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An Advanced, Physician-Strength Retinol Peel Improves Signs of Aging and Acne Across a Range of Skin Types Including Melasma and Skin of Color

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ABSTRACT

Background: Facial chemical peels are highly sought after by patients with photodamage, acne, and melasma. An advanced, physician-strength superficial peel, containing 3% retinol with other firming and volumizing ingredients was developed to exfoliate, improve the appearance of fine lines and wrinkles, and plump and firm skin, while promoting a bright, even complexion.

Objective: A clinical study was conducted to evaluate the tolerability, safety, and efficacy of the 3% retinol peel with a supportive homecare regimen across a range of peel candidates, females aged 18-65 years, with photodamage, acne, hyperpigmentation or melasma, and skin of color, over a series of 2-4 peels.

Method: The 3% retinol peel formulation was administered under physician direction in 6-week intervals. Subjects with photodamaged skin, acne, hyperpigmentation/melasma, or skin of color (Fitzpatrick skin types IV-VI) received 2-4 peels along with a supportive homecare regimen. Dermatologist grading, self-assessment, and digital photography documented tolerability and efficacy parameters.

Results: 24 subjects participated in the study with a total of 78 peels administered (Photodamage group, n=14 [with an Acne subgroup, n=5]; Melasma group, n=5; Skin of Color, n=5). The 3% retinol peel along with the homecare regimen was well tolerated under physician direction in all skin types and conditions assessed. Obvious peeling was noticeable in many subjects 3 days post-peel and resolved by day 7. In the photodamaged group, dermatologist clinical grading of fine lines, wrinkles, pore size, laxity, mottled pigmentation, lack of clarity/radiance, and overall photodamage was significantly improved ($P<0.05$). Benefits were observed in all groups and supported by self-assessment. Digital photography demonstrated tolerability in the days immediately post-peel, along with benefits to photodamage.

Conclusion: The 3% retinol superficial peel was well tolerated and an efficacious cosmetic treatment under physician supervision in subjects of all skin types to firm skin, improve fine lines and wrinkles, and promote a bright, even complexion.

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INTRODUCTION

Physician-strength chemical peels are consistently the third most common cosmetic procedure next to neurotoxin and soft-tissue filler injections.[1] Superficial chemical peels are common and safe peeling procedures.[2] Facial chemical peels are highly sought after by aging patients who desire improvements to fine lines and wrinkles, pigmentation, clarity, and laxity, as well as patients with acne, hyperpigmentation, or melasma. As a complementary procedure to hydroquinone homecare products, patients have used chemical peels to improve hyperpigmentation or melasma.[3] While chemical peels are considered safe for all skin types, post-inflammatory hyperpigmentation can be a concern of higher strength chemical peels, particularly in those with darker skin.[2]

Retinol is a proven ingredient for the management of acne and is used as adjunctive care for photodamage due to its ability to enhance exfoliation, increase epidermal thickness, and reduce matrix metalloproteinase (MMP) activity (collagenase) while increasing collagen.[4-7] Studies have demonstrated that topical prescription retinoids are safe and effective in patients with dark skin for the treatment of post-inflammatory hyperpigmentation.[8] Cosmetic retinol products have been shown to affect hyperpigmentation and provide a more even skin tone.[5]

An advanced, physician-strength superficial peel containing 3% retinol was developed to exfoliate and improve the appearance of fine lines and wrinkles, plump and firm skin, and reduce hyperpigmentation while promoting a bright, even complexion. Formulated with bisabolol to help calm the skin, and Vitamin E as an antioxidant, this peel provides additional benefits to overall skin appearance with the addition of triethyl citrate and acetyl tyrosinamide to enhance the skin's matrix for plumping and firming effects.[9-11]

A single center, prospective clinical study evaluated the tolerability and effectiveness of a series of cosmetic retinol peels, in conjunction with a homecare regimen, to improve the appearance of fine lines, wrinkles, skin firmness, and overall complexion brightness on subjects with mild to moderate photodamage across a range of peel candidates, including those with moderate acne, hyperpigmentation or melasma, and skin of color.

