



Original Article

Evaluation of hypoallergenic and skin irritation potential of Venusia Ureka cream using human repeat insult patch test

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ABSTRACT

Objectives: This study evaluated the skin irritation and sensitization potential (allergenicity) of Venusia Ureka Cream™ (Dr. Reddy's Laboratories Ltd., Hyderabad, India), using the Human Repeat Insult Patch Test (HRIPT) technique.

Materials and Methods: This single-center, blinded, placebo/vehicle-controlled study evaluated Venusia Ureka Cream™ using HRIPT on adult men and women. Approximately 0.04 g of the cream and 0.04 mL of 0.9% isotonic saline (negative control) were applied occlusively to the back of participants using patch chambers. The study comprised three phases: The induction phase, where nine 24-h patches were applied over 3 weeks and scored using the Draize scale; a rest phase with no patch applications; and a challenge phase, involving one 24-h patch applied to naïve sites, scored at 48, 72, and 96 h using the International Contact Dermatitis Research Group scale.

Results: The study included 220 participants, with 217 completing it (142 with normal skin and 75 with sensitive skin, based on the lactic acid sting test). Venusia Ureka Cream™ demonstrated no irritation/hypersensitivity reactions after nine consecutive applications. Both normal and sensitive skin groups showed no adverse reactions.

Conclusion: Venusia Ureka Cream™ demonstrated non-irritant properties and was found to be hypoallergenic in the study population. The cream was well-tolerated by participants with both normal and sensitive skin.

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

INTRODUCTION

The skin, as the body's largest organ, plays a key role in overall health, largely due to the stratum corneum (SC) layer, which is vital for retaining moisture and providing a protective barrier against chemical, microbial, and physical stressors.^[1] This layer, along with its lipid coating, acts as a natural moisturizer, but when skin water content drops below 10%, dryness and flakiness become evident.^[2] Skin dryness often increases with age, impacting keratinization and lipid levels in the SC, though factors such as body size, gender, climate, ultraviolet (UV) exposure, pollution, and daily cycles also significantly affect moisture levels. Globally, nearly 75% of young individuals apply moisturizer creams daily.^[3] Ideal moisturizers meet four essential needs: They soften and smooth the skin, enhance hydration, improve skin appearance, and deliver beneficial components to the skin's surface. Although various moisturizers provide these effects, the best formulations offer prolonged benefits.

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Moisturizers are typically categorized based on their action as occlusives, humectants, emollients, or protein rejuvenators, with many commercial products combining these classes for optimal outcomes. Yet, increasing skin moisture levels to promote healthy, smooth skin remains a significant challenge in the cosmetic and pharmaceutical industries. Many products marketed as dry skin treatments often come with undesirable side effects.^[3]

Venusia Ureka offers an advanced formula with triple benefits of hydration, exfoliation, and itch relief. With urea, a clinically validated moisturizer for exfoliation and skin repair, alongside allantoin, phytosqualan, and shea butter, Venusia Ureka enhances hydration through a combination of ingredients, including purified water, propylene glycol, urea, cetanol, phytosqualan, sodium lactate, medium-chain triglycerides, isopropyl palmitate, shea butter, glyceryl stearate, polyethylene glycol-100 stearate, polyacrylamide (and) C13-14 isoparaffin (and) laureth-7, lactic acid, phenoxyethanol-ethylhexylglycerin, pramoxine hydrochloride, sorbitan monostearate, trolamine, allantoin, fragrance, butylated hydroxytoluene, and disodium edetate.

Due to the potential for skin irritants and allergic reactions with cosmetics, allergenicity testing is critical. Standard human tests, such as the primary irritation patch test and the human repeat insult patch test (HRIPT), are employed to assess skin irritation and sensitization potential. These tests align with the European Society of Contact Dermatitis guidelines, which emphasize patch testing for identifying type IV hypersensitivity reactions, the primary cause of contact allergies.^[4] This study evaluated the skin irritation and sensitization potential of Venusia Ureka Cream™, using the HRIPT technique.

