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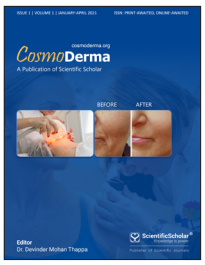

Original Article

Evaluation of skin irritation and skin sensitization potential of Venusia CeraPlus cream using human repeat insult patch test

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ABSTRACT

Objectives: This study evaluated the safety of Venusia CeraPlus Moisturizing Cream using the human repeat insult patch test (HRIPT).

Materials and Methods: A single-center, non-randomized, double-blinded, observational study was conducted from February 12 to March 27, 2024. 211 participants (aged 18–65, Fitzpatrick skin types III–V) completed the study. The HRIPT protocol included induction, rest, and challenge phases. Skin reactions were assessed using the Draize scale during induction and the International Contact Dermatitis Research Group scale during the challenge phase.

Results: The study demonstrated favorable results for Venusia CeraPlus moisturizing cream. During the induction phase, the product showed a mean cumulative irritation score of 0.37, which was well below the non-irritant threshold of 2. In the challenge phase, no participants exhibited strong positive reactions (++) at any time point. No adverse events were reported by any of the participants.

Conclusion: Venusia CeraPlus moisturizing cream demonstrated non-irritant properties after nine repeat applications and was found to be hypoallergenic in the study population.

Keywords: Allergic contact dermatitis, Human repeat insult patch test, Moisturizer, Skin Irritation

INTRODUCTION

The widespread use of moisturizers among young individuals is evident, with over 75% of the global youth population incorporating them into their daily routines.[1] This trend reflects the growing emphasis on skin health and hydration. Numerous studies highlight the important role of moisturizers in maintaining skin moisture, enhancing the skin's barrier function, and protecting against environmental stressors.[2] Moisturizers are also commonly used to manage conditions such as xerosis and atopic dermatitis.[3] However, while their benefits are well documented, research warns of potential risks with excessive use, such as increased susceptibility to food allergies.[4] This highlights the importance of mindful application and understanding individual skin needs.

Patch testing is a key method for assessing the potential of products to cause irritation or allergic reactions by applying a suspected allergen to the skin under occlusion and observing reactions. It

effectively distinguishes between allergic and irritant contact dermatitis, proving valuable in diagnosing persistent skin conditions and cutaneous adverse drug reactions. Studies highlight its utility in identifying specific allergens, such as fragrance mixtures, and its sensitivity can be enhanced with protocol modifications, especially for non-irritating products like feminine hygiene items. However, caution is needed due to the risk of false positives, particularly with rinse-off products.

Considering the critical role moisturizers play in skin health, it is imperative to evaluate the safety and efficacy of new formulations. Our study focuses on the Venusia CeraPlus Cream, specifically assessing its potential for skin irritation and sensitization using the human repeat insult patch test (HRIPT).

MATERIALS AND METHODS

This was a single-center, non-randomized, double-blinded, observational study to assess the skin irritation and skin sensitization potential of Venusia CeraPlus moisturizing cream using the HRIPT technique. The study was carried out under the supervision of the principal investigator/dermatologist. The study was conducted from February 12, 2024, to March 27, 2024. The study protocol was approved by an Independent Ethics Committee (ECR/245/Indt/MH/2015/RR-22). The study was conducted in compliance with the Declaration of Helsinki, Good Clinical Practices, and ICMR guidelines concerning medical research in humans. Potential risks and benefits were explained to the participants, and informed consent was obtained from all participants before entry into the study.

Study population

Participants were recruited from the dermatology outpatient department following a thorough screening by the principal investigator. To ensure the inclusion of individuals with normal, healthy skin, a comprehensive dermatological examination was performed. The test area (upper back) was assessed for any conditions such as dermatitis, eczema, scars, or infections that might influence the study results. For participants with sensitive skin, the lactic acid sting test [Appendix A] was used to confirm sensitivity without the presence of active dermatological conditions. The study population consists of 200 complete cases, as determined by the sample size guidelines outlined in IS 4011:2018 (Third Revision, July 2018).

Inclusion criteria

- Men and women aged 18–65 years with apparently healthy skin on the test area and Fitzpatrick skin types III–V.
- At least 50 participants with sensitive skin, as determined by the lactic acid sting test were included.
- Participants agreed to avoid water contact (such as swimming), excessive sweating activities (like exercise and sauna), and intense ultraviolet exposure on the test site during the study.
- In addition, they should be able to read and write in English, Hindi, or the local language and possess valid proof of identity and age.

Exclusion criteria

- Pregnancy, lactation, scars, tattoos, excessive terminal hair on the test area, previous hypersensitivity to cosmetic products, chronic illnesses that may influence the study outcome, current or recent (within one month) medical treatments that may interfere with the study, and participation in other clinical trials.

Study intervention and follow-up

The test product, Venusia CeraPlus Moisturizing Cream (Batch No. EOCMC0123–22; contains purified water, propylene glycol, glycerin, emulsifying wax, cyclomethicone, and a blend of natural butter and aloe), and negative control of 0.9% isotonic saline solution (Batch No. 82RL404101) were applied occlusively to the backs of healthy participants.

