge, Surrey, UK

Correspondence
Jane Snatchfold, CK Clinical, The Bridge Business Centre, Chesterfield, UK.
Email: jane.8.snatchfold@gsk.com

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Summary

Background: Topical cosmetic products can cause adverse reactions in some individuals, particularly those with sensitive skin who may develop irritations or allergic contact dermatitis. Evidence suggests that the frequency of self-reported sensitive skin is increasing in the general population, placing greater importance on clinical testing of topical cosmetics for potential skin reactivity.

Objectives: To confirm the cutaneous acceptability under normal conditions of use of a moisturizing cream in individuals with sensitive skin.

Methods: This was a prospective, single-center, open-label, noncomparative clinical trial conducted in female subjects aged 18-60 years with Fitzpatrick skin phototype I-IV and confirmed sensitive skin. Subjects applied the moisturizer twice daily to the body and/or face for 21 ± 2 days. Product acceptability was based on the occurrence of adverse events, investigator assessment of skin adverse reactions, and subjects' self-reported feelings of skin discomfort.

Results: Thirty-five female subjects initiated and completed the study; mean age was 43.2 years and most (89%) had Fitzpatrick skin phototype I-III. No adverse events or skin adverse reactions of erythema, edema, or skin desquamation were observed. There were no participant reports of skin dryness, prickling, or stinging on any occasion. One subject reported a single event of mild itching, which was considered by the investigator as probably not related to study product.

Conclusions: These findings suggest that the moisturizing cream was well tolerated under normal conditions of use and appropriate for topical use on sensitive skin.

KEYWORDS
acceptability study, safety, sensitive skin

1 | INTRODUCTION

Topical cosmetic products may cause adverse reactions in some people. UK-based research has shown that 57% of women and 31% of men have experienced an adverse reaction to a cosmetic at some stage in their lives, with 23% of women and 14% of men reporting such a reaction in the year prior to the analysis.[1] The most common adverse reactions to cosmetics are irritation, burning sensation, pruritus, and erythema.[2]

Sensitive skin may be defined as a noninflammatory response to cosmetics, characterized by stinging, burning, or itching, without visible skin changes.[3] Skin sensitivity is often determined by a stinging test, in which lactic acid or other irritants are applied to the nasolabial fold.[3] People with sensitive skin are likely to develop allergic contact

Presentation at a scientific meeting: This work has not previously been presented in part or in full.

dermatitis or irritation to some cosmetic products.[3-5] The frequency of self-reported sensitive skin is increasing, with data from a European study[6] and a U.S. study[7] showing that 38% and 45% of subjects, respectively, described their skin as sensitive or very sensitive. It is important, therefore, that topical cosmetic products undergo clinical evaluation for their suitability of use for this population.

Accordingly, due to the potential for adverse reactions and skin sensitization, topical cosmetic products need to be clinically assessed under normal conditions of use, prior to approval. Acceptability trials aim to confirm the absence of risk of irritation/discomfort of cosmetics in real-world settings of everyday use. Clinical evaluation should include the risk of sensitization at the product application site.[8] Clinical assessments conducted in such trials allow products to be labeled "clinically tested" and "dermatologically tested." This open-label safety study was conducted to confirm the cutaneous acceptability of a moisturizing cream under normal conditions of use in individuals with sensitive skin.

2 | MATERIALS AND METHODS

2.1 | Study design and subjects

This was a prospective, single-center, open-label, noncomparative, 3-week clinical trial investigating the cutaneous acceptability of a topically applied moisturizer in subjects with sensitive skin. The overall objective was to confirm the absence of adverse reactions and feelings of cutaneous discomfort related to application of the moisturizer under normal conditions of use.

The moisturizer evaluated in this study contained the following ingredients: acetamide MEA and aqua, acrylates/C10-30 alkyl acrylate crosspolymer, betaine anhydrous, *Butyrospermum parkii*, caprylic/capric triglyceride, caprylyl glycol, ceramide 3, *Cocos nucifera*, dehydroxanthan gum, glycerol, hydrogenated phosphatidylcholine, *Olea europaea*, palmitic acid monoethanolamide, pentylene glycol, purified water, sarcosine anhydrous, sodium carbomer, and squalane.

The study was conducted at LAL Clínica Pesquisa e Desenvolvimento Ltda, Brazil, between July and August 2015, in accordance with the Declaration of Helsinki, international guidelines for Good Clinical Practice, and the National Health Council (CNS) Ordinance 466/12. The study was approved by the Research Ethics Committee of Faculdade de Medicina de Jundiaí, Brazil. All subjects provided written informed consent.

Eligible participants underwent dermatological assessments at screening. Female subjects aged 18-60 years with a skin phototype classification of I-IV according to the Fitzpatrick scale[9] (Table 1), and who were confirmed to have sensitive skin based on a positive response (prickling, itching, burning, stinging, and/or numbness with an intensity score ≥2) to the lactic acid stinging test[10] at the screening visit, were included. Key exclusion criteria were as follows: the presence of skin marks or active dermatoses in the areas of product application; a history of allergic reactions to topical medications or cosmetics; intense sun exposure or use of tanning equipment within 15 days prior to enrollment or during the study; use of esthetic and/or dermatological treatments in the areas of study product application within 21 days prior to screening or during the study; and therapeutic, topical, or systemic use of immunosuppressants, antihistamines, nonsteroidal anti-inflammatory drugs, or corticosteroids within 14 days (30 days for systemic corticosteroids) prior to screening.

