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A Randomized, Double-blind, Placebo-controlled Clinical Trial Evaluating an Oral Anti-aging Skin Care Supplement for Treating Photodamaged Skin

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Abstract

Objective: Evaluate an anti-aging skin care supplement on the appearance of photodamaged skin. **Design:** Randomized, double-blind, placebo-controlled clinical trial. Following a one-month washout period, subjects received two anti-aging skin care formula tablets (total daily dose: marine complex 210mg, vitamin C 54mg, zinc 4mg) or placebo daily for 16 weeks. Subjects were restricted from products/procedures that may affect the condition/appearance of skin, including direct facial sun or tanning bed exposure. Participants utilized a standardized facial cleanser and SPF15 moisturizer. **Setting:** Single study center (Texas, United States; June-November 2007). **Participants:** Healthy women aged 35 to 60 years (mean, 50 years), Fitzpatrick skin type I-IV, modified Glogau type II—III. **Measurements:** Subjects were assessed at Weeks 6, 12, and 16 on clinical grading (0-10 VAS), bioinstrumentation, digital photography, and self-assessments. Analysis of variance with treatment in the model was used for between-group comparisons (alpha $P \leq 0.05$). **Results:** Eighty-two anti-aging skin care formula subjects and 70 placebo subjects completed the study. Significant differences in change from baseline to Week 16 scores were observed for clinical grading of overall facial appearance (0.26; $P<0.0001$), radiant complexion (0.59; $P<0.0001$), periocular wrinkles

(0.08; *P*<0.05), visual (0.56; *P*<0.0001) and tactile (0.48; *P*<0.0001) roughness, and mottled hyperpigmentation (0.15; *P*<0.001) favoring the subjects in the anti-aging skin care supplement group. Ultrasound skin density (Week 16) was significantly reduced for placebo versus anti-aging skin care supplement group (-1.4% vs. 0%; *P*<0.01). Other outcomes were not significant. Mild gastrointestinal symptoms possibly related to the anti-aging skin care supplement (n=1) and placebo (n=2) were observed. **Conclusion:** Women with photodamaged skin receiving anti-aging skin care supplement showed significant improvements in the appearance of facial photodamage. **Trial registry:** Not applicable. Study precedes FDAAA 801 clinical trial registration and results submission requirements.

The signs of skin aging, including the development of fine lines, wrinkles, and discoloration, are the result of both intrinsic and extrinsic factors.[1] The primary cause of extrinsic aging is exposure to ultraviolet (UV) radiation, which breaks down the skin's underlying structure and accelerates the appearance of aged skin.[2] Strategies to treat or prevent these processes have traditionally been performed locally, with topical and injectable treatments. Note, however, that systemically administered nutrients and other non-nutrient ingredients can also have positive effects on the appearance of skin by reducing the internal factors that lead to the changes associated with photoaging.[3] Essential nutrients, such as vitamins E and C, selenium, and zinc, have been shown to reduce the negative effects of UV radiation on skin by eliminating reactive oxidative species and reducing the erythema associated with UV exposure.[4,5] Additionally, vitamin C plays a role in collagen synthesis.[6,7] Therefore, oral intake of these nutrients and nutrients from fruit and vegetable extracts obtained through the diet and/or supplementation can have positive effects on the appearance of skin through their anti-oxidative, anti-inflammatory, and photoprotective properties.[8-11]

A number of commercially available products that contain complexes of nutrient and non-nutrient ingredients combined into a single matrix are available as oral formulations designed to improve the appearance and condition of the skin.[12-14] Imedeen® Derma One® (Ferrosan Laboratories S/A, Søeborg, Denmark, acquired by Pfizer in December 2011) is an oral skin care dietary supplement that includes a

proprietary marine complex that on its own has been shown to improve the structure of the skin and stimulate collagen and laminin synthesis using human skin equivalents.[15] Benefits of this supplementation have also been documented in randomized, placebo-controlled clinical trials and open-label, uncontrolled studies.[16-19] The current study was conducted to evaluate the efficacy of this anti-aging skin care formula in women with photodamaged skin using clinical grading, bioinstrumentation, subject self-assessments, and digital photography.

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METHODS

Study design. This study was a 16-week, randomized, double-blind, placebo-controlled, parallel-group clinical trial that was conducted at a single study center in the United States from June to November 2007. The study center is a commercial contract research organization (Thomas J. Stephens & Associates, Inc., Texas Research Center) located in Richardson, Texas.

Participants. *Inclusion criteria.* The enrolled study population consisted of Caucasian women who were 35 to 60 years of age. A representative range of ages was enrolled so that approximately one-third of subjects could be included in the following age groups: 35 to 41 years, 42 to 53 years, 54 to 60 years. Subjects were required to have a Fitzpatrick skin classification type I-IV, type II-III modified Glogau classification of skin photoaging, and self-reported dry skin. All eligible subjects were required to replace their current facial cleansers and moisturizers during the washout period with the assigned products and continue use of their usual glamour products if they had been in use for ≥1 month. To limit further photoaging throughout the study, all subjects were required to avoid direct facial exposure to the sun and/or tanning beds. Subjects who were currently taking estrogen and/or progesterone therapy for ≥3 months were required to sustain their use throughout the study and those who were not currently receiving hormonal therapies could not initiate use during the study. Subjects were required to refrain from facial treatments performed at

home or by a physician or skin care professional throughout the study, including peels, laser treatments, dermabrasion, botulinum toxin injections, and acid treatments and were restricted from smoking >10 cigarettes per day.

