PHYSICIAN STUDIES

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HYPERPIGMENTATION

Split-Face Comparison of an Advanced Non-Hydoquinone Lightening Solution to 4% Hydroquinone

Joel Schlessinger, MD

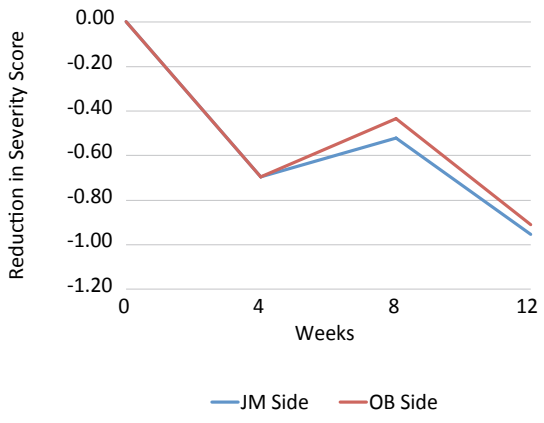
Method:

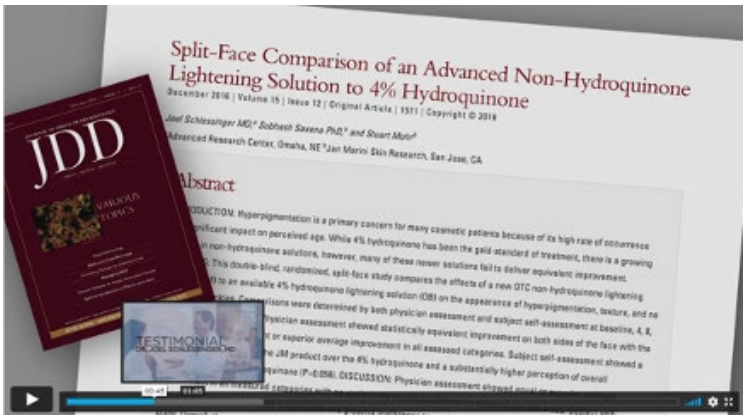
- Physician Assessment at baseline, 4, 8 and 12 weeks
- Usage of a generic gentle cleanser, Marini Luminate Face Lotion MD, a generic moisturizer and Marini Physical Protectant SPF45
- 3-month study

Study Summary:

- Statistically significant improvement in the appearance of hyperpigmentation, fine lines and wrinkles
- Rapid improvement: statistically significant after only 4 weeks
- Continued improvement over the course of the study
- Mild to moderate acclimation (due to high concentration of retinol)*

Figure 1: Reduction in Hyperpigmentation by Physician Assessment





*Published study. Schlessinger. J.MD. et al. Split-Face Comparison of an Advanced Non-Hydrquinone Lightening Solution to 4% Hydroquinone. Journal of Drugs in Dermatology, 2006; 15(12): 1571-1577

HYPERPIGMENTATION
Products Used | Marini Luminate Face Lotion MD

Split-Face Comparison of an Advanced Non-Hydroquinone Lightening Solution to 4% Hydroquinone

Joel Schlessinger, MD [a], Subhash Saxena, PhD [b], Stuart Mohr [b]

[a] Advanced Research Center, Omaha, NE
[b] Jan Marini Skin Research, San Jose, CA

INTRODUCTION
Hyperpigmentation is a primary concern for many cosmetic patients because of its high rate of occurrence and significant impact on perceived age. While 4% hydroquinone has been the gold-standard of treatment, there is a growing interest in non-hydroquinone solutions however many of these newer solutions fail to deliver equivalent improvement.

METHODS
This double-blind, randomized, split-face study compares the effects of a new OTC non-hydroquinone lightening product (JM) to an available 4% hydroquinone lightening solution (OB) on the appearance of hyperpigmentation, texture and fine lines and wrinkles. Comparisons were determined by both physician assessment and subject self-assessment at baseline, 4, 8 and 12 weeks.

RESULTS
Physician assessment showed statistically equivalent improvement on both sides of the face with the JM side showing equivalent or superior improvement average improvement in all assessed categories. Subject self-assessment showed a significant preference for the JM product over the 4% hydroquinone and a substantially higher perception of overall improvement over 4% hydroquinone ($p=0.058$).

CONCLUSION
Overall, the results of this study show the JM product to be equivalent if not superior to 4% hydroquinone for results and patient satisfaction.

INTRODUCTION

Hyperpigmentation is a primary concern for cosmetic patients because of its high rate of occurrence and significant impact on perceived age. In the United States, as many as 90% of Caucasians over the age of 60 and 20% of Caucasians under the age of 35 experience lentigines.[1,2] Further, 8.8% of individuals of Latino descent and up to 40% of persons of Asian descent experience melasma.[3]

Non-uniform color distribution is a visual indicator of perceived age and health. One study showed that, even in the absence of wrinkles, color distribution was highly positively correlated with the actual age of the person and perceived age. In addition, the homogeneity of pigment distribution on the face correlated positively with perceived attractiveness, healthiness, and youthfulness and was inversely correlated with perceived aging. Further, non-uniform color distribution could account for as much as 20 years of variance in perceived age.[4]

Hydroquinone has been the gold-standard topical solution for hyperpigmentation, due to consistency and quality of results. Additionally, studies have shown that concomitant use of hydroquinone and tretinoin is more effective than hydroquinone alone[5,6] functioning via multiple pathways to inhibit melanin production. Hydroquinone inhibits tyrosinase activity during melanin synthesis, while retinoids function upstream in the melanin production cycle by regulating tyrosinase transcription[7] and increase cellular turnover, helping to exfoliate pigmented skin.

This study was published in Volume 15 Issue 12 (December 2016) of *JDD [Journal of Drugs in Dermatology]*.

Additionally, retinoids are vital to the maintenance of optimal skin health and are utilized extensively by dermatologists. Retinoids have independently been shown to decrease the appearance of fine lines and wrinkles, increase epidermal proliferation leading to epidermal thickening, and increase compaction of the stratum corneum for greater luminosity of the skin and the biosynthesis & deposition of glycosaminoglycans to enhance collagen and elastin in the skin.

In response to consumer demand for non-hydroquinone lightening solutions, there is a continuous influx of new "lightening" products. Very few, however, combine the benefits of lightening agents and retinoids and many lack independent data to support their claims, instead relying on in-vitro or in-vivo data on individual ingredients to act as a surrogate for study data. Without testing the final formulation, however, it is impossible to know if the ingredients function as desired or if interactions in the final formulated product nullify anticipated benefits. Due to the lack of evidence and underwhelming results from many non-hydroquinone solutions, the gold standard recommendation for hyperpigmentation remains hydroquinone, often combined with a retinoid and/or in-office treatment.

This study investigates the effects of a new non-hydroquinone product combining two new lightening agents plus a host of established lightening technologies (Table 1) with all-trans-retinol to address multiple stages of melanin production for maximum results. One new ingredient, Nonapeptide-1, functions as an antagonist to Melanin Stimulating Hormone (MSH), effectively inhibiting melanin production upstream from classic tyrosinase inhibitors.[8] Another new ingredient, tetrahydrodiferuloylmethane (a colorless derivative of curcumin), is shown to function as a potent tyrosinase inhibitor and antioxidant and is shown to protect keratinocytes from hypoxanthine/xanthine oxidase injury in vitro. In addition, it is also shown to provide topical protection against UVB-induced inflammation and damage.[9]

METHODS

Twenty-nine subjects were enrolled in a 12-week, double-blind, split-face study comparing two products, Product JM (Marini Luminate Face Lotion MD, Jan Marini Skin Research) and Product OB (Obagi Nu-Derm Blender, 4% Hydroquinone, Obagi Medical).

Subjects were required to have mild-to-moderate hyperpigmentation (2-3 on a 0-4 scale) at baseline as determined by dermatologist assessment. Fine lines and wrinkles were assessed as part of the study but wrinkle score was not an enrollment criterion. Subjects were required to commit to the use of the study products, to follow protocol and to avoid significant intentional sun exposure over the course of the study.

Subjects were excluded from study participation if they were smokers, pregnant or nursing, used any prescription products on the areas undergoing treatment with the protocol items, used retinoids or tyrosinase inhibitors within three months of the study, had significant hormonal changes within three months of the study, demonstrated an inability to adhere to study protocols, had a known sensitivity or allergy to any of the ingredients, or had a conflicting condition.

Table 1: Key Ingredients Function and Mechanism of Action

Ingredient	Function	Reference
Reduce Melanin Stimulating Signaling		
Nonapeptide-1	Melanin Stimulating Hormone Antagonist	8
Inhibit Melanin Synthesis		
Tetrahydrodiferuloylmethane	Tyrosinase Inhibitor	11
Alpha-Arbutin	Tyrosinase Inhibitor	12
Hexylresorcinol	Tyrosinase Inhibitor	10
Retinol	Tyrosinase Transcription Inhibitor	7
Inhibit Tyrosinase Activity		
Dipotassium Glycyhrrizate	Tyrosinase Inhibitor	12
Glycyrrhiza Glabra	Tyrosinase Inhibitor	9, 12
Reduce Inflammation and Oxidative Damage		
Epigallocatechin Gallate	Antioxidant	13
Tetrahydrodiferuloylmethane	Antioxidant, anti-inflammatory. Protects keratinocytes from oxidative injury.	11
Alpha-Bisabolol	Anti-inflammatory	11
Glycyrrhiza Glabra	Antioxidant	9, 12

To prevent investigator bias during assessment, product labels were removed, product use was randomized to left/right application and the principal investigator was blinded

to product side usage. Subjects were randomized into two equal groups. Group 1 applied product JM to the right side of the face and OB to the left. Group 2 applied product JM on the left side of the face and OB on the right side. To control the remaining skin care routine, subjects used a generic gentle cleanser on both sides of the face, a generic moisturizer applied to each half of the face individually, with care to prevent the spread of products between sides, and a broad spectrum physical sunscreen (Marini Physical Protectant SPF 45), similarly independently applied to each half of the face.

Improvement was determined by direct physician assessment, subject self-assessment and Visia photography at baseline, 4, 8 and 12 weeks. Physician assessment rated three primary indicators on each side of the face: hyperpigmentation, fine lines, and wrinkles, using a 5-point increasing-severity assessment scale (4 = Severe, 3 = Moderate, 2 = Mild, 1 = Trace, 0 = None). Assessments of dryness, peeling and erythema were also recorded, using the same scale.

Subjects self-assessed the severity of discoloration, wrinkles and textural irregularities on each side of the face using a 5-point Severity Assessment (0= Very Significant Severity, 1=Significant Severity, 2=Neutral, 3=Minimal Severity, 4=flawless). Additionally, subjects were asked to rate their satisfaction with both the product and observed improvement using a similar 5-point scale (0=Highly Dissatisfied, 1=Dissatisfied, 2=Neutral, 3=Satisfied, 4=Highly Satisfied). Finally, to determine product preference, subjects were asked to identify a single preferred product "Overall, I prefer the product on this side of my face" and were asked whether or not they would choose to continue to use either product outside the study "Independent of this study, I would choose to continue to use the product on this side of my face".

RESULTS

Of the 29 enrolled subjects, 5 were lost to follow-up and one subject did not meet enrollment criteria with only trace pigmentation on one side of the face, resulting in a final "n" of 23 subjects.

Physician assessment showed statistically significant improvement vs. baseline in hyperpigmentation, fine lines and wrinkles at all time intervals for both sides of the face. Improvement in the appearance of hyperpigmentation, fine lines and wrinkles on the JM product side of the face is shown in Figure 1. Baseline and 12-week severity scores for improvement in the appearance of hyperpigmentation, fine lines and wrinkles are shown in Table 2. Irritation, dryness, peeling and erythema were also observed on both sides of the face with greater severity on Side A (the JM side). Average sensitivity scores for product JM were highest at week 4, deceasing by week 12. Maximum irritation was rated "trace" with a score of 1.35 (Trace = 1, Mild = 2).

Figure 1: Reduction in Hyperpigmentation by Physician Assessment

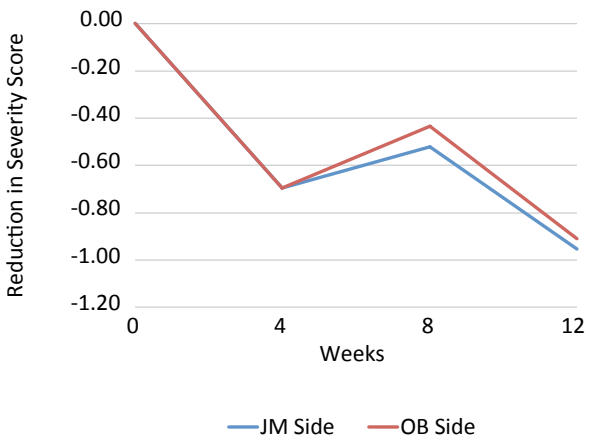


Table 2: Physician Assessed Severity Score & Statistical Significance (0-4 Scale)

	Product JM			Product OB		
	Base-line	12 Wks	p-value	Base-line	12 Wks	p-value
Hyperpig-mentation	3.00	1.96	0.0001	2.96	2.09	0.0002
Fine Lines	2.17	1.50	0.0152	2.17	1.55	0.0192
Wrinkles	2.09	1.50	0.0120	2.09	1.55	0.0194

- Figure 1: Compares the reduction in physician-assessed hyperpigmentation severity for both Products JM and OB.
- Figure 2: Shows the improvement in appearance of pigment, fine lines and wrinkles with product JM from baseline to week 12.
- Figure 3: Shows the improvement in appearance of pigment, fine lines and wrinkles with product OB from baseline to week 12.
- Figure 4: Measures subject-assessed satisfaction for both products.
- Figure 5: Shows the % of subjects preferring each product
- Figure 6: Shows the % of subjects indicating an intent to continue use for each product.
- Table 1: Shows key ingredient function and mechanism of action.
- Table 2: Shows the physician-assessed severity score for hyperpigmentation, fine lines and wrinkles.
- Table 3: Shows product acclimation severity
- Table 4: Measures subject assessed improvement across 4 factors.
- Table 5: Displays average product satisfaction and

improvement satisfaction at 4 and 12 weeks, along with significance of variance of the two sides at each time interval.

Figure 2: Improvement By Concern (JM Side)

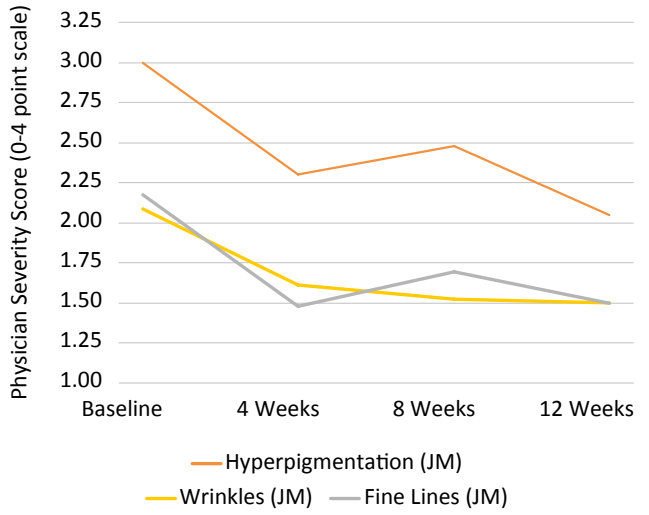


Figure 3: Improvement By Concern (OB Side)

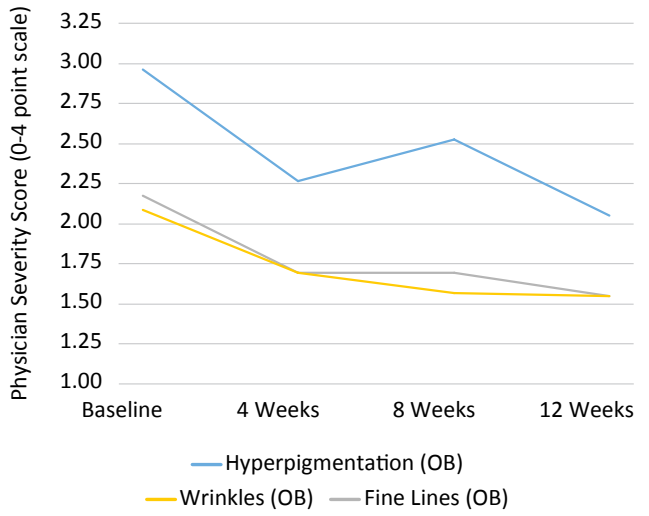


Table 3: Product Acclimation (0-4 scale)

	4 Weeks		8 Weeks		12 Weeks	
	JM	OB	JM	OB	JM	OB
Irritation	1.35	0.43	1.26	0.35	0.68	0.18
Dryness	1.17	0.35	1.43	0.35	1.05	0.27
Peeling	1.04	0.17	0.96	0.22	0.91	0.27
Erythema	1.04	0.35	0.74	0.17	0.55	0.05

Subject satisfaction (Figure 4) remained neutral (score range: 2.14 – 2.55) over the course of the study on the OB side of the face and progressed from neutral to satisfied (score range: 2.32 – 3.0) on the JM product side of the face. At the conclusion of the study, 57% of study participants stated that they preferred product JM over product OB. Further, a statistically significant difference was observed in the desire to continue to use each product with 80% of subjects indicating they would continue to use product JM and only 45% of subjects indicating they would choose to continue to use OB ($p = 0.03$) (Figure 5).

Figure 4: Subject Satisfaction

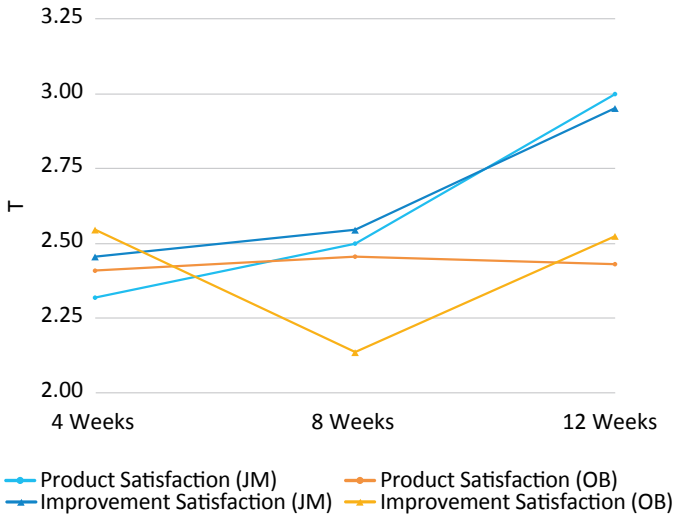
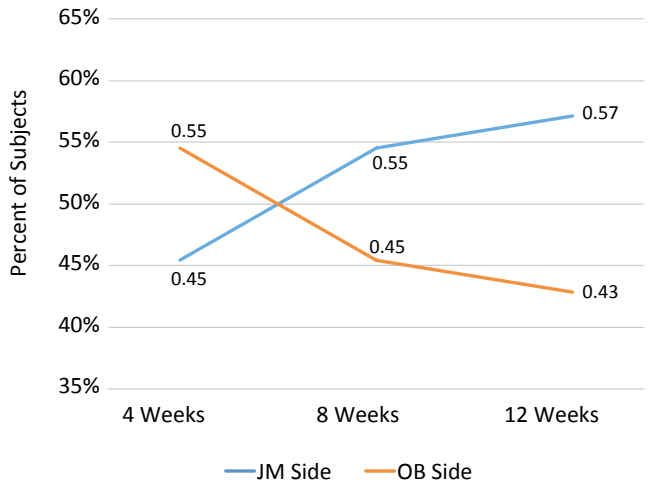


Figure 5: Overall Product Preference



DISCUSSION

This double-blinded, split-face study was designed to determine the efficacy of a new non-hydroquinone lightening solution vs. the gold standard lightening solution, 4% hydroquinone. Assessment by direct physician assessment and subject self-assessment show the test product (JM) to be equal or superior in all measured categories.

PHOTOGRAPHIC EVALUATIONS

BEFORE

AFTER | 12 WEEKS

BEFORE

AFTER | 12 WEEKS

Comparison of average physician-assessed hyperpigmentation scores on the two sides of the face showed slightly superior improvement on the JM product side of the face with an average improvement score of 0.91 compared to an average improvement score of 0.86 on the OB product side of the face (Figure 1). Improvement on both sides of the face were statistically significant with no statistically significant difference between the two sides of the face (p=0.77).

Physician assessment also showed rapid, statistically significant improvement in hyperpigmentation, fine lines and wrinkles, with a trend toward continued improvement over the course of the study on both sides of the face (Figure 2, Figure 3).

Average improvement in hyperpigmentation, fine lines and wrinkles was statistically significant on both sides of the face at weeks 8 and 12 (Table 2 shows results at week 12) with equivalent or superior average improvement scores on the JM product side of the face for all assessments at all time intervals. Only product JM, however, showed significant improvement in the appearance of wrinkles at week 4, indicating potentially more rapid anti-aging benefits. The observed faster response for wrinkles and greater overall improvement for the JM side may be attributable to its more comprehensive nature, as it includes 0.75% all-trans-retinol and multiple antioxidants in addition to lightening ingredients.

As expected, the high concentration of retinol in Product JM resulted in an acclimation period including greater irritation, dryness, peeling and erythema than that observed on the OB side. The OB side of the face did not include a secondary retinoid product as this study was designed to compare two single-product lightening solutions – an over-the counter product to a 4% hydroquinone product. Acclimation was most notable at the 4-week visit and decreased over the course of the study. It should be noted, however, that in practice it is not necessary to start individuals without prior retinoid usage on the studied 0.75% retinol formulation as another, less intense 0.3% formulation is available.

Subject satisfaction with improvement shows an increasing trend toward superior satisfaction on the JM product side of the face (Figure 4, Table 5) At the initial satisfaction assessment, average scores on both sides of the face were roughly equivalent (p=0.7) however, at 12 weeks, overall satisfaction on the JM side of the face increased notably while satisfaction on the OB product side of the face remained constant. While the difference between the two sides is not quite significant (p value = 0.058), there is a highly visible trend toward greater satisfaction on the JM product side of the face.

Subject assessment shows an increasing, and ultimately significant, preference for the JM product side of the face. At the 4-week visit there is a slight, non-significant (p=0.68) preference for the OB side of the face (Figure 5). Preference, however, changes to the JM side of the face at week 8, becoming statistically significant at week 12 (p=0.05). This study seems to show that when patients acclimate to both products, preference is highest for the JM side of the face.