Formulation Strategy

An anhydrous peel formulation was developed to deliver 3% retinol to the skin as the primary antiaging benefit ingredient.

Retinol, a precursor to retinoic acid with better tolerance, increases epidermal thickness and reduces MMP activity while enhancing collagen.[5-7] This peel contains triethyl citrate and the amino acid derivative acetyl tyrosinamide to collectively increase collagen and hyaluronic acid shown to plump and firm skin.[9-11] The formula also contains the soothing and calming agent bisabolol, a botanical derived from chamomile. Vitamin E acetate functions both as a skin protectant and provides antioxidant protection for retinol in the formulation. Additionally, the anhydrous vehicle solution contains a photostabilizer and is packaged in amber unit dose vials (2 mL) to preserve the stability of the retinol. The formulation is preservative free, fragrance free, oil free, and dye free (Table 1).

TABLE 1.

Key Benefit Ingredients in Retinol Peel		
Cosmetic Benefit for Skin	**Ingredient**	**Mode of Action**
Peeling Agent	Retinol 3%	• Precursor to retinoic acid with better tolerance • Increases epidermal thickness & reduces MMP activity (collagenase) while enhancing collagen
Firming Agent	Triethyl Citrate	• Increases collagen
Volumizing Agent	Acetyl Tyrosinamide	• Novel, amino acid derivative increases collagen and hyaluronic acid
Soothing/ Calming Agent	Bisabolol	• Botanical derived from chamomile
Protectant	Vitamin E Acetate	• Antioxidant/free radical scavenger
Anhydrous Solution Vehicle	Vehicle	• Contains photostabilizer to protect retinol • Preservative free (alcohol), fragrance free, oil free, dye free • Packaged in opaque unit dose vial

METHODS

The study protocol was approved by an institutional review board (IRB) and informed consent was obtained prior to enrollment. The study consisted of a group of 14 subjects with photodamaged skin (Photodamage group), including five subjects with acne (Acne subgroup). An additional 10 subjects with Fitzpatrick skin types IV-VI (Skin of Color group, n=5) or mild to moderate melasma or hyperpigmentation, as noted with a grade of 3-6 on the 0-9 modified Griffith's scale (Melasma group, n=5), were also included. The Photodamage group, Acne subgroup, Skin of Color group, and Melasma group consisted of females ages 18-65 years with mild to moderate photodamage on the face (fine lines, wrinkles, and/or mottled pigmentation with a grade of 3-6 on the 0-9 modified Griffith's scale). Females in the Acne subgroup had moderate global facial acne (grade 3 on a 0-4 scale).

To be eligible for inclusion, subjects were required to be free of disease or history of disease and without medication usage that could interfere with the study or expose study subjects to unacceptable risks. Subjects also could not have used prescription topical retinoids within 8 weeks, or systemic retinoids within 6 months. Furthermore, they could not have had facial chemical peels, or other resurfacing procedures within 6 months of study start, and could not have used topical cosmetic hydroxyacids, retinol, or other high-strength physician-dispensed antiaging formulations on their face within 4 weeks of study enrollment. Subjects who had regularly used any topical prescription or over the counter facial medications or cleansers on their face within 2 weeks of study enrollment were excluded. Subjects could not be pregnant or breastfeeding, planning to become pregnant during the course of the study, or have known allergies or sensitivities to topical skin products. Subjects who were required to spend excessive time in the sun were not eligible for the study.