MATERIALS AND METHODS

Study design

This was a single-center, non-randomized, interventional study conducted to evaluate the skin irritation and sensitization potential (allergenicity) of Venusia Ureka Cream™ (Dr. Reddy's Laboratories Ltd., Hyderabad, India) using the Human HRIPT technique. The study was carried out at C.L.A.I.M.S. Pvt. Ltd., Andheri, Mumbai, under the Principal Investigator's (Dermatologist) supervision. The study was conducted in compliance with the principles of the Declaration of Helsinki, Good Clinical Practice (GCP) guidelines (IS 4011:2018), New Drugs and Clinical Trials Rules, 2019, and Indian Council of Medical Research (ICMR) guidelines concerning medical research in human subjects. The study protocol was reviewed and approved by the Independent Ethics Committee (ECR/245/Indt/MH/2015/RR-22), and written informed consent was obtained from all participants before study enrolment. The study was conducted in compliance with the Protocol, Declaration of

Helsinki, GCPs BIS guidelines (IS 4011:2018 Third Revision, July 2018 guidelines), New Drugs and Clinical Trials Rules, 2019, and ICMR guidelines concerning medical research in humans.

Study population

This study included 220 participants (men and women) aged 18–65 years, with 50 participants having sensitive skin as determined by the lactic acid sting test. Participants with apparently healthy skin on the test area and Fitzpatrick skin types III to V were recruited. At least participants were required to refrain from intense UV exposure and activities leading to excessive sweating or water contact (e.g., swimming, exercise, and sauna) during the study. Participants were not on any systemic or topical medications before or during the study. Pregnant or lactating women, individuals with scars, tattoos, excessive terminal hair on the test area, dermatological pathologies, known allergies to cosmetic products, chronic illnesses that could influence study outcomes, and those on treatments that could interfere with the study were excluded.

Treatments and Follow-ups

The test product was Venusia Ureka Cream™ (approximately 0.04 g), and the negative control was 0.9% isotonic saline solution. The products were applied using occlusive patch chambers on the backs of participants. Patch applications and subsequent evaluations were conducted by trained personnel in two phases.

Induction phase

Patches were applied to participants 9 times over 3 weeks, on alternate days during specified visits (V1, V3, V5, V7, V9, V11, V13, V15, and V17). Following each application, the patches were removed, and skin reactions were graded using the Draize scale at designated intervals, starting from V2 through V19 [Supplementary File, Table S1].

Rest phase

A 14-day rest phase followed the induction phase, allowing any initial irritation to subside and ensuring that any reactions in the challenge phase could be attributed to sensitization rather than residual irritation.

Challenge phase

Patch applications were made to naïve sites adjacent to the original application sites during visit V20. After 24 h, the patches were removed (V21), and the skin reactions were evaluated and graded at 48 h (V22), 72 h (V23), and 96 h (V24) using the International Contact Dermatitis Research

Group (ICDRG) scale. Participants exhibiting any reactions were followed up 1 week later to confirm that all reactions had subsided [Supplementary File, Table S2].

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 ICDRG scale, which uses symbols to denote reaction severity from no reaction (–) to extremely positive (+++)^[6] [Supplementary File, Tables S3 and S4].

Evaluation

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

RESULTS

This study initially enrolled 220 participants, with a total of 218 completing the induction phase and 217 completing the challenge phase. Throughout the study, three participants were lost to follow-up, resulting in a final analysis based on the 217 individuals who completed both phases [Table 1].

Demographic characteristics

Among the 217 participants, the ages ranged from 18 to 60 years, with an average age of 38.96 years (standard deviation = 9.90). The gender distribution included 18 males and 199 females. Seventy-five participants were identified as having sensitive skin in the nasolabial area through a lactic acid sting test, while the remaining 142 participants were categorized as having non-sensitive skin [Table 2].

Product assessment criteria

In the induction phase, Venusia Ureka Cream™ recorded a mean cumulative score of 0.25, while the 0.9% isotonic saline solution, as a negative control, had a score of 0.00. Since the mean cumulative score for Venusia Ureka Cream™ was below 2, it was classified as a non-irritant, affirming its safety for use [Table 3]. In the challenge phase, at 48 h, 192 participants had no reactions, 18 showed doubtful reactions, and seven had weak-positive reactions. At 72 h, 208 participants exhibited no reactions, with five doubtful and four weak positive. By 96 h, 211 participants reported no reactions, while two had doubtful and four weak-positive reactions [Table 4].

Adverse events

No adverse events were reported.

Table 1: Participant numbers and reasons for dropout.

Participant number	Reason for dropout	Participant number	Reason for dropout
Batch I		Batch II	
A79	Lost to follow-up	Z81	Lost to follow-up
A109	Lost to follow-up	-	-

Table 2: Demographic and other baseline characteristics.

Total number of cases (n)	211
Age (years)	
Mean	38.96
SD	9.90
Range	18–60 years
Gender	
Males	18
Females	199
Skin	
Sensitive skin	75
Normal skin	142

SD: Standard deviation.

