Facial Aging Improvement Case Study Using a Novel Combination of Retinol, Niacinamide, and Terminalia Chebula

Marc Z. Handler MD,[a,b,c] Alison Adams-Woodford BA LE,[d] Patty Ayres LE CMLT,[e]
Giorgiana Giancola PhD,[f] Isabel Diaz BA[g]

[a]Department of Dermatology, Metropolitan Hospital, New York, NY
[b]Department of Dermatology, Rutgers-New Jersey Medical School, Newark, NJ
[c]Dermatology, Hackensack Meridian School of Medicine, Nutley, NJ
[d]R&D and Communications, Physicians Care Alliance (PCA) Skin, Scottsdale, AZ
[e]Physicians Care Alliance (PCA) Skin, Scottsdale, AZ
[f]Scientific Affairs, Colgate-Palmolive Company, Piscataway, NJ
[g]Dermal Clinical Research, Colgate-Palmolive Company, Piscataway, NJ

ABSTRACT

For decades, retinoids have been considered the gold standard of treatment for a variety of skin conditions.[1,2] As the bioavailable form of vitamin A, retinoic acid has demonstrated the ability to reduce skin discoloration, stimulate collagen production, reduce rhytids, improve acne, and uneven skin texture.[3,4] Retinoic acid is a potent drug with high bioavailability. Challenges with such a product include skin sensitivity and retinoid dermatitis.[1,5] This potential irritation and discomfort may hinder patient compliance reducing visible results. The non-prescription vitamin A ingredient retinol is an effective and less irritating alternative, as it is converted into retinoic acid within the skin, causing little to no irritation when used topically. Intensive Age Refining Treatment: 0.5% pure retinol night by PCA SKIN® contains 0.5% retinol, protected and delivered into the skin with a multi-layered liposomal delivery technology. This development addresses the inherent instability of retinol,[1,2,3] as well as the mitigation of irritation with the goal of enhancing patient compliance and visible results. This formulation also features niacinamide and terminalia chebula to further support the anti-aging benefits of retinol. The 12-week in vivo use of this potent, yet non-irritating retinol topical demonstrates improved patient compliance and satisfaction due to tolerability and enhanced efficacy in the improvement in overall signs of healthy skin.

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INTRODUCTION

Many patients avoid retinoic acid due to skin irritation after application, thus reducing perceived efficacy. Retinol is a less irritating topical that carries many of the same benefits as retinoic acid with less irritation and is available without a prescription. Additional ingredients, such as niacinamide and terminalia chebula have demonstrated anti-aging benefits as well.[7,8] Using a liposomal delivery system, a novel formulation was produced to provide an effective and tolerable facial treatment of rhytids, redness, discoloration, and texture. A 12-week facial study was conducted to evaluate the efficacy of a novel topical on the reduction of fine lines, erythema, dyspigmentation, as well as the improvement in skin texture. A self-perception questionnaire was also completed by all participants at the endpoint of the study.

CASE

In order to evaluate the efficacy of the PCA SKIN® Intensive Age Refining Treatment: 0.5% pure retinol night, a group of Fitzpatrick Type II women between the ages of 36 and 61 were recruited with an N=16 (subjects enrolled) and N= 13 (subjects completed and analyzed) for the study. Three withdrew due to issues unrelated to the study.

Following completion of an IRB approved informed consent (US Investigational Review Board, Miami, FL) and meeting all inclusion criteria and none of the exclusion criteria, baseline images were captured before the start of the study at week 0 as well as every two weeks until the study endpoint at week 12. For all participants, images and filter data were captured of the left, right, and front of the face using the Canfield Visia® imaging technology (model Generation 7, software version 7). Filter images specifically analyzed were those tracking changes in brown spots, red areas, wrinkles, and skin texture. Visia® images of all participants were evaluated by the dermatologist investigator.

A self-perception questionnaire was also completed by each participant at baseline and weeks two, four, six, eight, ten, and twelve, the endpoint of the study. The questionnaire measured perceived product performance and the improvements or outcomes the participants identified in their skin after use. The aggregate responses were assessed to determine statistical significance.

METHODS

The test product was dispensed to the participants at the day 0 appointment. Due to the known potential for irritation with the application of any retinoids, the study participants were advised to introduce the test product slowly into their nighttime regimen to allow for skin accommodation to the retinol. In the first two weeks, they were told to use the test product three times per week (day 0, day 2, day 4, day 7, day 9, day 11) in the evenings only. In weeks three to twelve, the participants were instructed to use the product nightly. No participants experienced irritation or sensitivity to the test product when used as directed; limited use in the first two weeks and every evening in weeks three to twelve of the study.