Exclusion criteria. Candidate subjects were excluded from enrollment if they had a medical condition that would interfere with participation in the study, including skin conditions (e.g., atopic skin, eczema), psychiatric disorders, hormone-related diseases, sensitivities or allergies to fish or soy, gastrointestinal diseases other than mild acid reflux, and uncontrolled metabolic illness (e.g., diabetes or hypertension). Individuals were also excluded from enrollment who had recently participated in the following: facial procedures (e.g., facial peel, laser treatment, dermabrasion) within six months, photoaging or prescription acne treatments within three months (including use of those containing alpha-, beta-, or polyhydroxy acid or salicylic acid within 30 days), prescription acne medication (e.g., Retin-A [Valeant Pharmaceuticals, Bridgewater, New Jersey], Renova [Valeant Pharmaceuticals], Tazorac [Allergan Inc., Irvine, California]) within three months, or vitamins, dietary supplements, or topical prescription products indicated for improving the appearance or condition of the skin within one month. Throughout the study, subjects were only permitted to continue use of their regular daily multivitamin if it was maintained throughout the study; they were required not to initiate any other dietary supplement regime during the study.

Ethical conduct. Subjects provided written informed consent prior to performing any study procedures, which is consistent with the requirements in 21 CFR 50.25. This study was conducted according to Good Clinical Practice regulations, and the study protocol and informed consent form were reviewed by an institutional review board (IntegReview IRB).

Study procedures. Following initial telephone screening, eligible subjects reported to the study site (Visit 1) for additional screening. Subjects were required to wash their faces ≥30 minutes prior to this visit and each subsequent visit using a standardized facial cleanser, including full removal of cosmetics from the face, eyes, and lips. The

standardized facial cleanser was Purpose Liquid Cleansing Wash (Valeant Consumer Products), which was to be used on the face in place of each subject's regular facial cleansers. Subjects were also provided with a standardized facial and body moisturizer (Purpose Dual Treatment Moisture Lotion with SPF 15 [Valeant Consumer Products]), which was to be used no more than twice daily. If the subject's makeup was not removed upon arrival to the study site, then she was required to cleanse her face at the study site and wait ≥15 minutes prior to being assessed. In addition, subjects were provided with diaries to record usage of study treatments and any other comments, including potential adverse reactions.

Subjects returned to the study site approximately one month after the screening visit for the baseline visit (Visit 2) to allow for washout of current facial care products and adjustment to the Purpose cleanser and moisturizer. During the three days before Visit 2, subjects could not use the standardized moisturizer. Subjects with very dry skin were permitted to reduce this washout period to 1 to 2 days as needed to prevent irritation. Subjects were required to acclimate to the room for ≥30 minutes before instrumental assessments and VISIA (Canfield Scientific, Fairfield, New Jersey) and digital photography were conducted in order to limit the impact of environmental exposure on these assessments. Throughout the study, the waiting and instrumentation rooms were maintained at a temperature of 64°F to 74°F and relative humidity of 28 to 55 percent.

Randomization. Following completion of baseline procedures, subjects were randomly assigned to either active treatment or placebo according to a predetermined randomization scheme. To ensure even distribution across treatment groups, subjects were stratified by age group (35-41 y, 42-53 y, 54-60 y). Randomization of the treatment groups and blinding of the test material packaging were conducted by an outside firm. Subjects, investigators, and evaluators were all blinded to the study randomization.

Study treatment. Subjects were instructed to take two tablets per day of either Imedeen Derma One or a matching placebo with a morning meal for 16 weeks. Active and placebo supplements were similarly appearing coated tablets in generic packaging. The active ingredients

(per daily dose) of the dietary supplement included the Imedeen marine complex[15] 210mg, vitamin C 54mg, and zinc 4mg. The placebo tablet included the following inactive ingredients: maltodextrin, microcrystalline cellulose, starch, croscarmellose sodium, silicon dioxide, and magnesium stearate. At the baseline visit, subjects were provided with a six-week supply of supplements and instructed to not discard any supplement and to return the remaining supplements and packaging (even if empty) at the next study visit. Treatment compliance was assessed based on tablet counts and review of subjects' diaries.

Outcome measures. Subjects returned to the study site (±5 days) at Weeks 6 (Visit 3), 12 (Visit 4), and 16 (Visit 5) and underwent the procedures described below.

Clinical grading. Subjects' faces were evaluated at each study visit by the same investigator using the following parameters: overall facial appearance and radiant complexion: 0 (worst possible score) to 10 (best possible score); periocular, perioral, and forehead wrinkling, visible and tactile roughness, mottled pigmentation, and under-eye darkness: 0 (none) to 10 (severe). The primary outcome of interest was the statistical difference between the active and placebo supplements for the change from baseline score in clinical grading of overall facial appearance at Week 16.