Table 4: Subject-Assessed Improvement from Baseline (0-4 scale)

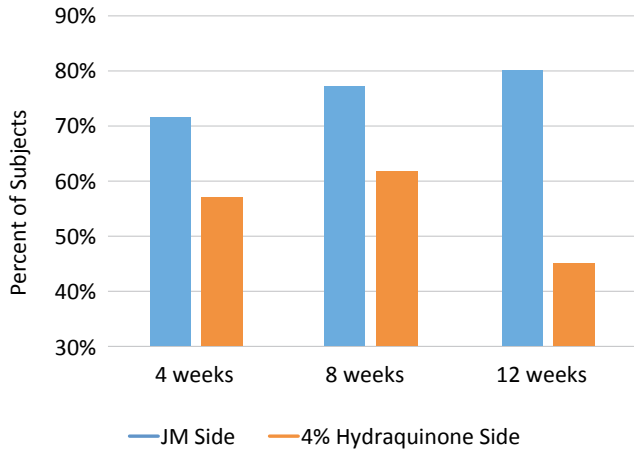
	JM	OB
Texture	0.81 (p<0.01)	0.76 (p<0.01)
Wrinkles	0.81 (p<0.01)	0.67 (p<0.01)
Pigment	0.90 (p<0.01)	0.90 (p<0.01)
Perceived Age	0.38 (p=0.10)	0.24 (p=0.23)

Table 5: Average Subject Satisfaction Scores

	4 Weeks			12 Weeks		
	JM	OB	p-value	JM	OB	p-value
Product Satisfaction	2.32	2.41	0.776	3.00	2.43	0.055
Improvement Satisfaction	2.45	2.55	0.715	2.95	2.52	0.058

Finally, the % of subjects indicating an interest in continuing to use each product outside the study showed a significant preference for the JM product (p=0.03 at 12 weeks) (Figure 6). Of particular interest is the divergent trend between the two products, with a continually increasing percent of subjects indicating intent to use the JM product.

Figure 6: Percent of Subjects Intending to Continue Use



One limitation of this study is the fact that the OB product is typically used in conjunction with prescription tretinoin. The goal of this study, however, was to compare the results of two comparably-priced, single-product lightening solutions with the only primary patient variable being an over-the-counter product vs. the gold-standard, 4% hydroquinone. This study shows superiority of the over-the-counter solution in many measured aspects. Further studies would be necessary to determine the results of more complete (and expensive) hydroquinone and OTC regimens.

CONCLUSION

Both direct physician assessment and subject self-assessment show equivalent to superior results for the over-the-counter study product (Product JM) vs. 4% hydroquinone (Product OB). Physician assessment showed statistically equivalent improvement in hyperpigmentation, texture and fine lines and wrinkles at 12 weeks with more rapid improvement noted in wrinkles on the JM product side of the face.

Subject-assessment showed superior satisfaction with both the JM product and their observed improvement on the JM product side of the face compared to use of 4% hydroquinone. Further, subjects showed a statistically significant preference for the test product and a greater preference to continue using the test product outside the study. Overall, the results of this study show the JM product to be equivalent if not superior to 4% hydroquinone for results and patient satisfaction.

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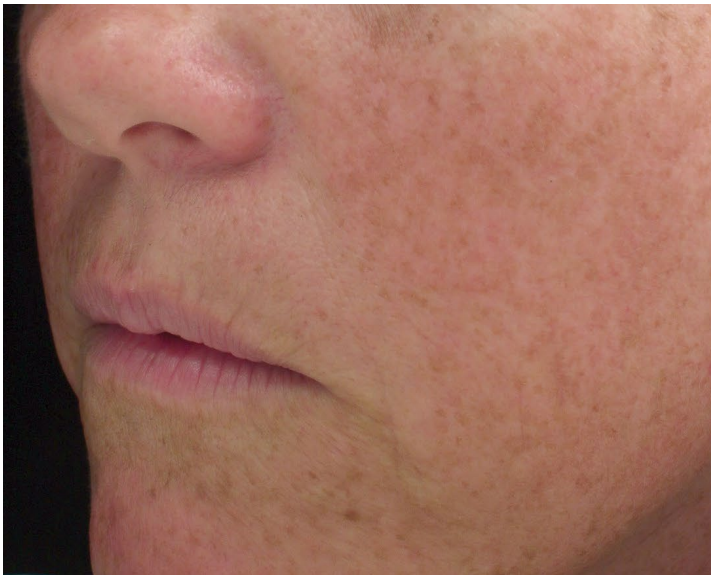
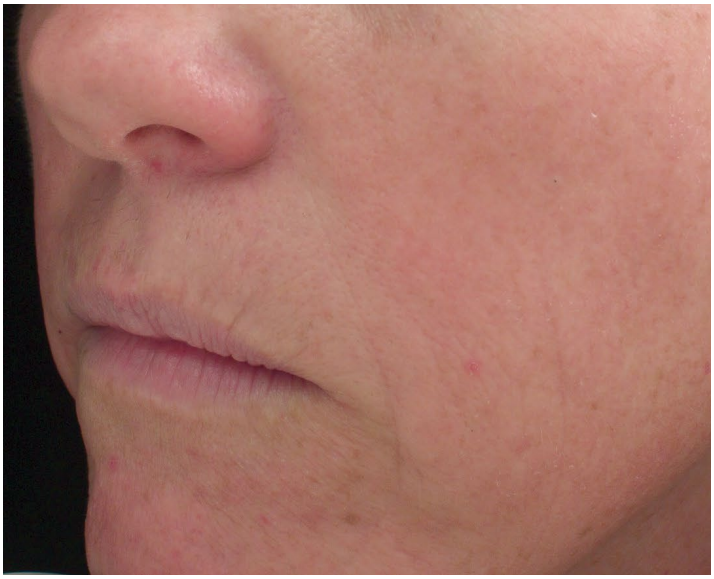
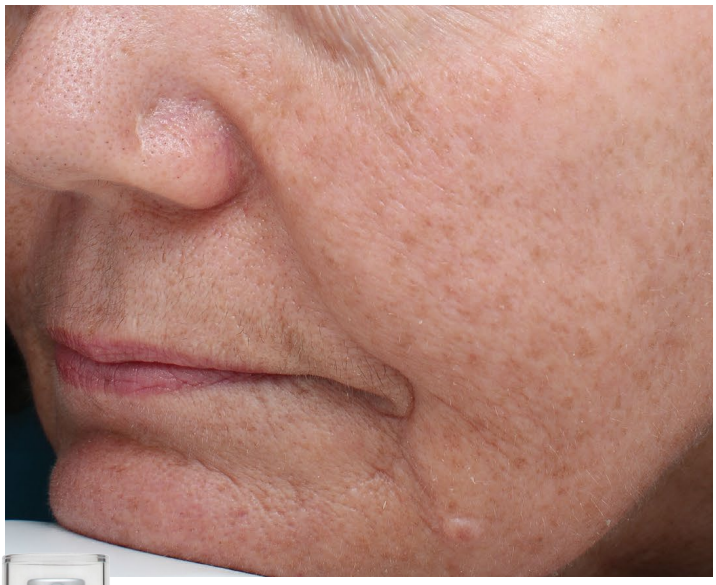
THE NEW 2-IN-1 GOLD STANDARD FOR WRINKLES AND DISCOLORATION.



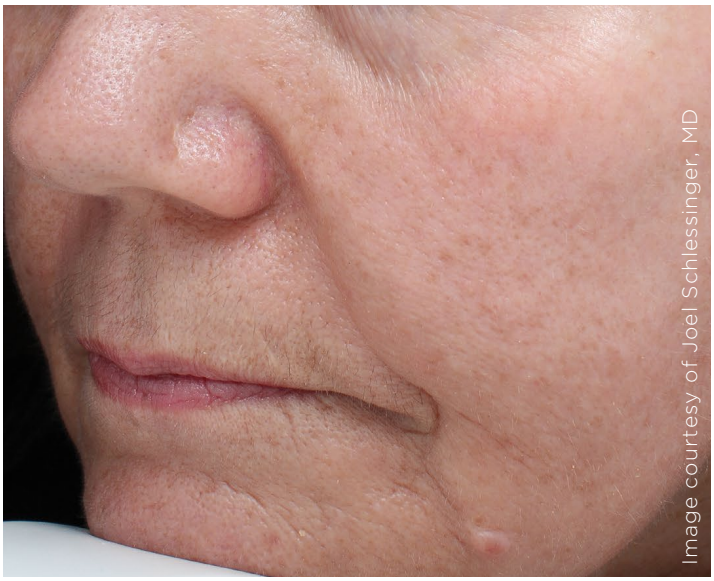
BASELINE



2 MONTHS



BASELINE



1 MONTH

Image courtesy of Joel Schlessinger, MD

A highly concentrated, non-hydroquinone solution with turmeric, peptides, licorice, arbuten, retinol and more, shown to reduce the appearance of discoloration, fine lines and wrinkles. Reveal brighter skin with Marini Luminate Face Lotion!

Jan MARINI SKIN RESEARCH®

FINE LINES & WRINKLES

Multi-Center Evaluation of a New Concentrated Retinol, Peptide and Antioxidant Anti-Aging Solution

Jacqueline Calkin, MD | Kelly Bomer, MD | Sanjay Grover, MD FACS

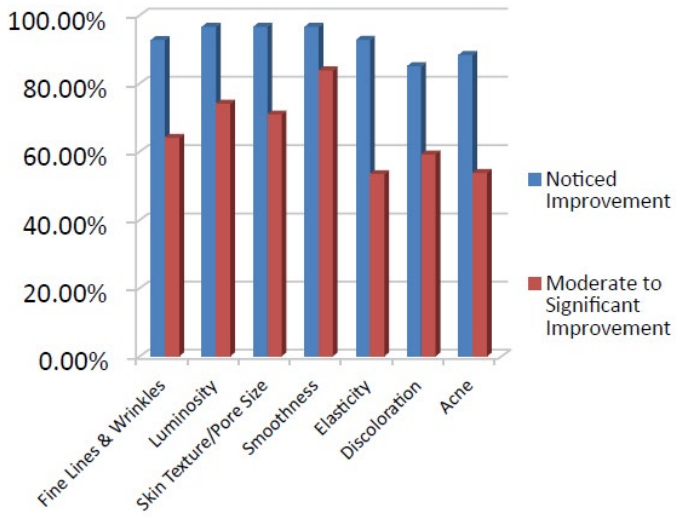
Method:

- 33 subjects ages 20-75 with moderate photo-aging on the face
- AM/PM usage of the Skin Care Management System™ [SCMS] and Retinol Plus MD
- 3-month study

Study Summary:

- 97% of subjects noted improvement in skin smoothness, luminosity, texture and pore size
- 93% of subjects noted improvement in skin elasticity and the appearance of fine lines and wrinkles
- 97% of subjects noticed improvement in overall skin quality
- 96% of subjects noted equal or superior results versus previously used prescription retinoids (n=13)
- 83% of subjects noted superior

Figure 1:
Subjects Noting Improvement In Appearance By Category



FINE LINES & WRINKLES
Products Used | Skin Care Management System, Age Intervention Retinol Plus MD

Multi-Center Evaluation of a New Concentrated Retinol, Peptide and Antioxidant Anti-Aging Solution

Jacqueline Calkin, MD, Sacramento CA
Kelly Bomer, MD, Scottsdale AZ
Sanjay Grover, MD FACS, Orange County CA

INTRODUCTION
Retinoids are utilized extensively among physicians and skin care professionals to achieve optimal skin health for their patients and clients. While there are many benefits from retinoid use, the higher concentration formulas necessary to produce maximum results typically come with longer acclimation periods. This study tests a new multi-ingredient technology combining retinol, peptides and antioxidants to enhance anti-aging benefits and mitigate the irritation and acclimation problems typically associated with high concentration retinoids.

METHODS
Thirty-seven adult subjects (ages 20-75) with moderate photo-aging on the face were enrolled in a 12-week, open-label satisfaction study. Subject surveys, administered at the initial visit and again at weeks 6 and 12, evaluated multiple skin aspects including overall skin quality, the appearance of fine lines and wrinkles, skin texture/pore size, smoothness, elasticity, discoloration from sun damage (spots), acne/periodic breakouts, skin tone and suppleness.

RESULTS
This study demonstrated significant anti-aging benefits in as little as two to four weeks with 93% of subjects experiencing mild to non-existent acclimation issues by week 5. Improvement in all categories was significant with 96.9% of subjects noting improvement in overall skin quality, 96.8% of subjects noting improvement in the appearance of skin texture/pore size, smoothness and luminosity and 92.9% of subjects noting improvement in the appearance of fine lines, wrinkles and elasticity.

CONCLUSION
The tested product provided significant and rapid skin rejuvenation with minimal acclimation sensitivity. Subject satisfaction and compliance was high and subjects rated the test product superior to both prescription and non-prescription products.

INTRODUCTION

The market for professionally-dispensed topical anti-aging products continues to grow and evolve with new ingredients, advancements in formulations and bases and novel combinations of known proven ingredients to achieve synergistic benefits. Economic changes and increased consumer interest in less invasive cosmetic solutions are driving demand; and both consumers and physicians are recognizing the value of topicals as a means of enhancing office-based procedures. Expected market growth for professionally-dispensed topicals is significant. It is estimated that from 2011 to 2015 global sales of physician-dispensed topicals will increase by 12.2% per year.[1]

Retinoids are essential for maintaining optimal skin health. They are utilized extensively among physicians and skin care professionals and continue to be the gold standard for providing dramatic results. However, the high concentrations of retinoids necessary to provide these dramatic benefits often cause flaking, irritation and sensitivity, and can require significant periods of acclimation. For that reason, although the benefits are significant, compliance continues to be an issue. A product that provides a high concentration retinoid with reduced acclimation for maximum results when used alone or in combination with procedures would be extremely desirable for both consumers and physicians.

The tested product (Retinol Plus MD, Jan Marini Skin Research) combines the maximum allowed concentration of all-trans-retinol (1.0%) with anti-aging and collagen boosting peptides[2] and antioxidants plus green tea extract, chrysin, alpha-bisobolol, hydrators and skin soothing ingredients to minimize sensitivity and irritation. The combination of the high concentration of all-trans-retinol and additional ingredients allows this product to provide unparalleled skin rejuvenation benefits while minimizing the acclimation and downtime typically associated with high concentration retinoids.

METHODS

Thirty seven adult subjects between 20 and 75 with moderate photo-aging on the face were enrolled in a 12-week, open-label, multi-center study. Study sites included a Dermatologist, Dr. Calkin (Site A), a Facial Plastic Surgeon, Dr. Bomer (Site B) and a Plastic Surgeon, Dr. Grover (Site C). Inclusion criteria indicated that at least ½ of the subject population have prior personal experience with prescription retinoids.

The test product was added to subject's existing skin care routine. 15 subjects were current JMSR skin care users, 8 were new JMSR users implemented the entire Skin Care Management System (SCMS), and 17 subjects used a skin care regimen other than JMSR. Subjects were instructed to apply the investigational product prior to their hydrator. Subjects followed a 3-week acclimation protocol with every other day PM application week one, daily PM application week 2, and increasing to AM/PM application as tolerated week three.

Results were determined through subject self-assessment surveys. Surveys were administered at study initiation, six weeks and twelve weeks. Assessments included pre- and post-study skin satisfaction assessments as well as perceived improvement in multiple categories. Categories measured included overall skin quality and the appearance of fine lines and wrinkles, skin texture/pore size, smoothness, elasticity, discoloration from sun damage (spots), acne/periodic breakouts, skin tone and suppleness.

Pre- and post-assessment utilized the following 4-point scale: 0=Dissatisfied, 1=Moderately Dissatisfied, 2= Moderately Satisfied and 3=Satisfied. Post study, subjects were also asked to grade the degree of improvement observed for each condition on a 4-point scale as follows: 0=none, 1=mild, 2=moderate and 3=significant. For both assessments subjects also had the option of selecting "Not Applicable" for any condition that did not apply to their skin. If a subject answered "not applicable" to any specific concern, individual responses to that concern were removed from the study population for that concern.

Images were taken using a Visia Camera of subjects at baseline, 1 and 3 months to observe photographic changes in both visible and UV illumination. Statistical significance was determined based on pre- and post-assessment values. Significance was determined using a two-tailed paired t-test with a p value of 0.05 being considered significant.

RESULTS

This study demonstrated notable anti-aging benefits and improvement with 96.9% of the subjects experiencing improvement in their overall skin quality. 71% of subjects noted moderate to significant improvement utilizing a 4-point scale, rating improvement as none, mild, moderate, or significant.

Of the 37 enrolled subjects, 32 (86%) subjects completed the study to protocol. Four subjects (11%) withdrew from the study due to sensitivity/irritation and one (3%) was lost due to follow up. Gender distribution consisted of 30 female and 2 male subjects. Age distribution was as shown in Table 1. Significant improvement was observed in satisfaction for all measured skin categories (Table 2) with a significantly high percentage of subjects reporting moderate to significant improvement in each of the specific categories (Table 3 and Figure 1). Included in the table are individual site enrollment numbers and results. The "n" for each specific condition is adjusted based on those that noted "N/A" for the measured condition.

Subjects with prior experience using prescription and non-prescription retinoids were asked to compare the test product to their previous experiences and rate the test product as inferior, equal or superior to prior experience. Over 50% of the study subjects had prior experience with both prescription and non-prescription retinoids. The test product rated significantly superior to all prior experiences (Table 4).

Table 1: Subject Age Distribution

Age:	25-29	30-39	40-49	50-59	60+
Quantity:	4	5	12	8	3

Table 2: Satisfaction In Appearance Pre/Post By Category

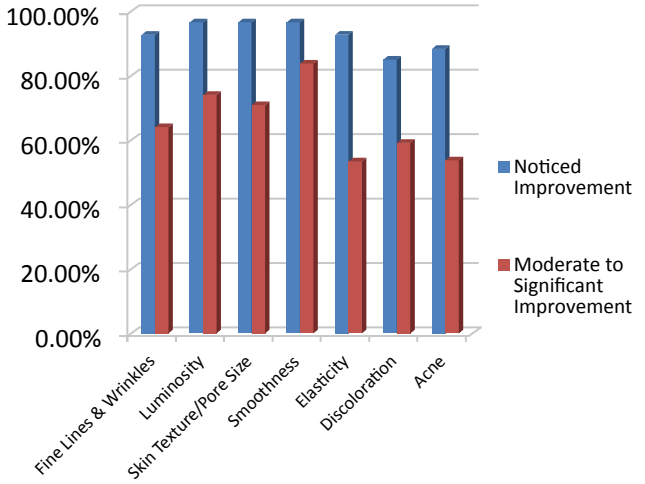
Area of Concern:	n (sum)	Average Value Pre	Average Value Post	Significance (two-tail)
Fine Lines & Wrinkles	29	1.03	2.07	p<0.001
Luminosity	31	1.32	2.29	p<0.001
Skin Texture/ Pore Size	31	1.35	2.07	p<0.001
Smoothness	31	1.68	2.36	p<0.001
Elasticity	29	1.41	2.17	p<0.001
Discoloration	28	0.97	1.93	p<0.001
Acne	25	1.64	2.24	p=0.02

Acclimation sensitivity was minimal with over 80% of subjects reporting none to mild sensitivity during the first 5 weeks of acclimation. By week 5, 93% of subjects reported none to mild acclimation. (Figure 2) 90% of the subjects were able to use the product 1-2 times daily and only 10% of the subjects limited use to once every other day.

Table 3:
Subjects Noting Improvement In Appearance By Category

		Noticed Improvement			Moderate to Significant Improvement	
Area of Concern:	n (sum)	Site A	Site B	Site C	Sum of All Sites	
Total Subject Enrollment		16	11	5	32	
Fine Lines & Wrinkles	28	93%	100%	80%	92.9%	64.3%
Luminosity	30	100%	100%	80%	96.8%	74.2%
Skin Texture/ Pore Size	30	100%	100%	80%	96.8%	74.2%
Smoothness	30	100%	100%	80%	96.8%	83.9%
Elasticity	28	93%	100%	80%	92.9%	53.6%
Discoloration	27	75%	100%	80%	85.2%	59.3%
Acne	26	83%	100%	80%	88.5%	53.8%

Figure 1:
Subjects Noting Improvement In Appearance By Category



Of note, three of the four subjects that withdrew from the study due to sensitivity reported previous sensitivity problems associated with retinoid usage.

Subject satisfaction was high with 97% of subjects noticing overall improvement in skin and 84% of subjects stating they would purchase and/or recommend the tested product to a family member or friend.

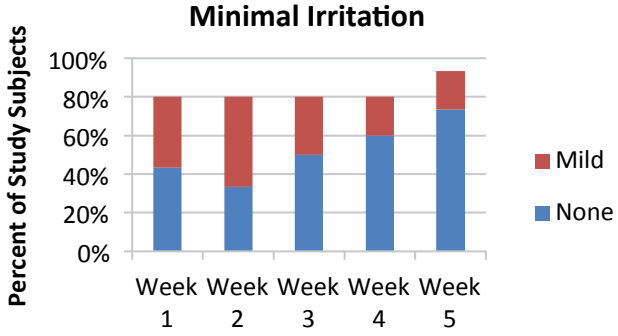
DISCUSSION

Anti-aging is the primary driver for the cosmetic industry, and now more than ever, adults in all age categories are seeking solutions to address the visible signs of aging. Among the many technologies used for anti-aging benefits, three of the most common are retinoids, peptides and green tea. These technologies are shown to enhance collagen production,

Table 4:
Subject Experience vs. Other Anti-aging and Retinoid Product

	"n"	Inferior	Equal	Superior
Retinol Products (Non-Prescription)	24	4.2%	8.3%	87.5%
Prescription Retinoid	23	4.3%	26.1%	69.6%
Anti-Aging Products	28	7.1%	14.3%	78.5%
Acclimation vs. Prescription Retinoid	23	13.0%	4.3%	82.6%

Figure 2:
Rapid Acclimation with Minimal Irritation



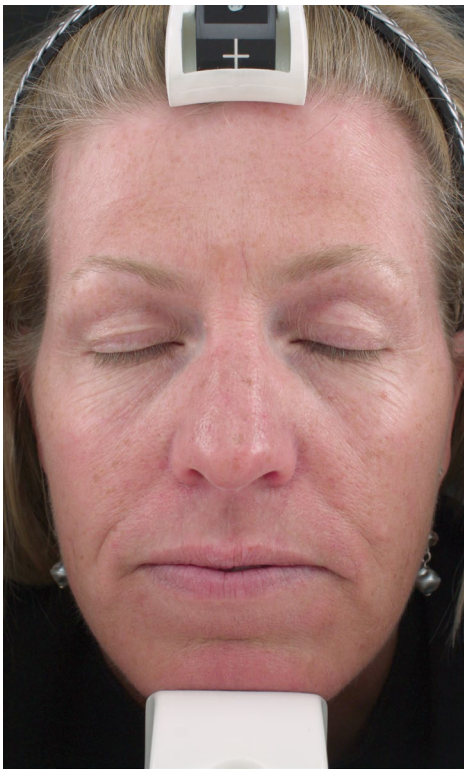
increase dermal thickness and reduce inflammation, abnormal pigmentation and diffuse redness.[3,4,5]

Retinoids are vital to the maintenance of optimal skin health and are utilized extensively among dermatologists. They yield many benefits for the skin and are used to treat a variety of skin conditions. Retinoids provide significant anti-aging benefits by increasing skin thickness and cellular turnover,[6] promoting healthier skin. Many dermatologists believe that the use of retinoids should begin at a young age in order to stave off the visible signs of aging.

The benefits of retinoids are well-known amongst doctors and consumers alike and are used in a wide range of topical products, including over-the-counter and prescription products. Several well-known department store brands promote retinol in their products, emphasizing little to no acclimation as a part of the promotional messaging, but these brands typically employ concentrations below those proven necessary to provide significant results.

