

An evaluation of prescription device moisturizers

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Summary

Moisturization of the skin is important for both medical and cosmetic purposes. The development of prescription device moisturizers, receiving 510K approval on the basis of the physical reduction in transepidermal water loss, provided a new dermatologic category. This investigator-blinded research utilized a split body model in 60 subjects to examine the effect of a traditional moisturizer as compared to a prescription device moisturizer in the treatment of mild to moderate symmetrical eczema of the arms or legs. This study demonstrated parity between the two moisturizers based on subject and investigator assessments.

Keywords: therapeutic moisturizer, prescription moisturizers, 510K moisturizers

Introduction

Moisturizers hydrate the skin by decreasing transepidermal water loss (TEWL) and attracting water to the dehydrated stratum corneum and epidermis.¹ Substances that reduce TEWL are oily occlusive substances, such as petrolatum, paraffin, mineral oil, dimethicone, cyclo-methicone, etc. Substances that attract water to the skin are known as humectants and include glycerin, sorbitol, propylene glycol, hyaluronic acid, sodium PCA, proteins, etc. The most efficacious moisturizers contain both occlusive and humectant ingredients. The sum of these skin effects results in an environment optimal for barrier repair.² In short, moisturizers do not moisturize the skin, but rather facilitate barrier repair by encouraging the natural restorative process.

Moisturizers are the most widely used cosmeceutical; yet, the word itself is a misnomer. Moisturizers do not add water to the skin, even though the first or second ingredient on many moisturizer formulations is water. Most mois-

turizers function by placing a water impermeable film over the skin surface that decreases evaporation of water from the skin to the lower humidity atmosphere.^{3,4} Any water in a moisturizer formulation is a vehicle that evaporates, possibly drying the skin further, without enhancing skin water content. Water-based moisturizers may further damage xerotic skin, due to repeated wetting and drying of the skin surface.

Moisturizers were traditionally sold in the over-the-counter (OTC) realm, until recently when several prescription moisturizers were introduced to dermatologists in the United States. These moisturizers were not approved as drugs, but rather as devices. The drug approval route requires filing of an Investigational New Drug application with the Food and Drug Administration (FDA) followed by clinical testing to demonstrate the safety and efficacy of the formulation. This is an expensive undertaking requiring 5–7+ years. The drug approval route is distinct from the 510K device approval route where safety, not efficacy, is of primary concern. Devices were traditionally machines that were placed on the skin surface, although this stereotype is changing.

Several moisturizers were approved as prescription devices in last 5 years, containing a variety of ingredients such as petrolatum, paraffin, hyaluronic acid, and botanically derived extracts. The moisturizers qualified as devices because they changed the water content of the

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skin, demonstrated by measuring TEWL. This physical skin change allowed approval of non-mechanized devices and the marketing of prescription moisturizers that were FDA approved, but not through the drug route. This was a new concept in dermatology raising the question as to whether other moisturizers in the marketplace could also be considered moisturizing devices, if the 510K approval process were undertaken.

A moisturizer with longevity in the OTC marketplace is a combination of agents that retard TEWL such as mineral oil, petrolatum, paraffin, and ceresin (Albolene, DSE Healthcare Solutions, Edison, NJ). An approved medical device formulation contains olive oil and vegetable oil to retard TEWL and the humectants glycerin and pentylene glycol (MimyX®, Stiefel, Coral Gables, FL). The prescription product is labeled as deep dermal hydrating anti-irritant cream designed to improve dry skin and relieve itching and burning. The goal of this study was to determine whether a time-tested OTC formulation could deliver equivalent improvement in eczema as a prescription medical device.

Method

The objectives of this study were to demonstrate the equivalence of an OTC moisturizer (Albolene) and an Rx device (MimyX) in the treatment of mild eczema for 4 weeks and in combination with 0.1% triamcinolone cream (TAC) for moderate eczema for 4 weeks. Sixty subjects (30 with mild eczema, 30 with moderate eczema) aged 18+ years were enrolled in this single-site, double-blind, split-body study after completion of an Institutional Review Board–approved informed consent (Concordia Institutional Review Board, New Jersey). The study could only be investigator blinded, as it was not possible to make the two study moisturizers appear identical, since the products were studied as currently marketed. Subjects with symmetrical mild to moderate eczema of the arms or legs were enrolled.

