

Novel AHA-Retinoid Ester in Combination with Salicylic Acid for the Treatment of Acne

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INTRODUCTION

Acne vulgaris is a common condition, especially among adolescents and women. Fundamental elements denoting the pathogenesis of acne include inflammation, bacterial colonization by *Propionibacterium acnes* within the pilosebaceous unit, abnormal keratinization, and excessive production of sebum, resulting in the formation of inflammatory and non-inflammatory

lesions that may cause scarring and negatively affect quality of life.

Alpha hydroxy acids (AHA),¹ salicylic acid (BHA),² and retinoids (RC)^{3,4} each have their own mechanism of action when employed to treat acne, including (but not limited to) therapeutic exfoliation—in hydrophilic areas via AHA and in lipophilic areas via BHA—and normalization of cellular differentiation (an effect of RC).

NOVEL RETINOID AHA CONJUGATE

Unfortunately, therapeutic doses of topically applied retinoids frequently cause skin irritations that interfere with treatment. Figure 1 shows relationship between commonly used retinoids and general irritation level and the process by which they are converted from one form to another.

Attempts to reduce retinoid irritation by esterifying Vitamin A with fatty acids or other common organic acids such as palmitic acid and acetic acid to produce “retinyl” esters (e.g. retinyl palmitate, retinyl acetate) also result in reduced efficacy.

Ethyl lactyl retinoate (AHA retinoid conjugate, or AHA-RC) is a “retinoate” ester created by first combining lactic acid (as the carboxylic acid) with ethanol (as the alcohol) to create ethyl lactate and further combining this molecule (as the alcohol) with retinoic acid (as the carboxylic acid).

The resulting AHA-RC is the first double conjugate retinoid to deliver both AHA and RC to skin on a hydrolysis-based time released mechanism, biologically designed to be efficient and minimally irritating to patients. Figure 2 shows the molecular model of this novel ester.

Figure 1. Vitamin A Derivatives, Method of Conversion & Irritation Potential

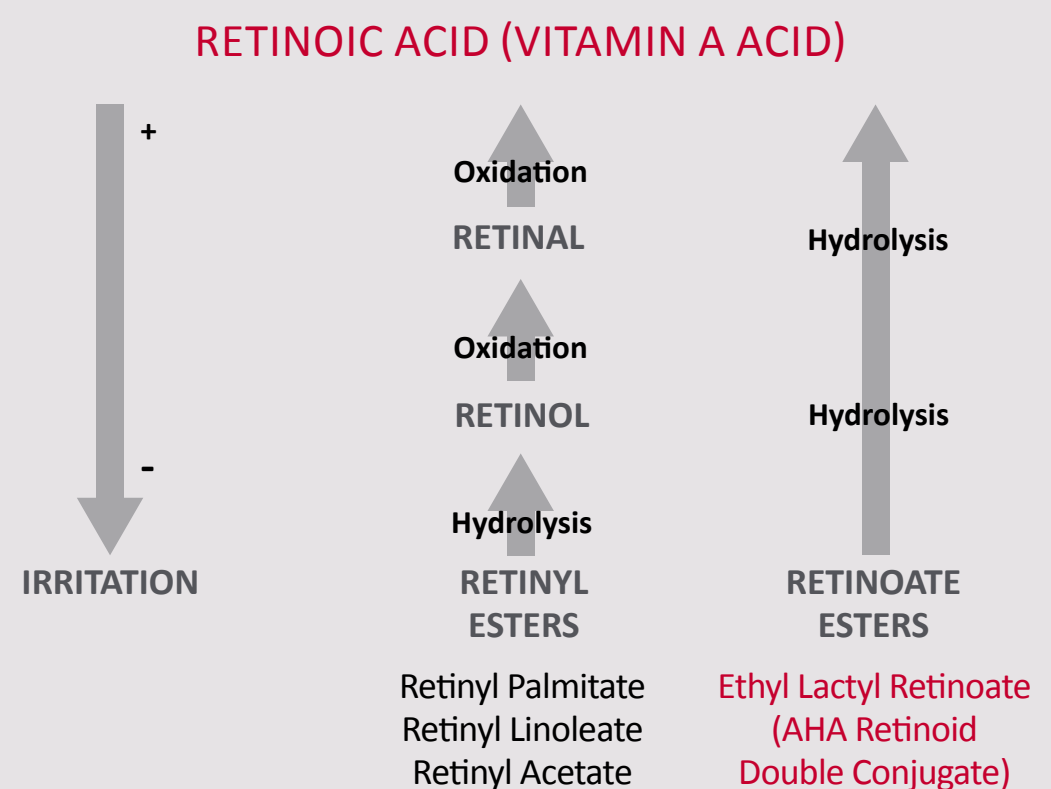
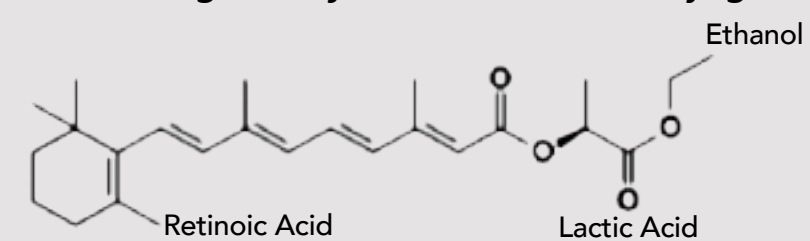


Figure 2. Molecular Diagram of AHA Retinoid Conjugate (AHA-RC)



STUDY PURPOSE & METHODS

The purpose of this clinical study was to evaluate the safety, efficacy and tolerability of an AHA-RC and BHA combination topical product for moderate to severe acne.