There are many forms of retinoids, the two most well-known being all-trans retinol (retinol) and all-trans-retinoic acid (tretinoin). All-trans-retinol undergoes a conversion to tretinoin upon application to the skin, and studies confirm that results are equivalent for topically applied all-trans-retinol and all-trans-retinoic

PHOTOGRAPHIC EVALUATIONS



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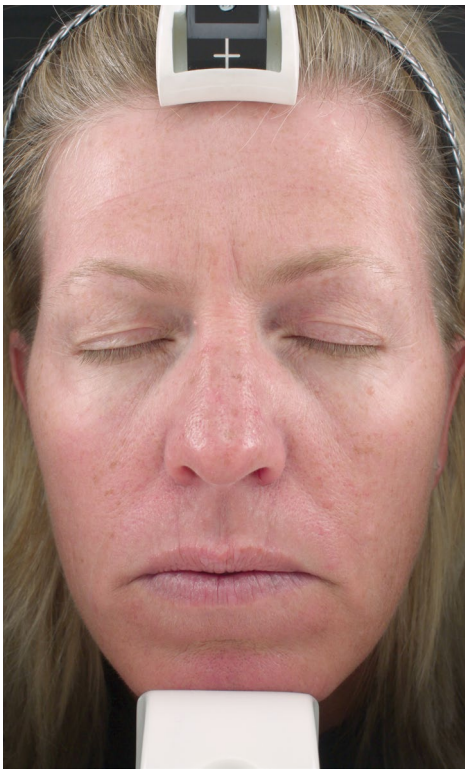

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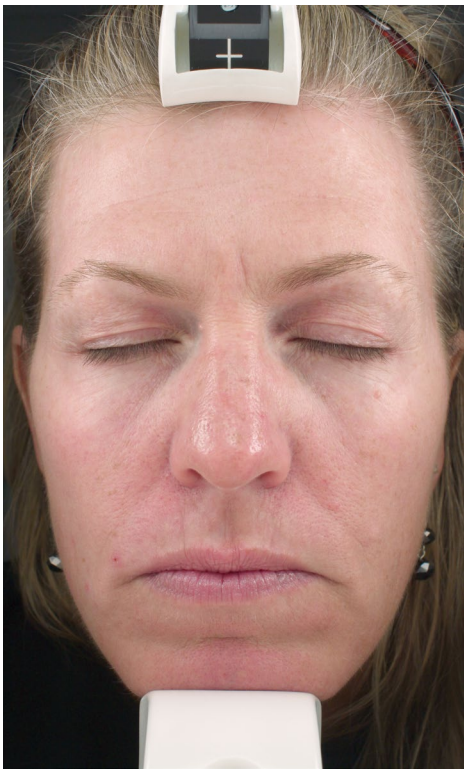

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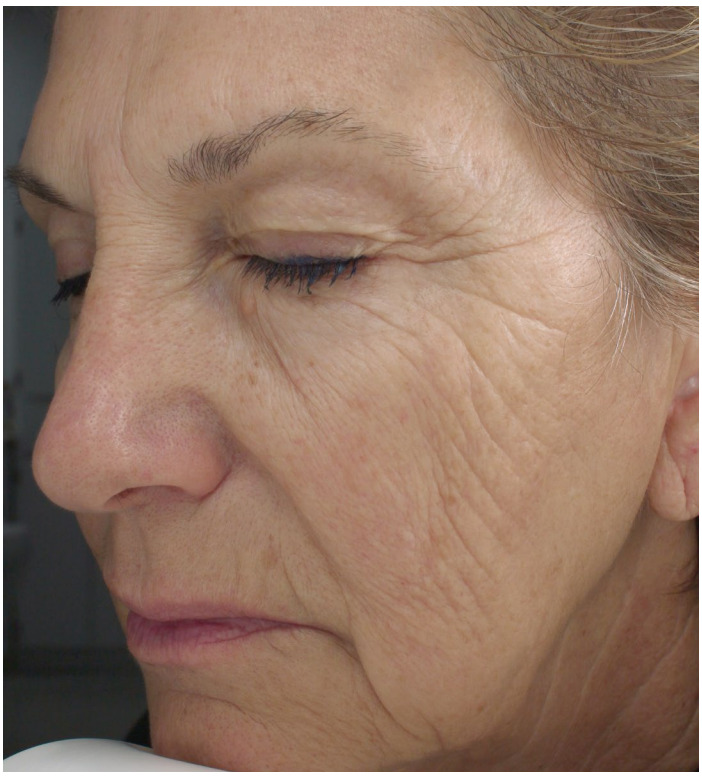

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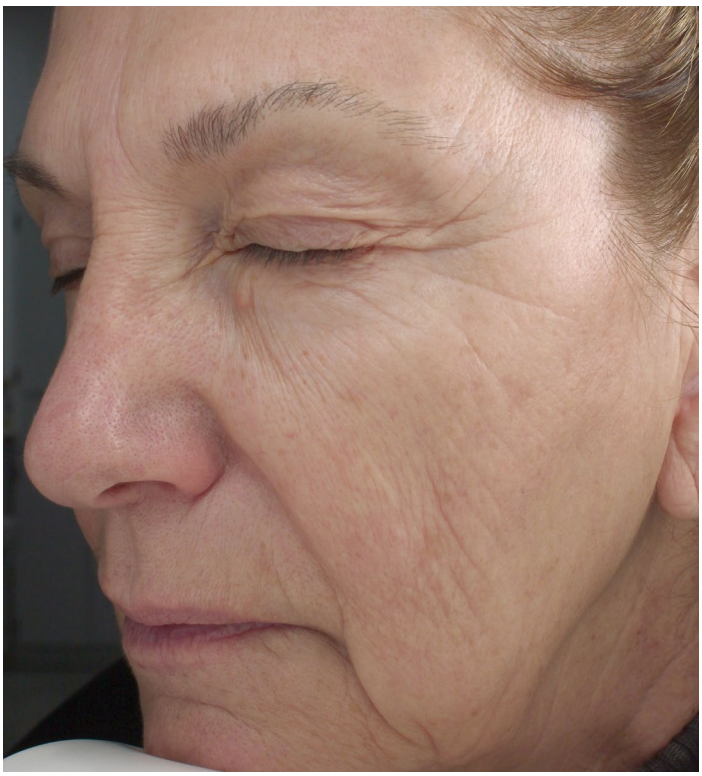

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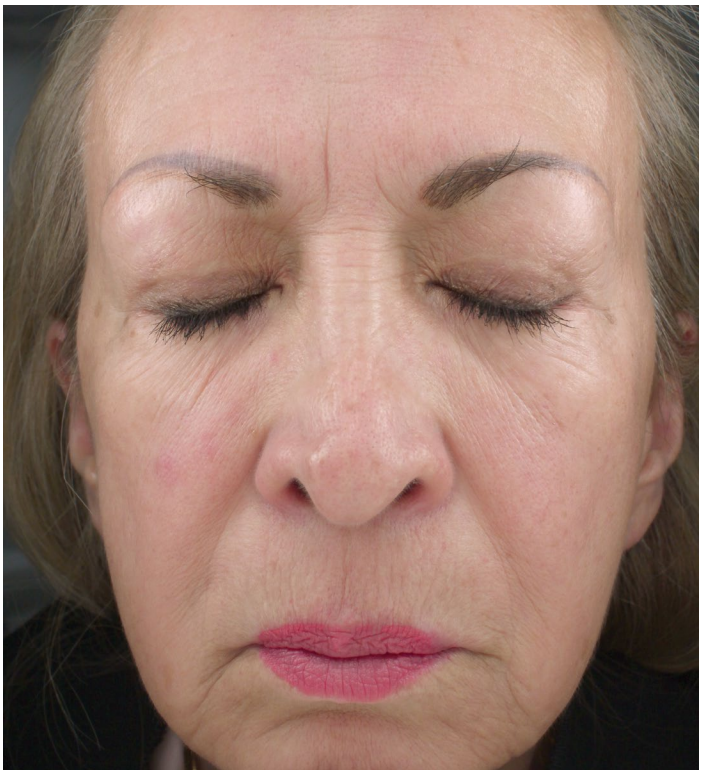

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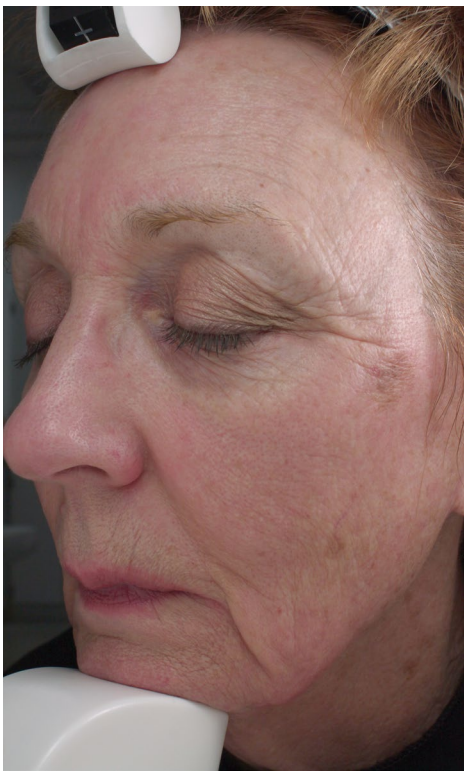
Images courtesy of Jan Marini Skin Research



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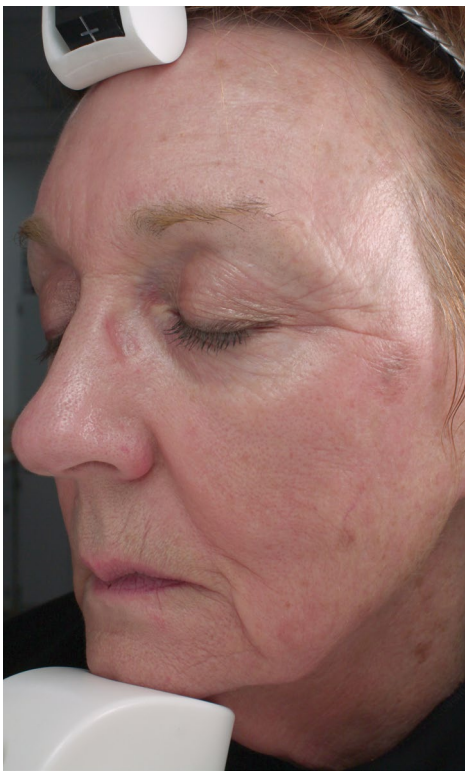

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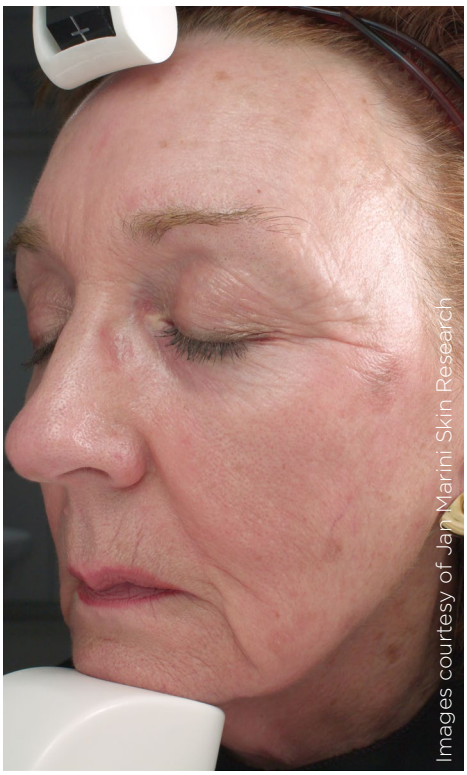


AFTER | 3 MONTHS

Images courtesy of Jan Marini Skin Research

acid for multiple indications.[7] A histologic control study comparing retinol concentrations observed increased epidermal thickness and skin changes at concentrations of 0.15% with increased keratinocytes orderliness and decreased melanin content in 100% (6 of 6) subjects at concentrations at and above of 0.3% vs. no changes (0 of 3) in the control group.[7] Another study noted that to achieve comparable results, the necessary concentration of all-trans-retinol is approximately 10 times the equivalent concentration of all-trans-retinoic acid[8] (example 1.0% all-trans-retinol is roughly equivalent 0.1% all-trans-retinoic acid).

The standard prescribed retinoid, tretinoin, is typically prescribed with concentrations ranging from 0.025% to 0.1%. Results from tretinoin are significant but irritation and sensitivity is also high with irritation ranging from 67-82% of subjects using 0.1% tretinoin.[9,10]

The proven technologies combined in the tested product - multiple peptides, antioxidants and anti-inflammatories (green tea extract, chrysin, alpha-bisobolol, n-hydroxysuccinimide (NHS), and hydrators) - were specifically selected to enhance anti-aging benefits and mitigate the irritation and acclimation problems typically present with high concentration retinoids. The peptides in the product, palmitoyl tetrapeptide-7 and oligopeptide are shown to reduce the appearance of wrinkles and increase skin firmness and smoothness after 1-2 months[2] and antioxidants are considered an essential component in helping to prevent many of the visible signs of aging.[11] Green tea extract is a powerful antioxidant that significantly decreases the appearance of lines and wrinkles and is shown to reduce the damage from oxidative stress thus decreasing cellular damage, providing great benefits to photo-damaged and aging skin.[12,13,14]

In addition to green tea extract, the tested product contains other calming/anti-inflammatory ingredients including alpha-bisabolol, chrysin and N-hydroxysuccinimide (NHS). Each of these ingredients has significant anti-inflammatory properties and assists in mitigating the irritation and inflammation from the high concentration of retinol.[15,16]

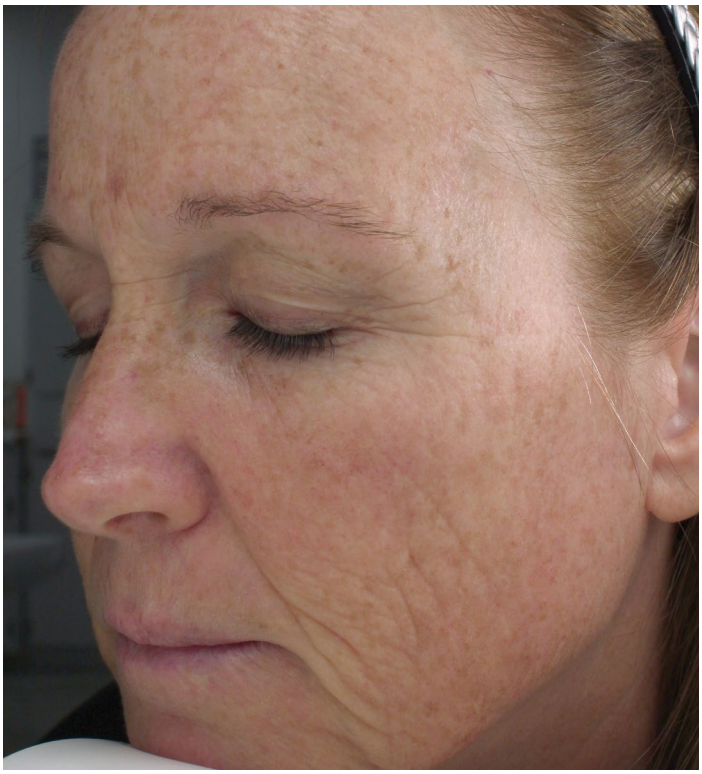
Interestingly, although the concentration of retinol in the test product is high (1.0%) which is roughly equivalent to a 0.1% tretinoin, 81% of study subjects with previous retinoid experience (n=21) indicated a superior acclimation experience compared to a high percentage topical retinoid.

CONCLUSION

The tested product is a revolutionary new topical anti-aging concept. It provides rapid and clinically proven improvement for smoother, more uniform looking skin with marked reduction in the appearance of fine lines and wrinkles. The revolutionary combination of high concentration all-trans-retinol with key integrated peptides, antioxidants, hydrators and soothing agents enhance the benefits beyond those of simple retinoids while simultaneously reducing the acclimation and sensitivity historically associated with high concentration retinoids.

The benefits of rapid improvement and minimal irritation/ sensitivity lead to high subject satisfaction and compliance. The tested product is safe for long-term use and, as with any retinol product, the benefits will continue with use. No other single product offers the same complete anti-aging solution.

PHOTOGRAPHIC EVALUATIONS



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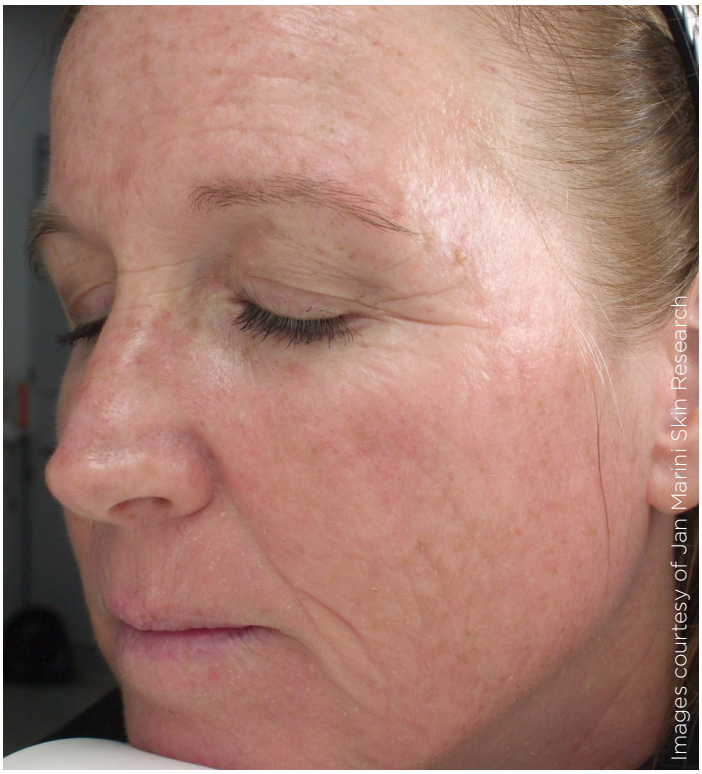

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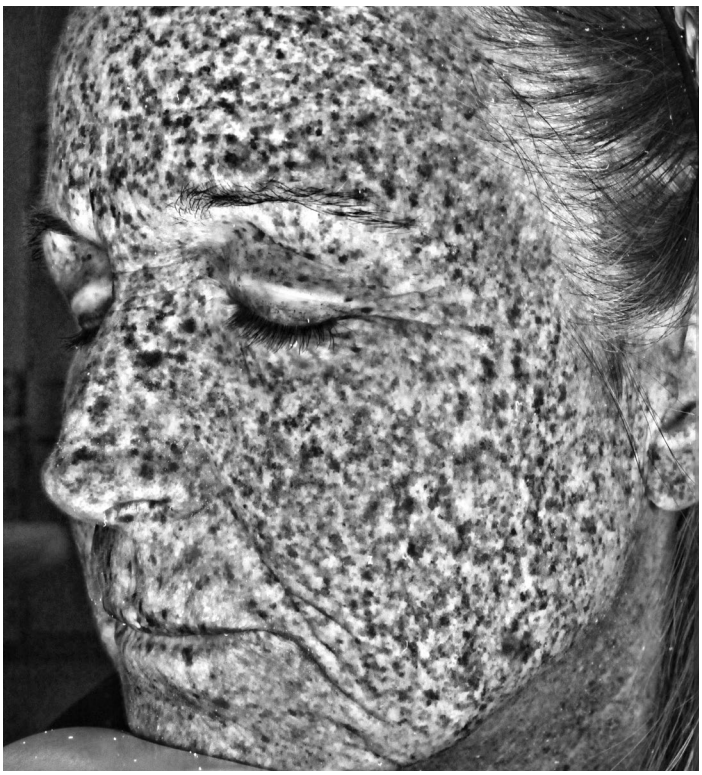

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AFTER | 3 MONTHS | UV LIGHT

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ACNE

Multi-Center Evaluation of a New Concentrated Retinol, Peptide and Antioxidant Anti-Aging Solution

Jaggi Rao, MD

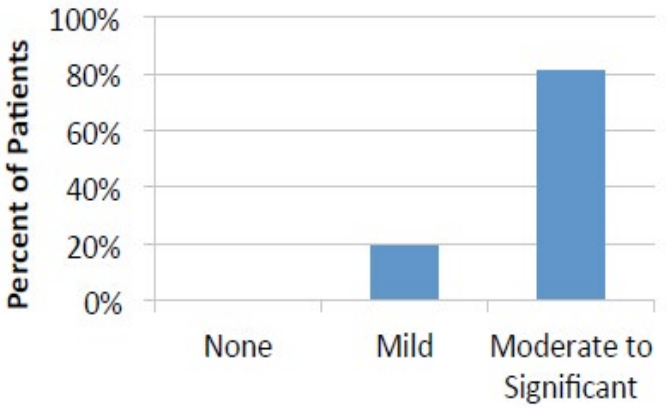
Method:

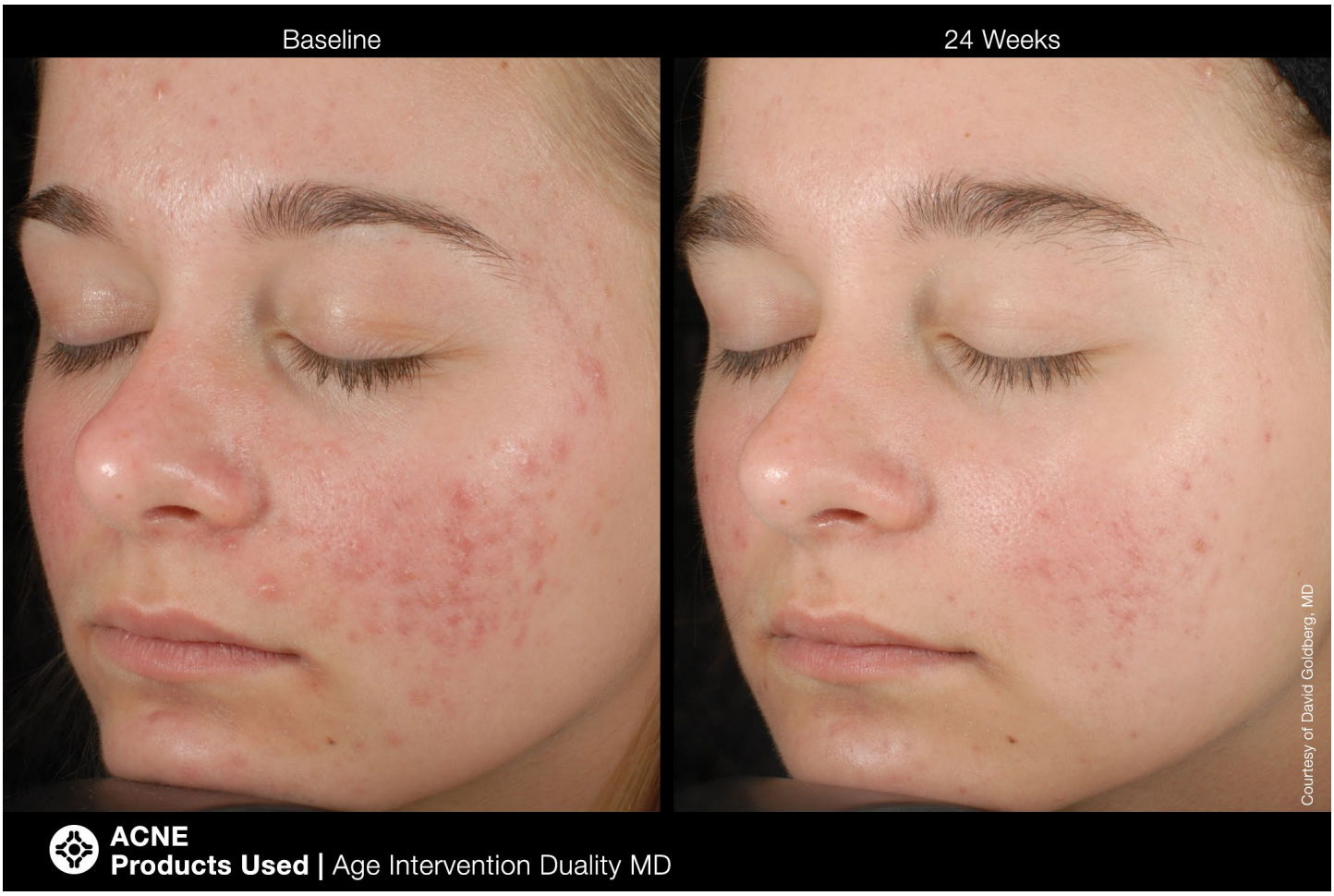
- 21 subjects ages 20-29 with mild to moderate acne
- AM/PM usage of the Skin Care Management System™ and Duality MD™ following a 3-week acclimation period
- 3-month study

Study Summary:

- 100% of subjects experienced a reduction in acne lesion counts
- Improvement was statistically significant by week 4 and continued to improve through study completion
- 64% average lesion count reduction (range 36% to 78%)
- 100% of subjects experienced significant improvement in skin quality by blinded photographic review
- High subject satisfaction with no reported irritation or excessive drying

Figure 5:
Degree of Acne Improvement





ACNE
Products Used | Age Intervention Duality MD

Novel Dual-Chamber Anti-aging and Acne Solution Utilizing 10% Benzoyl Peroxide and 1% Retinol

Jaggi Rao, MD
Associate Clinical Professor of Medicine,
University of Alberta,
Edmonton, Alberta, Canada

INTRODUCTION
Acne and anti-aging are two of the most significant skin concerns affecting the population today. Nearly 54 million people in the US alone are affected with acne each year, and anti-aging is recognized as the primary driver for the entire cosmetic skin care industry. With nearly 50% of female adults experiencing acne, an increasing rate of adult acne and ever increasing attention on new anti-aging technologies, there is a significant demand for a combination acne and anti-aging solution for adults.