Subjects received the 3% retinol peel at the study physician's office approximately every 6 weeks. Each peel procedure was identical for all treatment groups and utilized a pre-peel cleanser followed by application of the retinol peel. Subjects were instructed to remove the peel at home after at least 8 hours with a 4% polyhydroxy acid (PHA) facial cleanser. The study dermatologist monitored the skin's reaction to the peel for 10 minutes in the office. After washing the peel off the skin and for up to one week after, subjects used the 4% PHA facial cleanser twice daily, a 12% Bionic/PHA post-peel face cream or 10% Bionic post-peel face serum, with sunscreen (10% Bionic/PHA day cream SPF 23, or 4% Bionic/PHA physical sunscreen SPF 50). Thereafter, subjects followed a homecare regimen consisting of the 4% PHA facial cleanser (morning and night), 10% Bionic/PHA day cream SPF 23 (morning), 4% Bionic/PHA physical sunscreen SPF 50 (as desired), and a 10% PHA night cream (night). Test materials were packaged in blinded containers. The Photodamage group and Acne subgroup received a total of four peels,

the Melasma group received three peels, and the Skin of Color group received two peels. The first peel was administered on day 0 and subjects visited the office on day 3 and day 7 to observe the skin's response. Additional peels were administered at subsequent visits with a final follow-up visit two weeks after the last peel.

Each study visit consisted of dermatologist clinical grading, objective and subjective tolerability grading, digital photography, and self-assessment questionnaires. Dermatologist visual clinical grading was conducted for each group using a modified Griffith's scale (0=none to 9=severe) and included efficacy grading for fine lines, wrinkles, mottled pigmentation/melasma, pore size, lack of clarity/radiance, laxity, overall global photodamage, and overall global acne evaluation (Acne Subgroup; 0-4 scale). Tolerability was assessed before, during, and 10 minutes post-peel application by the dermatologist (erythema; 0-3 scale) and subject (burning/stinging; 0-3 scale). General objective and subjective irritation were assessed throughout the study by the dermatologist (dryness, erythema, peeling, roughness; 0-3 scale) and subject self-report (burning/stinging, tightness/dryness, and skin sensitivity; 0-3 scale). Days 3 and 7 were included as additional visits to assess tolerability and the skin's visible response to the peel. Adverse events were recorded and tabulated as a measure of safety. Self-assessment questionnaires were administered to capture subject's perception of benefits to skin. Standardized digital photography was conducted (VISIA-CR and Omnia; Canfield Scientific, Inc.) before the first peel, at day 3, day 7, prior to each subsequent peel, and at the final follow-up visit.

Statistics

Primary clinical endpoints included dermatologist visual grading scores of photodamage in the Photodamage group after the series of 4 peels with comparisons to baseline conditions for each subject at each visit. Statistical comparisons were made using the Wilcoxon Signed Rank test and significance was determined at $P \leq 0.05$. The Melasma group, Skin of Color group, and Acne Subgroups were included as case studies, and as such, their data was not statistically analyzed due to the small population size of each group. These case studies, however, provide an assessment of the peel across a range of skin types, and thus, offer valuable safety and tolerability data for the peel. Self-assessed benefits to skin were summarized using mean scores. Tolerability was tabulated using mean scores for objective and subjective irritation during the peel. Safety was recorded through adverse event reporting.

RESULTS

Twenty-four subjects completed the study for tolerability and safety endpoints, including 14 subjects in the Photodamage group (inclusive of five subjects in the Acne Subgroup), five subjects in the Melasma group, and five subjects in the Skin of Color group. A total of 78 retinol peels was administered. Tolerability of the 3% retinol peel on the skin showed only 4 instances of mild erythema and 5 instances of mild stinging/burning over the 78 peels. Mean scores for objective and subjective irritation were assessed over the course of the study and were less than or equal to baseline after the series of peels. A visible skin response in the days following the retinol peel was observed by the dermatologist and subjects. Dermatologist visual grading showed up to moderate increases in peeling, dryness, roughness, and erythema by day 3, which decreased or resolved by

FIGURE 1. Visible peeling and flaking following the 3% retinol peel: 3 days (obvious peeling) and 1 week (peeling resolved) post-peel.