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

Product	Mean cumulative scores (n=218)
Venusia Ureka cream	0.25
0.9% Isotonic saline solution	0.00

n: Total number of cases

DISCUSSION

The HRIPT for Venusia Ureka Cream™ in our study population showed non-irritant after nine repeat applications and was hypoallergenic. In this study, we utilized HRIPT, regarded as the most reliable method for obtaining conclusive human data on skin reactions. HRIPT enables the evaluation of a formulation's irritation and allergic potential. For an accurate assessment of sensitization potential, a larger sample size, ideally up to 100 subjects, is recommended. This study, however, included 220 participants, thus exceeding the guideline requirements for this type of evaluation. According to the European Commission's Scientific Committee on Consumer Safety, if a confirmatory HRIPT involving 100 subjects shows no sensitization, the statistical confidence interval suggests that a maximum of 3% of a larger population could still exhibit sensitivity. Therefore, completing the HRIPT protocol with around 100 subjects

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

	48 h (n=217)	72 h (n=217)	96 h (n=217)
0.9% isotonic saline solution	217 participants had no reactions.	216 participants had no reactions, one participant showed doubtful reaction	216 participants had no reactions, one participant showed doubtful reaction
Venusia Ureka cream	192 participants had no reaction (–) 18 participants had doubtful reactions (?) seven participants had weak-positive reactions (+) None of the participants had any strong positive reactions.	208 participants had no reaction (–) five participants had doubtful reaction (?) four participants had weak-positive reactions (+). None of the participants had any strong positive reactions.	211 participants did not react (–) two participants had doubtful reaction (?) four participants had weak-positive reactions (+). None of the participants had any strong positive reactions.

provides a robust safety evaluation, supported by historical data from Henderson and Riley (1945), which indicates that if no positive reactions are observed in the initial 100 subjects, the rate of positive reactions in a larger population is unlikely to exceed 2.9%.^[7]

Estimates suggest that 1–5.4% of the general population may be sensitive to a cosmetic or its ingredients,^[8] with common allergens such as synthetic fragrances and preservatives contributing to cosmetic dermatitis and potential skin sensitization. Irritant dermatitis and allergic contact dermatitis (ACD) are among the most frequent adverse effects related to cosmetic use,^[9] with approximately 15–20% of individuals hypothesized to be sensitive to common allergens and an estimated 7% incidence of contact dermatitis each year. Therefore, patch tests play a crucial role in identifying substances that may cause ACD.^[10]

The findings from our study demonstrated that Venusia Ureka Cream™ did not elicit any adverse events when tested using HRIPT. These results are consistent with previous research where a similar study on Venusia Max lotion (PAMA-free), where HRIPT similarly revealed no irritant or allergenic reactions.^[11] A similar study by Nisbet also evaluated the safety of a lamellar moisturizer, comparing it to a saline control.^[12] 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.

Strengths and limitations

This study demonstrates that Venusia Ureka Cream™ is non-irritant and hypoallergenic, as evidenced by the results from HRIPT. The robust study design, featuring a substantial cohort of 220 participants, ensures the reliability of the findings while adhering to rigorous ethical standards. The comprehensive evaluation showed no adverse reactions, supporting the cream's safety for use, particularly in individuals with sensitive skin. However, limitations such as the single-center design and the low number of male participants ($n = 18$) may limit the generalizability of

findings. In addition, since the product was tested only on the backs of participants, regional differences in skin response could not be assessed. Further research is necessary to confirm these findings across diverse populations and body sites and to establish the product's long-term safety profile.

CONCLUSION

The findings from this study indicate that Venusia Ureka Cream™ is safe for use, exhibiting non-irritant and hypoallergenic properties as determined by HRIPT. Given the increasing prevalence of skin irritations and allergies associated with cosmetic products, the results highlight the importance of thorough allergenicity testing. Future studies, ideally involving diverse populations, varied anatomical test sites, and extended follow-up periods, are warranted to further substantiate the long-term safety and efficacy of Venusia Ureka Cream™ in various demographics.

Ethical conduct of the study: The study was conducted by the approved protocol and adhered to established ethical and regulatory standards, including the Declaration of Helsinki, GCP as per BIS guidelines (IS 4011:2018, 3rd Revision, July 2018), the New Drugs and Clinical Trials Rules, 2019, and the ICMR guidelines for biomedical research involving human participants.

Ethical approval: The research/study was approved by the Institutional Review Board at Claims Independent Ethics Committee, number CL/037/0624/STU, dated January 07, 2024.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest: 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.

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