A High-Potency, Multimechanism Skin Care Regimen Provides Significant Antiaging Effects: Results From a Double-Blind, Vehicle-Controlled Clinical Trial

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ABSTRACT

Skin aging is a multifaceted biological process characterized by the appearance of wrinkles, pigmentation irregularities, and loss of firmness. These symptoms cannot be fully addressed by any single skin care ingredient or noninvasive cosmetic procedure. A comprehensive treatment approach, including the use of clinically proven topical skin care formulations, provides optimal antiaging effects. A high-strength skin care regimen (NeoStrata® Skin Active, NeoStrata Company, Inc, Princeton, NJ) was developed to deliver a combination of more than 35% active benefit ingredients, including the α-hydroxy acid glycolic acid, the polyhydroxy acid gluconolactone, maltobionic acid, N-acetylglucosamine, retinol, peptides, antioxidants, and apple stem cell extract. The products (cleanser, day cream, night cream, eye cream) were formulated to provide antiaging benefits across all skin layers via multiple mechanisms of action. The regimen was evaluated in a randomized, double-blind, vehicle-controlled clinical trial over 16 weeks, with a subset continuing to 30 weeks. Sixty-nine Caucasian women (active group, n=44; vehicle group, n=25) completed 16 weeks of twice-daily treatment. Results showed the active group improved significantly better than the vehicle group for: all clinician-graded aging symptoms beginning as early as 2 weeks, pinch recoil as a measure of firmness/elasticity; dermal density, which was measured using ultrasound; and total skin thickness, which was measured using digital calipers. Clinical photography revealed younger-looking skin. Seventeen subjects from the active group continued to receive the active regimen until week 30. Improvement in all parameters of aging was shown to be significantly greater at week 30 than at week 16, and dermal density continued to increase. The comprehensive benefits observed in this study over the cosmetic vehicles are believed to have been achieved through the synergistic actions of the benefit ingredients in the active regimen.

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INTRODUCTION

Aged skin is characterized by the appearance of wrinkles, pigmentation irregularities, and loss of firmness due to diminished functionality of skin cells from both intrinsic and extrinsic factors, of which exposure to ultraviolet (UV) light and free radicals have the largest negative impact.[1] These extrinsic factors notably cause a reduction in the production of collagen and extrafibrillar matrix components, leading to wrinkles, loss of firmness, and abnormal pigment production, causing age spots and other pigmentation irregularities. Skin aging, a multifaceted biological process with multiple symptoms, cannot be fully addressed by any single skin care ingredient or noninvasive cosmetic procedure.[2] Therefore, a comprehensive treatment approach, including the use of clinically proven topical skin care formulations, provides optimal antiaging effects. Well-formulated antiaging products can address many signs of skin aging when used as monotherapy[3,4] and can enhance and extend the effects of cosmetic procedures when used in combination.[5]

A high-strength skin care regimen that delivers a combination of more than 35% active benefit ingredients, including α-hydroxy and polyhydroxy acids, maltobionic acid (MBA), N-acetylglucosamine (NAG), retinol, peptides, antioxidants, and apple stem cell extract, was developed to provide antiaging benefits across all skin layers via multiple mechanisms of action. The regimen consists of a facial cleanser, a day cream with sunscreen, a night cream, and an eye cream. The tolerability and effectiveness of this regimen were evaluated in a randomized, double-blind, vehicle-controlled clinical trial.

Comprehensive antiaging therapy addresses both prevention and reduction of various physiologic mechanisms and visual signs associated with aging of the skin. To this end, the benefit ingredients in the test regimen were chosen to target multiple mechanisms of action in skin (Table 1). Preventive agents, including broad-spectrum sunscreens and antioxidants such as Chardonnay grape seed extract, were selected to reduce exposure to and damage

TABLE 1.

