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ORIGINAL ARTICLE

Improvement in skin barrier function and itch relief on dry skin: a short-term, placebo-controlled study of the efficacy of Bioakè Xerophy Cream

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ABSTRACT

Background: Dry skin is often present in chronic skin diseases, such as atopic dermatitis, and can affect different areas of the body. It is caused by several factors that affect the integrity of the cutaneous barrier, resulting in an increased transepidermal water loss (TEWL) and an itching sensation. This short-term, placebo-controlled study aims to evaluate the effect of a cosmetic product (Bioakè Xerophy anti-scratching cream) on skin barrier function and hydration, and assess its soothing effect after an irritant stimulus.

Methods: Twenty healthy female subjects aged between 18 and 60, with sensitive, dry, and reactive skin, were recruited. Skin properties (TEWL and hydration) and soothing effects were assessed before and after a single application of Bioakè Xerophy cream, compared to a skin area treated with a placebo formulation and an untreated area.

Results: Bioakè Xerophy cream determined a statistically significant decrease in transepidermal water loss (-3.4%) and a statistically significant increase in skin hydration (+53.4%) after 4 hours from the application. A statistically significant decrease in the stinging/itching sensation induced by the capsaicin solution was observed.

Conclusions: A single application of Bioakè Xerophy cream facilitated skin barrier restoration and good hydration of the stratum corneum, also providing an early itch relief, compared to the placebo formulation and the untreated area.

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Key words: Skin; Pruritus; Atopic dermatitis.

The presence of dry skin is a standard key aspect of many chronic diseases, such as psoriasis and atopic dermatitis, as well as diabetes and kidney diseases.[1] Dry skin affects different areas of the body and, even if it is not a critical condition, impacts on the patient's quality of life in terms of discomfort and itching. The appearance and the feelings associated with dry skin can impair the quality of life.[2] Dry skin might be red, rough, and scaly, with the presence of fissuration, and often, it is strictly related to chronic itch.[3, 4] Chronic itch, which lasts more than six weeks, is an unpleasant sensation that can negatively affect the quality of life.[4] It often accompanies pathological dry skin-based conditions, such as xerosis, psoriasis, atopic dermatitis, liver and kidney diseases and diabetes mellitus.[5] In these cases, pruritogens, substances eliciting an itching sensation, are released inducing a vicious cycle which is defined as the "itch-scratch cycle" that can exacerbate skin discomfort. Scratching temporarily relieves the itching sensation through the activation of pain-sensory fibers that can inhibit itching sensation at the level of the spinal cord.[6, 7] This symptomatology, characteristic of dry skin, is often associated with aesthetic and social discomfort. A severe pathological manifestation can negatively affect productivity at work, mainly if the areas involved are the hands.[2] For a quick and effective resolution of the symptomatology caused by skin dryness and improving skin health, preventive actions must be taken using emollient, soothing and moisturizing products. To have this kind of preventive effect, there are two essential cellular elements involved: the intercellular lipids, responsible for the skin barrier against diffusion of water across the stratum corneum (SC), and the natural moisturizing factor (NMF), able to absorb water in the SC. In every case in which a condition of skin dryness appears, there is damage to the skin barrier, which loses an excessive amount of water. The pathological condition leading to skin barrier damage is the initial step in the developing skin dryness.[8, 9] In order to remain supple and keep its elasticity, the SC must contain 10% to 15% water.[10] Skin dryness is characterized by a simultaneous increase in transepidermal water loss (TEWL), a measure of the steady-state water vapor flux crossing the skin to the external environment, and a decrease in the water content in SC.[11]

Hence, a cream combining moisturizing action with a repairing action is needed. The ability of this product to repair the skin barrier makes it possible to restore the skin barrier efficiently and counteract problems related to it, such as dryness. The essential role of a moisturizer is to reduce the moisture loss from the skin and quickly restore the normal barrier, fighting dryness and protecting the skin from internal and external pruritogens.[12] When the moisturizer functions appropriately in the skin, the skin maintains homeostasis despite changes in the external environment, so that the stratum corneum can maintain proper hydration.[13]