In addition to the test product, participants were given marketed ancillary products (facial cleanser, a moisturizer, and a broad-spectrum sunscreen product) for daily use. The regimen was as follows:

Morning: wash with facial cleanser and apply the sunscreen product. No additional products are to be used.

Evening: wash with facial cleanser and apply retinol test product. Apply moisturizer as needed. No additional products are to be used.

Each participant returned to the test site every two weeks for an assessment by the Study Originator/Supervisor. At these appointments, images and data were captured using the Canfield Visia® imaging technology. This enabled the capture of consistent light images as well as detailed filters that elucidated changes that may not be clinically apparent to the naked eye. Percentages of improvement in comparison to the broader population was also provided through the Visia® technology.

RESULTS AND STATISTICAL ANALYSIS

The dermatologist assessment, self-assessment, and instrument filter data were analyzed by first calculating the 12-week change from baseline (t=0). In all cases, the change was calculated such that a larger, more positive difference ("Diff") indicated a better/more favorable outcome. A two-sided Wilcoxon signed rank test was used to test if the median change in each case was statistically different from zero (ie, no change). A test resulting in a *P*-value of 0.05 or less indicated a statistically significant change.

Dermatologist Assessment

After the 12-week timepoint, the dermatologist investigator determined through analysis of Visia® images that over half of the participants (7 of 13) to have had a statistically significant improvement (P=0.022) in their overall skin condition and appearance. (Figures 1a, 1b, 2a, and 2b) Additionally, during the course of the study, there was no evidence of product irritation visually observed by clinical staff or reported by participants, demonstrating product tolerability.

FIGURE 1A. Photographic assessment for participant #1: redness and uneven texture. (Left) Front view image: baseline- day 0. (Right) Front view image: week 12.

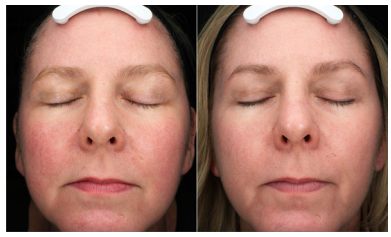


FIGURE 1B. Photographic assessment for participant #1: redness and uneven texture. (Left) Front view image: baseline- day 0. (Right) Front view image: week 12.

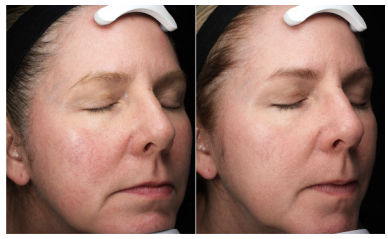


FIGURE 2A. Photographic assessment for participant #2 uneven texture and fine lines. (Left) Front view image: baseline- day 0. (Right) Front view image: week 12.

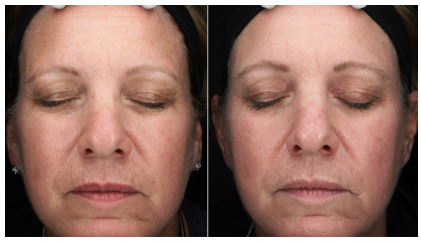


FIGURE 2B. Photographic assessment for participant #2 uneven texture and fine lines. (Left) Front view image: baseline- day 0. (Right) Front view image: week 12.