Key Antiaging Benefit Ingredients in the Active Product Regimen

Ingredient	Photoprotective Effect	Reduces the Activation of Elastase and/or MMP Enzymes	Preserves Epidermal Stem Cell Activity	Increases Epidermal Cell Turnover	Increases Dermal Matrix Components (GAGs and/or Collagen)	Apparent Smoothing
Meltobionic acid		X		X	X	X
Glycolic acid				X	X	X
Retinol		X		X	X	X
N-Acetylglucosamine				X	X	X
Gluconolactone		X		X		X
Palmitoyl oligopeptide and tetrapeptide					X	
Apple stem cell extract			X			
UVA- and UVB-absorbing sunscreens	X					
Antioxidants	X	X				

GAGs, glycosaminoglycans; MMP, matrix-degrading metalloproteinase; UVA, ultraviolet A light; UVB, ultraviolet B light.

from UV radiation and to help neutralize resultant free radicals. Well-established antiaging ingredients, including retinol and polyhydroxy/bionic acids (eg, MBA), were selected to help protect the skin by reducing the activity of matrix-degrading metalloproteinase enzymes, such as collagenase.[4,6,7] The polyhydroxy acid gluconolactone was chosen to help protect skin against solar activation of elastase, thereby helping to preserve the quality of healthy, elastic tissue.[4] A relatively recent ingredient in antiaging therapy with growing consumer interest, Swiss apple stem cell extract (PhytoCellTec Malus Domestica extract; Mibelle AG Biochemistry, Buchs, Switzerland), was selected because it provides a source of phytonutrients and epigenetic factors that have been shown in vitro to preserve youthful characteristics and functionality of essential human epidermal stem cells.[8]

Reduction of the signs of skin aging can be achieved via multiple mechanisms, including increased biosynthesis of dermal matrix components, such as glycosaminoglycans (GAGs; eg, hyaluronic acid). An increase in the skin's natural GAG content promotes significant water binding and building of the dermal gel matrix, resulting in a natural volume-building effect that helps to reduce the appearance of wrinkling and increase firmness. The test regimen utilized glycolic acid,[9] MBA,[4,7] retinol,[9] and NAG[10] to provide this effect. Furthermore, retinol and NAG were combined in the daytime formulation because they have been shown to bring about a synergistic increase in hyaluronic acid production when used together.[10] Likewise, the regimen was formulated to target an increase in the skin's primary structural protein, collagen. Collagen-building ingredients were chosen, including palmitoyl oligopeptide and palmitoyl tetrapeptide (Matrixyl; Sederma SAS, Paris, France),[11] which were observed in vitro to stimulate collagen synthesis, as well as retinol[12] and glycolic acid[13] which have data to support in vivo increases in human collagen. Many of these same ingredients, including NAG and retinol, impact melanogenesis by reducing the activation of tyrosinase and reducing melanin production.[14,15]

MATERIALS AND METHODS

Study Design

The initial phase of this study was a 16-week, randomized, double-blind, vehicle-controlled assessment of the efficacy and tolerability of the high-potency, multimechanism skin care regimen. To determine whether additional antiaging benefits could be achieved beyond 16 weeks, a subgroup of participants in the active group continued to receive the active regimen for an additional 14 weeks. The protocol received institutional review board approval, and all subjects provided written informed consent before participating.

Caucasian women aged 45 to 65 years who were willing to use high-strength skin care products were enrolled in the study. To be included, subjects had to present with mild to moderate general facial photodamage (4-7 on a 0-9 grading scale for fine lines, coarse wrinkles in the periocular area, and mottled pigmentation on the face). Subjects were excluded if they had known allergies to skin care products, skin or eye conditions, or uncontrolled chronic diseases that could interfere with evaluations; if they were currently using medications for skin or eye conditions or had routinely used antiaging topical products, including prescription retinoids, within the previous 6 months; if they had used hydroxy acids, retinol, or other antiaging cosmetics within the previous 2 months; if they had undergone a cosmetic procedure (eg, peel, laser, or light treatment) within the previous 6 months.

Participants were randomly assigned in a 2:1 ratio to either the active group or the vehicle group. They used the entire regimen on the face twice a day (cleanser, eye cream, and day or night cream); the day and eye creams were applied after cleansing in the morning, and the night and eye creams were applied after cleansing in the evening. Subjects also applied the day cream and night cream or their vehicles on one outer forearm, leaving the other forearm untreated as a control. The effects of the

active regimen and the vehicle were assessed with respect to several parameters at numerous intervals during the 16 weeks.