METHODS
This study investigates a new acne and anti-aging product capable of simultaneously delivering stable formulations containing 10% Benzoyl Peroxide (BPO), 1% retinol, antioxidants and peptides. Twenty-one adult patients were enrolled in a 12-week, open label, non-placebo controlled study. Patients were assessed at each visit by a dermatologist to determine improvement in acne and photo-aging. Pre- and post- photographic assessments were conducted by four independent dermatologists reviewing global acne and skin quality. Finally, patients completed pre and post self-assessments to determine perceived improvement and satisfaction.

RESULTS
Acne lesion counts improved in 100% of all patients. Improvement was statistically significant by week 4 ($p<0.0001$) and continued to improve through study completion. Average lesion reduction was 64% ranging from a low of 36% to a high of 78%. Global acne assessment scores improved significantly ($p<0.0001$) with an average reviewer assessment of 70% of patients improving by 1 or more grades. Improvement in photo-aging was significant ($p=.02$) with photographic review indicating significant improvement in skin quality ($p<0.0001$) in 100% of all patients. Patient assessment showed significant improvement in both skin quality ($p<0.0001$) and acne ($p<0.0001$). Patient satisfaction was high with no reported cases of irritation or excessive drying.

CONCLUSION
The simultaneous application of BPO, retinol, antioxidants and peptides delivered statistically significant improvement in acne and anti-aging without the common acne medication side-effects of skin irritation and excessive drying. Lesion count improvement was comparable or superior to prescription topical medications and over 70% of patients improved by at least one full grade using the 4-point global acne assessment scale. Skin quality improvements were significant by both patient self-assessment and investigator assessment. The tested solution represents a new and highly effective acne and anti-aging solution for adults with mild to moderate acne vulgaris.

INTRODUCTION

Acne and anti-aging are two of the most significant skin concerns affecting the adult population today with nearly 54 million people affected each year in the US alone. In an effort to control acne, American physicians write nearly eleven million prescriptions (The Lewin Group, 2004) with an estimated annual cost of $2.2 billion. In terms of dollars spent to control a skin condition, acne is second only to hair and nail diseases. In fact, it is estimated that acne patients are willing to spend an average of $4.00 per day to alleviate their acne conditions, indicating a potential market of $12 billion (The Lewin Group, 2004).

Anti-aging is the primary driver for the cosmetic industry and, now more than ever, adults in all age categories are seeking solutions to address the visible signs of aging. Among the many technologies used for anti-aging benefits, three of the most common topical solutions are retinoids, peptides and green tea. These technologies have been shown to enhance

collagen production, increase dermal thickness and reduce inflammation, abnormal pigmentation and diffuse redness (Fowler JF Jr., 2010) (Atkin DH, 2010) (Fu JJJ, 2010).

Acne, while often thought of as an adolescent condition, greatly affects the adult population and the prevalence is growing. In recent years the average age of individuals with acne has increased from 20.5 to 26.5 years of age (Goulden V, 1999), with the typical age ranging between 15-42. Studies show that approximately 50% of women between 20-29 years old and 25% of women 40-49 years old are affected by some form of acne with 12% of all adult women having clinically significant acne (Goulden V, 1999). Self-assessment data show that for the age groups of 20-29, 30-39 and 40-49, respectively, acne affects 50.9%, 35.2% and 26.3% of women and 42.5%, 20.1% and 12.0% of men (Collier CN, 2008). Studies also show that this disease can have a dramatic influence on a patient's quality of life (QOL), more so even than psoriasis. 25% of all people with acne suffer from anxiety and 13% exhibit depression ranging from mild to severe (The Lewin Group, 2004).

Two of the first-line solutions to treat acne are retinoids (vitamin A derivatives) and benzoyl peroxide (BPO) (Zaeinglein AL, 2006) (Sinclair W, 2005). Retinoids are highly keratolytic thereby enhancing desquamation of the follicular epithelium, reducing the number of microcomedones. They also exhibit significant anti-inflammatory properties (Zaeinglein AL, 2006) and are used very successfully as a primary treatment for inflammatory acne (Sinclair W, 2005). Finally, retinoids can help enhance the penetration of other topical drugs such as BPO and antibiotics (Zaeinglein AL, 2006) (Gollnick H, 2003) (Mills OH Jr., 1978).

BPO is a potent antibacterial agent, which also has mild anti-inflammatory and keratolytic effects. Because of its ability to rapidly destroy P. acnes bacteria, it is an important component of acne therapy as both a stand-alone technology and in combination with many other acne treatments. For severe acne treated with oral and topical antibiotics, BPO and retinoids are recommended to be used in combination to enhance efficacy, suppress the emergence of resistant strains of P. acnes bacteria and sustain results after a course of antibiotics (Zaeinglein AL, 2006) (Sinclair W, 2005) (Gollnick H, 2003).

Over time, the oxygen created by BPO breaks down retinoids – preventing stable combination formulations. Because of this, many protocols prescribe separate application of retinoids and BPO in an AM/PM routine. These protocols are sub-optimal as they limit the number of applications of both retinol and BPO, require multiple products and complicate the application process leading to decreased compliance. A recent study disproved the need for separate application protocols finding no difference in efficacy or skin irritation when both BPO and retinoids were applied in the AM vs. separate AM/PM applications (Pariser D, 2010).

Additional technologies such as anti-bacterial peptides and green tea are also becoming more popular treatments to control acne. Green tea is shown to have anti-inflammatory characteristics and functions as a 5-alpha reductase to help control inflammatory and hormonal acne. Since oxidative stress is speculated to be a factor in the pathogenesis of acne, green tea and other antioxidants that reduce reactive oxygen and oxidative stress in the skin (Elsaie ML, 2009) (Katiyar SK, 2001) can independently improve acne (Elsaie ML, 2009).

The product under investigation is a new combination acne and anti-aging solution (Age Intervention Duality by Jan Marini Skin Research). This new product utilizes a dispensing system with independent internal chambers comprised of stable formulations of 10% BPO and 1% Retinol plus antioxidants (green tea, bisabolol and Chrysin), an anti-bacterial peptide, anti-aging peptides and moisturizers. The ingredients in this new acne and anti-aging product are specifically designed to maximize results in acne and anti-aging improvement without drying or excessive irritation to the skin.

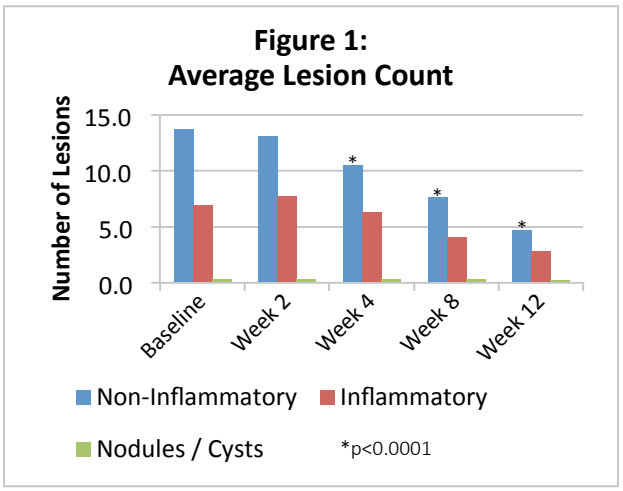
METHODS

Twenty-one adult subjects were enrolled in a 12-week, open-label, non-placebo controlled acne study with a total of 5 office visits (initial, 2 weeks, 4 weeks, 8 weeks and 12 weeks). Inclusion criteria specified individuals with mild to moderate acne of both genders between the ages of 20-65, in good health, non-smoking and with no known diseases or conditions causing their acne.

Subjects in the study used the investigational BPO, retinol and anti-aging formulation with The Skin Care Management System (Jan Marini Skin Research). The Skin Care Management System is a complete pre-packaged skin care system consisting of a glycolic cleanser, a Vitamin C serum, a resurfacing gel, a hydrating product and a sunscreen. The complete system was used to ensure uniform incorporation of a daily skin care regimen, including cleanser, moisturizer and sunscreen as each of these components could affect results. An acclimation period of 2-weeks was utilized to minimize skin sensitivity with patients applying Duality MD every other evening during week one, every evening during week two finally twice daily for weeks 3-12. The protocol followed recommended procedures for the Skin Care Management System.

Assessments included principal investigator review, patient self-assessment, and blinded photographic review at study completion by four independent dermatologists. Quantification of acne was determined by both total lesion count (TLC) and global acne assessment. TLC quantified the total number of non-inflammatory lesions, inflammatory lesions (papules / pustules) and nodules / cysts (>5mm) on the forehead, right cheek and mouth/chin/nose area. Global acne assessment was determined following the FDA Guidance for Industry Acne Vulgaris: Developing Drugs for Treatment (Table 1).

Improvement in anti-aging was determined by the principal investigator using a 10-point scale for overall photo-damage (pigmentation, wrinkles, elastosis, elasticity, etc.), overall skin pigmentation (including hyperpigmentation from acne), and overall appearance of skin quality (texture, luminosity, tone and general appearance).



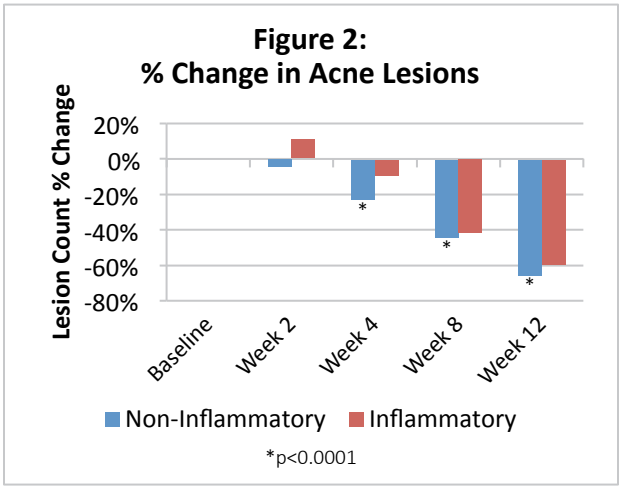
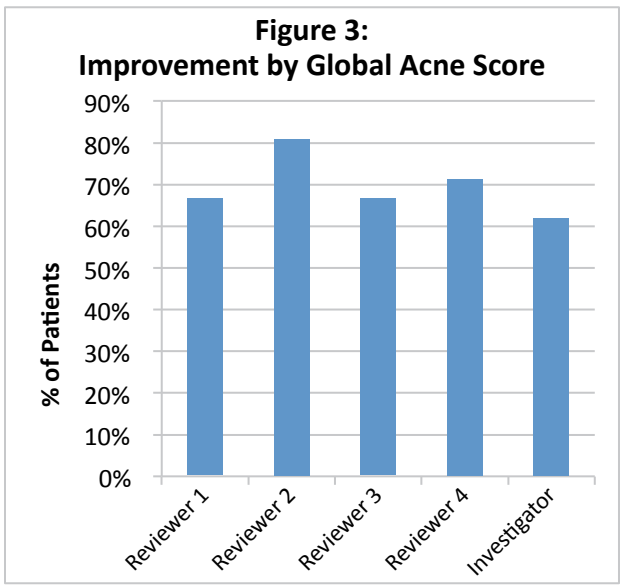


TABLE 1 – INVESTIGATORS GLOBAL ACNE ASSESSMENT

1	Clear skin with no inflammatory or non-inflammatory lesions
2	Almost clear; rare non-inflammatory lesions with no more than one small inflammatory lesion
3	Mild severity; greater than Grade 1; some non-inflammatory lesions with no more than a few inflammatory lesions (papules / pustules only, no nodular lesions)
4	Moderate severity; greater than Grade 2; up to many non-inflammatory lesions and may have some inflammatory lesions but no more than one small nodular lesion
5	Severe; greater than Grade 3; up to many non-inflammatory and inflammatory lesions but no more than a few nodular lesions

Photo-aging was also assessed using a published multi-factorial 4-point scale developed by Dr. Macrene Alexiades-Armenakas published in *JDD* Sept. 2006 for assessing



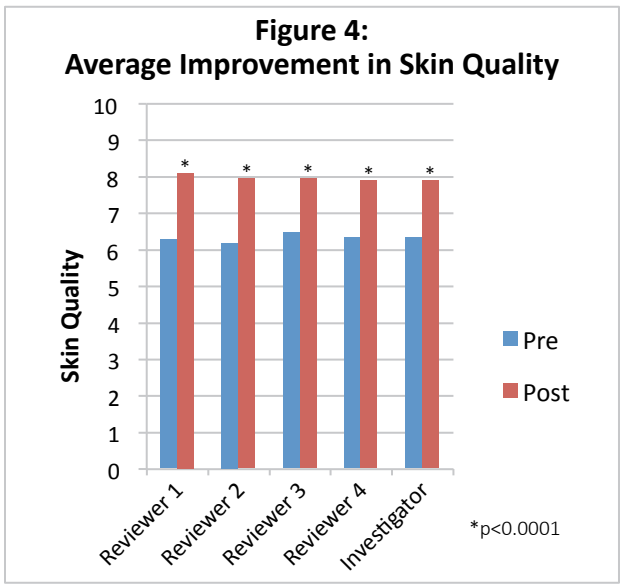


photo-aging pre- and post-non-ablative laser treatments. This scale was used in place of a standard wrinkle score due to its increased granularity to measure changes in texture, erythema, elastosis and wrinkles.

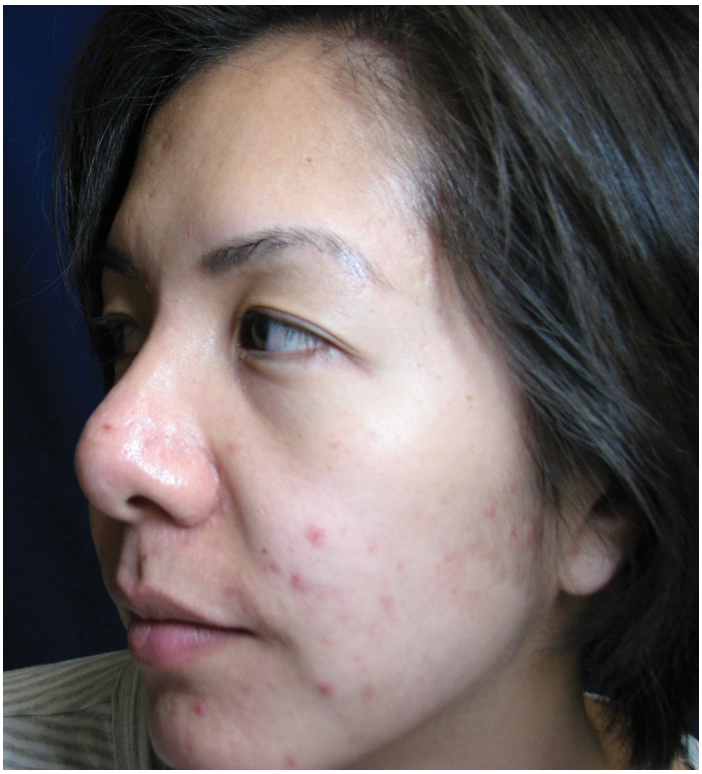
To determine patient satisfaction, patients were asked to complete pre -and post- study questionnaires. Finally, upon study completion, patients were asked to rate their perceived degree of improvement in acne, discoloration, rosacea, wrinkles, skin texture, pore size, skin smoothness, elasticity and luminosity / brightness of the skin.

Statistical significance was determined by paired t-test. Unless otherwise specified, statistical significance was determined by comparing pre and post-treatment data. A p value of less than 0.05 was used to determine significance.

RESULTS

Patient compliance was extremely high with no reports of drying or skin irritation. There were also no drop-outs in the

PHOTOGRAPHIC EVALUATIONS



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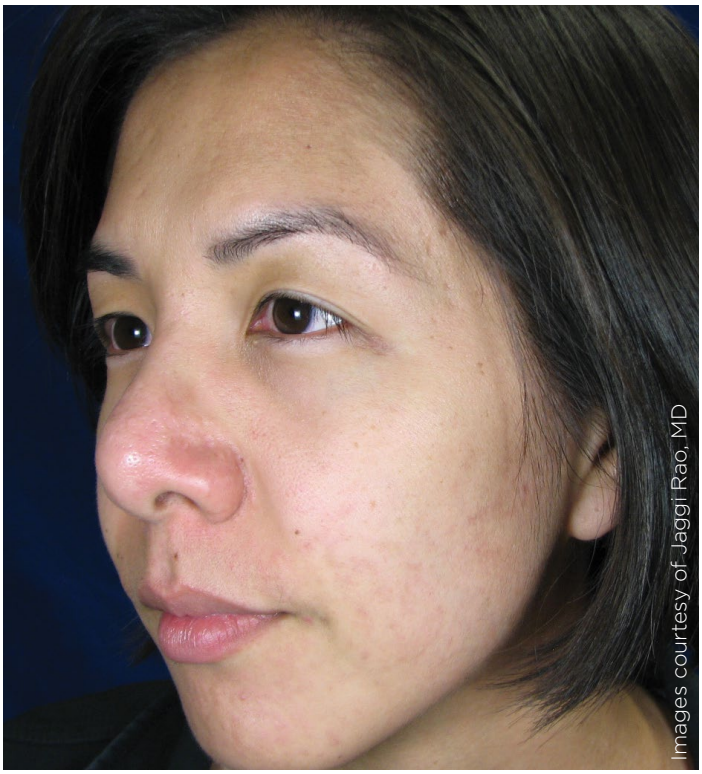
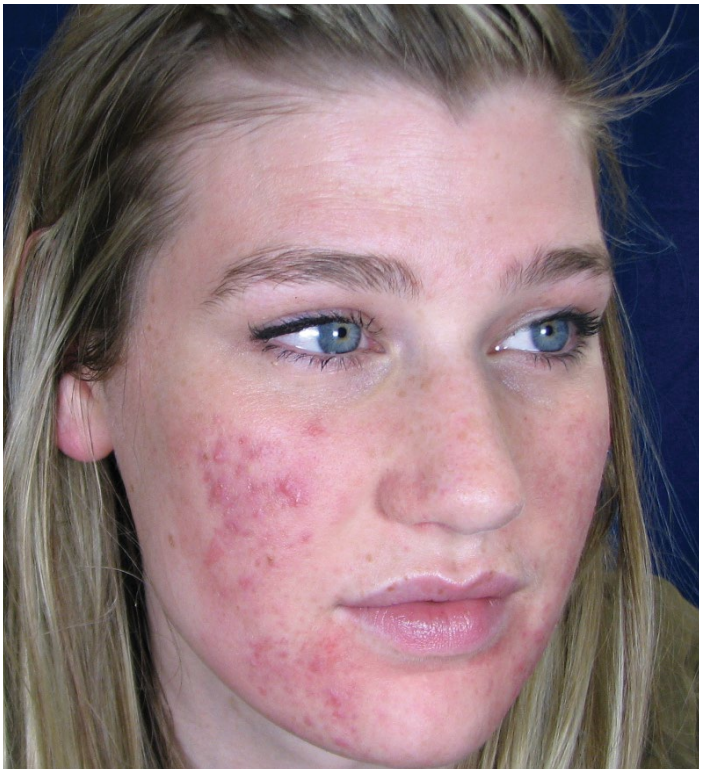


AFTER | 3 MONTHS



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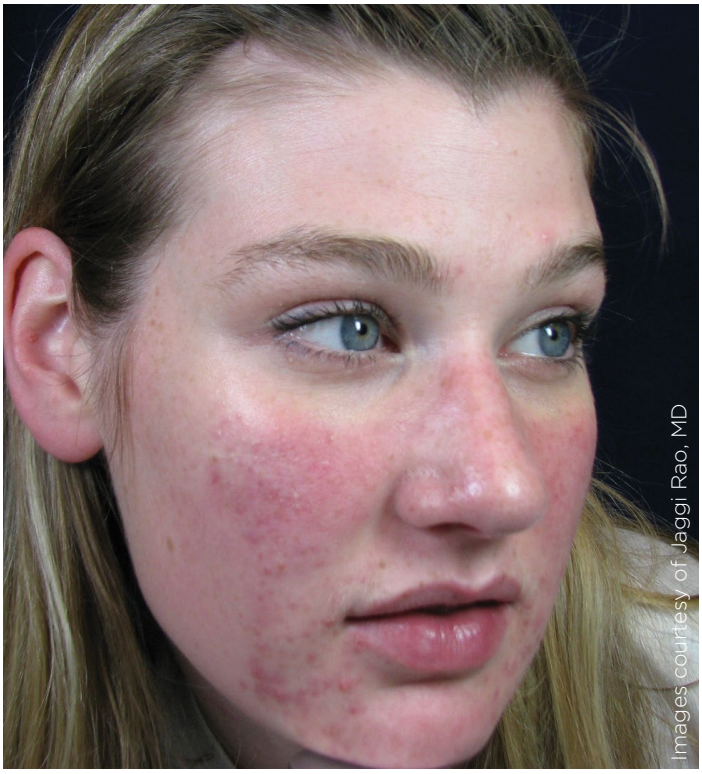