It is expected to think that a moisturizer cream adds water to the skin; however, this is a misunderstanding. Instead, a moisturizer prevents or reduces water evaporation from the skin.[8]

This action allows the skin to rehydrate from within. Three classes of chemical ingredients regularly serve as moisturizers: occlusives, humectants and emollients.[7, 9]

The new generation of moisturizers arises precisely from the need to combine hydrating, moisturizing, and repairing action synergistically, so they are characterized by the presence in their formulation of ingredients that repair the barrier, in addition to the traditional moisturizer components. The most common ingredients are ceramides, free fatty acids and cholesterol, which help replace the deficient lipids in some skin diseases characterized by barrier impairment, such as eczema and psoriasis.[13, 14]

This short-term, placebo-controlled study aimed to assess the effect of a cosmetic product (Bioakè Xerophy repairing anti-scratching cream, Ekuberg Pharma, Italy) in improving the skin barrier function and skin hydration, together with the assessment of its soothing effect in decreasing the skin discomforts induced by a chemical irritant (capsaicin).

Materials and methods

Study design and participants

A new concept formulation, Bioakè Xerophy cream, containing a combination of carefully selected ingredients, was tested. A placebo cream, which did not include the active ingredients, was also formulated. Details of both formulas are reported in Table I.

To reach this goal, an instrumental study was carried out on 20 healthy female subjects between 18 and 60 with sensitive, dry and reactive skin. Bioakè Xerophy cream and placebo were applied on the volar surface of the arm of each participant (2 mg/cm^2) under controlled conditions by the experimenter. Another area of the forearm was left untreated and acted as control. The subjects participating in the study were screened and enrolled under the supervision of a board-certified dermatologist from a panel of healthy subjects, by inclusion and exclusion criteria. The

TABLE I.—*Ingredients of Bioakè Xerophy Cream and placebo.*

Action of the ingredient	Bioakè Cream	Placebo formula
Base	Water	Water
Filming	Panthenol	
Humectant	Glycerin, xanthan gum	Xanthan gum
Emollient	Shea butter, ethylhexyl stearate, glyceryl stearate, sweet almond oil, hydrogenated ethylhexyl olivate, hydrogenated olive oil unsaponifiables, caprylic/capric triglyceride	Ethylhexyl stearate, caprylic/capric triglyceride, glyceryl stearate
Soothing	Allantoin, tocopherol, calendula officinalis flower extract, hydroxyphenyl propamidobenzoic acid, tocopheryl acetate	
Skin barrier boost	Ceramide NP	
Preservatives	Phenoxyethanol	Phenoxyethanol
Other	Cetearyl alcohol, sodium polyacrylate, ethylhexylglycerin, polyglyceryl-6 stearate, polyglyceryl-6 behenate, butylene glycol, pentylene glycol, phenethyl alcohol, caprylyl glycol, ascorbyl palmitate, citric acid, fragrance	Cetearyl alcohol, sodium polyacrylate, caprylyl glycol, ethylhexylglycerin, polyglyceryl-6 behenate, phenethyl alcohol, polyglyceryl-6 stearate

evaluations were conducted in a temperature and humidity-controlled environment (respectively T: 22±2 °C and RH: 50±10%). Before the visit, the subject observed a 20-minute acclimatization period in these conditions. The study protocol has been registered in the ISRCTN registry (ISRCTN16954825).

Evaluation of transepidermal water loss and skin hydration

Transepidermal water loss and skin hydration were evaluated at baseline (T0) and four hours after the single application of the products. The measurement of the transepidermal water loss was based on the internationally recognized TEWAMETER® method. The used instrument was a Tewameter® TM 300 (Courage+Khazaka, electronic GmbH, Cologne, Germany). The probe was positioned on the affected area until a steady state was reached, and an average value was obtained. The Tewameter® was a standard equipment for evaluating skin barrier function, and TEWL was measured in g/h/m^2.[14] The measurement of skin hydration was based on the internationally recognized CORNEOMETER®. This measurement was based on the entirely different dielectric constant of water[15] and other substances (mostly <7). The instrument used was a Corneometer® CM 825 (Courage+Khazaka, electronic GmbH, Cologne, Germany).