Efficacy and Safety Assessments

Visual Grading and Pinch Recoil (Weeks 0, 2, 4, 8, 12, and 16)
A trained clinical grader assigned scores to either the right or the left side of the face for fine lines, wrinkles, clarity, laxity, visual roughness, tactile roughness, dyschromia, pore size, sallowness, eyelid crepiness (wrinkling), lifted appearance of the eyelid (droopiness), and overall appearance, using a scale from 0 (none) to 9 (severe) with half-point increments. A decrease in baseline score is associated with improvement in a clinical sign of aging. Pinch recoil was tested as previously described on the lateral side of the left eye for each subject.[18] Briefly, the skin was pinched and held for approximately 2 seconds and then released. The time taken for the skin to return to its original conformation was recorded to the nearest 100th of a second. A decrease in pinch recoil time is associated with an improvement in skin firmness/elasticity.

Skin Thickness (Weeks 0, 8, and 16)
Skin density in the crow's feet area was measured via ultrasound imaging for half the subjects in each group, randomly selected at baseline. An increase in dermal density was interpreted as a thickening of the tissue, resulting from deposition of matrix components. In addition, total skin thickness measurements of the dorsal side of each forearm were taken in duplicate approximately 4 cm from the flexor joint using a hinged pinching device and digital calipers, as previously described.[19] Using this method, scores increase as the skin thickens or becomes denser. The 2 scores for both the treated and untreated forearms were averaged.

Silicone Replicas (Weeks 0, 8, and 16)
The other half of the subjects in each group, randomly assigned at baseline, had a silicone replica taken in the crow's feet area (on the same side as was chosen for clinical efficacy scoring). The replica produced a negative impression of the skin's surface. Image analysis was applied to each replica, providing a view of the skin's topography to visually demonstrate any change in wrinkles.

Digital Photography (Weeks 0, 8, and 16)
Subjects were photographed using digital photography by a single medical photographer at all time points under standardized light conditions. Subjects' faces were placed in a facial-positioning device to ensure that the position could be reproduced at each study visit. A color chart was incorporated into each image to ensure light reproducibility. Images were unretouched and were cropped to show changes in target areas.

Self-Assessment (Weeks 0, 2, 4, 8, 12, and 16)
Self-assessment questionnaires were administered at each visit in order to capture both self-perceived efficacy and tolerability.

Tolerability/Safety (Weeks 0, 2, 4, 8, 12, and 16)
A trained clinical grader assessed all subjects for irritation/tolerability and elicited feedback from the subjects. Parameters included objective measures of erythema and dryness together with subjective measures of burning, stinging, itching, tingling, and tightness using a 0 (none) to 3 (severe) scale with half-point increments. Adverse events were also collected and tabulated.

> "In this study, a new high-potency, multimechanism skin care regimen, including a facial cleanser, a day cream with broad-spectrum sunscreen, a night cream, and an eye cream, delivered comprehensive antiaging benefits to photodamaged skin as early as week 2, with continued improvement over the 16- and 30-week durations of the study"

Continuation Phase to 30 Weeks

A subset of subjects was randomly recruited to continue beyond the initial 16-week study duration to receive the active regimen for an additional 14 weeks. Subjects returned to the clinic at weeks 21 and 30 for clinical efficacy and tolerance grading, pinch recoil, forearm caliper measurements, ultrasound imaging and silicone replicas, photography, and completion of a self-assessment questionnaire.

Formulations

Participants in the active group used the high-potency, multimechanism skin care regimen, comprising a facial cleanser, a day cream, a night cream, and an eye cream. The eye cream was applied twice daily to the periocular area, including the upper lids. These formulations contained cosmetic benefit ingredients (Tables 1 and 2), including α-hydroxy and polyhydroxy acids (glycolic acid, gluconolactone, and MBA), a neutral amino sugar compound (NAG), palmitoyl oligopeptide and tetrapeptide, retinol, antioxidants (Chardonnay grape seed extract, vitamin E, fruit/berry extracts), broad-spectrum sunscreens, and apple stem cell extract.

The products were formulated in moisturizing vehicles that were paraben free and lightly scented with a botanical oil (the eye cream was unscented). The day cream contained sunscreens and was formulated to protect the integrity of retinol with a triple-stabilizing complex of chelating agents, lipophilic and hydrophilic antioxidants, and a photostabilizing agent and was packaged in an airless, light-proof laminate tube.

TABLE 2.