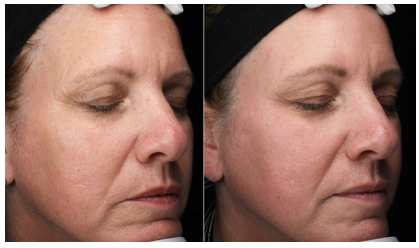
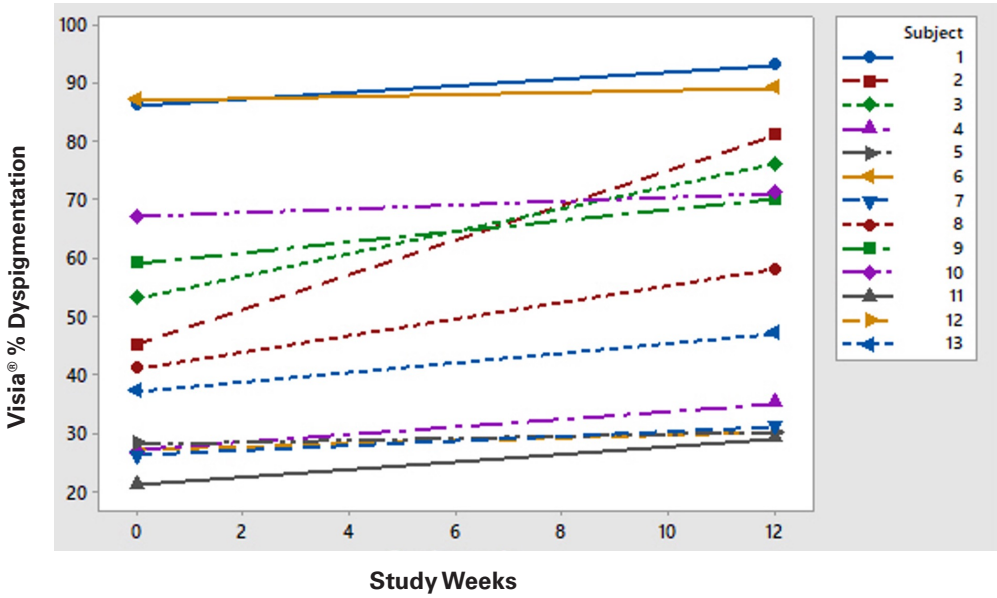


FIGURE 3. Visia filter data; brown dyspigmentation.



Visia® Filter Data

The Canfield Visia® assigns percentages to each participant's photos at each time of imaging. A lower percentage indicates a worse condition in relation to other people of their age globally. Improvement is indicated by a percentage that increases, closer to 100%. The statistical analysis indicated significant improvement in brown spots (*P*=.002; Figure 3), rhytids (*P*=.002; Figure 4), and skin texture (*P*=.003). Directional improvement in red areas was indicated (*P*=.055).

Self-Assessment Questionnaire

The self-assessment questionnaires were completed at each visit. Participants were asked: "On a scale of zero to four, how would you rate the overall appearance of your facial skin? Zero - no improvement, One - mild improvement, Two - moderate improvement, Three - moderately significant improvement, Four - significant improvement", at week 12, 100% of participants rated themselves a four, "significant improvement" (Figure 5).

FIGURE 4. Visia filter data; facial rhytids.

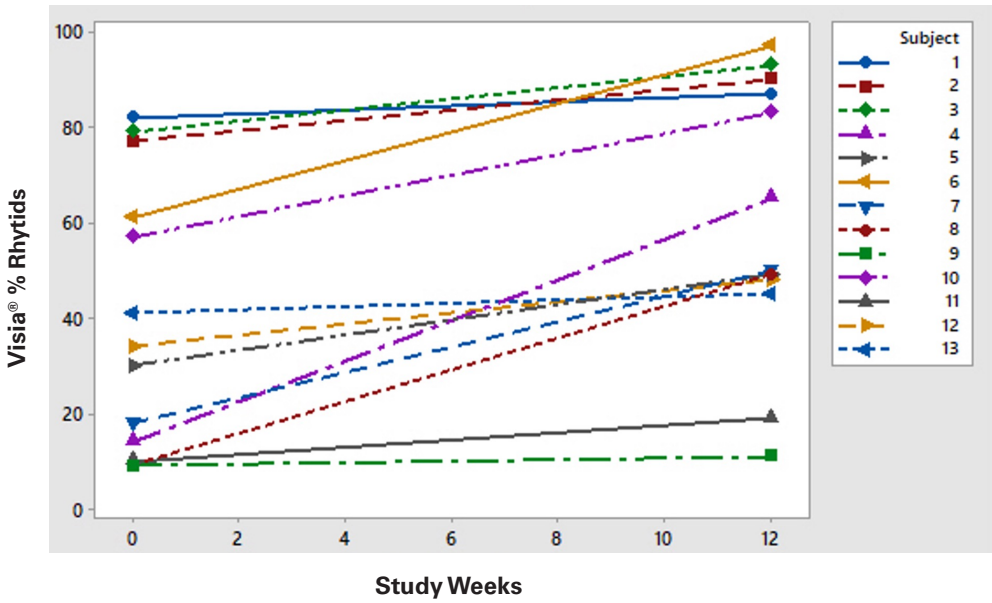
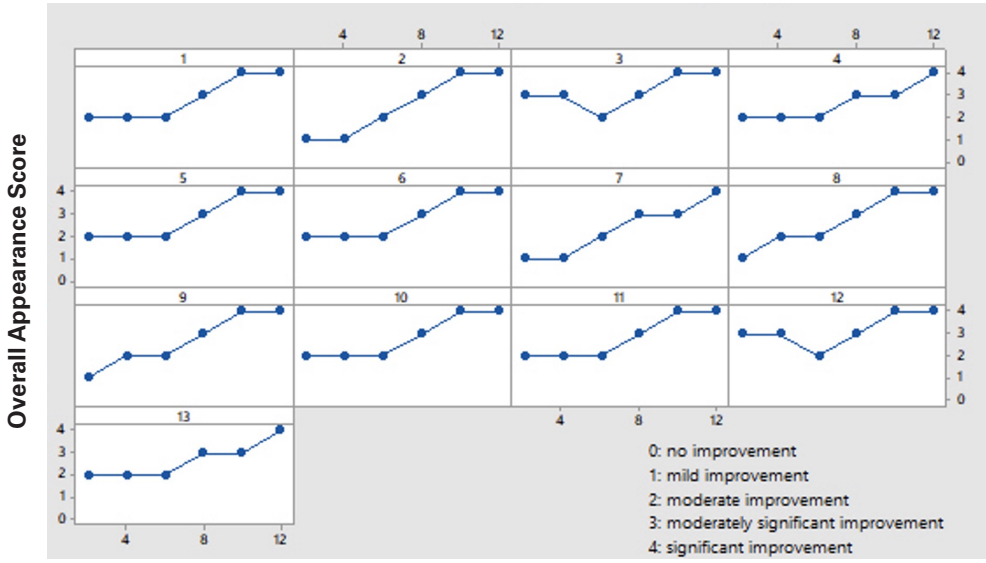