Thirty subjects with mild eczema, as assessed by the dermatologist investigator, were asked to use the OTC moisturizer twice daily to the randomized right or left target limb and an Rx device to the other randomized target limb. In addition, 30 subjects with moderate eczema, as assessed by the dermatologist investigator, were asked to use the OTC moisturizer and TAC twice daily to the randomized right or left target limb and an Rx device and TAC to the other randomized target limb. The arms or the legs were designated as the target site for each subject by the investigator. Subjects used the moisturizers on top of the TAC in all cases and were allowed to continue their self-selected cleanser unchanged for the duration of the

study. No other arm or leg moisturizers or medications were allowed.

Subjects were at baseline, week 1, week 2, and week 4. The dermatologist investigator performed all visual assessments of the arm or leg target site on a 6-point ordinal scale (0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = moderately severe, 5 = severe). The parameters evaluated included erythema, desquamation, lichenification, excoriation, stinging/burning, itching, and overall eczema severity. Subjects with an overall eczema score of less than 3 were entered into the mild eczema group and subjects with an overall eczema score of 3–4 were entered into the moderate eczema group. Only the arm or leg target sites were evaluated to obtain the severity rating. Subjects evaluated their target site skin appearance for redness, peeling, dryness, stinging/burning, and overall eczema appearance on the same 6-point ordinal scale.

Subject compliance was determined from diary sheets. Only subjects who completed the study per protocol were included in the final analysis. A two-tailed Mann–Whitney *t*-test for non-parametric data was used to analyze the study results with significance defined as $P < 0.05$. The primary efficacy endpoint was the parity of the OTC and device moisturizer as treatment for mild eczema. The secondary efficacy endpoint was the parity of the OTC and device moisturizer accompanied by TAC as treatment for moderate eczema.

Results

Fifty-nine of 60 subjects completed the 4-week study per protocol. One subject was unable to complete the study due to relocation. No adverse events or adverse experiences occurred during the administration of the study. The groups were properly balanced at baseline between arm and leg target sites and eczema severity, as no statistically significant differences between groups were present at baseline.

The data were examined as change from baseline to evaluate treatment success. All subjects with mild and moderate eczema were rated as clear by the dermatologist investigator at the end of the study on the arm or leg target sites. Each target site limb was evaluated separately and at no time point during the study, meaning at week 1, 2, or 4, were any statistically significant differences noted between the OTC and device moisturizer (Fig. 1). The subject assessments also showed no statistically significant differences between the OTC and device moisturizer at any time point (Fig. 2). Thus, parity was established in the treatment of mild to moderate eczema with both products.

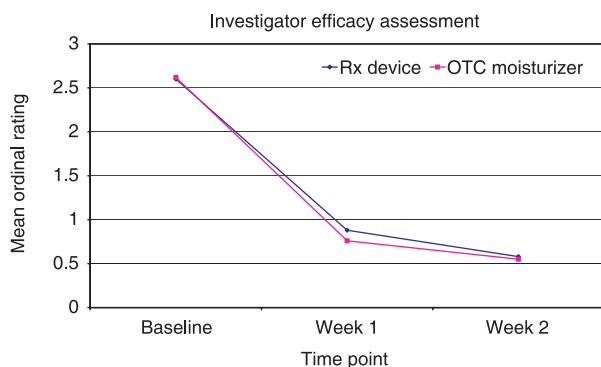


Figure 1 Equivalent investigator-assessed excellent results in resolution of mild to moderate eczema with both the prescription device and the OTC moisturizer.

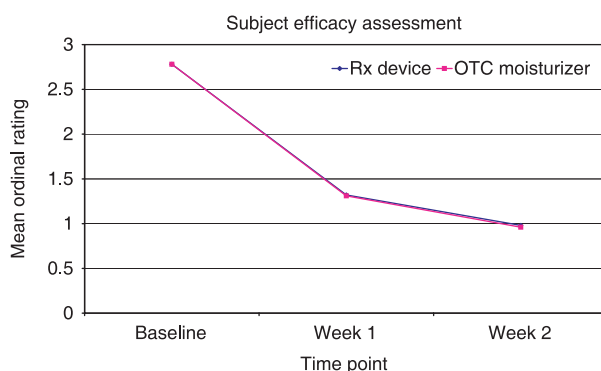


Figure 2 The inability of the subjects to distinguish between the prescription device and the OTC moisturizer in terms of disease resolution.