Description of Test Products

Product and Use	Key Benefit Ingredients
Facial Cleanser* (NeoStrata® Skin Active Exfoliating Wash) • Day and night use	8.5% polyhydroxy bionic acids (gluconolactone + maltobionic acid), botanical complex (extracts of aloe, chamomile, cucumber, *Althaea officinalis*, and rosemary), and soap-free surfactants
Day Cream* (NeoStrata® Skin Active Matrix Support SPF 20) • Day use	8% N-acetylglucosamine, 0.1% retinol, palmitoyl oligopeptide and tetrapeptide, vitamin E, pomegranate and coffee berry extracts, UVA/UVB sunscreens
Night Cream* (NeoStrata® Skin Active Cellular Restoration) • Night use	15% α-hydroxy/polyhydroxy bionic acids (glycolic acid, gluconolactone, and maltobionic acid), palmitoyl oligopeptide and tetrapeptide, Chardonnay grape seed extract, apple stem cell extract, extracts of acai fruit, pomegranate, and blueberry, vitamin E
Eye Cream* (NeoStrata® Skin Active Intensive Eye Therapy) • Day and night use	6% N-acetylglucosamine, palmitoyl oligopeptide and tetrapeptide, apple stem cell extract, caffeine, sodium hyaluronate, vitamin E, optical blurring agents
Vehicles (4) • Same daily regimen use as active product	No key benefit ingredients; base formulations were provided in identical packaging as active products; the vehicle day cream was formulated with identical UVA/UVB sunscreens (SPF 20)

SPF, sun protection factor; UVA, ultraviolet A light; UVB, ultraviolet B light.
*All products in the active regimen were manufactured by NeoStrata Company, Inc, Princeton, NJ.

Analytical studies confirmed the stability of retinol. The acid-containing night cream was formulated at pH 3.8 to promote bioavailability of the hydroxy acids.

Participants in the vehicle group applied identical facial cleanser, day cream, night cream, and eye cream preparations that did not contain benefit ingredients (except for the day cream, which contained identical sunscreens; Table 2).

Statistical Analysis

All scores were recorded using an electronic data capture system. The primary outcome measure was the difference in improvement in all visually graded signs of aging between the active group and the vehicle group after 16 weeks of treatment. In addition, postbaseline scores were compared with baseline scores within each group, and changes from baseline scores were compared between groups at each postbaseline visit for each visually graded sign of aging, pinch recoil times, forearm skin thickness measurements, and ultrasound measurements. All within-group comparisons were performed using paired *t* tests, and all between-groups comparisons were performed using analysis of variance with pairwise comparisons. All statistical tests were performed at $P \leq .05$ level of significance. Self-assessment questionnaire scores were tabulated.

RESULTS

Sixty-nine Caucasian women (active group, n=44; vehicle group, n=25) completed 16 weeks of treatment. The mean ages of the subjects were 59 years in the active group and 56 years in the vehicle group. Visual signs of aging significantly improved over the course of treatment in both groups (Table 3). However, participants in the active group showed significantly more improvement than participants in the vehicle group ($P<.001$) on all parameters, including fine lines (33% vs 17%; Figure 1a), wrinkles (20% vs 7%; Figure 1b), clarity (44% vs 29%), laxity (30% vs 15%; Figure 1c), visual roughness (49% vs 31%), tactile roughness (68% vs 44%), dyschromia (31% vs 12%; Figure 1d), pore size (21% vs 10%), sallowness (40% vs 13%), eyelid crepiness (24% vs 14%), lifted appearance of eyelid (19% vs 13%), and overall appearance (26% vs 18%) by the end of the 16-week initial phase. Pinch recoil also improved significantly more in the active group than in the vehicle group by the end of treatment (18% vs 8%; $P<.0001$).

Dermal density measured by ultrasound imaging increased by approximately 20% over the first 8 weeks in the active group ($P<.05$ vs baseline and between treatments; Figure 2a) vs 6% in the vehicle group (not significant). Week 16 data were not included in data analysis for dermal density measured by ultrasound imaging because of a malfunction of the ultrasound probe. Thickness of the forearm skin, determined by digital caliper measurements, also increased significantly more with active treatment (8.3%) compared with either vehicle (3.4%) or no treatment (0.3%; $P<.01$ between treatments; Figure 2b).