Bioinstrumentation. ***Moisturization.*** The NOVA Dermal Phase Meter (DPM) 9003 (NOVA Technology Corp, Manchester, Massachusetts) was used at all study visits to quantify the moisture content in the stratum corneum using an electrical capacitance method. Measurements were taken in triplicate on the right or left sides of the center of each cheek in line with the pupil and bottom of the nose based on a randomization schedule. On the same side (right or left), measurements were taken in triplicate on the lateral aspect of the lower leg approximately midway between the knee and ankle. Increasing values indicate that the skin is becoming more hydrated.

Transepidermal water loss (TEWL). At each study visit, the Tewameter TM 3000 (Courage + Khazaka Electronic GmbH, Cologne, Germany) was used to measure the amount of water escaping the

stratum corneum (i.e., TEWL). Measurements were taken on the right or left cheek, matching the cheek that was assessed with the NOVA DPM. Data were analyzed using a microprocessor and reported as $g/m^2/hr$. A significant increase in TEWL indicates damage to normal, healthy skin, reflecting a compromise in barrier function.

Ultrasound. A DUBplus (Taberna Pro Medicum GmbH, Lueneburg, Germany) ultrasound unit was used to take a B scan of the crow's foot area or lower cheek to measure skin density and thickness at baseline and at Weeks 12 and 16. The system uses a standard 20MHz transducer with a focal distance of 12mm and 40dB amplification. Measurements were taken perpendicularly to the body axis on the opposite side from where the NOVA and Tewameter measurements were taken. The density assessment reflects the level of collagen and elastin present in the dermis, while the skin thickness reflects the degree of age-related thinning of the skin and the potential to improve the dermal structure.

VISIA imaging. A single digital image was taken with the VISIA Complexion Analysis System (VISIA-CA; Canfield Scientific) of the right or left side of each subject's face as determined by the evaluator at baseline and at Weeks 12 and 16. The VISIA system uses multispectral imaging to quantify the following six photoaging parameters: wrinkles, spots, pores, evenness of skin tone, porphyrins, and UV spots. VISIA photographs were taken using a constant fluorescent lighting source for the standard white light and a UV light source for the UV images.

Digital photography. At the baseline and Week 12 and Week 16 visits, a single, full-face, digital visible light photograph was taken of either the right or left side of the face (matching the side of the VISIA image) or, alternatively, a full-frontal facial view as determined by the evaluator, which was to be used as a reference point for performing clinical grading. Photographs were taken using the same digital imaging setup at each visit: a Nikon D100 digital camera body (Nikon Corp, Tokyo, Japan) with a Nikkor AF 70-180mm Micro-NIKKOR lens (Nikon Corp). Digital images (RAW; 12 bits/channel) were recorded using Nikon Capture software and saved as Nikon RAW (NEF) files.

Subject self-assessment. Subjects completed a questionnaire that asked them to rate their degree of improvement in facial and body skin condition from the start of the study to the Week 6, 12, and 16 visits. The questionnaire included an assessment of 16 photoaging characteristics, including wrinkling, pigmentation, tone, clarity, hydration, and suppleness.

Safety. The occurrence of adverse events (AEs) was monitored throughout the study by the study investigators and based on subjects' diary entries. Investigators rated the observed and reported AEs as being either severe or non-severe based upon their potential relationship to study treatment.

Statistical methods. An analysis of variance with treatment in the model was used to make comparisons between treatment groups on clinical grading, moisturization, bioinstrumentation, and VISIA imaging. A 2-sided Fisher's exact test was used to make comparisons between treatment groups on the subject self-assessments. Statistical significance was indicated as $P \leq 0.05$.

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RESULTS

Study population. Two hundred-one subjects were enrolled and 152 subjects completed the study (anti-aging skin care supplement: n=82; placebo: n=70). Forty-nine subjects discontinued the study (voluntary discontinuation [n=15], failure to attend scheduled visits [n=30], serious AEs [n=2], non-adherence/investigator request [n=2]). Two serious AEs (i.e., hysterectomy, ovarian cancer) were observed in the placebo group, and neither was considered to be related to the study supplement. Baseline demographics and clinical characteristics for the anti-aging skin care supplement and placebo groups are presented in Table 1.

TABLE 1

Subject baseline demographics

	ANTI-AGING SUPPLEMENT (N=82)	PLACEBO (N=70)
Age, years		
Mean (SD)	50.1 (7.4)	49.6 (7.7)
Fitzpatrick, n (%)		
II	51 (62.2)	31 (44.3)
III	30 (36.6)	36 (51.4)
IV	1 (1.2)	4 (4.3)
Glogau, n (%)		
II	59 (72.0)	47 (67.1)
III	23 (28.1)	23 (32.9)
Clinical grading, mean (SD)		
Overall facial appearance	5.2 (1.0)	5.0 (1.0)
Radiant complexion	3.4 (0.9)	3.3 (1.0)
Periocular wrinkling	3.8 (1.6)	3.9 (1.6)
Perioral wrinkling	1.9 (2.0)	2.6 (2.4)
Forehead wrinkling	5.1 (1.6)	4.8 (1.9)
Visual roughness	5.5 (1.2)	5.6 (1.1)
Tactile roughness	5.1 (1.2)	5.2 (1.3)
Mottled pigmentation	3.8 (1.7)	4.0 (1.6)
Under-eye darkness	3.8 (1.6)	3.9 (1.8)
Moisturization, mean (SD)		
NOVA DPM		
Cheek	123.5 (52.4)	113.6 (25.3)
Leg	102.6 (15.2)	101.4 (11.2)
TEWL	12.0 (5.3)	11.9 (6.3)