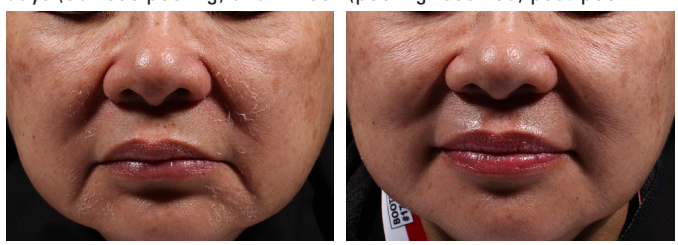


TABLE 2.

Skin Tolerability Over Series of 3% Retinol Peels, Objective and Subjective Irritation Grading

		Mean Score on 0-3 scale (0=none, 1=mild, 2=moderate, 3=severe)						
	Parameter	Baseline (n=24)*	Day 3 (n=23)	Day 7 (n=23)	After 1 Peel (n=23)	After 2 Peels (n=22)	After 3 Peels (n=16)	After 4 Peels (n=14)
Objective Irritation (Dermatologist Graded)	Dryness	0.3	1.0	1.0	0.4	0.2	0.1	0.0
	Erythema	0.3	0.8	0.4	0.1	0.1	0.3	0.3
	Peeling	0.0	1.0	0.7	0.0	0.0	0.0	0.0
	Roughness	0.5	1.1	0.7	0.3	0.4	0.3	0.0
Subjective Irritation (Subject Reported)	Stinging/ Burning	0.0	0.3	0.1	0.0	0.0	0.0	0.0
	Tightness/ Dry Feeling	0.1	0.8	0.6	0.2	0.1	0.0	0.0
	Skin Sensitivity	0.0	0.4	0.2	0.1	0.0	0.0	0.0

*Photodamage group (n=14; inclusive of n=5 acne), Melasma (n=5), Skin of Color (Fitzpatrick skin type IV-VI; n=5)

FIGURE 2. Overall Photodamage significantly improved after 1 peel, fine lines and pore size significantly improved after 3 peels, and all parameters significantly improved after 4 peels, n=14 (P<0.05).

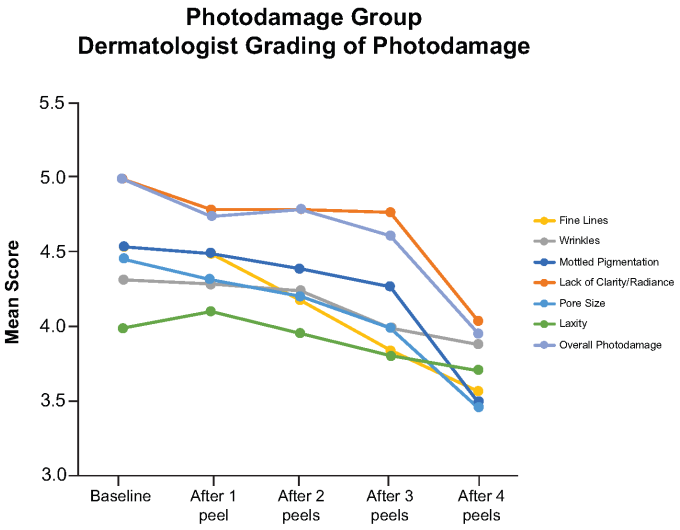
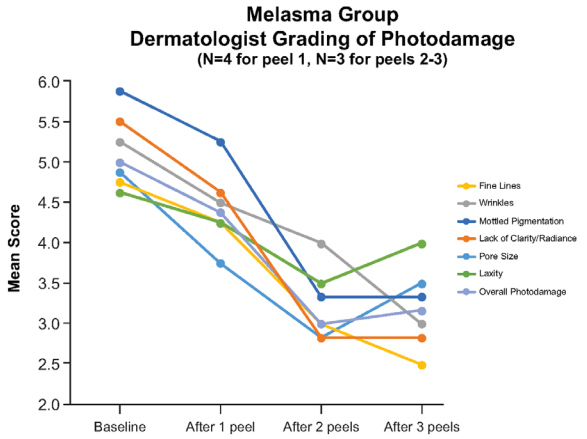


FIGURE 3. Photodamage parameters decreased throughout the series of peels; (A) Melasma; 3 peels (B) Skin of Color (Fitzpatrick skin types IV-VI); 2 peels and (C) Improvement in the appearance of acne; 4 peels (0-4 scale).