Clinical photography showed improvement in the visual signs of aging (Figures 3a and 4). Silicone replicas of the crow's feet area demonstrated improvement in skin texture and reduction in fine lines and wrinkles that corresponded to the visual changes seen in clinical photographs (Figure 3b).

After 16 weeks, almost all subjects in the active group reported antiaging benefits: 96% noted that their skin was more firm and radiant, 91% indicated that they looked younger and

TABLE 3.

Improvement in Visual Signs of Aging Over 16 Weeks: Active Group vs Vehicle

	Group	Week 0	Week 4		Week 16		Week 16	Weeks at Which Active Group Improved Significantly More Than Vehicle Group, $P \leq .05$
		Mean Score	Mean Score	Mean Change	Mean Score	Mean Change	Active Regimen Outperformed Vehicle Regimen by X Factor	
Fine lines	Active	4.42	3.82	−0.60	2.94	−1.48	2.0X	2, 4, 8, 12, 16
	Vehicle	4.26	3.92	−0.34	3.52	−0.74		
Wrinkles	Active	4.43	4.11	−0.32	3.55	−0.89	3.0X	8, 12, 16
	Vehicle	4.28	4.20	−0.08	3.98	−0.30		
Clarity	Active	5.16	3.94	−1.22	2.90	−2.26	1.5X	2, 4, 8, 12, 16
	Vehicle	5.16	4.22	−0.94	3.68	−1.48		
Laxity	Active	6.66	4.99	−0.67	3.99	−1.67	2.3X	2, 4, 8, 12, 16
	Vehicle	5.10	4.64	−0.46	4.36	−0.74		
Visual roughness	Active	5.17	3.90	−1.27	2.61	−2.56	1.6X	8, 12, 16
	Vehicle	5.34	4.36	−0.98	3.70	−1.64		
Tactile roughness	Active	5.10	2.66	−2.44	1.65	−3.45	1.5X	2, 4, 8, 12, 16
	Vehicle	5.36	3.60	−1.76	2.98	−2.38		
Dyschromia	Active	4.18	3.73	−0.45	2.89	−1.30	2.3X	4, 8, 12, 16
	Vehicle	4.52	4.30	−0.22	3.96	−0.56		
Pore size	Active	3.85	3.72	−0.14	3.05	−0.81	2.4X	12, 16
	Vehicle	3.56	3.52	−0.04	3.22	−0.34		
Sallowness	Active	3.92	3.42	−0.50	2.34	−1.58	3.3X	4, 8, 12, 16
	Vehicle	3.56	3.44	−0.12	3.08	−0.48		
Eyelid crepiness/ wrinkling	Active	5.56	5.13	−0.43	4.24	−1.32	1.8X	2, 4, 8, 12, 16
	Vehicle	5.20	5.02	−0.18	4.48	−0.72		
Lifted appearance of eyelid/droopiness	Active	5.98	5.73	−0.25	4.83	−1.15	1.6X	12, 16
	Vehicle	5.56	5.38	−0.18	4.82	−0.74		
Overall appearance	Active	5.09	4.43	−0.66	3.76	−1.33	1.5X	2, 8, 12, 16
	Vehicle	4.82	4.32	−0.50	3.94	−0.88		

All signs of aging were significantly improved in the active group vs baseline condition by week 4 except for lifted appearance of eyelid/droopiness, which reached significant improvement from baseline at week 8. The vehicle group did not achieve significant improvement in all signs of aging vs baseline until week 12.

FIGURE 1. Improvement in **a)** fine lines, **b)** wrinkles, **c)** skin laxity, and **d)** dyschromia over 16 weeks in the active group vs the vehicle group. *Significantly better than baseline ($P<.05$). †Significantly better than vehicle ($P<.05$).