	ANTI-AGING SUPPLEMENT (N=82)	PLACEBO (N=70)
Ultrasound, mean (SD)		
Density	28.4 (6.8)	29.3 (7.2)
Thickness	1570.3 (70.3)	1573.8 (70.8)
VISIA, mean (SD)		
Wrinkles	19.6 (8.2)	18.4 (7.6)
Spots	83.3 (24.7)	86.5 (24.7)
Pores	368.5 (120.4)	373.2 (129.5)
Evenness of skin tone	575.9 (240.9)	574.3 (258.5)
Porphyrins	226.2 (175.1)	255.3 (221.5)
UV spots	229.7 (29.8)	227.4 (29.8)

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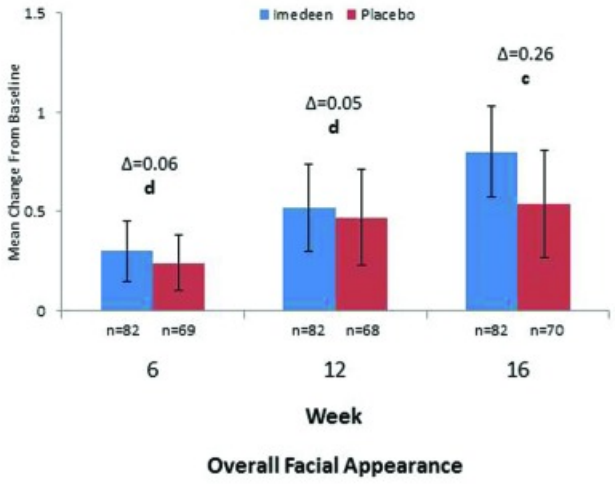
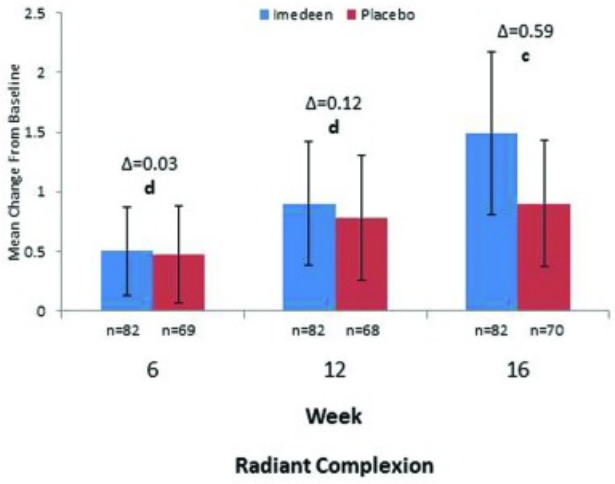
DPM=dermal phase meter; SD=standard deviation; TEWL=transepidermal water loss; UV=ultraviolet

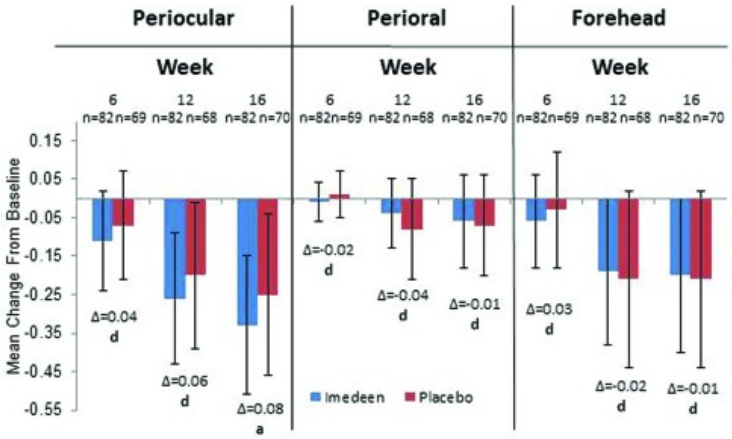
Clinical grading. A significantly greater degree of improvement ($P<0.05$) was observed at Week 16 for individuals taking the anti-aging skin care supplement versus placebo on a number of clinical grading parameters. The clinical grading of overall facial appearance and radiant complexion improved for both treatment groups, but the degree of improvement was significantly greater ($P<0.0001$) for subjects treated with the anti-aging skin care supplement versus those who received placebo (Figure 1). Subjects in the anti-aging skin care supplement group also experienced significantly greater decreases in periocular wrinkling, visual and tactile roughness, and mottled pigmentation ($P<0.05$) than those in the placebo group. Although subjects in both groups experienced improvements on the other clinical grading parameters (i.e., perioral and forehead wrinkles, under-eye darkness), the differences between groups were not significantly different.