TABLE 1 Skin phototype classification according to the Fitzpatrick scale[9]

Phototype	Response to sun exposure	Typical minimal erythema dose (mJ/cm^2 eff)[a]	Pigmentation scale[b]
I	Always burns, never tans	15-30	35-50
II	Always burns, tans minimally	25-35	51-60
III	Burns moderately, tans gradually	30-50	61-75
IV	Burns minimally, tans well	45-60	76-85
V	Rarely burns, tans intensely	60-100	86-100
VI	Never burns, deeply pigmented skin	100-120	101-127

[a]Dose of UVA and UVB radiation.[12]
[b]As measured using a DermaTone Skin Analyzer™.[13]

2.2 | Study procedures and assessments

The study comprised 2 scheduled clinic visits. At the screening/enrollment visit (Visit 1; Day 1), participants were instructed in the use of the study product by clinical staff and were supplied with a sufficient quantity to enable self-application at home throughout the duration of the study. Topical application of the study product was performed to the body, including the face, at the discretion of individual participants (reflecting normal use), twice daily for 21 ± 2 days. Throughout this period, participants completed a treatment diary to record daily use of the study product and occurrence of any skin discomfort/sensations. During the study, participants were asked not to apply any product in the experimental area that could interfere with study assessments; change their other cosmetic habits (including hygiene products); perform skin cleansing, exfoliation, or other esthetic treatments in the application area; expose themselves to excessive sunlight/artificial tanning beds; change their eating habits; or change hormonal treatments.

At the end of the treatment period, participants returned to the clinic (Visit 2; Day 21 ± 2) for final dermatological evaluation and assessment of treatment compliance. Cutaneous acceptability of the study product was determined by evaluation of occurrence of adverse events (local or generalized), skin adverse reactions, and sensations of skin discomfort. Adverse events were defined as any medical occurrence, regardless of causality with the study product, and included expected and unexpected symptoms, abnormal laboratory results, and/or concomitant diseases. Clinical assessment of skin adverse reactions was performed by a dermatologist and graded for severity according to a modified Draize and Kligman scale.[11]

TABLE 2 Criteria for assessment of skin adverse reactions[a]

Score	Appearance of erythema[b]	Formation of edema[b]	Skin desquamation[c]
0	None	None	None
1	Very mild erythema	Very mild edema (almost imperceptible)	Dryness
2	Well-defined erythema	Mild edema (defined area, beginning of swelling)	Thin scales
3	Moderate erythema	Moderate edema (swelling of ~1 mm)	Moderate scales
4	Severe erythema	Intense edema (growth >1 mm and beyond the application area)	Large scales

[a]The sum of the scores for each category was used to classify the reaction intensity as follows: 0-2, No reaction/equivocal; 3-4, Mild reaction; 5-8, Moderate reaction; >8, Intense reaction.
[b]Scale according to Draize et al.[11]
[c]Adapted from the Kligman scale that scores skin desquamation on a scale of 1-3.

Specifically, the area of product application was evaluated for the appearance of erythema, edema, and skin desquamation, and scored on a scale ranging from 0 to 4 (Table 2). The intensity of the reaction was calculated as the sum of the scores for the individual components, classified as: 0-2, no reaction/equivocal; 3-4, mild reaction; 5-8, moderate reaction; and >8, intense reaction. Feelings of skin discomfort associated with study product use, including sensations of dryness, prickling, itching, and stinging, were self-recorded by subjects in their treatment diaries; the severity (mild or moderate/intense) and duration (≤15 or >15 minutes) of these events were noted.

2.3 | Statistical considerations

No sample size calculation was made. Thirty-five subjects were planned for inclusion to ensure that at least 30 would complete the study. For analysis of product acceptability, only data from subjects with a minimum treatment compliance of 80% (equivalent to a minimum of 30 applications of study product) were considered. All subjects with at least one application of the study product were considered for the safety analysis.

3 | RESULTS

Thirty-five female subjects underwent screening, all of whom were confirmed eligible to participate in the study. Mean age was 43.2 years (range 20-58 years). The majority of subjects (31/35, 89%) had Fitzpatrick skin phototype I-III (Type I, n = 13; Type II, n = 9; Type III, n = 9; and Type IV, n = 4). All participants completed the study per protocol and achieved the minimum compliance requirement for inclusion in the analysis of study product acceptability.

TABLE 3 Frequency of skin adverse reactions and reports of discomfort (n = 35)

	Subjects, n (%)
Reaction classification by dermatologist	
No reaction (mild, moderate or intense)	35 (100)
Equivocal	0 (0)
Reaction without causal relationship	0 (0)
Complaint of sensation by subject	
Dryness	0 (0)
Prickling	0 (0)
Stinging	0 (0)
Itching	1 (3)[a]
Other	0 (0)

[a]Itching of mild intensity reported on a single occasion following study product application.