FIGURE 5. Participant self-assessment.



The questionnaire also asked participants to comment on their perception of fine lines, wrinkles, and discoloration. An analysis of these data demonstrated a statistically significant improvement in all categories (P=.003).

DISCUSSION

All-trans-retinol has been used in cosmetic products since the mid-1980s but has been further investigated in numerous studies in the subsequent decades. Some of the demonstrated anti-aging benefits of retinol are increased collagen synthesis, reduced activity of the MMP collagenase[1], and reduced melanogenesis.[6] Recent technological advances have boosted the penetration of retinol. By using an encapsulation system via a thermodynamically stable multi-layered liposomal delivery, retinol penetration is increased in the skin. In addition to improved epidermal penetration, time release of the 0.5% retinol into the skin also minimizes topical irritation due to application.

The addition of 4% niacinamide to a 0.5% retinol formulation enhances anti-aging outcomes, by reducing glycation-related yellowing of the skin.[7] Additionally, the improvement in skin discoloration due to the inhibition of melanosome transfer from melanocyte to keratinocyte and the reduction of wrinkle depth are additional anti-aging contributions of topically applied niacinamide.[7]

To further support the reduction in age-related skin degradation, the tannin-rich botanical extract, terminalia chebula, naturally found in the fruit of the myrobalan tree, was included. Terminalia chebula has demonstrated efficacy as an antioxidant, anti-glycation, and anti-aging component in topical formulations.[8]

CONCLUSION

Since Kligman et al research on vitamin A derivatives and skin, such products have become a staple in an anti-aging regimen. Additional ingredients, such as niacinamide and terminalia chebula have been reported to reduce dyspigmentation and improve skin texture. This is the first study testing the benefit of using these ingredients in combination.

The unique 0.5% retinol formulation of Intensive Age Refining Treatment demonstrated efficacy in reducing the visible signs of facial aging in a majority of subjects, with 100% of subjects reporting overall global improvement. In addition to efficacy, Intensive Age Refining Treatment produced no topical irritation amongst subjects, a benefit over other similar products. This study validated the use of this unique retinol topical for aging skin.

DISCLOSURES

Dr. Handler is a consultant for the Colgate-Palmolive Company. Alison Adams-Woodford and Patty Ayres are employed by PCA SKIN®. Dr. Giancola and Isabel Diaz are employed by the Colgate-Palmolive Company.

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AUTHOR CORRESPONDENCE

Alison Adams-Woodford BA LE
E-mail:..... aadams@pcaskin.com