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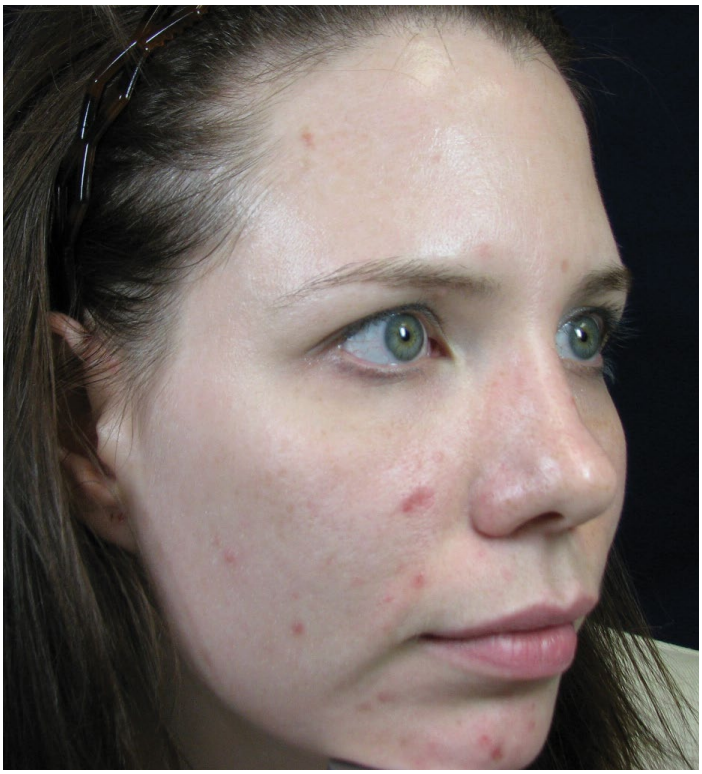

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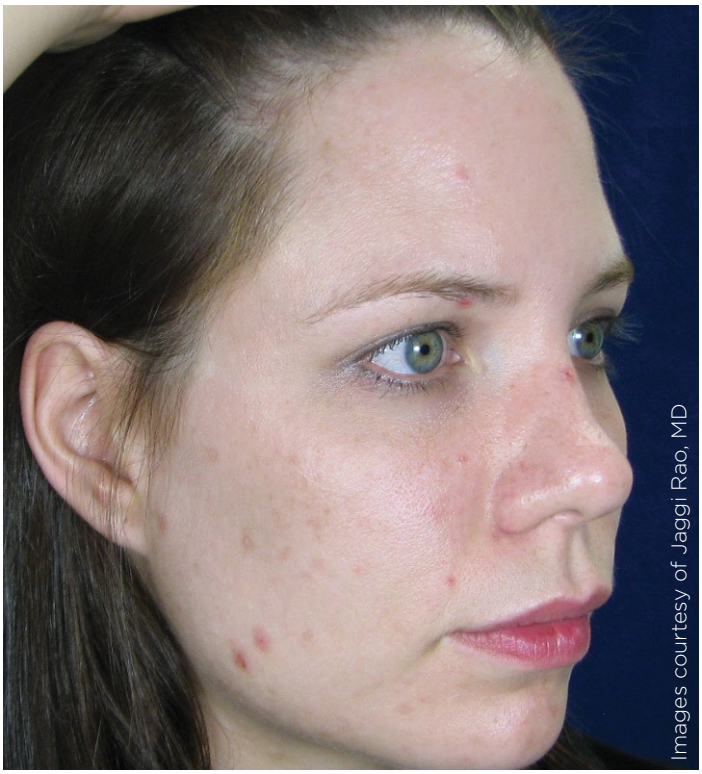

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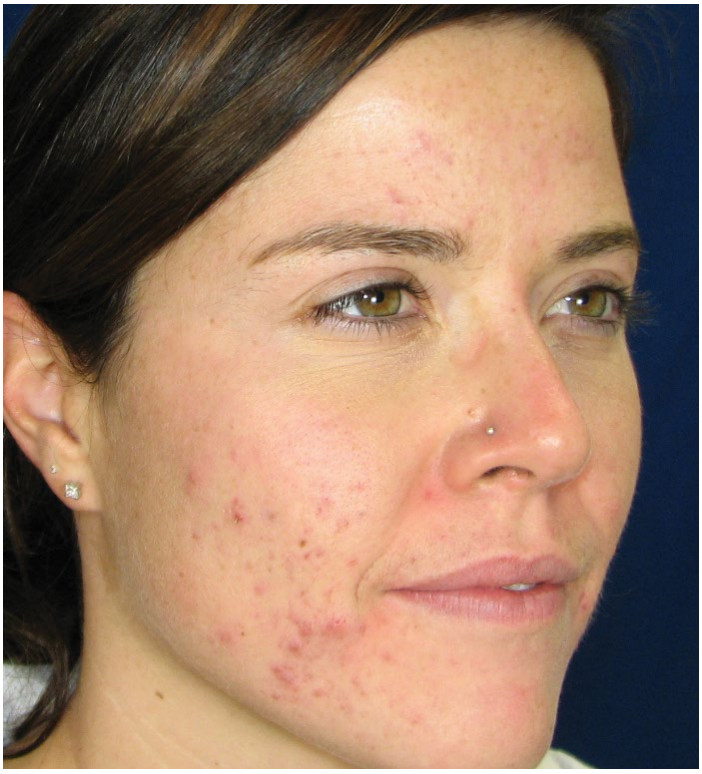

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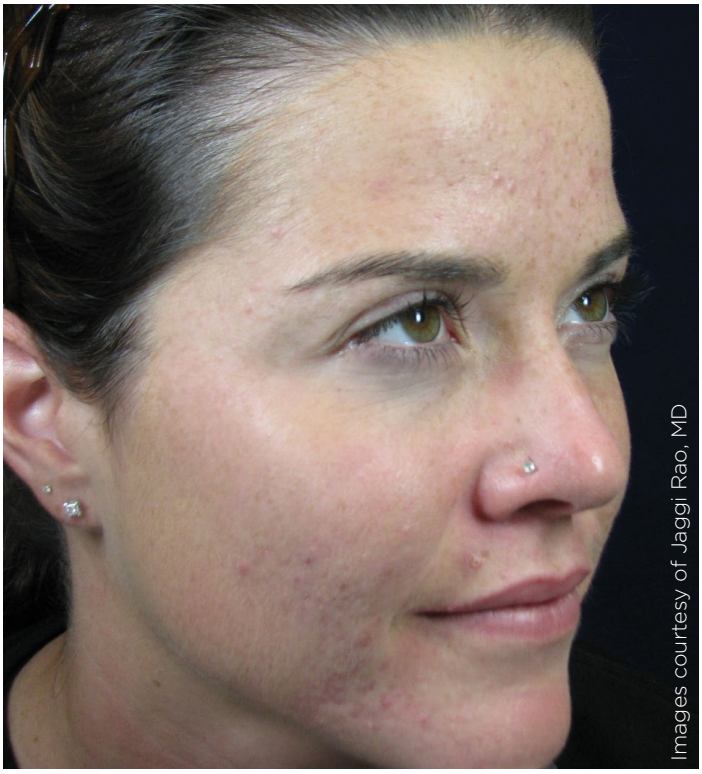


AFTER | 3 MONTHS

Figure 5:
Degree of Acne Improvement

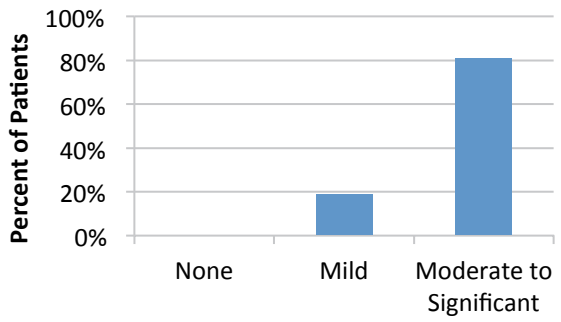


Figure 6:
Average Satisfaction with Skin Quality

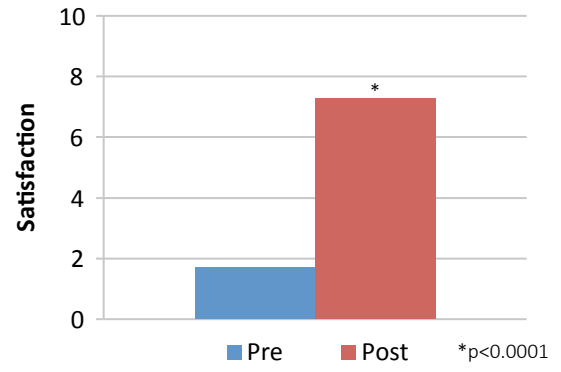
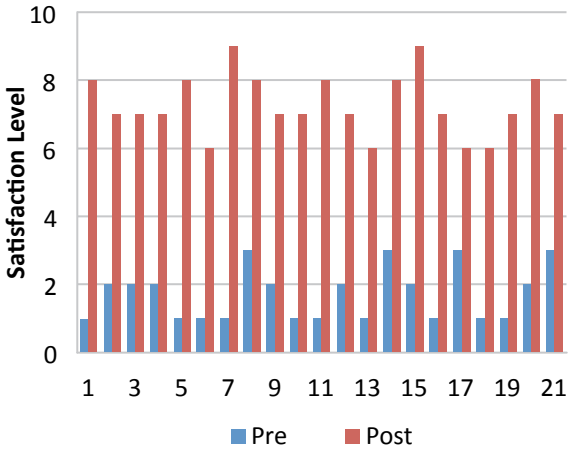


Figure 7:
Skin Quality by Individual Patient



study - all patients initially enrolled completed the study. Enrollment consisted of twenty one individuals between the ages of 20-29. Nineteen of the enrolled patients were female and two were male. Data is separated into two categories, physician assessment and patient self-assessment.

PHYSICIAN ASSESSMENT

Reduction in lesion count was significant (p<0.0001) with 100% of patients showing a significant reduction in lesion count.

Figure 8:
Improvement in Appearance of Aging

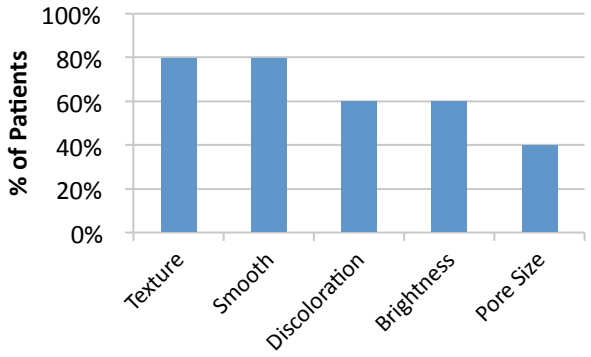
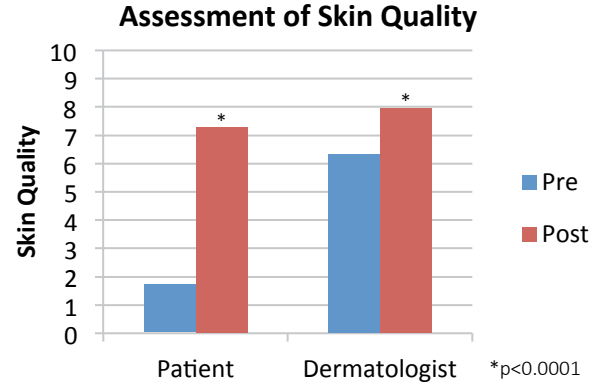


Figure 9:
Patient vs. Dermatologist Assessment of Skin Quality



The average per-patient reduction was 64% ranging from a minimum reduction of 36% to a maximum of 78%. Average lesion counts and % improved significantly by week 4 (p<0.0001) and increased in significance through week 12 (Figures 1 and 2).

Acne improvement using the 4-point global assessment scale was determined by 5 individual dermatologists (4 blinded photographic reviewers plus the principal investigator). Data showed statistically significant improvement (p<0.0001) in all reviewers with an average of 70% of patients improving by at least one full grade (Figure 3). Anti-aging measurements all showed statistically significant improvement. Both assessments using the published photo-aging scale and 10-point assessment of skin quality by all five dermatologists showed statistically significant improvement (p<0.0001). Improvement in pigment was also statistically significant (p=0.002).

Blinded physician reviewers were asked to identify the correct before and after image and then grade the skin quality in both before and after images. There was a 100% success rate selecting before and after images by all four investigators. Correlation between the reviewers and the principal investigator was also high (Figure 4).

PATIENT SELF-ASSESSMENT

100% of patients noted an improvement in acne ranging from mild to significant. Measurements grading acne pre and post study showed a statistically significant improvement

($p<0.0001$) in self-assessed acne (Figure 5). Periodic acne flare-ups were reduced in both frequency and severity.

Additionally, 100% of patients showed significant improvement in overall skin quality ($p<0.0001$) with very high consistency in degree of perceived improvement. Average satisfaction increased from 1.7 pre-treatment to 7.3 post-treatment on a 10 point scale (Figure 6). Degree of improvement was significant among all individuals with very high patient-to-patient consistency (Figure 7). Anti-aging scores using the published multi-factorial score also showed significant improvement ($p=0.028$).

DISCUSSION

The primary limiting factors to the use of both BPO and retinoids is typically skin irritation. Skin irritation will often result in decreased compliance including: discontinued usage, sporadic usage, use only when acne is present or spot treatment to acne lesions only. Any form of non-compliance can significantly decrease treatment efficacy. The lack of a single product and different AM/PM routines further complicates therapy and reduces compliance. The tested solution has the ease of use of a single product with 2X daily application leading to greater patient compliance.

This study was conducted between the months of November and March in Edmonton, Alberta with average monthly temperatures of -4°, -8.7°, -13.9°, -5.4° and -3.6° Celsius for each of the sequential months. In this climate, dry irritated skin is a significant problem and concern even without medications. Acne medications, in particular, tend to be drying and irritating to the skin, particularly in harsh climates. This issue is particularly true for BPO and retinol. One of the most notable findings from this study was the complete lack of irritation or sensitivity associated with use. In fact, many patients commented that the formulations were not overly drying, but rather moisturizing, and very tolerable compared to OTC products and topical prescription retinoids. Fourteen of the subjects in the study previously tried OTC and prescription products and services to treat acne – nine ProActiv, two Clindoxyl Gel, two chemical peels and one Stievamycin Gel. Finally, cosmetic elegance was high with patients commenting that the formulations felt smooth and elegant to apply and had a pleasant odor. These observations and results further increase the probability of compliance and lasting acne maintenance.

Patient satisfaction with this product and protocol was extremely high with 100% study retention and 18 patients (86%) indicating intent to purchase and or recommend the product to a friend or family member. All three patients that did not indicate intent to purchase observed improvement by both dermatologist and self-assessment but had the lowest percent improvement in acne and post-treatment skin quality perceptions.

Anti-aging improvement assessed by both dermatologist and self-assessment were statistically significant. When patients with mild or greater pre-study photo-damage were broken out as a subset, the improvement was significantly more notable. Of the twenty-one patients, only ten showed minor photo-damage with cumulative photo-aging scores of 4-5 out of 20 by dermatologist assessment (5 categories with a 0-4 scale each). These ten patients when viewed as a subset (Figure 8) witnessed a significant improvement in the appearance of key components commonly associated with aging.

An interesting observation was the variation in pre-treatment perception of skin quality between patients and the reviewing dermatologists (Figure 9). Pre-treatment, the average patient assessment had an average score of 1.7 out of 10 compared to an average score of 6.3 by the principal investigator and independent reviewing dermatologists. The variation between scores was far less notable post-treatment (after acne improvement) where patient self-perception of skin quality much more closely matched that of the reviewers. The excessively low perception of skin quality pre-treatment by patients compared to trained reviewers is presumably due to the presence of acne and exemplifies the significant impact of acne on QOL and self-perception.

The dual-chamber dispensing solution utilized in this study effectively combined BPO and retinol plus antioxidants, peptides and moisturizers in a single product eliminating the problem of multiple and incompatible products. Additionally the protocol studied combinatory application in both the AM and PM and found highly effective results. This indicates that the formulations in this product are stable and effective when simultaneously applied to the affected area.

CONCLUSION

The technologies tested in this skin care regime yielded statistically significant improvement in acne and anti-aging as assessed both by test subjects and multiple dermatologists. The dual chamber packaging solution effectively eliminates the challenges of simultaneously delivering and dispensing these key acne and anti-aging technologies and the specific formulations combine to yield results with little to no skin irritation. Patient satisfaction was exceptionally high with 100% of patients experiencing a significant reduction in the number of acne lesions (average = 68% reduction, ranging 36% to 78% reduction) and 100% experiencing significant improvement in skin quality with no cases of skin irritation or drying.

Age Intervention Duality MD with the Skin Care Management System effectively treats adult acne and offers statistically significant anti-aging improvement with little to no skin irritation. Acne improvement is statistically significant by week 4 and continues to improve through week 12.

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VITAMIN C SPLIT FACE STUDY

Multi-Center Evaluation of a New Concentrated Retinol, Peptide and Antioxidant Anti-Aging Solution

Leslie Baumann, MD

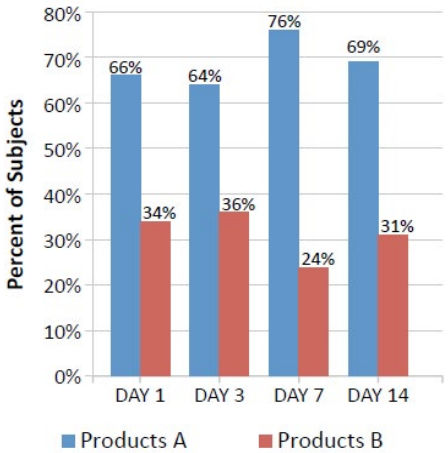
Method:

- 40 subjects ages 30-65 with lines & uneven skin tone
- 2-week blinded consumer split-face study
- Comparing C-ESTA® Face Serum and Marini Physical Protectant SPF 45 to SkinCeuticals' CE Ferulic® and Physical Fusion UV Defense SPF 50

Study Summary:

- 86% of subjects preferred the smell of C-ESTA over CE Ferulic
- 83% preferred the feel/application of C-ESTA over CE Ferulic
- 71% of subjects preferred the feel/application of Marini Physical Protectant SPF 45 over Physical Fusion UV Defense SPF 50
- Statistically superior improvement in texture with JMSR products
- 50% less irritation with JMSR products
- Subjects willing to pay more for JMSR products over SkinCeuticals

Figure 1:
Overall Product Preference



Baumann, L. MD. et al. Split-Face Vitamin C Consumer Preference Study. Journal of Drugs in Dermatology. 2014; 13(10): 1208-1213.

Figure 2:
Vitamin C Application / Feel Preference

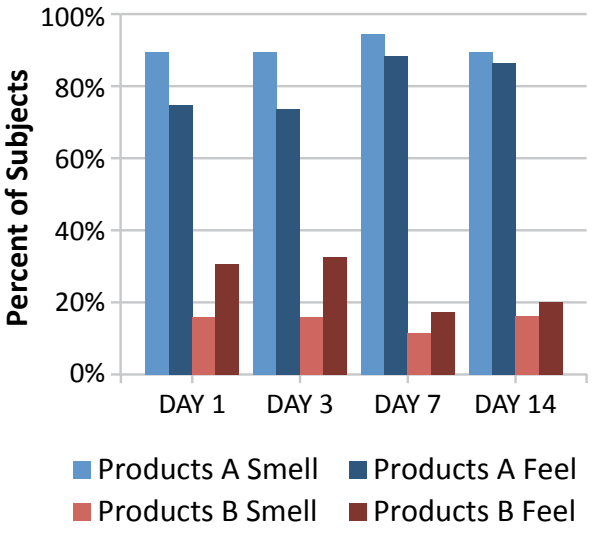
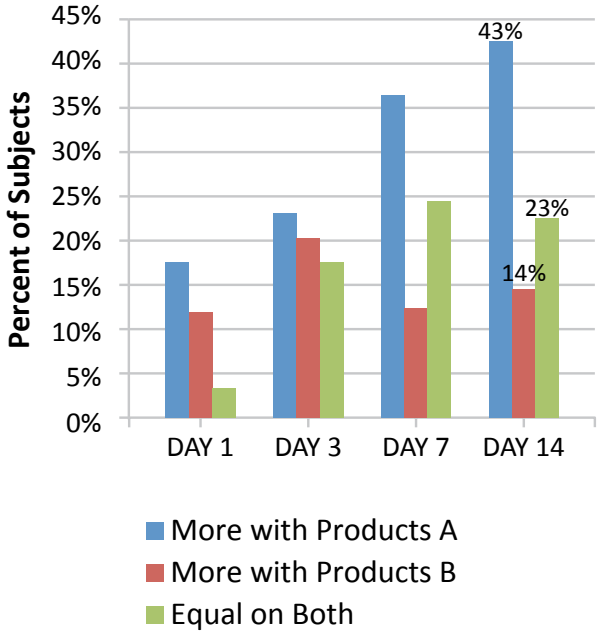


Figure 3:
Improvement in Texture



Split-Face Vitamin C Comparison Consumer Preference Study

C-ESTA® Serum and CE Ferulic®

Leslie Baumann MD [a], Deysi K. Duque MS [a], and Michael J. Schirripa PhD [b]

[a] Baumann Cosmetic & Research Institute, Miami, FL
[b] Private Consultant, Miami, FL

INTRODUCTION

Vitamin C is commonly used to treat aged skin because of its regenerative effects on skin wrinkles, texture, strength, and evenness of tone through its roles as an antioxidant, tyrosinase inhibitor, and inducer of collagen synthesis. There are many vitamin C formulations on the anti-aging skin care market that vary by their pH, packaging, and vehicle, which can affect the absorption, and therefore, the efficacy of the product. The purpose of this study was to assess the subjective efficacy, wearability, tolerance and overall preference of two professional vitamin C topical serums and sunscreens in Caucasian females using a split-face method and to assess subject preferences.

METHODS

An online "virtual" split-face study of thirty-nine Caucasian women compared two popular vitamin C and SPF product combinations – C-ESTA® Serum and Marini Physical Protectant SPF 45 from Jan Marini Skin Research (Products A) and CE Ferulic® and Physical Fusion UV Defense SPF 50 from SkinCeuticals (Products B). The products were assigned to each subject's left or right side of the face in a split-face manner. Subjects rated / compared products on each side of the face through 5 online surveys at baseline, 24 hours, 3 days, 7 days and 14 days.

RESULTS

Thirty-five of the thirty-nine subjects completed the study. Over 86% of subjects preferred the smell and 83% preferred the feel / application of vitamin C Serum "A" over Serum "B". 71% of subjects preferred the application / feel of Sunscreen "A" over Sunscreen "B". Skin texture results showed significant difference between Products A and B with more than 3 times the number of subjects noting superior skin texture improvement with Products A as compared to Products B. Products A outperformed Products B in skin tone (brightness / luminosity) and trended higher for multiple additional categories. Products A also caused notably less irritation than Products B at all intervals.

CONCLUSION

Subjects noted superior improvement in skin texture with significantly less irritation on the Product A side of the face. Subjects also preferred the product smell, feel and application of both the vitamin C and SPF with Products A vs. Products B. Subjects did not note superior improvement with Products B in any measured category. Overall, subjects preferred Products A over Products B and were willing to pay more for Products A than Products B.