Evaluation of the soothing effect in decreasing the skin discomforts induced by a chemical irritant (capsaicin). A 10% capsaicin hydroalcolic solution (3.6 x 10-3%) was applied to under alar grooves' skin to induce a stinging/itching sensation. When the discomfort peaks were at their maximum sensation (approximately 2 minutes after the application of the capsaicin solution) the subjects in collaboration with the experimenter scored the intensity of the perceived discomfort. They applied the test products using a soaked cotton stick on the right/left under alar groove according to a previously defined randomization list. The contralateral side was treated with the placebo formulation.

The intensity of the perceived stinging/itching discomfort (Timm) was immediately measured soon after the application and 1, 2, 3, 4, 5, 7 and 10 minutes after the first application of the products. At each checkpoint, the experimenter registered the intensity of the discomfort reported by the subject. The intensity of the perceived discomfort sensations (stinging/itching sensation) was scored as follows: 1 = no reaction; 2 = mild reaction; 3 = moderate reaction; 4 = severe reaction.

Inclusion criteria

Healthy female subjects registered with the National Health Service (NHS) between 18 and 60 and Caucasian ethnicity. Subjects with sensitive, dry and reactive skin. Subjects with a positive reaction to stinging test with capsaicin (10% hydroalcoholic capsaicin 3.6 x 10-3%). Subjects who certified the integrity of the personal data reported to the investigator. Subjects who were able to understand the language used in the investigation and the information provided by the investigator, as well as respect the instructions given by the investigator, and the study constraints and specific requirements. The pharmacological therapy (with the except that indicated in the exclusion criteria) had to be stable for at least one month without any changes expected or planned during the study. Commitment not to change one's daily routine and lifestyle. Subjects who were aware of the test procedure and had signed an informed consent form.

Exclusion criteria

Subjects with acute or chronic diseases (diabetes, chronic skin allergies, psoriasis vulgaris, pemphigus vulgaris, chronic kidney disease, or hormonal disorders such as hyperthyroidism/hypothyroidism) that could interfere with the outcome of the study or were considered dangerous to the subject or incompatible with the study requirements. Subjects who were participating or intended to participate in other clinical trials and who participated in a similar trial without observing an appropriate washout period. Subjects undergoing drug therapies are considered by the investigator to be reactions incompatible with the study requirements, and subjects with a clinical history of irritation to cosmetics, drugs, patches, or cosmetic devices. Subjects who were breastfeeding or pregnant.

Ethical requirements

All the subjects participating in the study were healthy volunteers of at least 18 years old and they were selected under the supervision of a dermatologist according to inclusion/exclusion criteria. Before the volunteers were exposed to the product to be tested, all relevant safety information about the product and each ingredient was collected and evaluated. All the study procedures were carried out in accordance with the ethical principles for medical research (Ethical Principles for Medical Research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964 and subsequent amendments). In case of non-expected/adverse skin reaction occurrence, the medical experimenter evaluated the severity of the reaction (reporting it in the data collecting sheet) and, consequently, he proceeded with the appropriate therapy.

Statistical analysis

Instrumental data (TEWL and skin hydration) were submitted to the two-way Student's *t*-test for paired data. The intra-group statistical analysis was carried out *vs.* T0, and the inter-group statistical analysis was carried out on treated *vs.* placebo-treated and untreated areas. Clinical data (stinging/itching sensation) were submitted to Wilcoxon signed-rank Test. The intra-group statistical analysis was carried out *vs.* Tmax and the inter-group statistical analysis was carried out *vs.* the placebo-treated area. Variations were considered statistically significant when P value was <0.05. The statistical software used for statistical analysis was NCSS 10 (version 10.0.7 for Windows; NCSS, Kaysville, UT, USA).

