

Efficacy and patients' satisfaction of anti-inflammatory ointment in xerotic conditions

Norramon Charoenpipatsin MD,
Thanisorn Sukakul MD,
Supenya Varothai MD,
Pichaya Limphoka MD,
Waranya Boonchai MD.

ABSTRACT:

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DEPARTMENT OF DERMATOLOGY, FACULTY OF MEDICINE SIRIRAJ HOSPITAL, MAHIDOL UNIVERSITY, BANGKOK, THAILAND.

Background: Xerotic conditions are the conditions of severely dry skin which commonly co-manifest in varieties of skin diseases such as eczema or ichthyosis. The mainstay of treatment for patients with xerosis was to well moisturize the skin. Moisturizer with anti-inflammatory and antioxidant properties may provide treatment benefit in patients with xerosis.

Objective: To examine the efficacy and patients' satisfactory of anti-inflammatory ointment (Ezerra ointment®) in xerotic conditions.

Materials and methods: We performed a 5-week open-labelled prospective study on 25 patients with xerotic conditions. Patients applied the product for a 4-week period and then discontinue during the

From: Department of Dermatology, Faculty of Medicine Siriraj Hospital Mahidol University, Bangkok, Thailand

Corresponding author: Waranya Boonchai MD., email: waranya.boonchai@gmail.com

last week. The two selected areas were assessed by a same physician at weeks 0, 2, 4 and 5 using symptoms severity assessment, physician global assessment, and bioengineering assessments consisting of Corneometer® to assess skin hydration and Tewameter® to assess transepidermal water loss. Patients assessed severity of their symptoms at week 0, 4, and 5. Product satisfaction was assessed at week 4.

Results: All patients completed the study. Dryness, scale, and overall assessment assessed by physician and dryness assessed by patients decreased significantly during the application of the ointment and maintained even one week after stopping the treatment. Both physician and patient global assessments significantly improved. The skin hydration evaluated by Corneometer® significantly increased during the application of the ointment but at one week after the skin hydration decreased significantly from during the usage.

Conclusion: This anti-inflammatory ointment help to improve symptoms, increase skin hydration and reduce signs of skin inflammation in patients with xerotic conditions.

Key words: xerosis, xerosis cutis, anti-inflammatory ointment; moisturizers

Introduction

Xerotic conditions are among the most frequent encountered conditions in dermatological practice¹. Symptoms of xerosis include dry, scaly, rough, itchy and dull skin appearances and can occur anywhere in the body but was usually predominantly found in skin areas with fewer sebaceous glands such as hands, feet, forearm, or lower legs¹. Xerosis can also present as one of the symptoms in other skin conditions such as eczema, psoriasis, and ichthyosis with notably accompanying symptoms of pain and redness². It may be caused by an impaired function of the skin barrier resulting from filaggrin mutation^{1,3}. Other factors such as eczema or exposure to irritant substances also play a role¹. Exposure to sunlight, friction, low humidity, and

using too much soap could be the risk factors².

Xerosis occurred more frequently in the elderly patients and in patients who had mixed co-factors of dermatological, systemic and psychological issues⁴.

The mainstay of treatment for patients with xerosis is well moisturizing and hydrating the skin^{2,5}. Moisturizing products that could achieve the hydrating level for this condition should, therefore, contain active ingredients that acted as an occlusive substance to prevent trans-epidermal water loss, a humectant to absorb the water from both dermis and outside environments into epidermis, and an emollient to improve skin texture and directly hydrate the skin². Example of occlusive substances are lanolin, paraffin, petrolatum, and stearyl alcohol⁶.

Humectants include glycerin, urea, ammonium lactate, gelatin, and hyaluronic acid^{6,7}; while petrolatum, dimethicone, propylene glycol, and castor oil have an emollient effect⁷.