INTRODUCTION

Photo-aging is characterized by sagging and thinning of the skin, discoloration, fine lines, and skin fragility. It is mainly induced by sun exposure, including UVA and UVB rays. Clinical signs of photo-aging are caused by loss of elastin, hyaluronic acid (HA), and collagen. Loss of elastin tissues leads to skin sagging resulting in nasolabial fold (NL) wrinkles, sagging of the jaw line, and crow's feet wrinkles. Loss of collagen in skin leads to fine lines, thinness, fragility and textural change. Loss of hyaluronic acid in skin results in decreased skin plumpness and fine lines.

Protection against UV exposure helps prevent or minimize many of the visible signs of aging. The American Academy of Dermatology recommends daily use of a broad spectrum sunscreen with a minimum SPF of 30. While many consumers recognize the need for sunscreen, many are challenged by the smell or feel of sunscreens, resulting in non-compliance and loss of sun protection. Hence, a broad-spectrum sunscreen with high user appeal is critical to any anti-aging solution. Collagen levels can be increased by using topical alpha hydroxy acids, retinoids and vitamin C.1 Vitamin C has the added benefit of improving skin tone and color and providing

antioxidant benefits in addition to its ability to increase collagen production. As humans are unable to synthesize vitamin C, thus the intake of dietary supplements or application of topical formulations of vitamin C is necessary to delay the process of aging or diseases related to vitamin C deficiency. Vitamin C is commonly used to treat aged skin because of its regenerative effects on skin texture, color, and inflammation through its roles as an antioxidant, tyrosinase inhibitor, and inducer of collagen synthesis.

HA is composed of repeated units of sugars (saccharides). The size of the HA molecule determines the ability of topically applied HA to penetrate into skin.2 HA that is applied to the surface of the skin is a humectant; therefore it draws water into itself which can increase skin hydration in a humid environment.

Vitamin C is one of the most recognized antioxidants in consumer surveys and has had a surge in popularity over the last 10 years with many topical products entering the market making it difficult for the products to differentiate themselves to consumers. This study compares consumer preference between two commercially available topical vitamin C and sunscreen products.

Study Products

In this study, a combination of sunscreen and vitamin C from two different companies were compared in a split-face study to compare efficacy and consumer preference. Products A, by Jan Marini Skin Research, San Jose, CA, consisted of "C-ESTA Serum" ($93 retail) and "Marini Physical Protectant SPF 45" ($49 retail) – combined retail value of $142. Products B, by SkinCeuticals Inc., Garland, TX consisted of "CE Ferulic" ($159 retail) and "Physical Fusion UV Defense SPF 50" ($34) – combined retail value of $193.

"C-ESTA Serum" is an anti-aging and antioxidant product containing vitamin C (ascorbyl palmitate), dimethylaminoethanol (DMAE), hyaluronic acid (sodium hyaluronate), vitamins B5 (pantethine) and E (tocopheryl acetate), tyrosine and zinc. "CE Ferulic" is an anti-aging and antioxidant product containing vitamin C (L-ascorbic acid), vitamin E and ferulic acid (see Table 1 on p. 4).

"Marini Physical Protectant SPF 45" is an 80-minute water resistant broad spectrum SPF containing zinc oxide, titanium dioxide, green tea extract, alpha-bisabolol and CoEnzyme Q10 and microscopic oil-absorbing particles. "Physical Fusion UV Defense SPF 50" is a 40-minute water resistant broad spectrum sunscreen containing zinc oxide, titanium dioxide and artemia selina (see Table 1 on p. 4).

Antioxidants

Antioxidants have the capacity to neutralize free radicals by giving oxygen the missing electron it needs, reducing oxidative stress and their ability to cause damage. By neutralizing free radicals, antioxidants mitigate damage to the skin and lessen the effects of aging. Vitamin C and vitamin E are two antioxidants shown to significantly reduce the damage produced by free radicals. Free radicals are compounds formed when oxygen molecules combine with other molecules yielding an odd number of electrons. An oxygen molecule with paired electrons is stable; however, oxygen with an unpaired electron is "reactive" because it seeks and seizes electrons from vital components leaving them damaged.3 DNA, cytoskeletal elements, cellular proteins, and cellular membranes may all be adversely affected by reactive oxygen species (ROS).4,5

Many factors need to be considered when selecting an optimal vitamin C. Nearly all forms of vitamin C, and L-ascorbic acid in particular, are sensitive to degradation from exposure to air and light.6 Products exposed to air and light will lose efficacy over the life of the product. Ascorbyl Palmitate is a more stable form of vitamin C and the test product is packaged in an airless container to eliminate degradation over time.

Different forms of vitamin C also have different formulation requirements for efficacy. To penetrate the skin, L-ascorbic acid (a polar water-soluble molecule) must be applied in a high concentration with a low pH of 2.0 to 2.5. This low pH can cause skin stinging, redness and persistent irritation in some skin types. Ascorbyl Palmitate is a lipid soluble form of vitamin C, effective over a broader pH range, allowing for significantly greater penetration with less irritation.

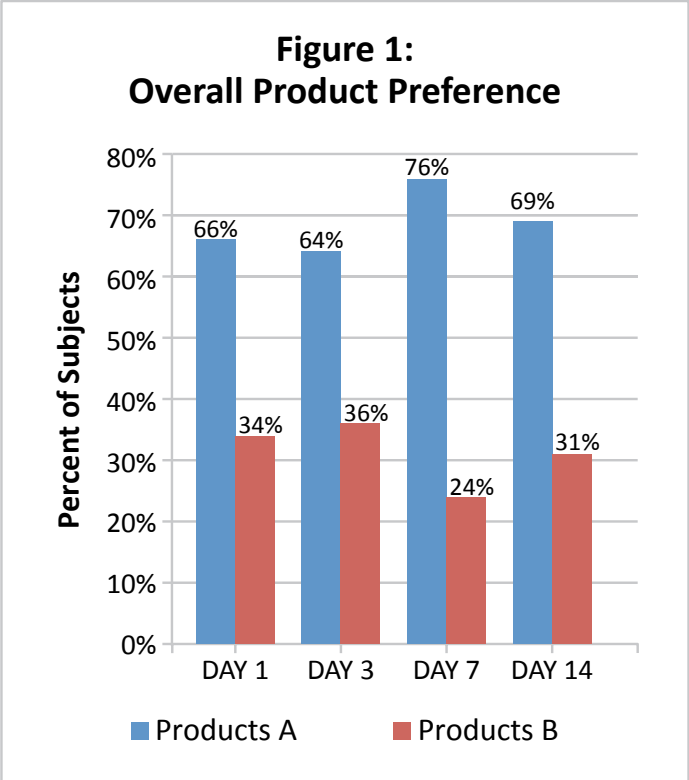
Ascorbyl Palmitate is shown to be effective as an intact molecule7 in-vivo and in-vitro, and hydrolysis of Ascorbyl Palmitate yields ascorbic acid in the skin with greater penetration due to its lipid soluble nature. Its increased absorption and ability to reside in the lipid portion of the cell membrane may give it a protective advantage over water soluble forms of ascorbic acid. In an oxidative stress induced tumor study, Ascorbyl Palmitate was found to be more than 30 times more effective than L-ascorbic acid and effective at significantly lower concentrations. This is hypothesized to be due mainly to the poor dermal penetration of the polar, water-soluble L-ascorbic acid.8

Ascorbyl Palmitate is further shown to have a photo-protective and anti-inflammatory benefit in-vivo. When applied post UV exposure, skin pre-treated with Ascorbyl Palmitate showed lower rates of erythema and required a higher minimum UV dosage to induce erythema. Further, in post-UV induced erythema, redness resolved 50% faster on areas treated with Ascorbyl Palmitate vs. untreated skin. Benefits were also observed in Asteatic Dermatitis, Psoriasis and dry skin.9

Green tea extract is a powerful antioxidant that significantly decreases the appearance of lines and wrinkles and is shown to reduce the damage from oxidative stress, thus decreasing cellular damage. This provides great benefits to photo-damaged and aging skin.10

DMAE, a precursor to acetylcholine which plays a role in proliferation, differentiation, locomotion, and secretion. A study by Grossman observed that topically

applied DMAE facial gel resulted in improvement of multiple signs of skin aging including improvement in skin tensile strength, lip fullness and overall appearance of facial skin with improvement in the reduction of forehead lines and periorbital fine wrinkles.11 These improvements remained after 2 weeks of cessation of the product. The mechanisms of action in the skin of acetylcholine and DMAE remain to be elucidated but evidence suggests that the skin is an active site of acetylcholine synthesis, storage, secretion, metabolism, and receptivity. Muscarinic acetylcholine receptors have been localized to keratinocytes, melanocytes and dermal fibroblasts, whereas nicotinic acetylcholine receptors have been found in keratinocytes.[12]



METHODS

Survey Subject Population

Subject screening was conducted via an online virtual trial. A total survey group of 40 subjects was completed to allow for dropouts while maintaining a minimum of 25 subjects at study completion. All subjects recruited for this study were Caucasian females between the ages of 30 and 65, and Fitzpatrick skin types II through IV. All subjects received 5 surveys at the following time points: baseline, 24 hours, 3 days, 7 days and 14 days.

The target population was defined as those who met the following criteria: 1) able to read, understand, and sign the approved informed consent; 2) able to limit their sun exposure and willing to daily wear sunscreen for the duration of the study; 3) able to avoid becoming pregnant, breast feeding, and willing to use a reliable method of birth control throughout the course of the study; 4) subjects who feel their skin was dull with a loss of radiance or have fine lines on the face; and 5) subjects who have uneven skin tone.

Survey Materials

Subjects received the study materials with home instructions to use throughout the two-week study period. Email notifications and reminders were provided to give instructions on how to fill out the 5 online surveys to determine the consumer preference for each of the products.

C-ESTA Serum and SkinCeuticals CE Ferulic were labeled as either Products A or B, and were used in combination with study-provided sunscreens. Subjects and investigators did not know the identity of Products A or B.

All subjects were instructed to apply Products A to one side of their face and Products B to the other side of their face. Products A and B were assigned to the left or right side of the face respectively. Subjects were also allowed to use daily facial cleanser and moisturizer and to continue wearing their makeup throughout the duration of the study.

Data Collection

Data was collected at baseline and days 1, 3, 7 and 14. Study surveys were provided to all enrolled subjects, ensure confidentiality of their individual responses and personal information. Surveys 2 to 5 for each respective time point allowed subjects to rate each product based on smell, feel and application as well as perceived impact on skin texture, pore size, skin tone, laxity, eye wrinkles and irritation / sensitivity with a final assessment of overall product preference.

Statistical Analysis

This report made use of statistics and graphics to draw inferences and conclusions. Choices were numerically coded to properly prepare for statistical testing with lower values representing negative skin perception and higher values representing positive skin perception. To assist in the visualization of results, some graphics used percentage even though statistical tests used numerical scores. A repeat measure Analysis of Variance (ANOVA) was used to test for significant difference at the $p = 0.05$ level. A paired two-tail t-test was used to compare preferences between products at each time interval.

RESULTS

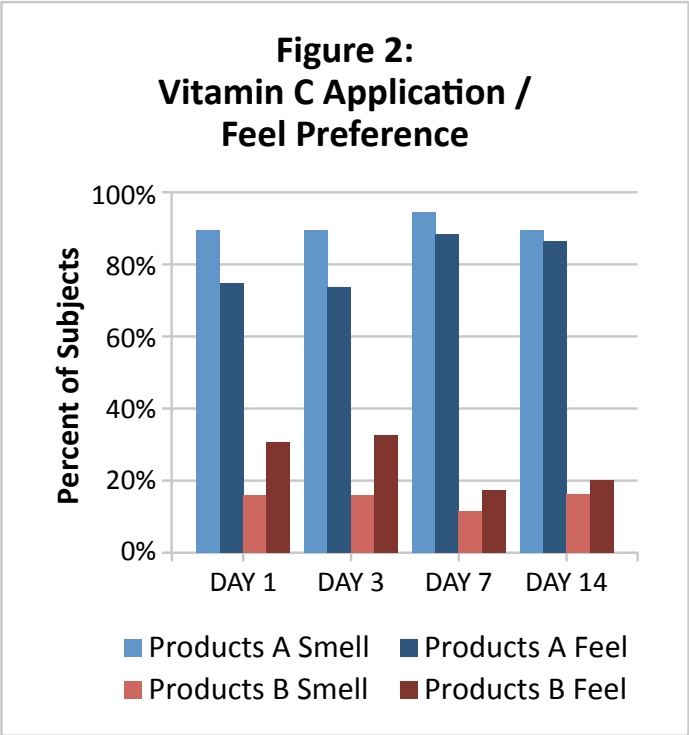
Thirty-five subjects completed the full study. Overall, subjects significantly preferred Products A over Products B at all measured time intervals with a significant number preferring Products A at days 7 and 14 ($p<0.05$) (see Figure 1 on page 3). Nearly two thirds of subjects (22 vs 13) were willing to pay more for Products A vs. Products B and two times the number of subjects indicated a preference of over $20 more for Products A than vs. Products B (8 vs. 4).

Subjects significantly ($p<0.001$) preferred the application/feel and smell of Product A's vitamin C serum (C-ESTA Serum) vs. the Product B serum (SkinCeuticals CE Ferulic) at all measured time intervals (see Figure 2).

Subjects also significantly preferred the Product A physical sunscreen over the Product B sunscreen. With topical

(Table 1: Key Ingredient Function and Comparison)

	Product Name	Key Ingredients	Ingredient Benefits
Products A	C-ESTA Serum	Ascorbyl Palmitate (Vitamin C)	Lipid soluble, neutralizes free radicals, promotes collagen synthesis, greater product penetration
		Dimethylaminoethanol (DMAE)	Skin rejuvenation, tightens skin, reduces laxity and fine lines & wrinkles
		Sodium Hyaluronate (Hyaluronic Acid)	Skin hydration
		Tocopheryl Acetate (Vitamin E)	Neutralizes free radicals, inhibits UV-induced melanogenesis; has anti-inflammatory properties
		Zinc Sulphate	Skin Conditioner
		Tyrosine	Skin Conditioner
		Pantethine (Vitamin B5)	Skin Conditioner
	Marini Physical Protectant SPF 45	Zinc Oxide 8%	Broad spectrum sun protection
		Titanium Dioxide 6%	Broad spectrum sun protection
		Ubiquinone (CoEnzyme Q10)	Neutralizes free radicals, reduces UV induced damage, helps build new collagen and elastin. May be more effective than Vitamin E at preventing oxidative damage to tissue.
		Alpha-Bisabolol	Anti-inflammatory, anti-irritant
		Camellia Oleifera (Green Tea Extract)	Neutralizes free radicals, skin conditioner, reduces lines & wrinkles
		Microscopic Sponges	Absorbs oil on skin
Products B	SkinCeuticals CE Ferulic	L-Ascorbic Acid (Vitamin C)	Neutralizes free radicals, promotes collagen synthesis
		Alpha Tocopherol (Vitamin E)	Neutralizes free radicals, inhibits UV-induced melanogenesis; has anti-inflammatory properties
		Ferulic Acid	Antioxidant, neutralizes free radicals
	Physical Fusion UV Defense SPF 50	Zinc Oxide 5%	Broad spectrum sun protection
		Titanium Dioxide 6%	Broad spectrum sun protection
		Artemia Selina	Decreases UV induced damage Anti-inflammatory, anti-irritant



products, most consumers expect to see a difference in the skin in 4 weeks' time. In this study subjects saw a difference in skin texture as early as day 3. When assessing skin texture, Products A outperformed Products B at all data points with statistical significance at days 7 and 14 ($p<0.05$). 3X the number of subjects noted superior improvement in texture on the Products A side vs. the Products B side (43% vs. 14%) with 2/3 of subjects indicated superior or equal improvement on the Products A side. Only 14% of subjects indicated superior improvement in texture with Products B (see Figure 3 on p. 6).

Irritation between the two products was notably different at all measured time intervals with Products B exhibiting nearly two times the amount of irritation of Products A. However, due to the lower number of subjects experiencing irritation, the difference was not significant ($p=0.08$ at day 3) (see Figure 4 on p. 7).

While not statistically significant, Products A trended toward superior performance at all measured time intervals for skin tone (brightness/ luminosity) (31% vs. 23% at day 14) and laxity (23% vs. 11% at day 14). Longer follow-up or a larger population size may show differences in these categories.

No meaningful difference or trend was observed regarding nasolabial folds and wrinkles under the eyes and pore size.

DISCUSSION

Overall, subjects preferred Products A over Products B. This was due to both superior results and superior aesthetic experience.

Application, feel and smell of a product play a large role in consumer preference, the ability to wear daily for best results and willingness to repurchase the product. In this study subjects preferred the smell and feel of Products A at all measured intervals with 86% and 83% respectively preferring Products A at Day 14. While a strong preference like this can lead to biases or a placebo effect on other questions, the notable percent of subjects indicating no improvement with either product for lifting, laxity and nasolabial folds suggests that the preference of the feel and smell of Products A did not bias the results of the survey.

Skin texture and associated fine lines are one of the most common visible signs of aging skin and showed the greatest difference between Products A and B in the study. Products A statistically outperformed Products B at day 7 and day 14 with increasing differentiation over time and the greatest difference observed at day 14. This question is the most targeted question in respect to the expected results with an anti-aging skin care regimen. Changes over time were expected in both products due to the increased production of collagen by the fibroblasts (skin cells). Due to the low pH, exfoliation and secondary irritation and micro swelling of Product B we (principal investigator) incorrectly expected superior results with Products B. Products A, however, exhibited superior performance at all time-intervals despite its non-acidic pH and significantly lower irritation rate. The superior improvement observed with Product A is likely due to a combination of increased collagen production, hydration from the HA, firming of skin from DMAE and skin conditioning from green tea extract, zinc, tyrosine and vitamin B6.

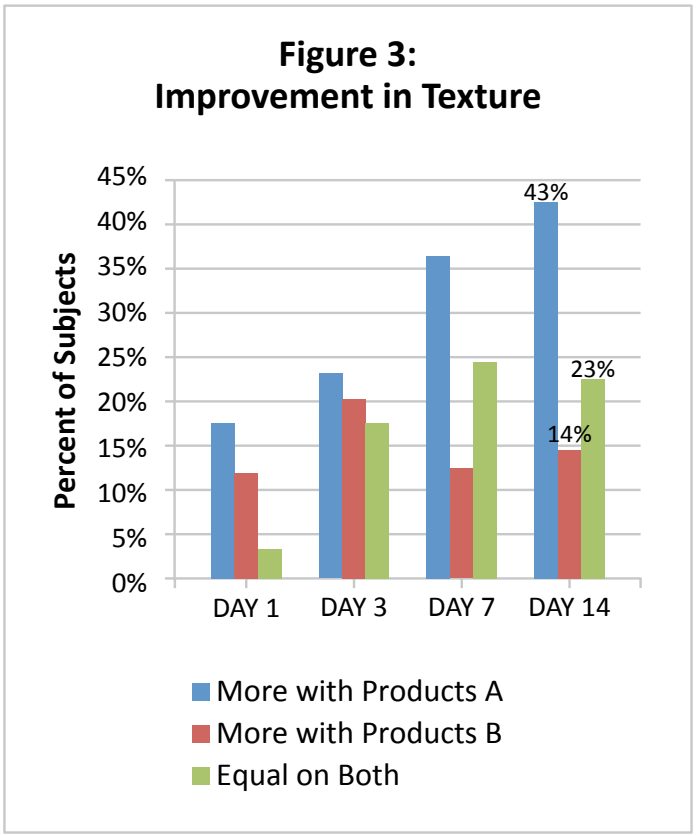
Wrinkles under the eyes can be improved by increased collagen production, increased skin hydration and slight skin swelling from irritation. Fine lines seen in photo-aging studies may improve based upon moisturizing and plumping ingredients in the formulation alone, however, improvement is often due to the additive effects of increased skin hydration and increased collagen production. As these lines are often deep and difficult to improve in a short study such as this, we did not expect significant improvement. Nearly 70% of subjects, however, noted improvement with either or both products, indicating the quality of both products.

Skin tone improvement is expected with vitamin C as it inhibits tyrosinase, which is needed to make melanin (skin pigment). If the ascorbic acid was efficacious, we would expect to see improvement in skin tone (color) over time but pigmentation studies usually note improvement at 8-12 week time points. Surprisingly, when asked on Day 14 about skin tone, brightness and luminosity, subjects noted improvement. Products A performed slightly better than Products B (11 vs. 8 subjects) with and 9 subjects indicating both sides improved equally. Only 7 subjects said that neither side improved illustrating that changes in the appearance of skin pigmentation can occur earlier than can be explained by tyrosinase inhibition alone and may be partly due to effects of vitamin C, HA, green tea, vitamin E and or other key ingredients on hydration and reflectivity.

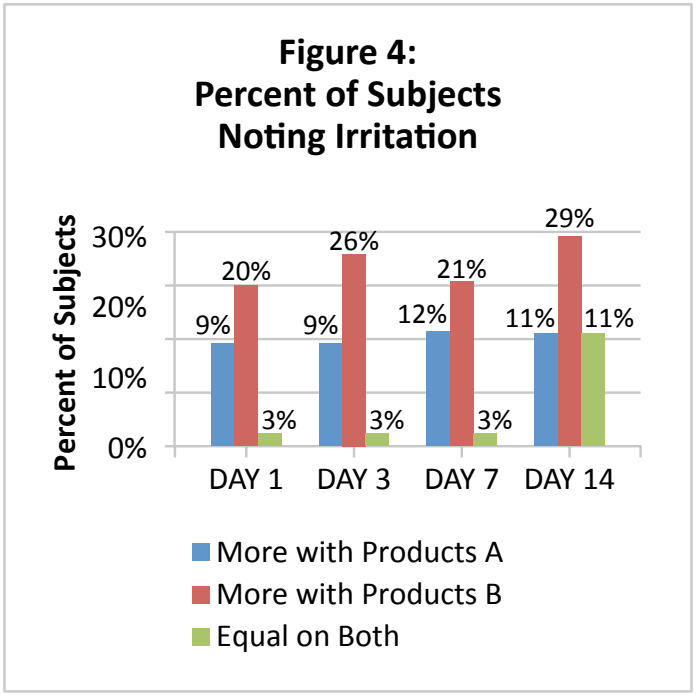
Pore size reduction may be observed due to tightening of skin, increased collagen production, astringent characteristics of ingredients or from swelling of the skin from irritation. On day 7 Products A had a greater effect on pore size than Products B but by day 15 there was no significant difference between Products A and B on pore size. As there was less irritation seen from Products A than Products B, irritation and swelling would not account for the improved appearance of the pores. A larger number of subjects would be needed to assess if there were a difference in the effects on pore appearance between the two groups.

Laxity, nasolabial folds and lifting along the jawline may be improved by increased collagen production as well as skin tightening. The magnitude of change necessary to visually observe these changes, however, is not likely to occur in a short-term 14-day study. While there was a slight but consistent observed bias toward Products A across all of these observations, most subjects noted no improvement from either product. The observed bias may be due to superior collagen stimulation or a combination of stimulation with lifting effects and hydration due to DMAE and HA but a longer term study with a larger number of subjects would be required to demonstrate statistical significance.