Overall Facial Appearance



Radiant Complexion


Periocular
Perioral
Forehead
Week
Week
Week
6 n=82 n=69
12 n=82 n=68
16 n=82 n=70
Mean Change From Baseline
0.15
0.05
-0.05
-0.15
-0.25
-0.35
-0.45
-0.55
Δ=0.04 d
Δ=0.06 d
Δ=0.08 a
Δ=-0.02 d
Δ=-0.04 d
Δ=-0.01 d
Δ=0.03 d
Δ=-0.02 d
Δ=-0.01 d
Imedeen
Placebo

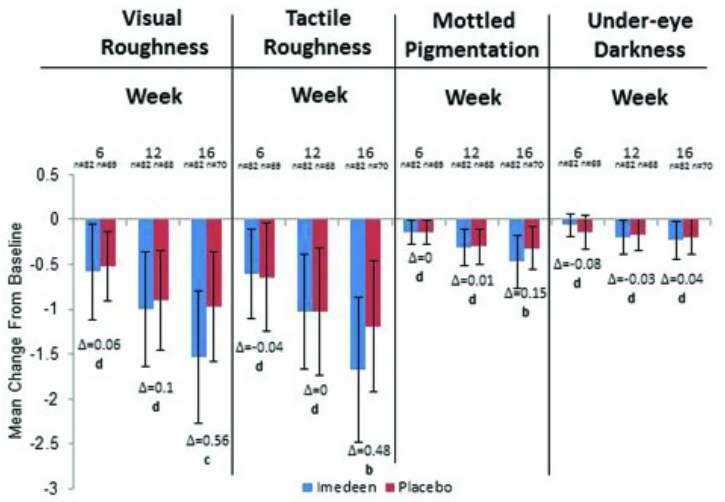


Figure 1

Mean change in clinical grading. (A) Overall Facial Appearance; (B) Radiant Complexion; (C) Wrinkling; (D) Roughness and Discoloration. [a]*P*<0.05; [b]*P*<0.001; [c]*P*<0.0001; [d]*P*=NS

Moisturization and TEWL. NOVA DPM measurements increased to a similar degree for both the anti-aging skin care supplement and placebo groups, particularly at Week 12, while at Week 16 the values decreased for both groups. No significant differences between treatment groups were observed at any time point (Table 2). Assessments of TEWL decreased for all subjects from baseline to Week 16, particularly in the cheek, but the difference between treatment groups was not statistically significant.

TABLE 2

Bioinstrumentation outcome measures

WEEK 6	**WEEK 6**			**WEEK 12**			**WEEK 16**		
	ANTI-AGING SUPPLEMENT	**PLACEBO**	***P* VALUE**	**ANTI-AGING SUPPLEMENT**	**PLACEBO**	***P* VALUE**	**ANTI-AGING SUPPLEMENT**	**PLACEBO**	***P* VALUE**
Moisturization									
NOVA DPM	n=70	n=67		n=67	n=63		n=66	n=63	
Cheek									
Mean (SD) change	+6.0 (23.3)[a]	+2.2 (22.3)	NS	+13.5 (29.4)[a]	+9.4 (31.9)[a]	NS	-3.6 (18.1)	-0.1 (24.5)	NS
Change from baseline, %	+5.3	+2.0		+12.4	+8.6		-3.3	-0.1	
Leg									
Mean (SD) change	-3.9 (9.5)[a]	-3.1 (9.3)[a]	NS	-4.3 (9.4)[a]	-3.4 (11.8)[a]	NS	-5.2 (12.5)[a]	-4.3 (13.7)[a]	NS
Change from baseline, %	-3.8	-3.1		-4.3	-3.4		-5.2	-4.3	
TEWL	n=80	n=69		n=81	n=69		n=81	n=70	
Mean (SD) change	-1.4 (5.4)[a]	-1.5 (6.7)	NS	-1.9 (4.0)[a]	-1.7 (6.8)[a]	NS	-0.6 (5.8)	-0.3 (6.4)	NS
Change from baseline, %	-11.8	-12.3		-15.6	-14.2		-4.6	-2.4	

WEEK 6	WEEK 6			WEEK 12			WEEK 16		
	ANTI-AGING SUPPLEMENT	PLACEBO	*P* VALUE	ANTI-AGING SUPPLEMENT	PLACEBO	*P* VALUE	ANTI-AGING SUPPLEMENT	PLACEBO	*P* VALUE
Ultrasound									
Density				n=81	n=66		n=80	n=66	
Mean (SD) change	-	-	-	+4.3 (4.0)[a]	+4.5 (4.2)[a]	NS	+7.0 (5.0)[a]	+6.2 (4.8)[a]	NS
Change from baseline, %	-	-		+15.3	+15.4		+24.5	+21.2	
Thickness				n=81	n=66		n=77	n=64	
Mean (SD) change	-	-	-	-2.9 (15.6)[a]	-14.6 (47.5)[a]	**<0.05**	0.2 (34.2)	-22.1 (57.2)[a]	**<0.01**
Change from baseline, %	-	-		-0.2	-0.9		0.0	-1.4	

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DPM=dermal phase meter; NS=not significant; SD=standard deviation; TEWL=transepidermal water loss
[a]*P*≤0.05 versus baseline value

Ultrasound. A significantly greater decrease in skin thickness was observed at Weeks 12 (-0.9% vs. -0.2%; *P*<0.05) and 16 (-1.4% vs. 0%; *P*<0.01) with placebo versus anti-aging skin care supplement, respectively (Table 2), while the anti-aging skin care supplement group maintained a constant level of skin thickness throughout the study. Increases in skin density from baseline to Week 16 were observed for both the anti-aging skin care supplement and placebo

groups (+24.5% vs. +21.2%, respectively; *P*=0.361); this degree of change was numerically, but not significantly higher for anti-aging skin care supplement versus placebo.