(A)



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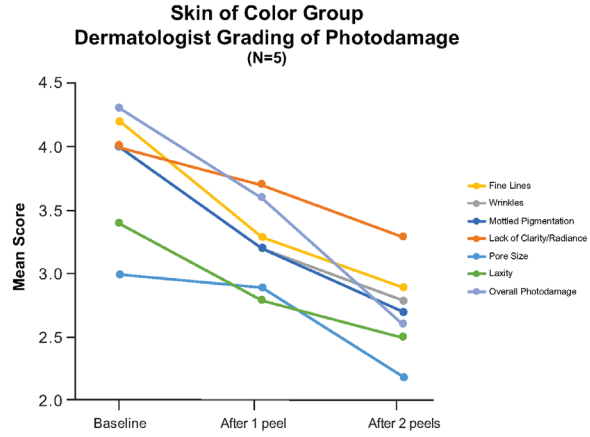

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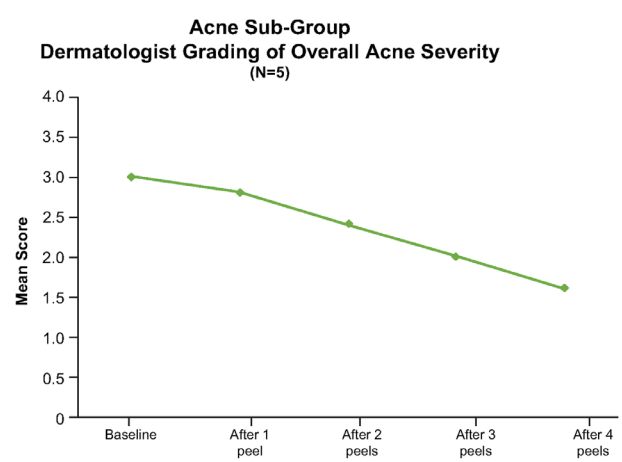
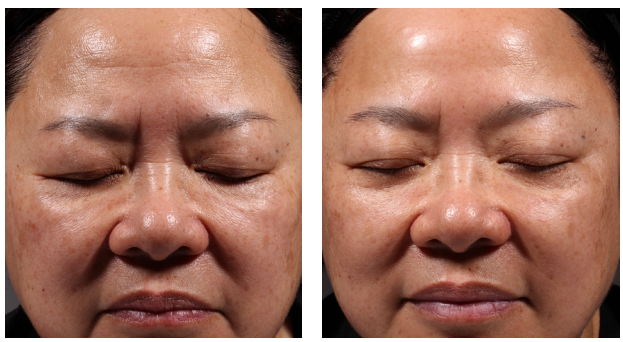


FIGURE 4. Obvious antiaging benefits with 3% retinol peel before and after 2 peels (A) Photodamage group, smoother forehead lines and more even skin tone (B) Skin of Color group, improved hyperpigmentation on forehead and better overall clarity.

(A)



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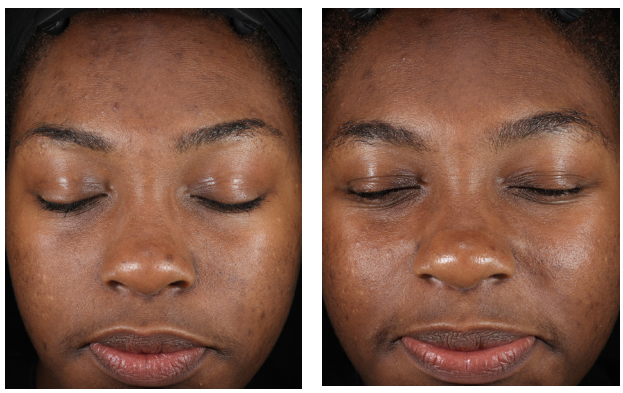


FIGURE 5. Improvement in acne, skin texture, and diminished pigmentation before and after 2 peels with 3% retinol peel; Acne subgroup.