The significant percent of subjects noting no improvement by either product (approximately 50% for each) or equal improvement with both products (15-20%) indicates integrity of the data on other measurements, as this shows a lack of bias and willingness to grade "no-response" for both products.



Irritation is commonly experienced with vitamin C products due to typically low-pH formulation. Notably fewer subjects reported irritation with Products A vs. Products B at all time-intervals during the study. Nearly two times the number of subjects indicated irritation on the Product B side at all measured intervals with very few subjects indicating equal irritation on both sides (Figure 4). While not statistically significant (p=0.08 on Day 3, p=0.1 on Day 14) the trend was notable. The lack of statistical significance is likely due to the small total number of people experiencing irritation.



The lack of irritation and improvement seen with Products A suggests rapid improvement mechanisms other than short term irritation and inflammation.

Price plays an important role in product selection and value and consumers are much more likely to repeat purchases where they perceive superior value.

In this study, 22 of 35 of subjects were willing to pay more for Products A than for Products B with nearly twice the number of subjects willing to pay over $20 more for Products A than Products B. The strong preference to pay more for Products A is amplified in the market where Products A cost significantly less than Products B ($142 vs. $193 respectively). This indicates a value gap of more than $50 between the two products.

CONCLUSION

Overall, Products A were significantly preferred over Products B. Statistical analyses showed that subjects observed significantly superior improvement in texture with Products A over Products B. Further, subjects significantly preferred application, feel and smell of both the vitamin C serum and the sunscreen of Product A over Product B. Finally, Products A caused less sensitivity and irritation. This combination lead to a clear user preference and willingness to pay more for Products A over Products B.

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REDNESS

Combined laser-topical therapy improves erythema associated with rosacea

Brian Beisman, MD, Nashville, TN

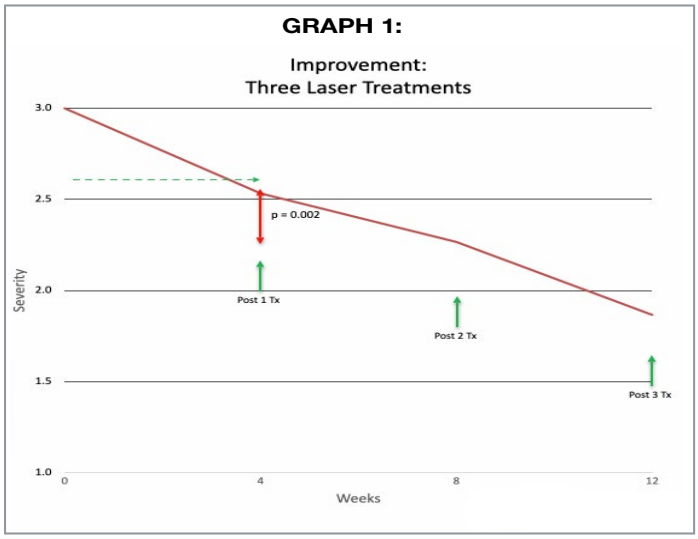
Method:

- 12 week study
- 30 subjects randomized into 2 equal groups (Group 1 - 2 Laser Treatments + Topical and Group 2 - 3 Laser Treatments)

Study Summary:

- Adding topical solutions enhanced results vs. laser alone
- Results were superior at 4, 8 and 12 weeks
- The addition of topical solutions enhanced results by as much, if not more than, one additional laser treatment
- The Skin Care Management System and RosaLieve Redness Reducing Complex should be added to laser treatment protocols for superior end results

GRAPH 1:



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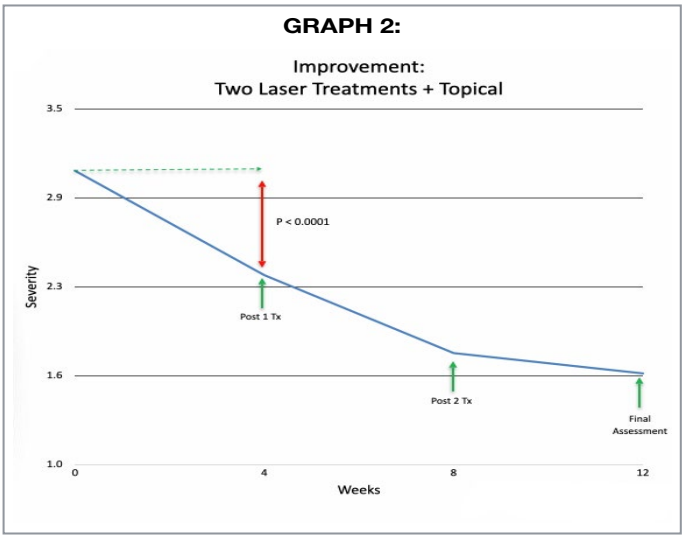

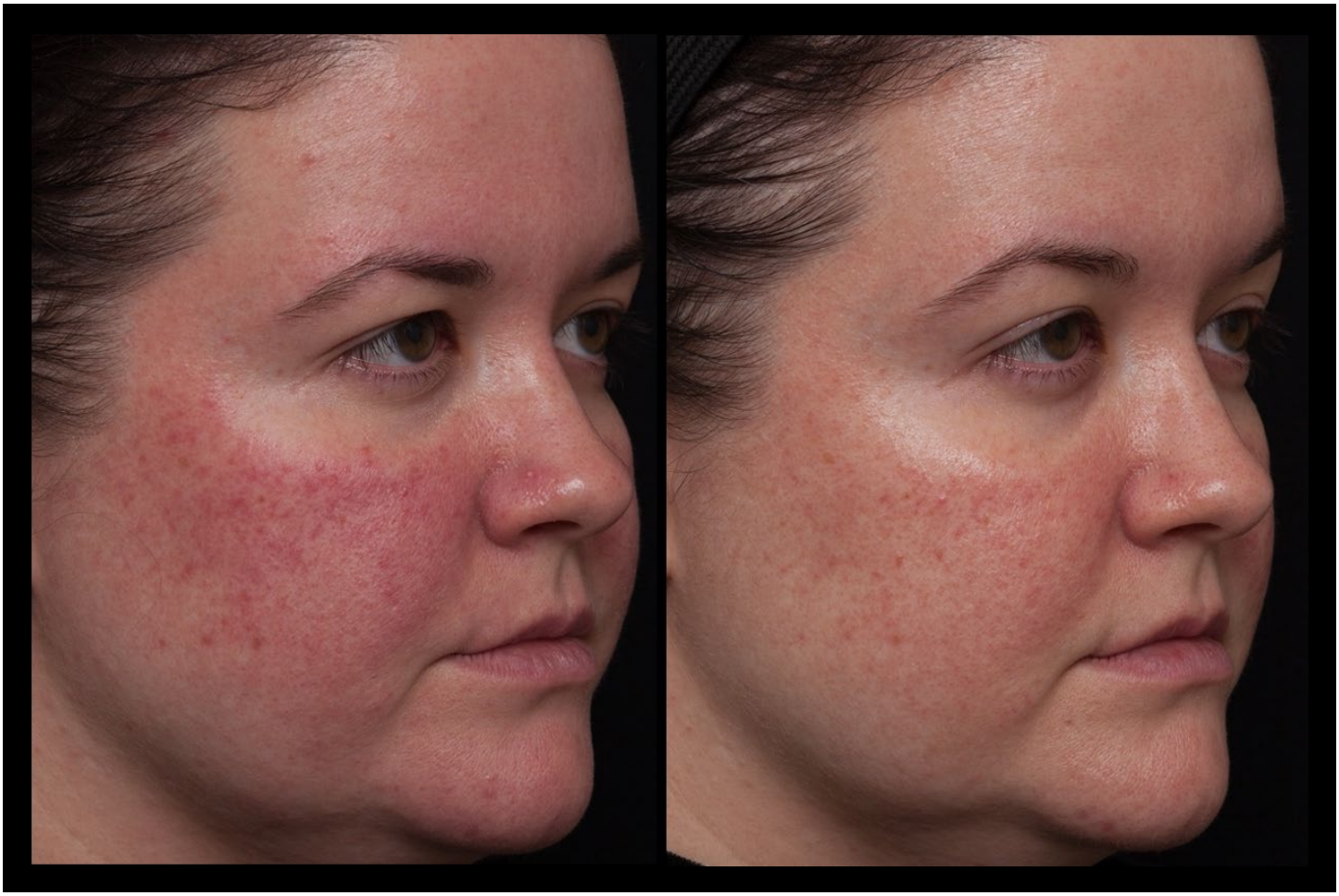


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Combined laser-topical therapy improves erythema associated with rosacea

RosaLieve®

Brian Biesman, MD, Nashville, TN

INTRODUCTION

DENVER – Among patients with facial erythema associated with erythrotelangiectatic rosacea, combining a long-pulsed 532 nm laser with daily application of a topical skin care regimen achieved equivalent to superior results in fewer treatments, compared with long-pulsed laser treatment alone.

The findings come from a pilot trial that Brian S. Biesman, MD, presented at the annual conference of the American Society for Laser Medicine and Surgery. "Vascular laser therapy is the standard of care for reduction of facial erythema associated with erythrotelangiectatic rosacea," said Dr. Biesman, an oculofacial plastic surgeon who practices in Nashville, Tenn. "The question was, if we combine topicals plus laser, can we get an enhanced outcome relative to laser treatment alone?"

STUDY DESIGN

To find out, he and his colleagues conducted a blinded, controlled prospective study of 30 subjects with mild to moderate erythrotelangiectatic rosacea who were evenly split into two groups. Those in group 1 received three treatments with the Excel V 532 nm long-pulsed laser by Cutera. Those in group 2 received two laser treatments with the Excel V long-pulsed 532 nm long-pulsed laser plus concurrent daily use of the topical Jan Marini Skin Care Management System, which included a glycolic acid cleanser, vitamin C serum, active containing glycolic, salicylic and azelaic acids, peptide, and growth factor moisturizer and a broad-spectrum sunscreen. It also contained RosaLieve, a proprietary redness-reducing complex.

RESULTS

(See Chart 1 & 2, Graphs 1, 2 & 3)

The researchers performed laser treatments at 4-week intervals and evaluated subjects at baseline, 4, 8, and 12 weeks by physician and subject self-assessment using 5-point (0-4) standardized scales: the Clinician Erythema Assessment (CEA) and patient self-assessment as well as a dermatology Quality of Life Assessment. In both treatment groups, reduction in facial erythema as assessed by CEA and patient self-assessment showed statistically significant improvement at all measured intervals. Specifically, average CEA scores improved from 3.00 to 1.87 among patients in group 1, and from 3.07 to 1.64 among those in group 2.

DISCUSSION

"These were both statistically significant from baseline," Dr. Biesman said. "What does it really say? The laser plus topical was superior to the laser-only treatment at all measured intervals. I didn't expect to see that. There was continued improvement noted from week 8 to week 12. That was more of a trend; it was not statistically significant. There were no complications or adverse reactions in either group. The

CHART 1:
Both groups observed statistically significant improvement at all time intervals

Statistically Significant Reduction in both Groups			
	4	8	12
Laser + Product (p=)	1.15E-05	1.34E-06	5.64E-08
Laser Only (p=)	1.77E-03	1.45E-04	3.91E-06

Paper presentation at the American Society for Lasers in Medicine and Surgery 2019
This study was published in Dermatology News
https://www.mdedge.com/dermatology/article/198848/rosacea/combined-laser-topical-therapy-improves-erythema-associated#

CHART 2::
Laser + Topical delivered superior results at all time intervals with statistically superior improvement by 8 weeks

Average Improvement & Differential Significance						
	Physician Assessed Erythema			Subject Assessed Erythema		
	4	8	12	4	8	12
Laser + Product	-0.73	-1.29	-1.43	-0.73	-1.29	-1.43
Laser Only	-0.47	-0.73	-1.13	-0.53	-0.73	-1.13
Significance (p=)	0.07	0.01	0.09	0.17	0.01	0.13

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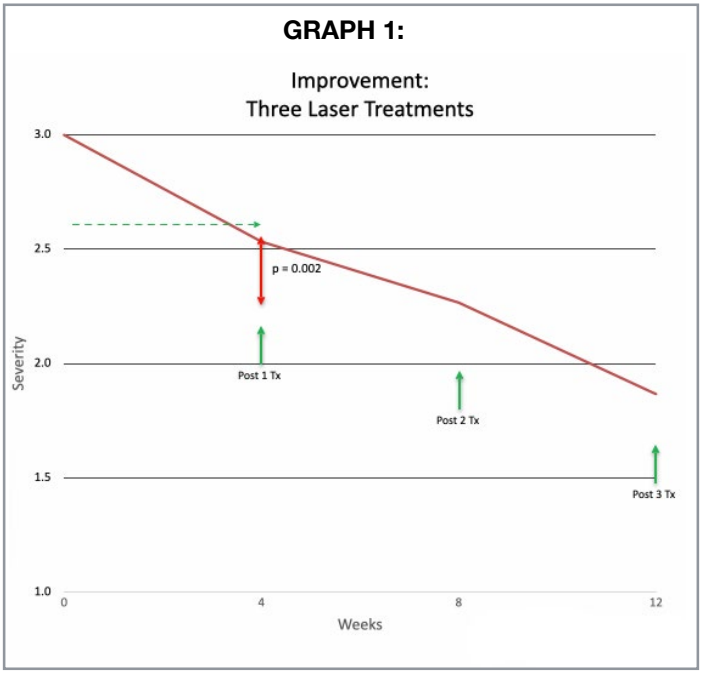

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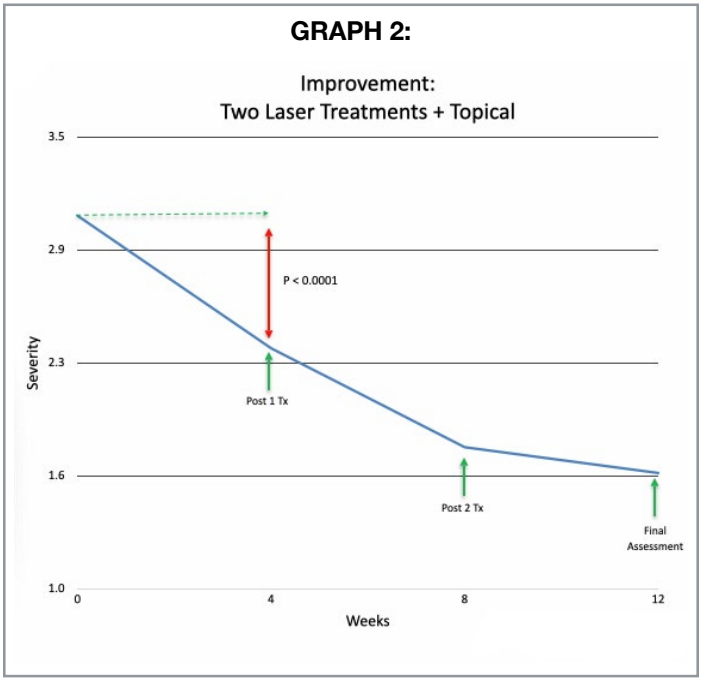

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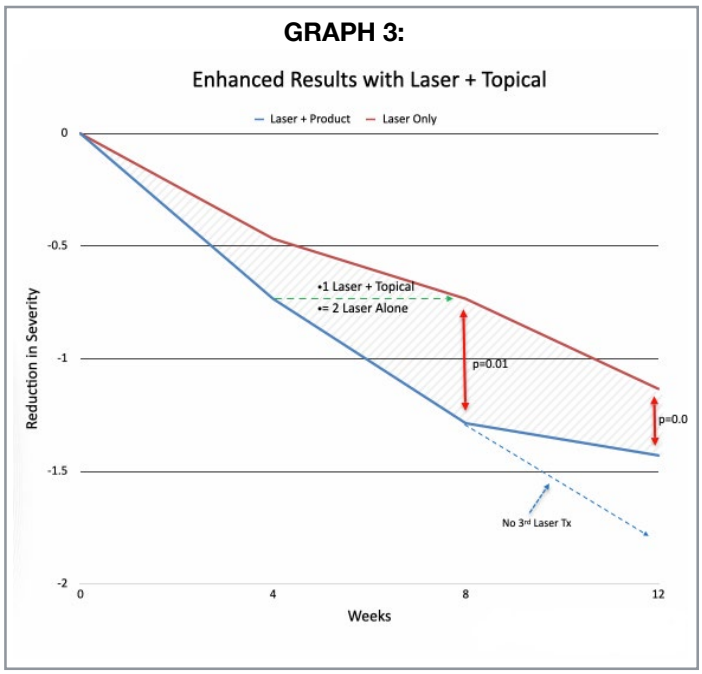


study data indicate that best results may be achieved with a combination of laser and home care."

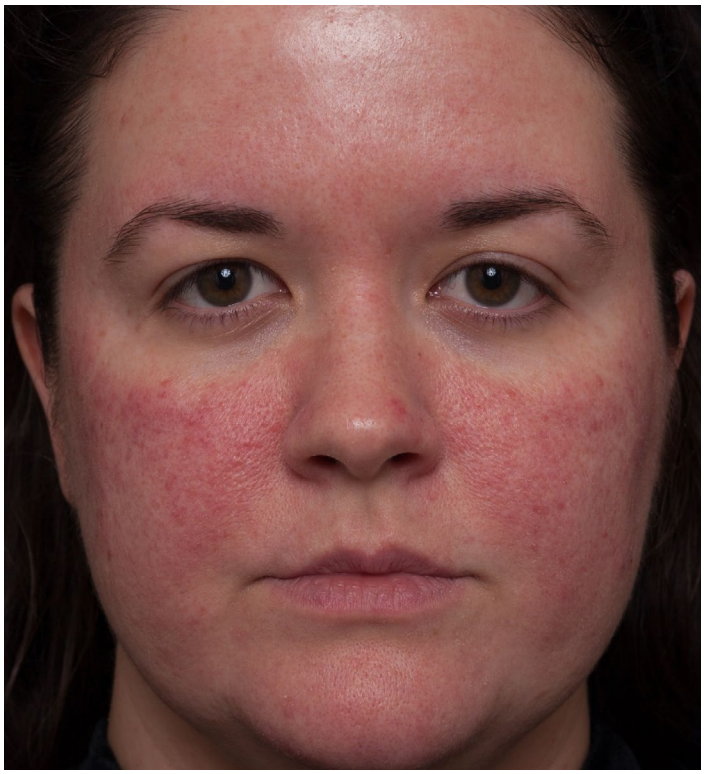
He acknowledged certain limitations of the study, including its small sample size and relatively short course of follow-up. "We didn't have standardization of topical therapy in the laser-only group," Dr. Biesman said. "Those patients were told to use their usual topical regimen. They were not allowed to use retinoids. We also didn't have a control arm."

He disclosed that he has received grant funding from Jan Marini Skin Research and Cutera.

SUMMARY

Both groups delivered safe and effective results. The addition of topical solutions enhanced results by as much, if not more than, one additional laser treatment. Based on this study data: The Skin Care Management System and RosaLieve Redness Reducing Complex should be added to laser treatment protocols for superior end results

PHOTOGRAPHIC EVALUATIONS



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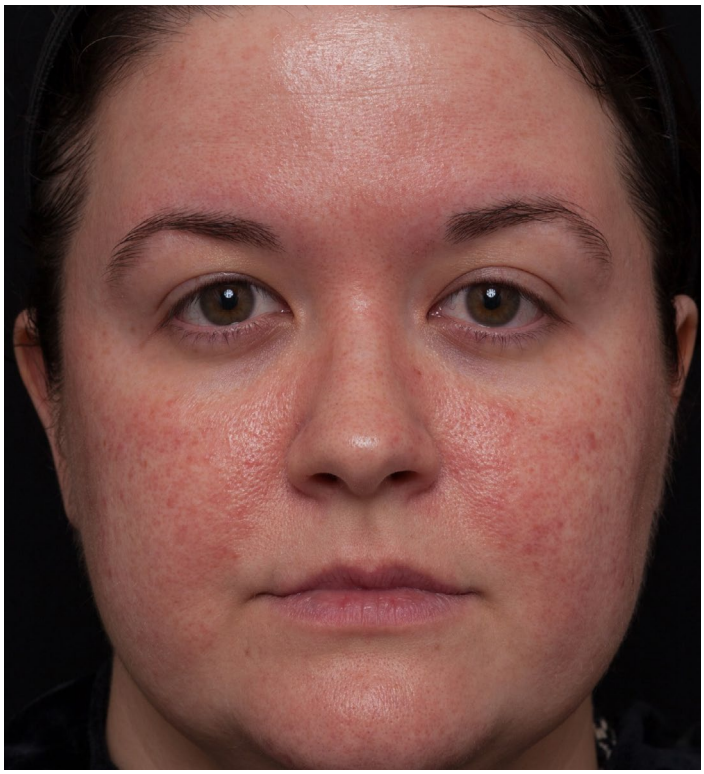

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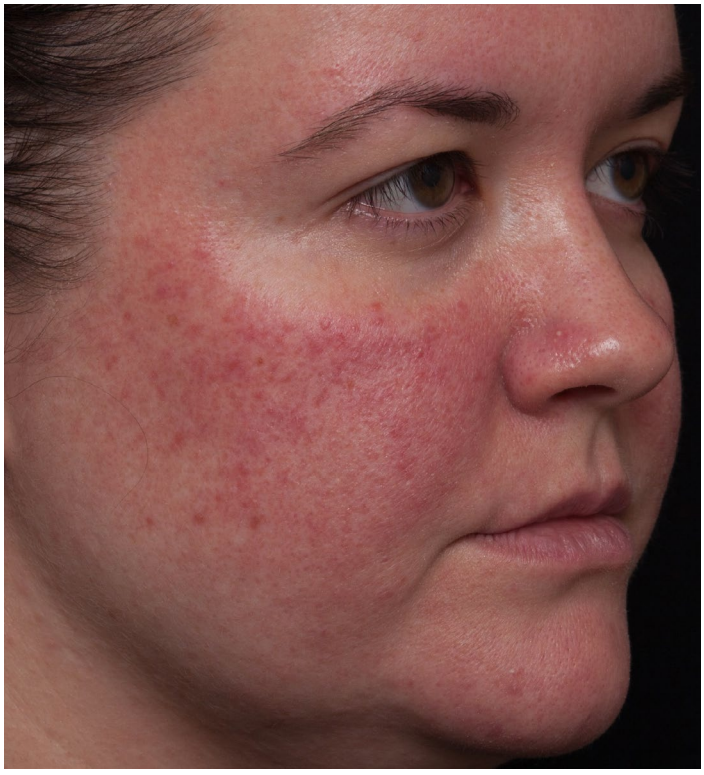