A three arm, 30 subject, 8 week clinical trial was conducted and one arm (n=10) was dedicated to AHA-RC for acne; subjects in the acne arm included women (mean age 30.7±9.56 years, range 19 to 44) with moderate to severe acne. Standard inclusion and exclusion criteria were parameters affecting participation in the study.

Patients employed a three product treatment regimen consisting of twice daily (morning and evening) application of foaming cleanser (6.5 % lactic acid, 2% salicylic acid) followed by acne

serum (0.05% AHA-RC, 2% salicylic acid & 10.4% lactic acid), with a broad spectrum SPF 50 sunscreen in the morning and as needed. Subjects also received 50% AHA superficial chemical peel at time point zero and at 4 weeks, and used 30% AHA home peel pads 2-3 times per week depending on patient tolerability. A light mineral powder foundation was provided for use in place of ordinary foundation. The clinical investigator evaluated acne by counting total inflammatory (papules, pustules) and non-inflammatory (open comedones, closed comedones) lesions before treatment and at 4- and 8-week follow-up.

RESULTS & DISCUSSION

All patients completed the study without reported side effects; the products were well tolerated. Two patients were lost to follow-up by week 8. Investigator-rated improvement in acne grade (on a 7 point scale) was approximately 26% at week 4 and 42% at week 8; both results were statistically significant (p<0.05). The study clinical results are reported in Table 1. Subject before and after pictures are shown in Figures 3 & 4. These outcomes are noteworthy because treatment of moderate to severe acne using topicals is a challenge, resulting in a trade-off between tolerability (due to irritation associated with RC and other strong compounds) and efficacy (because more tolerable compounds tend toward more modest outcomes).

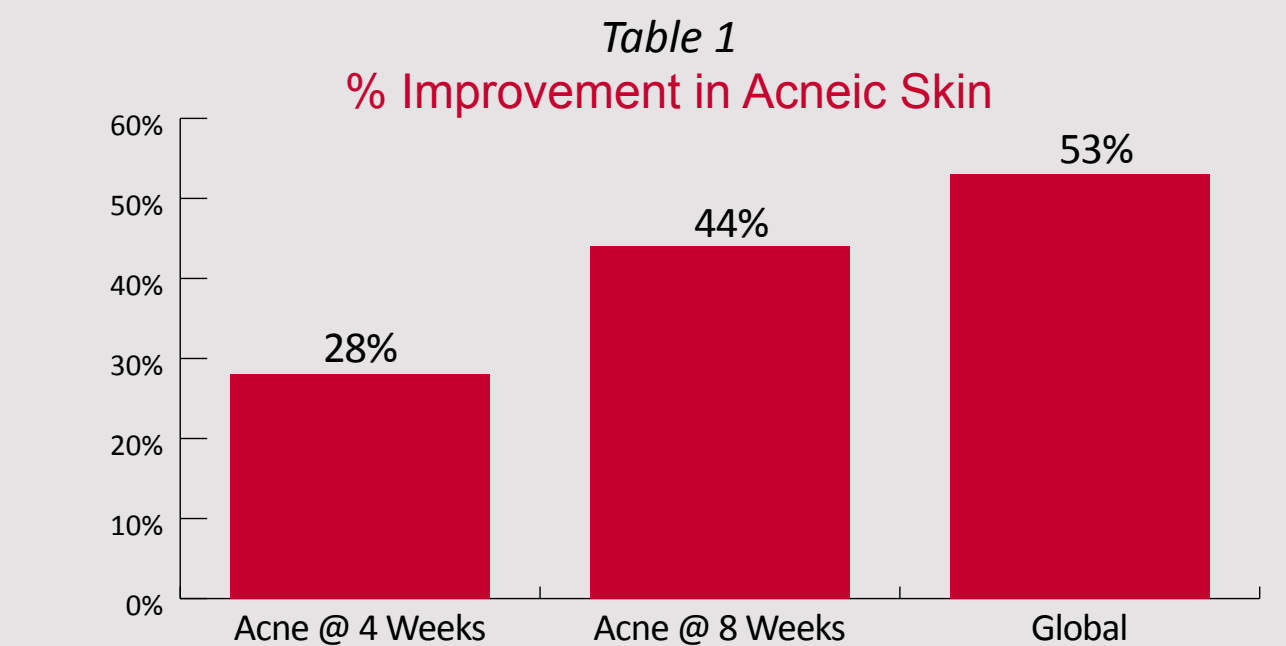


Figure 3 SUBJECT 29/0 & 8 WEEKS



Figure 4 SUBJECT 23/0 & 8 WEEKS



CONCLUSIONS

0.05% AHA-RC combined with 2.0% salicylic acid is safe, effective, and tolerable for the treatment of moderate to severe acne.

DISCLOSURES

This study was sponsored by US Cosmeceutechs, LLC and conducted on their behalf by Dr. Gold. The primary author holds no interest or stock or direct affiliation with US Cosmeceutechs except in the capacity of a paid independent research consultant.

Joseph Lewis BS and Laura McHugh MS are employed by US Cosmeceutechs, LLC, owner of pending patents for technologies used in this study.

Arthur Pellegrino BS and Lavinia Popescu MS, MBA are employed by Elizabeth Arden, Inc., investor in US Cosmeceutechs, LLC.

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