

Clinical Evaluation of a Nature-Based Bakuchiol Anti-Aging Moisturizer for Sensitive Skin

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ABSTRACT

Background: Patients with sensitive skin find topical retinoid use for anti-aging purposes challenging due to irritation. Bakuchiol, a meroterpene from the *Psoralea corylifolia* seed, has retinol functionality through retinol-like regulation of gene expression.

Objective: This research examined the tolerability, efficacy, and barrier effects of a nature-based bakuchiol-containing cleanser and moisturizer in subjects with sensitive skin.

Methods: 60 female subjects Fitzpatrick skin types I–V age 40–65 years with sensitive mild to moderate photodamaged skin were enrolled in this 4-week study. A sensitive skin panel was constructed: 1/3 eczema/atopic dermatitis, 1/3 rosacea, 1/3 cosmetic intolerance syndrome. Subjects used a nature-based cleanser and moisturizer twice daily and underwent transepidermal water loss (TEWL), corneometry, tolerability assessments, and efficacy assessments at baseline, 5–10 minutes post-application, and week 4.

Results: The skin care products were well tolerated and efficacious ($P < 0.001$) in terms of investigator assessed improvement in visual smoothness, tactile smoothness, clarity, radiance, overall appearance, and global anti-aging. Cheek corneometry measurements demonstrated a statistically significant 16% increase in skin moisture content ($P < 0.001$).

Conclusion: A bakuchiol nature-based anti-aging moisturizer is well tolerated and effective in individuals with sensitive skin.

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INTRODUCTION

The poor tolerability of the retinoids has limited their use in sensitive skin patients, even though retinoids are some of the most effective anti-aging cosmeceutical ingredients. Prescription retinoic acid, also known as tretinoin, and OTC retinol, which can be converted in the skin to retinaldehyde and then retinoic acid, can cause irritation due to an overload of the retinoic acid-dependent pathways with supraphysiological amounts of exogenous retinoic acid.¹ Retinoids are effective because they activate retinoic acid receptors and retinoid X receptors, each with three isotopes (alpha, beta, and gamma) and multiple isoforms, responsible for regulating growth, differentiation, and apoptosis.²

Sensitive skin patients desire to use anti-aging cosmeceuticals, but may find it difficult to combine retinoid efficacy with tolerability frequently experiencing pruritus, erythema, and xerosis with product use. In order to determine the suitability of anti-aging cosmeceuticals for sensitive skin subjects, a sensitive skin panel must be developed. One approach to studying sensitive skin is to enroll subjects with dermatologic conditions, such as rosacea, atopic dermatitis/eczema, and cosmetic intolerance syndrome. Cosmetic intolerance

syndrome is defined as individuals who frequently experience noxious sensory stimuli (stinging, itching, burning) when topical products are applied to the face.

Rosacea is characterized by vascular hyper-reactivity, atopic dermatitis/eczema by barrier disruption, and cosmetic intolerance syndrome by sensory hypersensitivity.

An ingredient with retinoid-like effects is bakuchiol, a meroterpene from the *Psoralea corylifolia* seed. Bakuchiol, a Sanskrit name derived from the plant name Bakuchi, has been used in Indian and Chinese medicine for its antioxidant, anti-inflammatory, anti-bacterial, anti-acne, and anti-tumor activities.^{3,4,5} Bakuchiol and retinol both modulate genes involved in the product of the extracellular matrix and dermal-epidermal junction.⁶ Thus, bakuchiol has been said to possess retinol functionality through retinol-like regulation of gene expression.⁷ Prior clinical studies have demonstrated the efficacy of bakuchiol in comparison with retinol.⁸ However, the goal of this research was to evaluate the tolerability, efficacy, and barrier effects of a cleanser and anti-aging cream containing bakuchiol in subjects with sensitive skin.

METHODS

60 female subjects Fitzpatrick skin types I–V age 40–65 years were enrolled in a 4-week single site study after completing informed consent (Allendale Institutional Review Board, Old Lyme, CT) and meeting all inclusion criteria and none of the exclusion criteria. Subjects possessed mild to moderate photodamaged skin defined as the presence of wrinkles and uneven skin tone rated 3–6 on the Fitzpatrick Wrinkle and Elastosis Scale.⁹ In addition, the subjects possessed self-perceived sensitive skin. The sensitive skin panel was constructed according the following guidelines: 1/3 eczema/atopic dermatitis, 1/3 rosacea, and 1/3 cosmetic intolerance syndrome. All subjects washed out of anti-aging or therapeutic skin care products for 4 weeks prior to study entry and topical retinoids or AHAs for 3 months prior to study enrollment. Subjects were not allowed to consume anti-inflammatory drugs, immunosuppressives, or anticancer medications.