No adverse events were reported during the study and, per dermatologist clinical evaluation, there were no recorded skin adverse reactions of erythema, edema, or skin desquamation (Table 3). None of the 35 participants reported experiencing sensations of skin dryness, prickling, or stinging on any occasion following application of the study product (Table 3). One participant reported a single experience of mild itching at the site of study product application, which occurred soon after the second application of the day and lasted for approximately 10 minutes. However, as this event was not associated with any clinically apparent skin adverse reaction, resolved spontaneously without treatment, did not interrupt product use by the subject, and did not recur, the investigator determined that the feeling was probably not related to the use of the study product and described the event as a discomfort sensation.

4 | DISCUSSION

This prospective, single-center, open-label, noncomparative clinical study, conducted in 35 adult female subjects with sensitive skin, assessed the skin acceptability of a novel moisturizing cream through evaluation of adverse reactions and cutaneous discomfort related to its application under normal conditions of use. Clinical assessments made by dermatologists identified no adverse events or skin adverse reactions of erythema, edema, or skin desquamation in any participant during the study. Furthermore, none of the participants reported experiencing sensations of skin dryness, prickling, or stinging on any occasion during the study period. There was a single event of mild itching in 1 participant; however, this was of short duration, resolved spontaneously, and was considered probably not related to study product application by the investigator.

This study achieved a high treatment compliance rate; all subjects completed the study, providing safety data based on more than 1000 separate product applications over the course of 3 weeks. The

complete absence of adverse events and skin adverse reactions during the treatment period therefore supports the tolerability of the study product in individuals with sensitive skin. Limitations of the study may include the following: the small sample size and female-only subject population, the absence of a control arm and associated treatment blinding, and the conducting of the study at a single center.

Based on the findings of this study, it was concluded that the moisturizing cream was well tolerated under normal conditions of use and is appropriate for topical use by individuals with sensitive skin.

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CONFLICT OF INTEREST

Jane Snatchfold discloses provision of independent consulting services to GlaxoSmithKline Consumer Healthcare.

ORCID

Jane Snatchfold http://orcid.org/0000-0002-3616-0159

REFERENCES

1. Willis CM, Shaw S, De Lacharriere O, et al. Sensitive skin: an epidemiological study. *Br J Dermatol*. 2001;145:258-263.
2. Lumelsky VJ, Shur MS, Wagner S. Sensitive skin. *IEEE Sensors J*. 2001;1:41-51.
3. Farage MA, Katsarou A, Maibach HI. Sensory, clinical and physiological factors in sensitive skin: a review. *Contact Dermatitis*. 2006;55:1-14.
4. De Groot AC, White IR, Flyvholm MA, Lensen G, Coenraads PJ. Formaldehyde-releasers in cosmetics: relationship to formaldehyde contact allergy. Part 1. Characterization, frequency and relevance of sensitization, and frequency of use in cosmetics. *Contact Dermatitis*. 2010;62:2-17.
5. Lundov MD, Johansen JD, Carlsen BC, Engkilde K, Menné T, Thyssen JP. Formaldehyde exposure and patterns of concomitant contact allergy to formaldehyde and formaldehyde-releasers. *Contact Dermatitis*. 2010;63:31-36.
6. Misery L, Boussetta S, Nocera T, Perez-Cullell N, Taieb C. Sensitive skin in Europe. *J Eur Acad Dermatol Venereol*. 2009;23:376-381.
7. Misery L, Sibaud V, Merial-Kieny C, Taieb C. Sensitive skin in the American population: prevalence, clinical data, and the role of the dermatologist. *Int J Dermatol*. 2011;50:961-967.
8. ANVISA (National Health Surveillance Agency). *Guide for Safety Assessment of Cosmetic Products*, 2nd edn. Brasilia, Version 2, 2012. http://portal.anvisa.gov.br/documents/106351/107910/Guia+para+Avalia%C3%A7%C3%A3o+de+Seguran%C3%A7a+de+Produtos+Cosm%C3%A9ticos/ab0c660d-3a8c-4698-853a-096501c1dc7c. Accessed 11 October 2016.
9. Fitzpatrick TB. The validity and practicality of sun-reactive skin types I through VI. *Arch Dermatol*. 1988;124:869-871.
10. Christensen M, Kligman AM. An improved procedure for conducting lactic acid stinging test on facial skin. *J Cosmet Sci*. 1996;47:1-11.
11. Draize JH, Woodard G, Calvery HO. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J Pharmacol Exp Ther*. 1944;82:377-390.
12. Pathak MA. Sunscreens and their use in the preventive treatment of sunlight-induced skin damage. *J Dermatol Surg Oncol*. 1987;13:739-750.
13. Sachdeva S. Fitzpatrick skin typing: applications in dermatology. *Indian J Dermatol Venereol Leprol*. 2009;75:93-96.

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