Ezerra ointment[®] contained active ingredients of the extractions from *Butyrospermum Parki* (shea butter), spent grain wax, argania spinosa kernel oil, petrolatum, stearyl ester, and tocopheryl acetate. *Butyrospermum Parki* (shea butter) had potent anti-inflammatory and antioxidant properties⁸. Spent grain wax was an effective moisturizer to rehydrate the skin with anti-inflammatory properties⁸. Argania spinosa kernel oil had been shown to restore skin barrier function resulting in improving skin elasticity and skin hydration⁹. Petrolatum and stearyl ester were effective occlusives that could help prevent epidermal water loss². According to active ingredients in the tested product, it might help repair and maintain the skin barrier, enhance skin hydration, and reduce skin inflammation with no obvious side effects. The ointment seems to suit for anyone suffering from xerosis or other skin conditions that might result in dryness and inflammation of the skin. The purpose of this study was to evaluate the effectiveness, safety, and also patients' acceptability of the ointment in xerotic conditions.

Materials and methods

Study design and patient population

An open-label prospective study was conducted between August 2019-Oct 2019 at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University. This study was ethically approved from Siriraj Institutional Review Board (SI131/2562). All patients were informed about the study and written consent was obtained.

Twenty-five patients took part in the current study which evaluated the efficacy of Ezerra ointment[®] and patient satisfaction. The inclusion criteria were patients of over 18 years of age having xerotic conditions such as xerosis cutis, eczema, ichthyosiform dermatoses, or cheilitis given by dermatologist. The exclusion criteria were patients who had active lesion of any skin diseases in the last 2 weeks, applied topical corticosteroids, calcineurin inhibitors or any moisturizer in the last 2 weeks, took systemic corticosteroids in the last 2 weeks, was pregnant or lactating, or had a history of allergy to any of the tested product ingredients. The withdrawal or termination criteria comprised of a patient who was unwilling or unable to continue to participate, was unable to withstand any reaction to the tested product, or had the active skin diseases that required additional treatment.

Demographic data, including age, sex, and underlying disease, were collected. Patients were assessed at weeks 0, 2, 4, and 5. All patients were requested to apply the tested product at the two

most obviously dry areas selected by a physician twice a day for four weeks (week 0 to 4). Then, patients discontinued applying the ointment during the last week (week 5). Other substances were not allowed to be applied to the study area throughout five weeks. The amount of the tested product that was left at each visit was measured to assess the levels of treatment compliance.

Assessments

The two selected area were assessed by the same physician at weeks 0, 2, 4 and 5. Symptoms severity consisting of dryness, scale, erythema, pruritus, fissuring, and overall severity were assessed¹⁰. The score ranged from 0 to 3; 0: none, 1: mild, 2: moderate, and 3: severe¹⁰. Physician global assessment¹⁰ which had the score ranging from 0-4 (0: absent, 1: faint scaling, faint roughness, and dull appearance, 2: small scales in combination with a few larger scales, slight roughness, and whitish appearance, 3: small and larger scales uniformly distributed, definite roughness, possibly slight redness, and possibly a few superficial cracks, 4: lesion dominated by large scales, advanced roughness, redness present, eczematous changes, and crack) were assessed. Bioengineering assessment consisted of Corneometer® CM825 and Tewameter® TM300 from Courage and Khazaka Electronics (Cologne,

Germany), were used to evaluate skin hydration and transepidermal water loss, respectively. Mean score of both sites was calculated as an overall score. Photograph and Visioscan® VC98 from Courage and Khazaka Electronics (Cologne, Germany) were taken at each visit.

At weeks 0,4, and 5, patient's grading of dryness and pruritus severity using a continuous scale of 0-10 and patient global assessment^{10, 11} using the scale of 0-3; 0: none, 1: mild, 2: moderate, and 3: severe were collected. At weeks 2 and 4, patients were asked of any side effects or irritation they experienced from using the tested product and patients' satisfaction for the product was assessed using a questionnaire at week 4. The questionnaire consisted of 7 question; question 1 asked if the product did not cause any irritation; question 2 asked if the product was well spread on the skin; question 3 asked if the product absorbed well; question 4 asked if the product was not greasy; question 5 asked if the product helped with the symptoms of dry skin; question 6 asked if the product had a good smell; and question 7 asked if the patients would be willing to purchase the product in the future. The answer consisted of 5 choices; 0: strongly disagree, 1: disagree, 2: neutral, 3: agree, and 4: strongly agree. (Fig. 1)