In order to evaluate the efficacy of each product as compared to baseline, both the investigator and subject data were evaluated longitudinally. The OTC and device moisturizer both showed statistically significant improvement in all parameters studied with identical rapidity of resolution of the mild or moderate eczema by the end of the 4-week study.

The primary efficacy endpoint was met, as parity was demonstrated between the OTC and device moisturizer as treatment for mild eczema. The secondary efficacy endpoint was also met, as parity was demonstrated between the OTC and moisturizer in combination with TAC for moderate eczema.

Discussion

Moisturization is necessary in the treatment of eczematous skin disease, which is one of the most common conditions for which patients seek dermatologic care.⁵ Damage to the

stratum corneum barrier, most commonly from excessive cleanser use, results in the erythema, desquamation, pruritus, and excoriation characteristic of xerotic eczema. Cleansers cannot distinguish between sebum and intercellular lipids; thus, if insufficient sebum and environmental dirt are present on the skin surface, the surfactant will remove the intercellular lipids. Removal of the intercellular lipids, which bind the corneocytes together in a waterproof barrier, increases TEWL signaling barrier damage has occurred. A burst of intercellular lipid synthesis follows, restoring the barrier. In this cascade of events, moisturizers can temporarily reduce TEWL until the barrier is restored, minimizing the signs and symptoms of eczema.⁶

Traditionally, moisturizers were considered cosmetics. They were sold without a prescription in an unregulated environment. However, moisturizers have a more profound effect on the skin than other cosmetics, such as face powder, blush, eye shadow, and mascara. This study demonstrated that twice daily application of moisturizers alone for 4 weeks could successfully treat mild eczema of the arms and legs. Furthermore, the combination of a mid potency topical corticosteroid with a moisturizer applied twice daily could treat moderate eczema of the arms and legs. These findings lend credence to the concept that moisturizers are not cosmetics, but should be more aptly classified as cosmeceuticals, since they have the ability to modify the functioning of the skin.⁷

It is unlikely that a cosmeceutical category will be created in the US skin care market in the near future. This has led several companies to apply for 510K approval of their moisturizer formulations. Dermatologists are familiar with the 510K approval process, which is used to insure the safety of laser, intense pulsed light, radio-frequency, and ultrasound devices. However, the 510K approval of moisturizers is a new concept. The 510K approval process is one way to demonstrate the profound effect moisturizers have on skin hydration, which is a physical skin change. Most moisturizers do not have 510K approval because it is expensive, not required, and confers no advantage to a product that cannot be patented to insure sales exclusivity.

The mineral oil, petrolatum, and paraffin OTC moisturizer evaluated in this research has been in the marketplace for over 100 years; yet, it was equally as efficacious as the prescription 510K device in the treatment of mild and moderate eczema. Both products performed well in the population examined. The OTC moisturizer sells for under \$10 in a half pound jar while the prescription device moisturizer sells for over \$100 in a 140-gram tube. Both products are oil-based, but the device moisturizer contains glycerin and a proprietary ingredient known as

palmitoylethanolamide (PEA). PEA is an endogenous fatty acid that binds to the cannabinoid receptor CB2, inhibiting the release of mast cell histamine, interleukin-4, and cyclooxygenase activity. PEA may be valuable in diminishing the itching associated with eczematous skin disease. This study did not examine the effect of the moisturizers in the treatment of severe eczema and utilized a topical corticosteroid to reduce itch in those subjects with moderate eczema.

In summary, it is interesting to note that this study demonstrated parity between an OTC and prescription moisturizer in the treatment of mild and moderate eczema. It lends credence to the concept that moisturizers are indeed highly effective cosmeceuticals creating physical changes in the skin and alleviating disease.

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