VISIA. In general, the VISIA output was the same on all parameters in both groups (Table 3). No significant differences between groups were observed for any of these outcomes.

TABLE 3

Results of VISIA image analyses

	WEEK 12			WEEK 16		
	ANTI-AGING SUPPLEMENT N=79	**PLACEBO N=65**	***P* VALUE**	**ANTI-AGING SUPPLEMENT N=81**	**PLACEBO N=69**	***P* VALUE**
Wrinkles						
Mean (SD) change	-1.4 (5.9)[a]	-0.8 (6.4)	NS	-0.1	-1.4 (5.6)[a]	
Change from baseline, %	-7.2	-4.4		-0.4	(7.5)	
Spots						
Mean (SD) change	-1.2 (9.9)	-0.9 (12.6)	NS	-4.6 (10.7)[a]	-5.2 (11.8)[a]	NS
Change from baseline, %	-1.5	-1.1		-5.6	-6.0	
Pores						
Mean (SD) change	-2.9 (57.9)	-12.8 (59.7)	NS	-24.1 (58.9)[a]	-36.7 (56.5)[a]	NS
Change from baseline, %	-0.8	-3.4		-6.5	-9.8	
Evenness of Skin Tone						

	WEEK 12			WEEK 16		
	ANTI-AGING SUPPLEMENT N=79	**PLACEBO N=65**	***P* VALUE**	**ANTI-AGING SUPPLEMENT N=81**	**PLACEBO N=69**	***P* VALUE**
Mean (SD) change	+1.5 (145.2)	-19.0 (121.2)	NS	-29.5 (165.7)	-67.3 (130.9)[a]	NS
Change from baseline, %	+0.3	-3.3		-5.1	-11.7	
Porphyrins*						
Mean (SD) change	+80.6 (209.6)[a]	+57.4 (187.2)[a]	NS	+104.1 (261.8)[a]	+48.3 (260.7)	NS
Change from baseline, %	+36.1	+22.6		+46.2	+19.0	
UV Spots						
Mean (SD) change	+3.2 (25.0)	+2.0 (22.6)	NS	-10.2 (54.9)	-5.3 (46.6)	NS
Change from baseline, %	+1.4	+0.9		-4.5	-2.3	

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NS=not significant; SD=standard deviation; UV=ultraviolet
[a]P- 0.05 versus baseline value

*Porphyrins: Anti-aging supplement: Week 12 (n=80); Week 16 (n=78); placebo: Week 12 (n=66); Week 16 (n=68)

Self-assessment. For any self-assessment questions, no significant differences between the anti-aging skin care supplement and placebo groups were observed, but subjects treated with the anti-aging skin care supplement reported improvements more frequently than the placebo group. At Week 16, subjects in both groups reported significant improvements from baseline on all outcomes.

Adverse events. No serious AEs related to study treatment were observed. Five non-serious AEs were observed in each treatment

group (Table 4). The AEs that were possibly related to anti-aging skin care supplement treatment were mild gastrointestinal distress, including nausea and diarrhea, and moderate facial rash. In the placebo group, one subject experienced moderate rash on her arms, neck, decolletage, and face that was deemed related to Purpose moisturizer. AEs possibly related to placebo included mild rash, constipation, and flatulence.

TABLE 4

Summary of non-serious adverse events

ANTI-AGING SUPPLEMENT			PLACEBO		
Adverse Event	**Severity**	**Relatedness**	**Adverse Event**	**Severity**	**Relatedness**
Gastrointestinal, including nausea and diarrhea	Mild	Possibly related	**Allergic dermatitis**	Moderate	Related (Purpose moisturizer)
Oral irritation, on roof of mouth and tongue	Mild	Not related	**Rash** on upper arm	Mild	Possibly related
Facial rash with itchiness and erythema	Moderate	Possibly related	**Flatulence**	Mild	Possibly related
Biopsy site infection	Mild	Not related	**Contact dermatitis**	Moderate	Not related (poison ivy)
Nausea	Moderate	Not related	**Constipation**	Mild	Possibly related

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DISCUSSION

Over the four-month study period, the anti-aging skin care supplement produced improvements in numerous parameters associated with photodamaged skin, particularly overall facial appearance, radiant complexion, periocular wrinkling, skin roughness, and mottled pigmentation. Subjects who received placebo experienced a significantly greater reduction in ultrasound-measured skin thickness, while subjects treated with the anti-aging skin care supplement

maintained the same degree of skin thickness, suggesting that untreated subjects experienced a decline in dermal structure. The differences between groups were not significantly different on the other outcomes that were assessed. In total, these results suggest that the anti-aging skin care supplement can have positive effects on the appearance of facial photodamage.