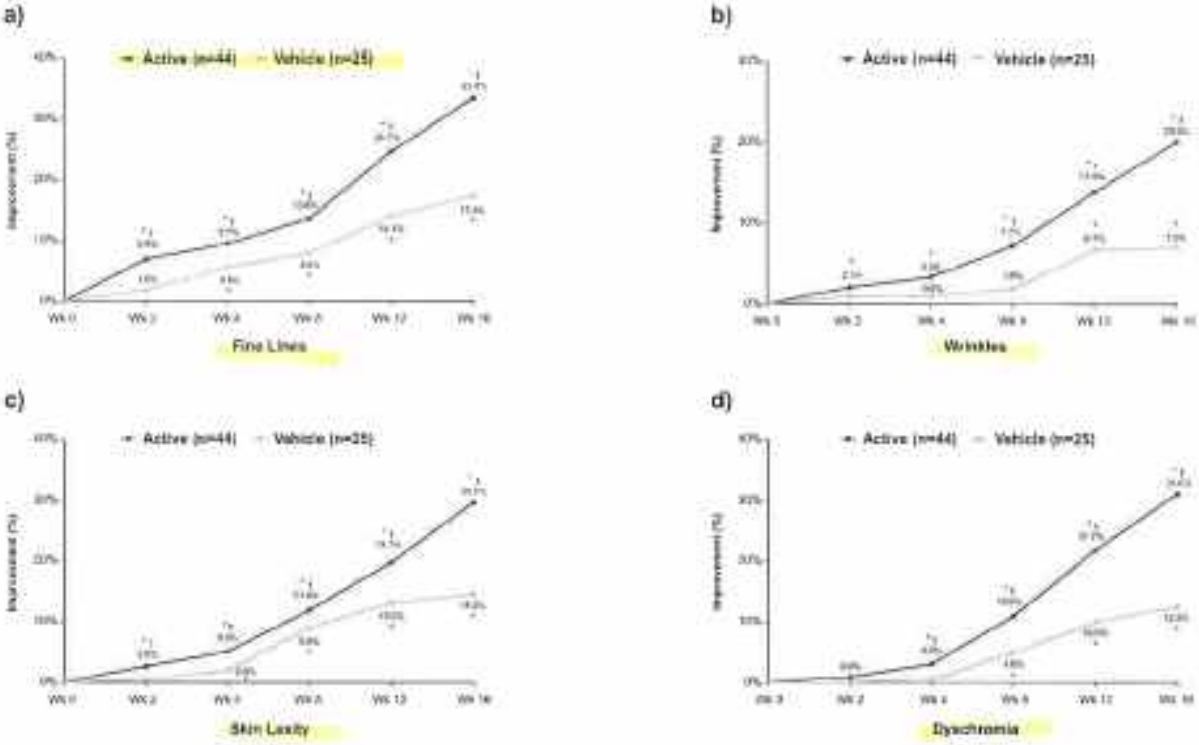
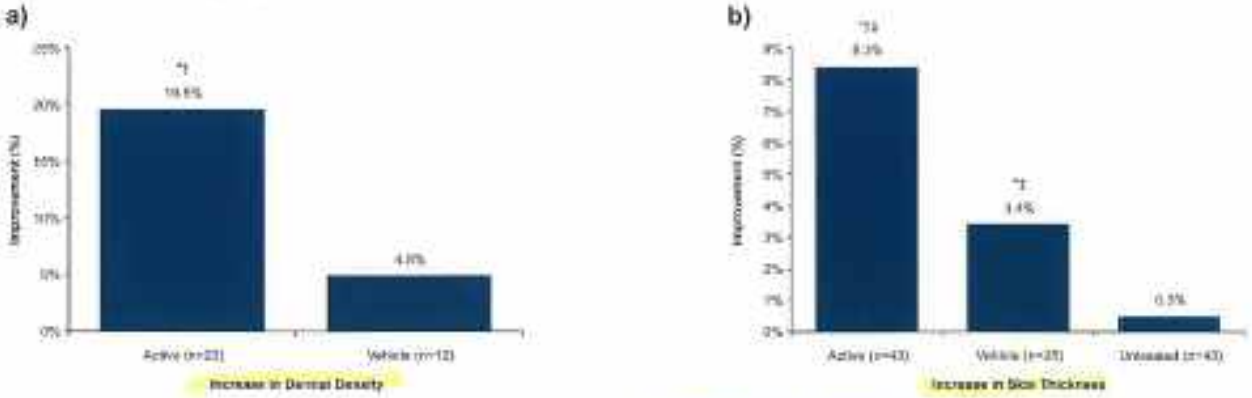


FIGURE 2. **a)** Increase in dermal density in the crow's feet area over 8 weeks and **b)** increase in forearm skin thickness over 16 weeks in subjects using the active regimen vs the vehicle regimen. *Significantly better than baseline ($P<.05$). †Significantly better than vehicle ($P<.05$). ‡Significantly better than untreated ($P<.05$).



that wrinkles were less noticeable, 98% reported that their skin texture was smoother, and 79% noted that brown spots were less apparent.