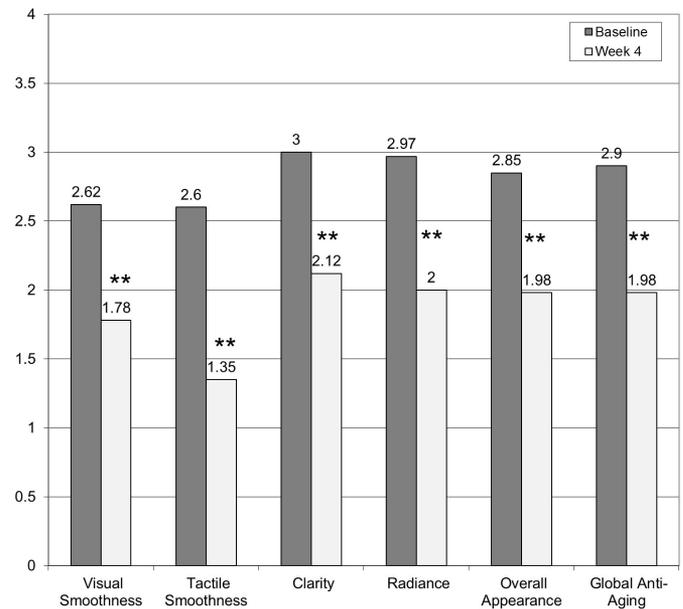
Subjects were dispensed a compliance diary, cleanser, and anti-aging moisturizer with the first application occurring at the research center. Study products were applied morning and evening to the face and neck. Investigator tolerability (investigator assessed erythema/redness, peeling/flaking, visual roughness, dryness and subject queried stinging, burning, itching, tightness) and subject tolerability (stinging, burning, itching, tightness, redness, flaking, roughness, irritation, dryness, overall sensitivity) assessments were performed on a 5-point ordinal scale (0=none, 1=minimal, 2=mild, 3=moderate, 4=severe). Investigator and subject efficacy assessments (visual smoothness, tactile softness, clarity, radiance, overall skin appearance, overall global photoaging) were also conducted on the same 5-point ordinal scale. All evaluations were repeated at week 4.

Instrumental noninvasive upper right cheek transepidermal water loss (TEWL)(Evaporimeter, Cyberderm, Broomall, PA) and lower right cheek triplicate pin probe corneometry (Dermalab Combo, Cortex Technologies, Hadsund, Denmark) measurements were recorded after subjects acclimated to the research center environment for 30 minutes. Measurements were obtained at baseline, 5–10 minutes post-application, and week 4.

RESULTS

60/60 subjects successfully completed the study. The investigator rated no tolerability issues and highly statistically significant improvement ($P<0.001$) in all parameters to include visual smoothness, tactile smoothness, clarity, radiance, overall appearance, and global anti-aging (Figure 1).

The subject ratings mirrored the investigator assessments with highly statistically significant improvement ($P<0.001$) in visual smoothness, tactile smoothness, clarity, radiance, overall

FIGURE 1. Investigator efficacy assessments.

appearance, and global anti-aging. The subjects assessed tolerability in terms of stinging, burning, itching, and tightness. In 10% of subjects primarily with eczema, minimal stinging occurred immediately after application ($P=0.008$) and persisted into week 4 ($P=0.031$). A few subjects noted minimal tightness at week 4 ($P=0.017$). Overall, the subject assessed tolerability profile was excellent given the sensitive skin panel composed of subjects with eczema, rosacea, and cosmetic intolerance syndrome.

TEWL readings did not change from baseline to week 4 indicating absence of barrier damage in sensitive skin subjects, which is crucial to skin health in this population. Corneometry triplicate measurements were taken from the cheek of all subjects. The skin care products produced a highly statistically significant 16% increase in skin moisture content ($P<0.001$), which is notable given the challenging sensitive skin population enrolled in the study.

DISCUSSION

The search for cosmeceutical ingredients suitable for use in patients with sensitive skin resulted in the development of a bakuchiol-based cleanser and moisturizer. Bakuchiol has been studied as an antioxidant for its ability to interfere with free radical-producing systems, inhibit microsomal lipid peroxidation, decrease translocation of mitochondrial apoptosis induced factor (AIF), and quench superoxide- and hydroxy-radicals in vitro.^{10,11} It also can inhibit matrix metalloprotease (MMP) MMP-1 more effectively than retinol.¹² Even though bakuchiol can function like retinol in the regulation of gene

expression, it has a much better tolerability profile than retinoids and does not require dose escalation. It is also photostable providing for greater formulation ease. Finally, bakuchiol is not phototoxic requiring the use of sunscreens.

The nature-based ingredient bakuchiol (1% w/w) was placed in a moisturizing vehicle that improved photoaging and did not damage the skin barrier, as noted by no increase in TEWL, resulting in enhanced moisturization, demonstrated by a 16% increase in corneometry. The major moisturizing ingredients in the formulation included the naturals glycerin and beeswax along with *Helianthus annuus* (sunflower) seed oil and Glycine soja (soybean) oil. Emollients to smooth the rough skin surface included cetyl alcohol and cetearyl alcohol, both derived from natural plant ingredients. The formulation was thickened with cornstarch and xanthan gum. Finally, the oil-based ingredients were emulsified into the water with decyl cocoate derived from coconut oil. Nature-based formulations are more challenging, but clever use of natural ingredients can provide products suitable for sensitive skin.

The nature-based bakuchiol cleanser/moisturizer combination had good tolerability in a challenging sensitive skin population while producing improvement in smoothness, clarity, radiance, overall appearance, and global anti-aging after 4 weeks of use. The minimal stinging observed in eczema subjects may be due to existing poor barrier function while the tightness could be related to winter weather during the study and the restriction that subjects could use the cleanser/moisturizer only twice daily for consistency. The subjects with eczema/atopic dermatitis did not experience worsening barrier function, the subjects with rosacea did not experience increased flushing or inflammatory papules, and the cosmetic intolerance syndrome subjects were able to use the products without facial sensory discomfort.

CONCLUSION

A bakuchiol based anti-aging cleanser and moisturizer was found to be suitable for use in sensitive skin subjects with eczema/atopic dermatitis, rosacea, or cosmetic intolerance syndrome.

DISCLOSURES

Zoe Diana Draelos, MD, received funding from Burt's Bees to perform the research. Hemali Gunt, PhD, is an employee of Burt's Bees. Joshua Zeichner, MD, and Stanley Levy, MD, have both received funding from Burt's Bees.

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