A six-month clinical trial that enrolled postmenopausal women and assessed a similar anti-aging skin care supplement formulation (Imedeen® Prime Renewal®; Ferrosan Laboratories S/A) produced results that were consistent with those observed in this study.[19] Imedeen Prime Renewal also contains the Imedeen marine complex, as well as vitamins and minerals with the addition of plant extracts. In the Imedeen Prime Renewal study, significant improvements ($P \leq 0.02$) versus placebo were observed on outcomes such as overall facial appearance, facial (forehead, periocular, perioral) wrinkling, mottled hyperpigmentation, laxity, and ultrasound skin density.[19] Imedeen® Time Perfection®, which contains the Imedeen biomarine complex and various plant extracts, has demonstrated efficacy in uncontrolled human trials for treating photoaged skin.[16,20] The results of these previous human studies and the *in vitro* study demonstrating that the anti-aging skin care supplement's proprietary marine complex produces benefits to the structure of the skin[15] support the overall effectiveness of the anti-aging skin care supplement for treating photoaged skin. Results from randomized, placebo-controlled trials that utilized other combination products formulated with nutrient and non-nutrient ingredients have also been suggestive of efficacy for producing improvements in similar objective and subjective outcomes to those used in the current study; however, some of the between-group differences did not reach statistical significance.[12,21-23] In some instances, the placebo group experienced deteriorations on certain parameters, while the active treatment groups maintained the same level or saw modest improvements.[12,21,23] Similar results were obtained with ultrasound-measured skin thickness in the current study.

The strengths of this study include the randomized, double-blind, placebo-controlled design, use of a third party for blinding the study products and randomization/ treatment allocation, equal distribution

of women across a broad range of age groups and severity of photodamage, and the relatively long duration of the assessment period. In addition, in relation to other studies conducted in this area, the study population size was relatively large. Additional strengths include the control of external variables (e.g., dietary supplement use, sun or tanning bed exposure) that could confound the observed results, as well as utilization of standardized facial cleanser and moisturizer throughout the study, a pre-treatment 30-day washout period, and the same rater throughout the study.

Despite these strengths, there are some limitations that are worth noting. The VISIA-CA imaging technology that was used in this study has since been updated to improve its sensitivity. The software used in the current study was able to quantify the number of wrinkles, spots, pores, evenness of skin tone, porphyrins and UV spots, while the most recent version utilizes a digital single-lens reflex camera and a pulsed xenon IntelliFlash (Canfield Scientific) illumination source for improved image resolution and lighting. The updated system also includes an additional lighting modality (i.e., cross-polarized to allow for RBX [Canfield Scientific] image processing) and other technologies. These updates to 11. the VISIA hardware and software provide better image quality and enhance the accuracy and repeatability of the skin complexion analysis.

Additionally, other image analysis software, such as Stephens Wrinkle Imaging using Raking Light (SWIRL; Thomas J. Stephens & Associates, Inc.), is now available and detects more subtle changes in facial photoaging 13. parameters.[24] The lack of significant effects on moisturization assessments, including TEWL and NOVA DPM, is not unexpected in a population with healthy, intact skin receiving an oral dietary supplement and using a topical moisturizing 14. sunscreen that contains skin conditioning ingredients. The value of these outcomes in this area of research is therefore unclear.

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CONCLUSION

In this four-month study, the anti-aging skin care supplement had a positive effect on the appearance of photodamaged skin across women of varying age, skin type, 16. and degree of photoaging.

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Footnotes

DISCLOSURE: Drs. Stephens and Sigler are employees of Thomas J. Stephens & Associates, Inc., and do not have a financial interest in Pfizer Consumer Healthcare. Dr. Hino is an employee of Dermatology Center of Dallas and Thomas J. Stephens & Associates, Inc. and does not have a financial interest in Pfizer Consumer Healthcare. Dr. Le Moigne and Ms. Dispensa are employees of Pfizer Consumer Healthcare and own stock and/or stock options in the company. This study was sponsored by Ferrosan Laboratories S/A, Søeborg, Denmark, which was acquired by Pfizer in December 2011. Medical writing support was provided by Dennis Stancavish, MA, of Peloton Advantage, LLC, and was funded by Pfizer.

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REFERENCES

1. Kohl E, Steinbauer J, Landthaler M, Szeimies RM. Skin ageing. *J Eur Acad Dermatol Venereol.* 2011;25(8):873–884. [PubMed] [Google Scholar]

2. Fisher GJ, Wang ZQ, Datta SC, et al. Pathophysiology of premature skin aging induced by ultraviolet light. *N Engl J Med.* 1997;337(20):1419–1428. [PubMed] [Google Scholar]

3. Fitzgerald R, Graivier MH, Kane M, et al. Update on facial aging. *Aesthet Surg J.* 2010;30(Suppl):11S–24S. [PubMed] [Google Scholar]

4. Fuchs J, Kern H. Modulation of UV-light-induced skin inflammation by D-alpha-tocopherol and L-ascorbic acid: a clinical study using solar simulated radiation. *Free Radic Biol Med.* 1998;25(9):1006–1012. [PubMed] [Google Scholar]