The study was conducted in three main phases: Induction, rest, and challenge. The induction phase, lasting three weeks, consisted of nine cycles of patch application and removal. On day 1 (Visit 1), patches containing either 0.04 g of the cream or 0.04 mL of saline solution on filter paper were applied occlusively to the participants' backs. These patches were removed the following day (Visit 2), and on the 3rd day (Visit 3), the patch areas were graded and scored before new patches were applied. This cycle was repeated throughout the induction phase, with patch removals occurring on alternate visits (4, 6, 9, 11, 13, 16, 18, and 20) and grading, scoring, and new patch applications on the subsequent visits (5, 7, 10, 12, 14, 17, and 19). The final grading and scoring of the induction phase took place on Visit 21.

Following the induction phase, participants entered a 14-day rest period. This break applied to both Batch I and Batch II of the study. After the rest period, the challenge phase began. On Visit 22, patches were applied to naïve sites adjacent to the original induction sites. These patches were removed after 24 h on Visit 23. Scoring was then conducted at 48 h (Visit 24), 72 h (Visit 25), and 96 h (Visit 26) post-application to assess any delayed reactions.

Throughout the entire study, clinical research associates, who were trained by the Principal Investigator, were responsible for weighing and applying the products. They also provided crucial support by counseling participants on how to follow the protocol

procedures during their site visits. Safety measurements were consistently assessed according to a predetermined schedule outlined [Appendix B, Tables S1 and S2].

The study concluded with a follow-up phase. Participants who showed any reactions during the challenge phase were followed up after one week. This follow-up was crucial to confirm their recovery and ensure that all reactions had completely subsided.

Scoring criteria

In the induction phase, scoring of the test area was done using the Draize scale, which evaluates erythema/dryness/wrinkles and edema on separate 0–4 scales.[5] In the Challenge Phase, reactions were scored using the international Contact Dermatitis Research Group scale, which uses symbols to denote reaction severity from no reaction (-) to extremely positive (+++)[6] [Appendix B, Tables S3 and S4].

Evaluation

Data from participants were analyzed for both the induction phase and the challenge phase.

RESULTS

Out of 220 participants recruited for the study, 211 successfully completed both the induction and challenge phases, resulting in 9 dropouts. The specific participant numbers and reasons for these dropouts were documented, ensuring that any factors influencing their withdrawal were noted [Table 1].

Participant demographics

211 completed the study (19 males and 192 females). The mean age was 37.09 years (range: 18–63 years). 59 participants had sensitive skin, whereas 152 had normal skin [Table 2].

Product assessment criteria

During the induction phase, Venusia CeraPlus moisturizing cream demonstrated a mean cumulative irritation score of 0.37, which fell below the threshold of 2, indicating it was non-irritant. The negative control (0.9% isotonic saline) had a lower mean cumulative score of 0.06 [Table 3]. In the challenge phase, none of the participants showed any strong positive reactions (++) at any time point for the test product. The negative control showed a similar trend of decreasing reactions over time, with 204, 209, and 210 participants showing no reactions at 48, 72, and 96 h respectively, and the number of doubtful reactions decreasing from 7 to 1 over the same period [Table 4].

Table 1: Participant numbers and reasons for dropout.

Participant number	Reason for Dropout	Participant number	Reason for Dropout
Batch I		Batch II	
A56	Lost to follow up	Z100	Lost to follow-up
A72	Lost to follow-up	Z108	Lost to follow-up
A73	Lost to follow-up	Z111	Lost to follow-up
A80	Lost to follow-up	Z115	Lost to follow-up
		Z129	Lost to follow-up

Table 2: Demographic and other baseline characteristics.

Total number of cases (*n*)	**211**
Age (years)	
Mean	37.09
SD	10.01
Range	18–63 years
Gender	
Males	19
Females	192
Skin	
Sensitive Skin	59
Normal Skin	152

SD: Standard deviation

Table 3: Scores for the induction phase for test product and saline.

Product	Mean cumulative scores *n*=211
Venusia CeraPlus Moisturizing Cream	0.37
0.9% Isotonic saline solution	0.06

n: Total number of cases

Adverse events

No adverse events were reported during the study.

DISCUSSION

The HRIPT for Venusia CeraPlus moisturizing cream in our study population showed non-irritant after nine repeat applications and was hypoallergenic.

In this study, we employed the HRIPT, which is widely regarded as the most reliable method for obtaining definitive human data on skin reactions. Studies demonstrate its sensitivity, with repeated exposure to irritants such as sodium lauryl sulfate leading to heightened skin reactions.[7,8] The HRIPT has also been useful in comparing barrier creams, showing significant differences in irritation levels.[9] Standardized protocols ensure reliable results across various settings, and the 4-h patch test has emerged as a reliable alternative to animal testing.[10]

Table 4: Scores for the challenge phase for the test product and saline.