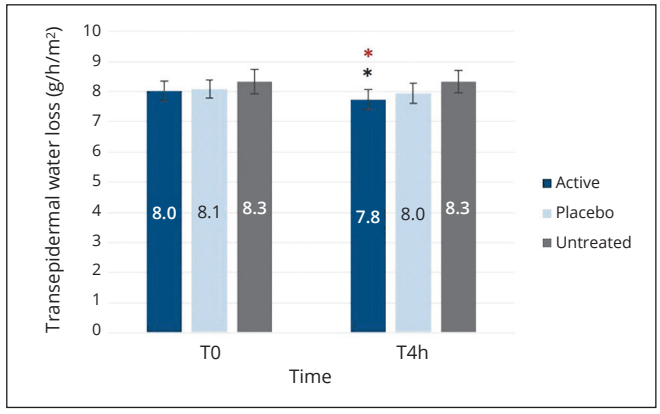

Figure 1.—The graph reports the mean data obtained at each experimental time. Data are expressed as a mean±SE. Above the error bar, the statistical analysis was reported as follows: *P<0.05; **P<0.01; ***P<0.001. Intra-group statistical analysis (*vs*. T0) is reported as black asterisks; inter-group statistical analysis (active/placebo *vs.* untreated) is reported as red asterisks.

Results

The single application of Bioakè Xerophy cream determined a statistically significant decrease in transepidermal water loss by -3.4% at T4h, both compared to baseline values and to the untreated area. A decrease in transepidermal water loss by -1.8% was also recorded with the application of the placebo formulation, although not statistically significant. No relevant variation of the monitored parameter was observed in the untreated area (Figure 1).

A statistically significant increase in skin hydration by +53.4% at T4h, both compared to baseline values and to the untreated area was registered too. A statistically significant increase in skin hydration by +17.8% was also recorded with applying of the placebo formulation (both compared to baseline values and to the untreated area). However, the results obtained with Bioakè Xerophy cream were statistically greater (inter-group statistical analysis active *vs.* placebo). No relevant variation of the monitored parameter was observed in the untreated area (Figure 2).

The single application of Bioakè Xerophy cream determined a statistically significant decrease in the stinging/itching sensation induced by the capsaicin solution, starting from Timm (immediately after product application) and at each checkpoint. A decrease in the stinging/itching sensation was also recorded starting from Timm, in the skin site treated with the placebo formulation. The inter-group statistical analysis highlighted that the decrease in the stinging/burning sensation was statistically faster due to the application of Bioakè Xerophy cream (Wilcoxon; active *vs.* placebo P<0.05) starting from T1' and up to T7'.

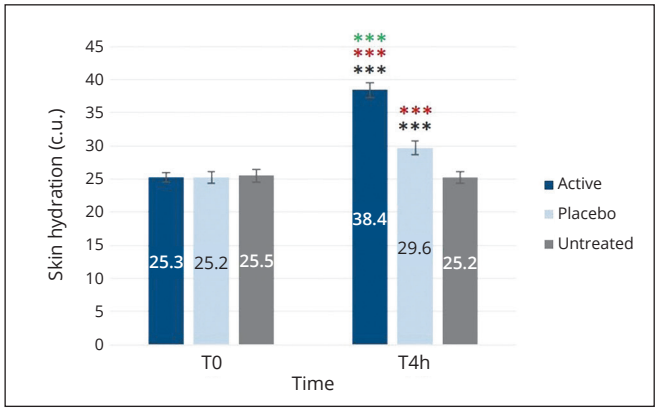

Figure 2.—The graph reports the mean data obtained at each experimental time. Data are expressed as a mean±SE. Above the error bar, the statistical analysis is reported as follows: *P<0.05; **P<0.01; ***P<0.001. Intra-group statistical analysis (*vs*. T0) is reported as black asterisks; inter-group statistical analysis (active *vs*. placebo) is reported as green asterisks; inter-group statistical analysis (active/placebo *vs*. untreated) is reported as red asterisks.