Continuation Phase

At the conclusion of the initial 16-week study, 17 subjects from the active group continued to receive the active regimen for an additional 14 weeks and returned to the clinic at weeks 21 and 30 for assessment. Improvement in all parameters of aging was shown to be significantly greater at week 30 than at week 16 ($P<.03$; Figure 5). Continued improvement in dermal density over the same period was demonstrated by ultrasound imaging with a mean improvement of 27% at week 30 ($P<.05$ vs baseline; Figure 6).

Tolerability

All the test products were generally well tolerated during both the initial 16-week treatment phase and the 14-week continuation phase (Table 4). There were 2 reports of facial irritation, 1 report of chest rash, and 1 report of forearm irritation in the

FIGURE 3. Improvement in periocular fine lines and wrinkles, eyelid tightening, and smoother skin texture observed in **a)** clinical photographs and **b)** silicone replicas from a subject using the active regimen for 16 weeks.

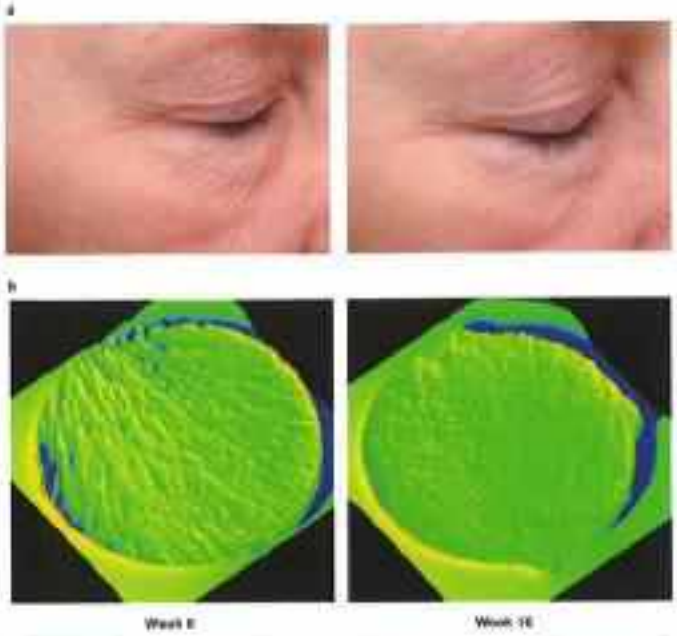


FIGURE 4. Reduced forehead wrinkling and pigmentation and smoother eyelid texture in a subject using the active regimen for 16 weeks.

active group, and 1 report of face, neck, and eye irritation and 1 report of eyelid irritation in the vehicle group.

DISCUSSION

Scientific studies have clearly demonstrated that skin aging involves several different biological processes. It is not realistic, therefore, to believe that the changes associated with aging of the skin can be fully addressed using any single skin care ingredient.[2] In this study, a new high-potency, multimechanism skin care regimen, including a facial cleanser, a day cream with broad-spectrum sunscreen, a night cream, and an eye cream, delivered comprehensive antiaging benefits to photodamaged skin as early as week 2, with continued improvement over the 16- and 30-week durations of the study. These antiaging effects were clinically measurable and statistically significant over the effect of the cosmetic vehicles, demonstrating the value of benefit antiaging ingredients. Moreover, the data further support

FIGURE 5. Improvement in signs of aging after use of the active regimen for 16 and 30 weeks. All improvements are significant compared with baseline ($P<.001$). All improvements at week 30 compared with week 16 are statistically significant ($P<.03$).