5. Leccia MT, Richard MJ, Beani JC, et al. Protective effect of selenium and zinc on UV-A damage in human skin fibroblasts. *Photochem Photobiol.* 1993;58(4):548–553. [PubMed] [Google Scholar]

6. Boyera N, Galey I, Bernard BA. Effect of vitamin C and its derivatives on collagen synthesis and cross-linking by normal human fibroblasts. *Int J Cosmet Sci.* 1998;20(3):151–158. [PubMed] [Google Scholar]

7. Otten JJ, Hellwig JP, Meyers LD. *Dietary Reference Intakes: The Essential Guide to Nutrient Requirements.* Washington, DC: The National Academies Press; 2006. [Google Scholar]

8. Aust O, Stahl W, Sies H, et al. Supplementation with tomato-based products increases lycopene, phytofluene, and phytoene levels in human serum and protects against UV-light-induced erythema. *Int J Vitam Nutr Res.* 2005;75(1):54–60. [PubMed] [Google Scholar]

9. De Spirt S, Sies H, Tronnier H, Heinrich U. An encapsulated fruit and vegetable juice concentrate increases skin microcirculation in healthy women. *Skin Pharmacol Physiool.* 2012;25(1):2–8. [PubMed] [Google Scholar]

10. Janjua R, Munoz C, Gorell E, et al. A two-year, double-blind, randomized placebo-controlled trial of oral green tea polyphenols on the long-term clinical and histologic appearance of photoaging skin. *Dermatol Surg.* 2009;35(7):1057–1065. [PubMed] [Google Scholar]

11. Kopcke W, Krutmann J. Protection from sunburn with beta-Carotene—a meta-analysis. *Photochem Photobiol.* 2008;84(2):284–288. [PubMed] [Google Scholar]

12. Fanian F, Mac-Mary S, Jeudy A, et al. Efficacy of micronutrient supplementation on skin aging and seasonal variation: a randomized, placebo-controlled, double-blind study. *Clin Interv Aging.* 2013;8:1527–1537. [PMC free article] [PubMed] [Google Scholar]

13. Segger D, Schonlau F. Supplementation with Evelle improves skin smoothness and elasticity in a double-blind, placebo-controlled study with 62 women. *J Dermatolog Treat.* 2004;15(4):222–226. [PubMed] [Google Scholar]

14. Thom E. A randomized, double-blind, placebo-controlled study on the clinical efficacy of oral treatment with DermaVite on ageing symptoms of the skin. *J Int Med Res.* 2005;33(3):267–272. [PubMed] [Google Scholar]

15. Rietveld M, Janson D, Siamari R, et al. Marine-derived nutrient improves epidermal and dermal structure and prolongs the life span of reconstructed human skin equivalents. *J Cosmet Dermatol.* 2012;11(3):213–222. [PubMed] [Google Scholar]

16. Costa A, Pegas Pereira ES, Favaro R, et al. Treating cutaneous photoaging in women with an oral supplement based on marine protein, concentrated acerola, grape seed extract and tomato extract, for 360 days. *Surg Cosmet Dermatol.* 2011;3(4):302–311. [Google Scholar]

17. Costa A, Pegas Pereira ES, Assumpcao EC, et al. Assessment of clinical effects and safety of an oral supplement based on marine protein, vitamin C, grape seed extract, zinc, and tomato extract in the improvement of visible signs of skin aging

in men. *J Clin Cosmet Investig Dermatol.* 2015;8:319–328. [PMC free article] [PubMed] [Google Scholar]

18. Kieffer ME, Efsen J. Imedeen in the treatment of photoaged skin: an efficacy and safety trial over 12 months. *J Eur Acad Dermatol Venereol.* 1998;11(2):129–136. [PubMed] [Google Scholar]

19. Skovgaard GR, Jensen AS, Sigler ML. Effect of a novel dietary supplement on skin aging in post-menopausal women. *Eur J Clin Nutr.* 2006;60(10):1201–1206. [PubMed] [Google Scholar]

20. Costa A, Lindmark L, Arruda LH, et al. Clinical, biometric and ultrasound assessment of the effects of daily use of a nutraceutical composed of lycopene, acerola extract, grape seed extract and Biomarine Complex in photoaged human skin. *An Bras Dermatol.* 2012;87(1):52–61. [PubMed] [Google Scholar]

21. Beguin A. A novel micronutrient supplement in skin aging: a randomized placebo-controlled double-blind study. *J Cosmet Dermatol.* 2005;4(4):277–284. [PubMed] [Google Scholar]

22. Udompataikul M, Sripiroj P, Palungwachira P. An oral nutraceutical containing antioxidants, minerals and glycosaminoglycans improves skin roughness and fine wrinkles. *Int J Cosmet Sci.* 2009;31(6):427–435. [PubMed] [Google Scholar]

23. Beer C, Wood S, Veghte RH. A randomized, double-blind, placebo-controlled clinical trial to investigate the effect of Cynatine((R)) HNS on skin characteristics. *Int J Cosmet Sci.* 2013;35(6):608–612. [PubMed] [Google Scholar]

24. Jiang LI, Stephens TJ, Goodman R. SWIRL, a clinically validated, objective, and quantitative method for facial wrinkle assessment. *Skin Res Technol.* 2013;19(4):492–498. [PubMed] [Google Scholar]