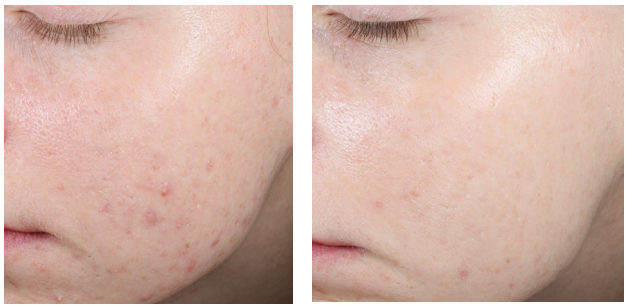


TABLE 3.

Self-Assessed Mean Scores Demonstrating Subject Perceived Improvement in Photodamage After 4 Peels; Photodamage group, n=14

Visit	Rough Skin Texture	Uneven Skin Tone/ Coloring	Fine Lines	Visible Pores
Baseline	1.1	1.9	2.0	2.3
After 1 peel	1.0	1.6	1.7	1.7
After 2 peels	1.2	1.7	1.5	1.7
After 3 peels	1.0	1.3	1.6	1.7
After 4 peels	0.7 (36%)	1.3 (32%)	1.5 (25%)	1.3 (43%)

Grading Scale: 0=none, 1=mild, 2=moderate, 3=severe with half point increments

FIGURE 6. Improvement in melasma along the jawline and overall skin texture before and after 3 peels with 3% retinol peel; Melasma group.

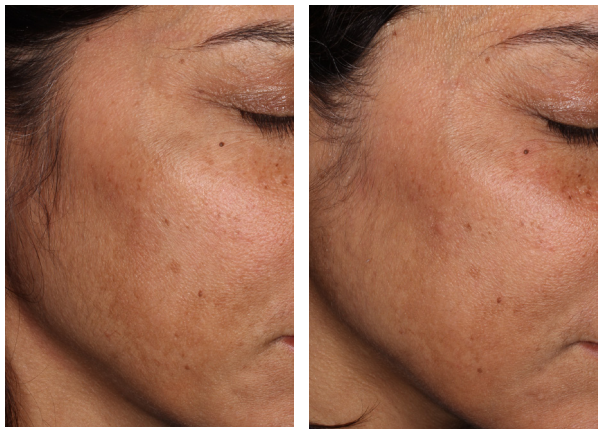
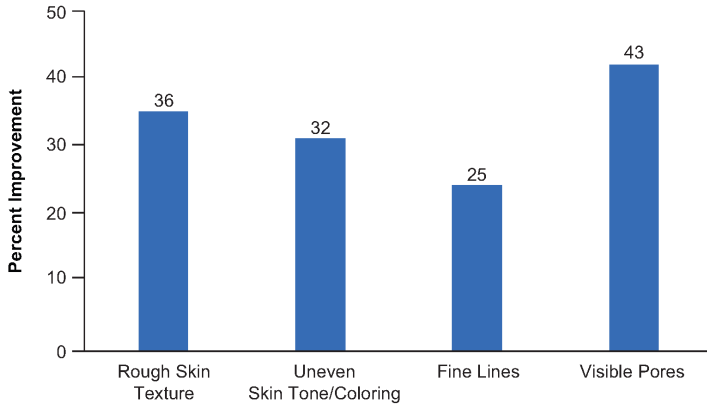


FIGURE 7. Self-assessed mean percent improvement from baseline demonstrates perceived benefits to skin after 4 peels; Photodamage group, n=14.



day 7 (Figure 1). Subjective irritation including up to moderate stinging/burning, tightness/dryness, and skin sensitivity was also reported at day 3 and diminished by day 7 (Table 2). One subject experienced an adverse event consisting of eye area irritation (puffiness/swelling, redness, itching) after the peel. She continued on the study avoiding application too close to the eye.