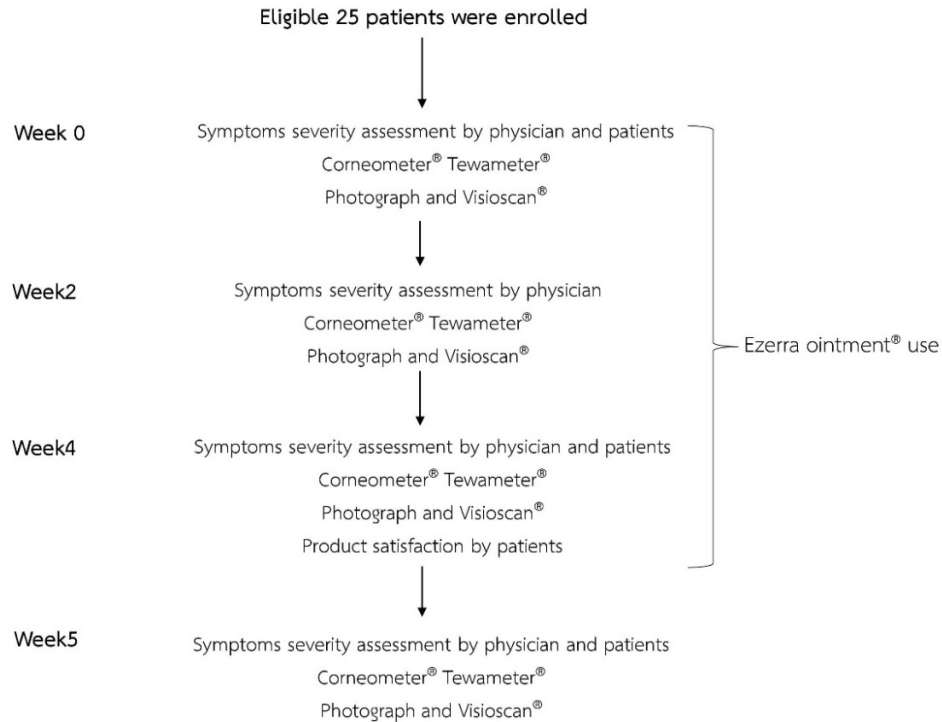


Figure 1 Flow of clinical and bioengineering assessment

Statistical analysis

The patients' baseline characteristics and the percentage of patients responding to each question in the patients' satisfaction questionnaire were presented as n (%) and analyzed using descriptive method. Friedman's 2-way ANOVA by ranks was used to compare the parameter that had been evaluated by a grading scale such as symptoms severity assessment consisting of dryness, scale, erythema, pruritus, fissuring, and overall severity assessment, physician global assessment, and patient global assessment between each visit. Differences were

further analyzed using the pairwise comparison method, with significance values adjusted by the Bonferroni correction for multiple tests. Friedman's 2-way ANOVA by ranks or repeated measures ANOVA were used to analyze the bioengineering assessment from Corneometer® and Tewameter®, and the patient's continuous grading of dryness and pruritus between each visit. Differences were further analyzed using the pairwise comparison method, with significance values adjusted by the Bonferroni correction for multiple tests.

Table 1 Demographic data

Characteristics	All patients (N = 25)	
	N	(%)
Mean age (\pm SD)	38.0 \pm 11.3	
Sex		
Female	22	88
Male	3	12
Skin conditions		
Xerosis cutis	17	68
Ichthyosis vulgaris	4	16
Eczema	3	12
Chelitis	1	4
Site of lesion		
Feet	8	32
Leg	6	24
Elbow	5	20
Hand	3	12
Trunk	1	4
Shoulder	1	4
Lip	1	4

Results

Demographic data

All of the 25 enrolled participants completed all of the visits in the experiment. Demographic data and site of lesion chosen were shown in Table 1. Skin conditions included in the study were xerosis cutis, ichthyosis vulgaris, eczema, and chelitis. Regarding the past medical history of patients, ten

participants (40%) had used moisturizers such as urea cream or Vaseline® lotion in the past. Two participants (8%) had received previous topical medication for their conditions; one used topical steroid and the other one with exfoliative chelitis used tacrolimus ointment. One participant (4%) had previously taken methotrexate and acitretin for his exfoliative chelitis.