	48 h (*n*=211)	72 h (*n*=211)	96 h (*n*=211)
0.9% Isotonic saline solution	204 participants did not react (-) 7 participants had doubtful reactions (?) None of the participants had any weak or strong positive reactions.	209 participants did not react (-) 2 participants had doubtful reactions (?). None of the participants had any weak or strong positive reactions.	210 participants did not react (-). 1 participant had a doubtful reaction (?). None of the participants had any weak or strong positive reactions.
Venusia CeraPlus Moisturizing Cream	185 participants did not react (-) 25 participants had doubtful reactions (?) 1 participant had a weak positive reaction (+) None of the participants had any strong positive reactions.	198 participants did not react (-) 13 participants had doubtful reactions (?) None of the participants had any weak or strong positive reactions.	209 participants did not react (-) 2 participants had doubtful reactions (?). None of the participants had any weak or strong positive reactions.

n: Total number of cases.

The findings from this study demonstrated that Venusia CeraPlus moisturizing cream did not elicit any adverse events when tested using the HRIPT. These results are consistent with previous research. A similar study on Venusia Max lotion (poly alkyl methacrylate free), where HRIPT similarly revealed no irritant or allergenic reactions.[1] A related study by Nisbet also evaluated the safety of a lamellar moisturizer, comparing it to a saline control.[11] Out of 233 participants, 214 completed the study, and 99.6% of participants had negative patch test results, further supporting the minimal allergenic risk associated with moisturizers.

Limitations

Limitations of the study include a relatively small sample size and the study being conducted at a single center, which may limit the generalizability of the findings. In addition, the exclusion of individuals with varying degrees of sensitivity could affect the results, and the reliance on subjective scoring systems may introduce variability in assessment outcomes.

CONCLUSION

The findings from this study indicate that Venusia CeraPlus moisturizing cream is a safe and well-tolerated option for individuals with sensitive skin, demonstrating low irritation and sensitization potential. The absence of adverse events and the high percentage of participants exhibiting no reactions highlight its suitability for this demographic. Future research should consider larger, multicenter trials to further validate these results and explore long-term effects, thereby enhancing the understanding of the product's efficacy in diverse populations.

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Ethical approval

Institutional Review Board (IRB) approval was obtained by Claims Independent EC for the study (ECR/245/Indt/MH/2015/RR-22), along with the clinical trial registration number CTRI/2024/02/062234.

Declaration of participant consent

The authors certify that they have obtained all appropriate participant consent.

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Conflicts of interest

All authors, Dr. Biswajit Aich, Preeti Kumbhar, Dr. Snehal Muchhala, Dr. Arti Sanghavi, Dr. Sagar Katare, and Dr. Bhavesh Kotak are employees of Dr. Reddy's Laboratories Ltd.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Gala MY, Muchhala SS, Charugulla SN, Rathod R, Mane A, Pandit S, *et al*. Evaluation of skin irritation and skin sensitization potential of Venusia max lotion (paraben-free, alcohol-free, mineral oil-free, animal origin free) using human repeat insult patch test. Int J Res 2022;8:26.
2. Bonté F. Skin moisturization mechanisms: New data. Ann Pharm Fr 2011;69:135-41.
3. Lynde CW. Moisturizers: What they are and how they work.

Skin Therapy Lett 2001;6:3-5.
4. Perkin MR, Logan K, Marrs T, Radulovic S, Craven J, Boyle RJ, *et al*. Association of frequent moisturizer use in early infancy with the development of food allergy. J Allergy Clin Immunol 2021;147:967-76.e1.
5. Farage MA, Maibach HI, Andersen KE, Lachapelle JM, Kern P, Ryan C, *et al*. Historical perspective on the use of visual grading scales in evaluating skin irritation and sensitization. Contact Dermatitis 2011;65:65-75.
6. Johansen JD, Aalto-Korte K, Agner T, Andersen KE, Bircher A, Bruze M, *et al*. European Society of Contact Dermatitis guideline for diagnostic patch testing-recommendations on best practice. Contact Dermatitis 2015;73:195-221.
7. Frosch PJ, Kurte A, Pilz B. Efficacy of skin barrier creams: (III). The repetitive irritation test (RIT) in humans. Contact Dermatitis 1993;29:113-8.
8. Freeman S, Maibach H. Study of irritant contact dermatitis produced by repeat patch test with sodium lauryl sulfate and assessed by visual methods, transepidermal water loss, and laser Doppler velocimetry. J Am Acad Dermatol 1988;19:496-502.
9. Schnetz E, Diepgen T, Elsner P, Frosch P, Klotz A, Kresken J, *et al*. Multicentre study for the development of an *in vivo* model to evaluate the influence of topical formulations on irritation. Contact Dermatitis 2000;42:336-43.
10. Robinson MK, McFadden JP, Basketter DA. Validity and ethics of the human 4-h patch test as an alternative method to assess acute skin irritation potential. Contact Dermatitis 2001;45:1-12.
11. Nisbet SJ. Absence of human skin irritation and allergenic potential after repeated patch applications of a lamellar moisturizer. J Cosmet Dermatol 2019;18:377-82.

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