Statistical analysis was conducted for dermatologist graded aging parameters in the Photodamage group; no statistical analysis of efficacy parameters was conducted for the case studies included in the Melasma group, Skin of Color group, or Acne Subgroup based on the small population sizes. All dermatologist graded aging parameters were significantly improved after 4 peels in the Photodamage group, $P<0.05$. Additionally, overall photodamage significantly improved after 1 peel, and fine lines and pore size significantly improved after 3 peels, $P\leq0.05$ (Figure 2). Although statistical analysis was not performed for the case study groups including the Skin of Color group, Melasma group, and Acne Subgroup, all dermatologist graded photodamage parameters and overall acne severity decreased over the course of the study (Figure 3). Digital photography demonstrated obvious antiaging effects (Figure 4), as well as benefits to acne (Figure 5) and melasma (Figure 6). Self-assessed aging parameters were improved, providing subjective support of the clinical data (Table 3, Figure 7). The PHA/Bionic supportive home care products were well-tolerated when used in conjunction with the retinol peel.

The 3% retinol peel, in conjunction with a homecare regimen, was well tolerated in subjects with photodamage, acne, hyperpigmentation/melasma, and skin of color (Fitzpatrick skin types IV-VI), and demonstrated visible improvements in antiaging parameters, acne, and melasma.

CONCLUSION

Patients seek non-invasive cosmetic treatments for aging concerns, acne, and hyperpigmentation. The tested high-strength retinol superficial peel formulation, containing 3% retinol, with triethyl citrate and acetyl tyrosinamide, significantly improved overall photodamage after one peel. In addition, after a series of 4 retinol peels, along with a polyhydroxy acid-based homec-

are regimen, the clinically graded signs of aging, including fine lines, pore size, lack of clarity/radiance, mottled pigmentation, wrinkles, and laxity, significantly improved. This unique retinol peel and homecare regimen provided benefits to acne and melasma as well. Subject self-assessment provided further support to the clinical grading. Obvious benefits and tolerability of the peels and homecare are further demonstrated through digital photography. The retinol peel was well tolerated under physician direction when applied and left on for 8 hours or overnight (>8 hours) across a range of skin types and conditions. Minimal irritation was observed during the peel procedure, though the physician must manage patient expectations for peeling and redness in the days following application of the peel. Peeling did not occur immediately, but usually by day 3 and resolved within approximately 1 week. Gentle, restorative post-procedure PHA products can be used post-peel until the skin returns to normal and thereafter to complement benefits of the peel. These results demonstrate that the 3% retinol superficial peel is well tolerated in all skin types and is an effective method of delivering clinical improvements in subjects with photodamage, as well as acne and hyperpigmentation or melasma.

Physicians have many modalities available in their armamentarium, and chemical peels continue to be a mainstay of therapy. This unique, high-strength retinol peel provides a new tool for the physician and their patient, particularly to those desiring a visual cue, or those without objection to the potential for obvious peeling. While still falling under the category of a superficial chemical peel the proven benefits of retinol are available with a high concentration of retinol, far above that available to a consumer. Additionally, compatibility of the retinol peel was shown in a variety of populations that can be difficult to treat and may be prone to post-inflammatory hyperpigmentation, such as patients with melasma or Fitzpatrick skin types IV-VI. The retinol peel provides a versatile option to the physician to offer to all patients desiring superficial skin rejuvenation.

DISCLOSURES

Ms. Edison, Ms. John, and Ms. Green are employees of NeoStrata Company, Inc. Dr. Sadick served as the study investigator and has been a speaker for NeoStrata Company, Inc. Ms. Bohnert was an employee of Sadick Research Group LLC and is now at Celgene.

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