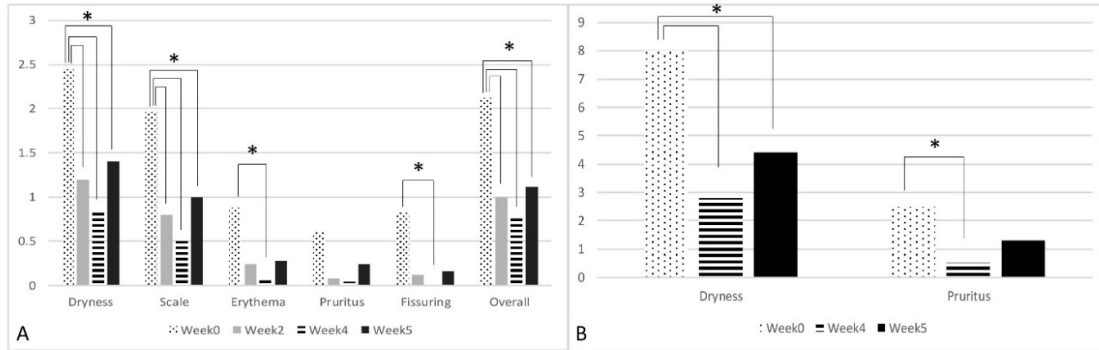


Figure 2 A) comparison of clinical parameter; dryness, scale, erythema, pruritus, fissuring, and overall assessed by a physician at week 0, week 2, week 4, and week 5; B) comparison of clinical parameter; dryness and pruritus assessed by patients at week 0, week 4, and week 5

Clinical assessment

Significant improvement for dryness, scale, erythema, fissuring, and overall assessment by a physician; and dryness and pruritus assessed by patients were observed (Fig. 2). Dryness assessed by a physician decreased significantly at week 2 compared to week 0 ($p < 0.001$), week 4 compared to week 0 ($p < 0.001$), and week 5 compared to week 0 ($p < 0.001$). Scale decreased significantly at week 2 compared to week 0 ($p < 0.001$), week 4 compared to week 0 ($p < 0.001$), and week 5 compared to week 0 ($p = 0.001$). Erythema and fissuring decreased significantly at week 4 compared to week 0 ($p = 0.007$ and 0.022 respectively). Overall assessment by a physician showed a significant decrease of symptoms at week 2 compared to week 0 ($p < 0.001$), week 4 compared to week 0 ($p < 0.001$), and week 5 compared to week 0 ($p = 0.001$). Dryness assessed

by patients decreased significantly at week 4 compared to week 0 ($p < 0.001$) and week 5 compared to week 0 ($p < 0.001$). Pruritus assessed by patients decreased significantly at week 4 compared to week 0 ($p = 0.003$).

Mean physician global assessment at week 0 was 2.9, which decreased significantly to 1.4 at week 2 ($p < 0.001$), to 0.9 at week 4 ($p < 0.001$), and to 1.5 at week 5 ($p < 0.001$). Mean patient global assessment at week 0 was 2.7, which decreased significantly to 1.0 at week 4 ($p < 0.001$), and to 1.5 at week 5 ($p < 0.001$).

Bioengineering assessment

Bioengineering assessments at week 0, 2, 4, and 5 were compared between each visit (Fig. 3). Corneometer® score increased significantly at week 2 compared to week 0 ($p < 0.001$), and at week 4 compared to week 0 ($p = 0.001$).

Corneometer® score at week 5 decreased significantly compared to week 2 ($p = 0.007$).

Tewameter® score showed no significant changes between any visits.

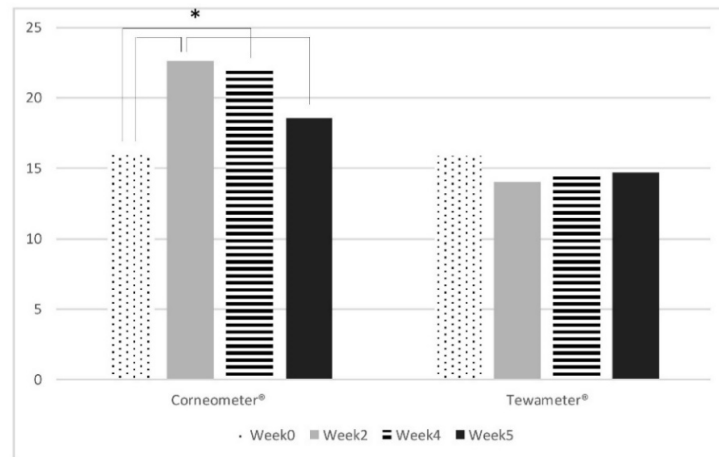


Figure 3 Comparison of bioengineering assessment; Corneometer® and Tewameter® at week 0, week 2, week 4, and week 5