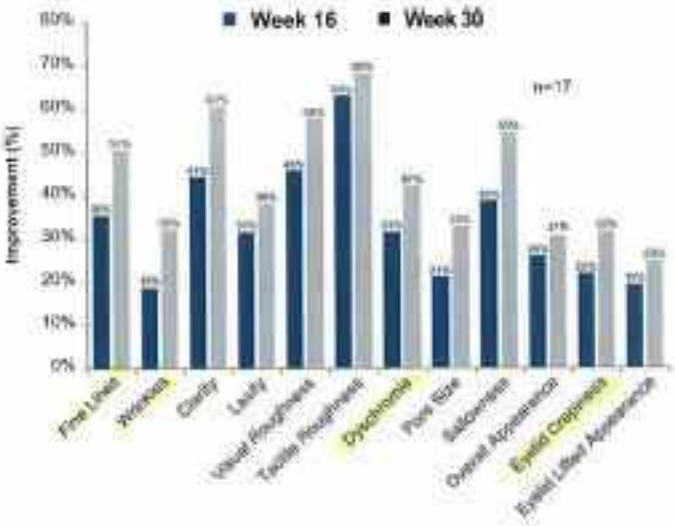
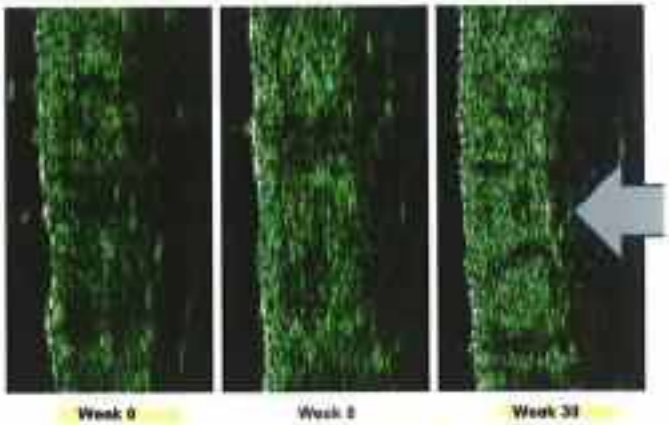


FIGURE 6. Increased dermal density over 30 weeks demonstrated by ultrasound imaging in a subject using the active regimen. Note the increase in echogenic substances in the dermal matrix over time.



the conclusion that visually apparent and objectively measured antiaging effects are achievable and are not simply due to moisturization and daily sunscreen protection.[4] In this study, the active group outperformed the vehicle group by a factor of 2 to 3 times at week 16 for fine lines, wrinkles, laxity, dyschromia, and other clinician-graded parameters. In addition, visually assessed changes were supported by instrumental, tactile, and skin structural assessments, all of which were consistent with the reversal of the photoaged skin phenotype. Ultrasound measurement of dermal density increased significantly in the active group but not the vehicle group; pinch recoil measurement of elasticity increased significantly more with active vs vehicle; and forearm skin thickness increased significantly more with active vs vehicle and untreated.

TABLE 4.

Mean Tolerability Scores Over 30 Weeks[a]

Parameter	Week							
	0	2	4	8	12	16	24	30
Erythema	0.28	0.40	0.40	0.42	0.41	0.44	0.32	0.53
Dryness	0.73	0.16[b]	0.07[b]	0.09[b]	0.11[b]	0.08[b]	0.00[b]	0.06[b]
Burning	0.00	0.20[c]	0.07	0.05	0.07	0.02	0.06	0.06
Stinging	0.00	0.36[c]	0.05	0.14[c]	0.09	0.07	0.06	0.06
Itching	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00
Tingling	0.00	0.11[c]	0.00	0.00	0.00	0.00	0.00	0.00
Tightness	0.30	0.02[b]	0.07[c]	0.09[b]	0.02[b]	0.00[b]	0.00	0.00
			n=44				n=17	

[a]Based on a 4-point scale where 0 = none, 1 = mild, 2 = moderate, and 3 = severe.
[b]Improved compared with baseline ($P<.05$).
[c]Worsened compared with baseline ($P<.05$).

The benefit ingredients in this regimen—α-hydroxy and poly-hydroxy acids, MBA, NAG, retinol, peptides, antioxidants, and apple stem cell extract—have previously been shown to reduce signs of skin aging. The comprehensive benefits observed in this study over the vehicle control are believed to have been achieved through the synergistic actions of these ingredients across formulations in the regimen.

DISCLOSURES

Ms. Edison, Ms. Brouda, Ms. Green, and Dr. Weinkauf are employees of NeoStrata Company, Inc, which provided funding for this study. Dr. Farris consulted to NeoStrata Company, Inc. as medical monitor for this study.

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