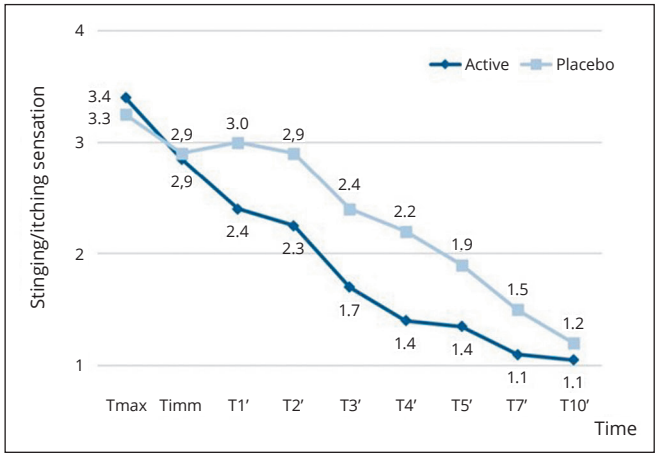

Figure 3.—The graph reports the mean data obtained at each experimental time.

Moreover, it was possible to notice that at T4', T5' and T7', the stinging/itching sensation induced by the capsaicin solution has almost disappeared in the area treated with Bioakè Xerophy cream (mean values respectively by 1.4 at T4', 1.4 at T5' and 1.1 at T7'). At the same time, it was still mildly perceptible in the area treated with the placebo formulation (mean values respectively by 2.2 at T4', 1.9 at T5' and 1.5 at T7') (Figure 3).

Discussion

The skin performs various complex functions because the epidermis is a permeability barrier which aims to create an optimal cellular environment.[16] It provides an essential environment for deeper tissues by separating them from the external environment and, simultaneously, ensures it through the exchange of substances and reception of stimuli.[17] Dry skin alters the functions of the skin, transforming a physiological condition into a pathological condition, which is highly dangerous for the patient's health.

This study aimed to demonstrate the efficacy of Bioakè Xerophy cream in restoring the normal skin barrier function of the skin, increasing hydration and soothing the itching sensation induced after an external stimulus.

Results demonstrated that Bioakè Xerophy cream decreased the transepidermal water loss by -3.4% and increased skin hydration by 53.4% at T4h compared to baseline values and the untreated area.

The product was responsible for a statistically significant decrease in the itching and stinging sensations induced by the capsaicin solution, starting from Timm and at each following monitored time. This effective decrease was statistically faster compared to the placebo formulation in the same conditions.

Limitations of the study

Our study had some limitations: sample size and study design should be adequately improved considering a randomized, placebo-controlled, double- or triple-blind clinical trial in order to better investigate these preliminary results.

Conclusions

Bioakè Xerophy cream described in this study worked by preventing excessive water loss by skin, maintaining a physiologically optimal hydration level in the stratum corneum. The optimal level of hydration was considered essential to guarantee the correct skin's function. Bioakè Xerophy cream also decreased the itching and stinging sensations, which produced discomforts affecting the patients' quality of life. By combining a repairing effect on the skin barrier and at the same time hydrating, the product highly demonstrated efficacy in the treatment of condition such as dry skin. Future research in this area with a large cohort of patients and collaboration between different centers will be of highly importance.

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Conflicts of interest

Davide Carati, Camilla Schinzari, Silvia Luperto and Carolina Mauro are employees of Ekuberg Pharma. This does not alter the author's adherence to all journal policies on sharing data and materials. The other authors declare no conflict of interest. The funder had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

Authors' contributions

Conceptualization: Vincenzo Nobile, Davide Carati, and Camilla Schinzari. Methodology: Vincenzo Nobile. Software: Vincenzo Nobile. Validation: Vincenzo Nobile, Davide Carati, and Camilla Schinzari. Formal analysis: Vincenzo Nobile. Investigation: Enza Cestone. Resources: Vincenzo Nobile. Data curation: Vincenzo Nobile. Writing—original draft preparation: Vincenzo Nobile and Davide Carati. Writing—review and editing: Vincenzo Nobile, Davide Carati, Camilla Schinzari, Carolina Mauro, Silvia Luperto. Visualization: Vincenzo Nobile. Supervision: Vincenzo Nobile. Project administration: Vincenzo Nobile. Funding acquisition: Vincenzo Nobile and Davide Carati. All authors have read and agreed to the published version of the manuscript.

History

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