Product satisfaction

Product satisfaction questionnaire at week 4 (Fig. 4) revealed that most patients agree that the product could relieve their symptoms and caused no irritation. The most troublesome aspects of the product were the ability of absorption and level of greasiness.

Compliance and adverse event

Regarding compliance during the study, only one participant (4%) had used the product less than the estimated amount throughout four weeks. We calculate the amount of estimated product use according to the fingertip unit.¹² The

only reported adverse event was mild irritation from one patient when first applying the product but it was subsided shortly after the usage and did not cause a patient to stop using the product.

Discussion

In the present study, the utilization of the tested product had led to significant improvement in every aspect including dryness, scale, erythema, pruritus, fissuring and overall assessment by both patients and physician. Interestingly, the effect of the tested product seemed to last one week after stopped using when compared week 5 to week 0.

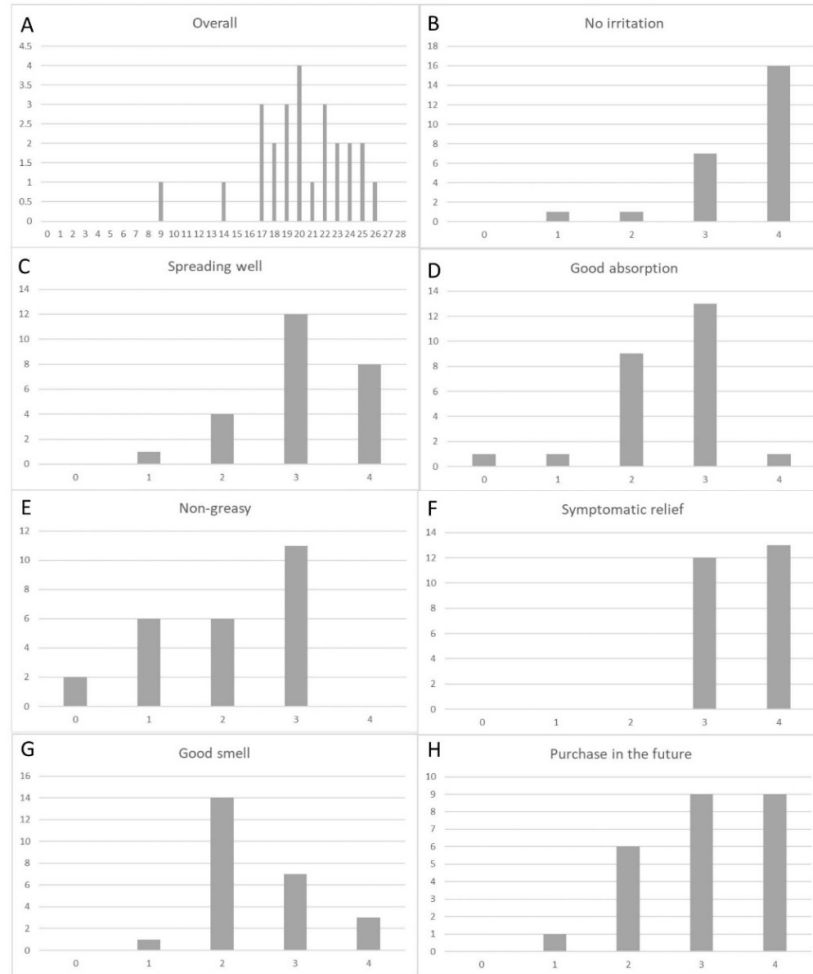


Figure 4 Product satisfaction at week 4; A) overall satisfaction which was the sum-up of each seven questions, a score ranging from 0-28; B) to H) satisfaction for each question. 0: strongly disagree, 1: disagree, 2: neutral, 3: agree, 4: strongly agree

Bioengineering assessment also yielded the results that were in accordance with the clinical assessment. The level of skin hydration (assessed by Corneometer®) increased significantly at week 2 and 4, and still maintained the higher level at

week 5 compared to week 0 even though this difference had no statistical significance. There were no significant changes in transepidermal water loss shown by Temameter®.



Figure 5 Patient with foot eczema; A) week 0; B) week 2; C) week 4; D) week 5

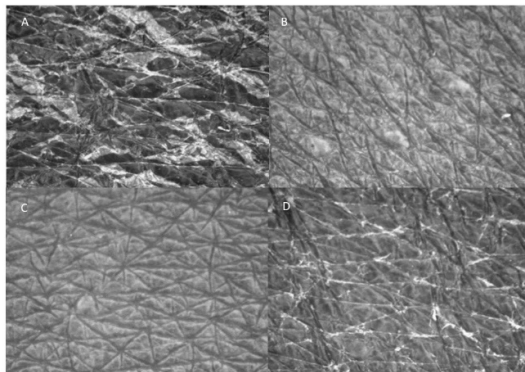


Figure 6 Visioscan® at abdomen; A) week 0; B) week 2; C) week 4; D) week 5

The pathogenesis of xerosis involved in the combination of defects in skin barrier function and external factors that might play a role such as skin inflammation or exposure to irritant substances^{1,3}. Typically, patients suffering from xerotic conditions have been treated with moisturizers that contained broadly classes of occlusives, humectants, and emollients substances. The studied product had several unique ingredients with different mechanisms such as *Butyrospermum Parki* (shea butter) and

spent grain wax which had potent anti-inflammatory and antioxidant properties⁸. The result from our study was in accordance to previous studies on the product containing shea butter extract. In a study by Hon et al.³, the usage of product containing shea butter could lead to significantly less pruritus in atopic dermatitis, while a study by Diluvio et al.¹³ also stated that topical application of emollients with shea butter could lead to significant improvement of itching and decreased severity of dry skin assessed by physician. *Argania spinosa* kernel oil also helped to restore skin barrier function resulting in improving skin elasticity and skin hydration as shown by significantly increased skin hydration assessed by Corneometer^{®9}.

The anti-inflammatory property of the tested product has been shown by the decrease of score in redness and itching. Therefore, this product not only acted as a moisturizer that can rehydrate the skin but also it could lead to a decrease in skin inflammation. Such a product could be recommended to be used alone in patients with xerotic conditions with or without mild inflammation. The product might be used in combination with topical steroids in more severe cases that accompanied with marked inflammation of the skin to help minimize the potential side effects of topical steroids such as skin thinning, telangiectasia, skin atrophy, or acne^{14,15}.

The tested product, Ezerra ointment[®], did not contain any fragrances or preservatives that might lead to allergies or irritations and according to our study it was found to be acceptable to, and well-tolerated by, almost every patient. Since patients with xerotic conditions usually have impaired skin barrier that is prone to have irritation from applied substances, only one patient reported mildly irritated sensation after the first few times of application which was subsided after continued using.

Patient-reported satisfaction for the product revealed that most patients seemed to be satisfied with the formulation of the product. Symptomatic relief was obvious as all patients either agree or strongly agree that the product provided some relief for them. Ninety-two percent of patients either agree or strongly agree that the product did not irritate. However, eight percent of patients disagreed that the product had good absorption, and even up to thirty-two percent reported that the product was greasy. This seemed to be a problem regarding the texture of the product which could be further solved and improved. Even though the product might cause some greasiness, most patients adhered well to the study as shown by the amount of the product applied that corresponded to the expected use.

In conclusion, Ezerra ointment[®] is an effective, considerable safe moisturizer for various xerotic

conditions which could decrease skin inflammation. Further study with a well-defined outcome preferably in randomized controlled trial should be conducted in the future to prove its efficacy over placebo. It might also be worthwhile to compare its anti-inflammatory property with other anti-inflammatory medications or to test its efficacy as an adjunction to topical steroids before it could be recommended to patients with more severe skin inflammation.

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Competing interests

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