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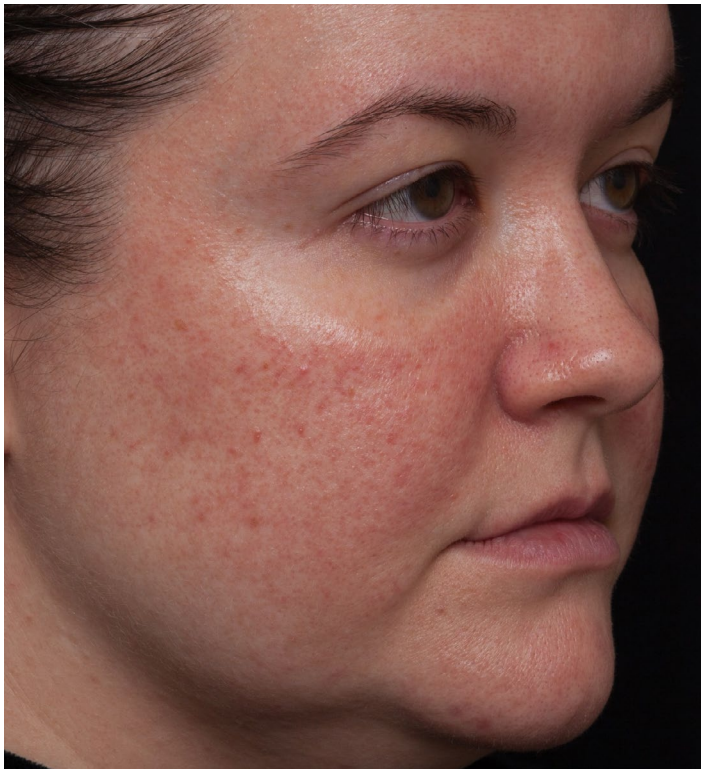

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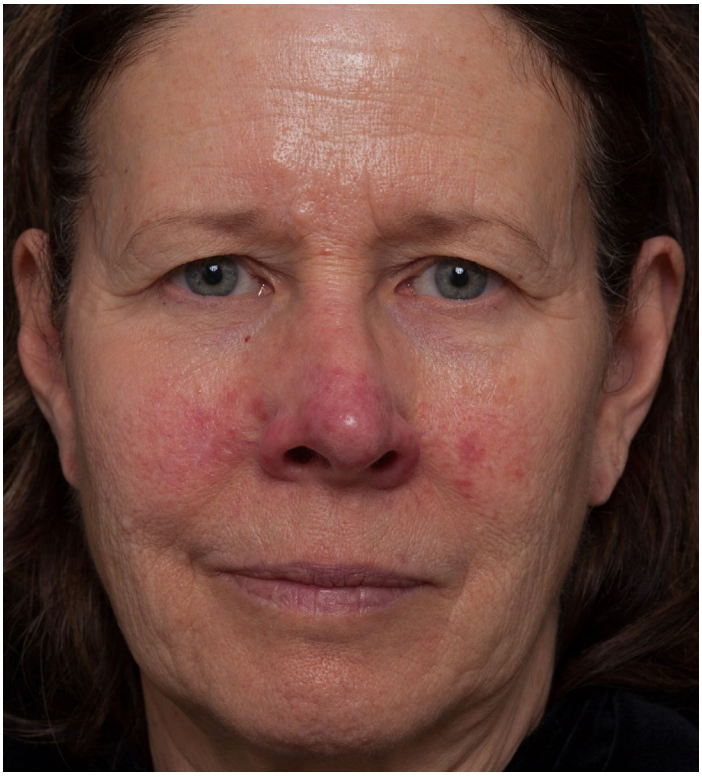

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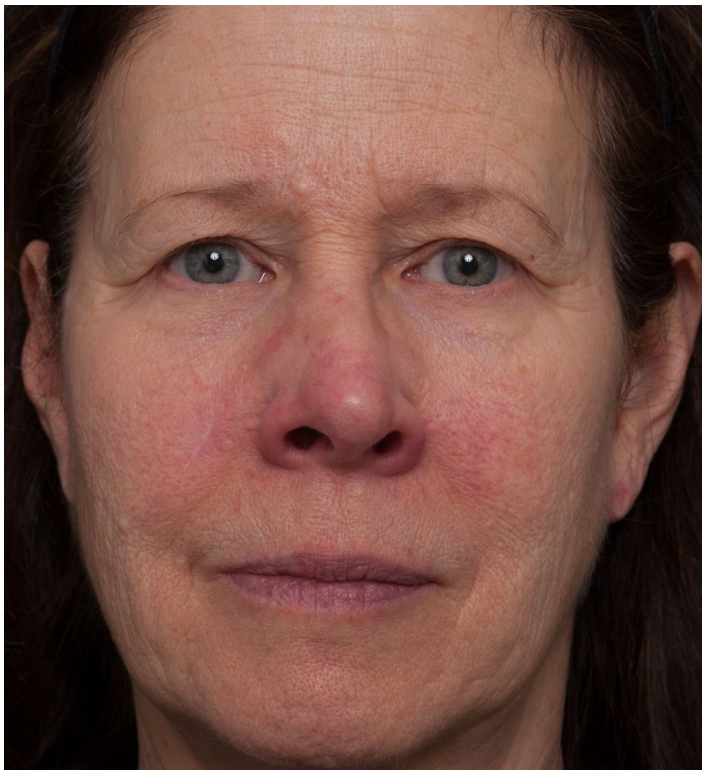

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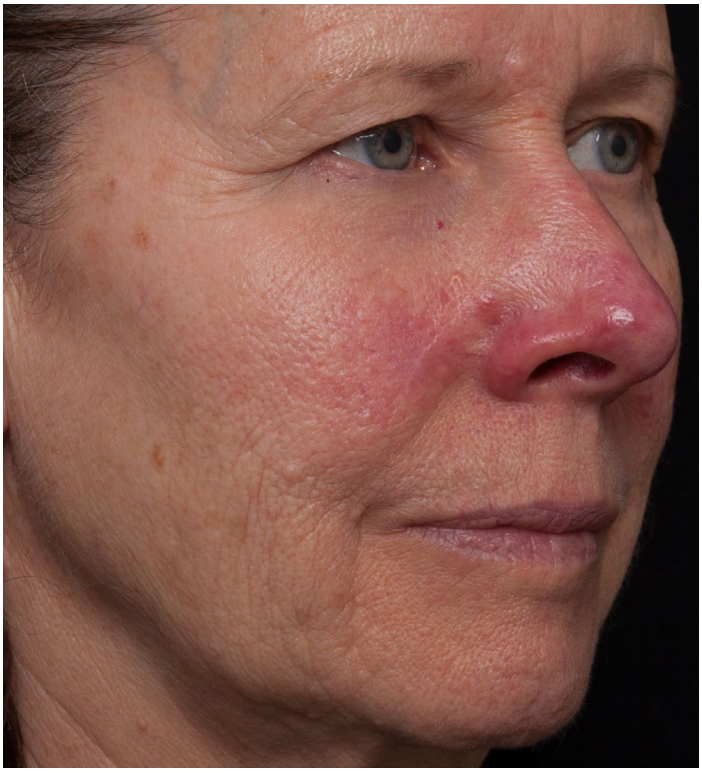

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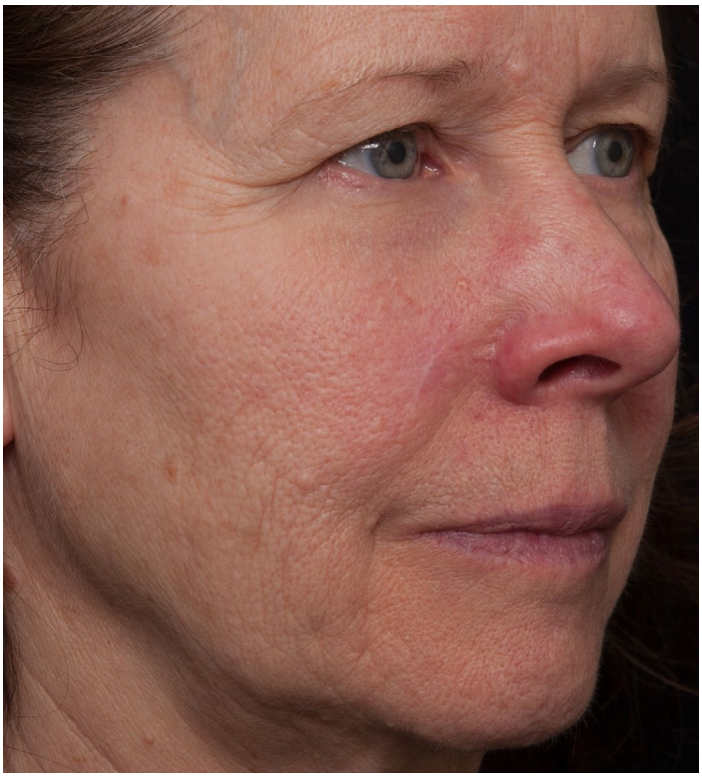


AFTER | 12 WEEKS

ANTI-AGING

Evaluation of a Novel Anti-aging Topical Formulation Containing Cycloastragenol, Growth Factors, Peptides and Antioxidants

Robert Weiss, MD

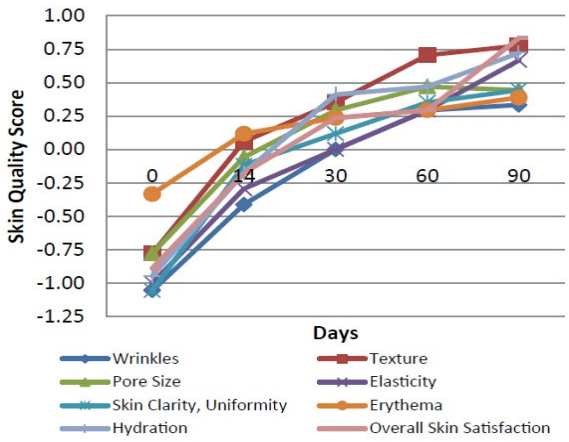
Method:

- 20 subjects ages 35-75 with moderate photo-aging on the face (Glogau wrinkle scale score II-III)
- Subjects used Regeneration Booster, gentle cleanser, & sunscreen
- 3-month study

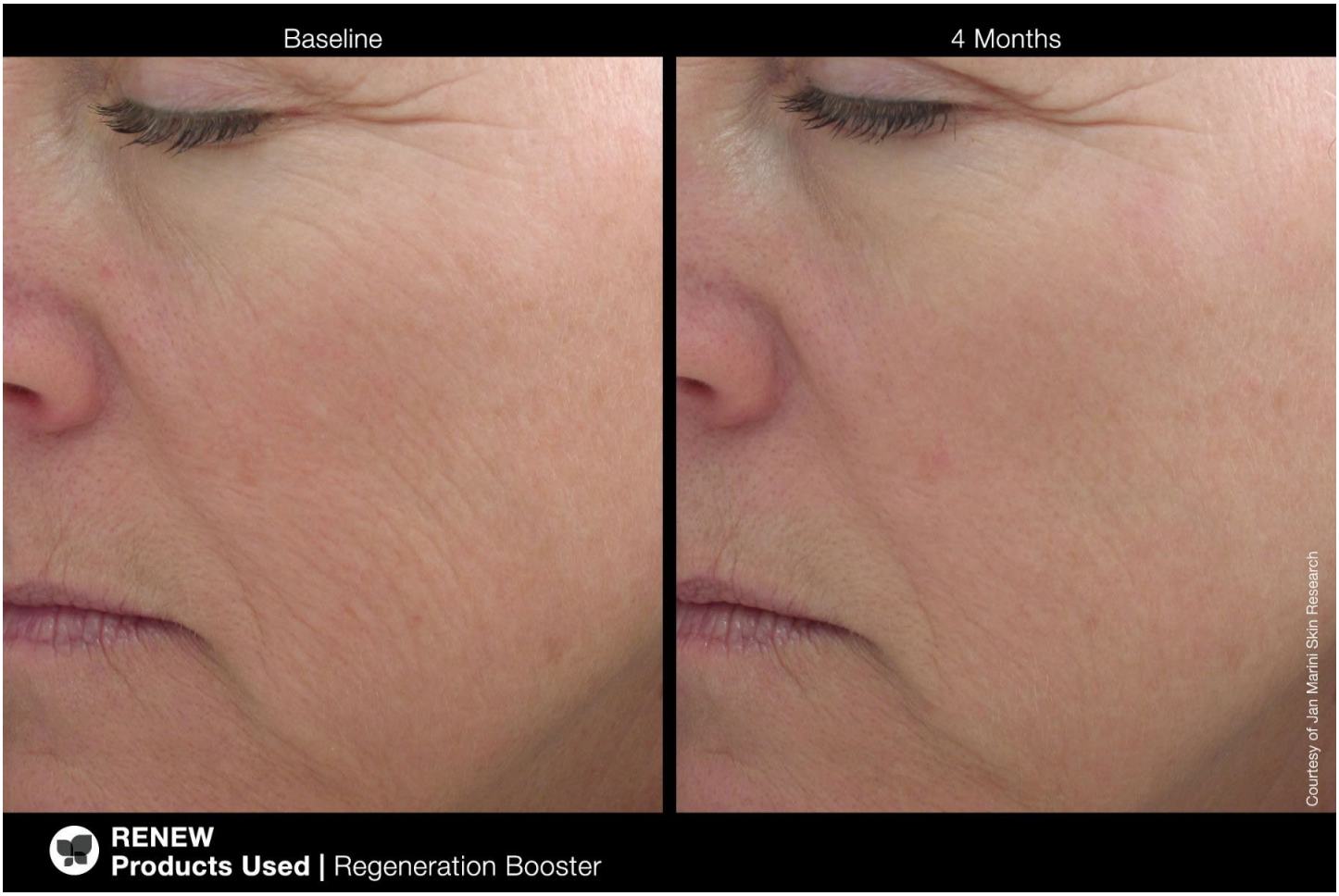
Study Summary:

- 100% of subjects noted improvement in overall skin quality with statistically significant improvement after just two weeks
- 100% of subjects noted improvement in at least 3 or more categories with an average improvement in 6.7 of 8 categories including: wrinkles, texture, pore size, elasticity, skin color/clarity, erythema, hydration and overall skin quality
- 100% of subjects noted positive user experience
- Significant improvement in wrinkles, texture, pore size, elasticity, skin clarity/uniformity, hydration, and overall skin satisfaction
- 0 cases of sensitivity, acclimation or irritation

Figure 1
Average Score By Concern



This study was published in Volume 13 Issue 9 (September 2014) of JDD [Journal of Drugs in Dermatology].


Baseline
4 Months
Courtesy of Jan Marini Skin Research
RENEW
Products Used | Regeneration Booster


REGENERATION
BOOSTER
Face Lotion
Lotion Pour Le Visage
JANMARINI

Evaluation of a Novel Anti-aging Topical Formulation Containing Cycloastragenol, Growth Factors, Peptides and Antioxidants

Robert Weiss, MD, Baltimore MD

INTRODUCTION
This study investigates the efficacy, tolerance and usability of a single product containing cycloastragenol, growth factors, peptides and antioxidants to decrease the visible signs of aging, including fine lines and wrinkles, texture, pore size, elasticity, skin color / clarity, redness, hydration and overall skin quality.

METHODS
Twenty subjects were enrolled in a 90-day, open-label, patient-assessment study. Subjects used a gentle cleanser, Regeneration Booster and a broad spectrum SPF for the duration of the 90-day study. Assessments were taken at baseline, 14, 30, 60 and 90 days. All assessments were compared against baseline for statistical significance.

RESULTS
18 of the 20 subjects completed the study. Improvement was significant after just 2 weeks of use for all measured categories except erythema and significant for all categories at 90 days. 100% of study subjects noted improvement in at least 3 or more of the 8 assessed categories with an average improvement in 6.7 categories. Improvement response rate for individual categories ranged from 67% to 100% of study subjects. There were zero cases of sensitivity or irritation and product smell, feel and ease of application were rated "positive" by 100% of study subjects. Photographic improvement was most notable in texture and lines on the cheeks and eye area.

CONCLUSION
Regeneration Booster when used as a stand–alone anti-aging solution delivers rapid and significant reduction in the visible signs of aging. Subject satisfaction was extremely high and there were zero reported cases of sensitivity or irritation. Based on these observations, Regeneration Booster is a safe and effective topical product for individuals seeking significant improvement in the appearance of aging skin.

INTRODUCTION

The professionally dispensed topical anti-aging market continues to grow and evolve driven by new ingredients, advancements in formulations and new utilizations of synergistic combinations of proven ingredients. It is estimated that from 2011 to 2015 global sales of physician-dispensed topicals will increase by 12.2% per year (Medical Insights Inc., June 2011).

The tested product, Regeneration Booster (Jan Marini Skin Research), is an advanced, patented, anti-aging formulation consisting of multiple anti-aging technologies. A key ingredient in Regeneration Booster's patented formulation is a new topical compound cycloastragenol. Cycloastragenol, is a purified extract from the astragalus plant. Cycloastragenol, a strong antioxidant, is also shown to significantly reduce many of the visible signs of aging. (Baumann, July 2011) (Valenzuela H, 2009)

In addition to cycloastragenol, Regeneration Booster contains high concentrations of three growth factors: Transforming Growth Factor Beta 1 (rh-polypeptide-22),

This study was published in Volume 13 Issue 9 (September 2014) of *JDD [Journal of Drugs in Dermatology]*.

Keratinocyte Growth Factor (sh-Polypeptide-3), Epidermal Growth Factor (sh-Oligopeptide-1) and four anti-aging / skin-conditioning peptides Myristoyl Tetrapeptide-12, Myristoyl Pentapeptide-11, Palmitoyl Pentapeptide-4 and Myristoyl Pentapeptide-8.

Finally, Regeneration Booster contains a broad range of topical antioxidants, hydrators and skin-protectants including Coenzyme Q10, Green Tea Extract, Hyaluronic Acid, Ceramides 2 and multiple essential fatty acids.

The purpose of this study is to determine Regeneration Booster's ability to decrease the visible signs of aging, including fine lines and wrinkles, texture, pore size, elasticity, skin color / clarity, redness, hydration and overall skin quality. In addition, this study also seeks to assess the product's user experience including smell, feel, ease of use, acclimation and irritation.

METHODS

Twenty subjects were enrolled in a 90-day, open-label patient assessment study to determine the efficacy of Regeneration Booster. The study was conducted by the office of Robert Weiss, MD of the Maryland Laser, Skin and Vein Institute.

Study protocol specified enrollment of subjects aged 35-75 with a moderate degree of photo-aging, defined by a starting Glogau score of II or III. Of these, a minimum of 70% of subjects were required to have a starting Glogau wrinkle score of III. Exclusion criteria included anyone with known allergies to product ingredients, anyone with recent hormonal changes including pregnant or nursing, a history of smoking, and use of any professional skin care products, retinoids or prescription topical medications in the past 90 days.

To control the environment, all subjects were required to use only the test product, (Regeneration Booster by Jan Marini Skin Research), Age Intervention Gentle Cleanser (Jan Marini Skin Research) and Antioxidant Daily Face Protectant SPF33 (Jan Marini Skin Research). Products were applied AM and PM, with the SPF being applied only in the AM or prior to outdoor activity. No other topical skin care products were allowed over the study period. Subjects were allowed to wear daily makeup per individual preference.

Results were determined through subject self-assessment surveys. Surveys were administered at study initiation and follow up visits at 14, 30, 60 and 90 days. Assessments graded 8 categories: the appearance of fine lines and wrinkles, texture, pore size, and skin color clarity / uniformity, skin elasticity, erythema, hydration and overall skin quality. Each assessment was performed using a 5-point scale: -2=Significantly Dissatisfied, -1=Dissatisfied, 0=Neutral, 1=Satisfied and 2=Significantly Satisfied. Subjects were also asked at each follow-up visit to rate their perceived change in each of the above categories as worsened, none, mild, moderate and significant.

To determine product usability, subjects rated the product as negative, neutral or positive for each of the following categories: ease of application, texture / feel, smell, and overall usage. Finally, subjects recorded adverse events to determine acclimation including sensitivity, tingling / burning or other.

Table 1:
Assessment Scores by Category at Time Intervals

Days	0	14	30	60	90
Wrinkles	-1.06	-0.41	0.00	0.29	0.33
Texture	-0.78	0.06	0.35	0.71	0.78
Pore Size	-0.78	-0.06	0.29	0.47	0.44
Elasticity	-1.00	-0.29	0.00	0.29	0.67
Skin Clarity / Uniformity	-1.06	-0.12	0.12	0.35	0.44
Erythema	-0.33	0.12	0.24	0.29	0.39
Hydration	-0.94	-0.18	0.41	0.47	0.72
Overall Skin Satisfaction	-0.89	-0.18	0.24	0.29	0.83

Table 2:
Improvement and Significance at 14 and 90 Days

	14 Days		90 Days	
	Delta	**Signif.**	**Delta**	**Signif.**
Wrinkles	0.64	p=0.017	1.39	p<0.001
Texture	0.84	p=0.004	1.56	p<0.001
Pore Size	0.72	p=0.018	1.22	p<0.001
Elasticity	0.71	p=0.014	1.67	p<0.001
Skin Clarity / Uniformity	0.94	p=0.010	1.50	p<0.001
Erythema	0.45	p=0.104	0.72	p=0.014
Hydration	0.77	p=0.014	1.67	p<0.001
Overall Skin Satisfaction	0.71	p=0.003	1.72	p<0.001

Finally, to assess overall satisfaction, subjects were asked on their 90-day assessment if they would recommend the product to a friend or family member.

Images were taken using a Visia camera at each visit to observe photographic changes. Statistical significance was determined based on pre and post assessment values. Significance was determined using a two-tailed paired t-test with a p value of <0.05 being considered significant.

RESULTS

Of the twenty enrolled subjects, eighteen completed the study. The two subjects lost to follow-up were lost after the 60-day follow-up, prior to the final 90-day follow-up. Results were significant in all measured categories with 100% of subjects experiencing improvement in 3 or more categories.

Self assessed satisfaction scores by category at each visit are shown in Table 1 and Figure 1. Figure 2 shows the percent of subjects with improvement in each category over the duration of the study.

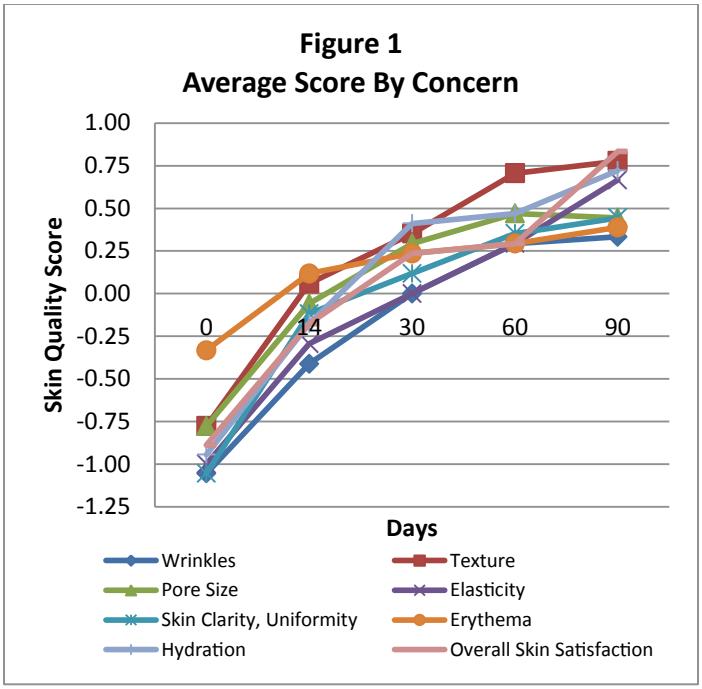
Scores are based on a 5-point scale. -2=Significantly Dissatisfied, -1=Dissatisfied, 0=Neutral, 1=Satisfied and 2=Significantly Satisfied.

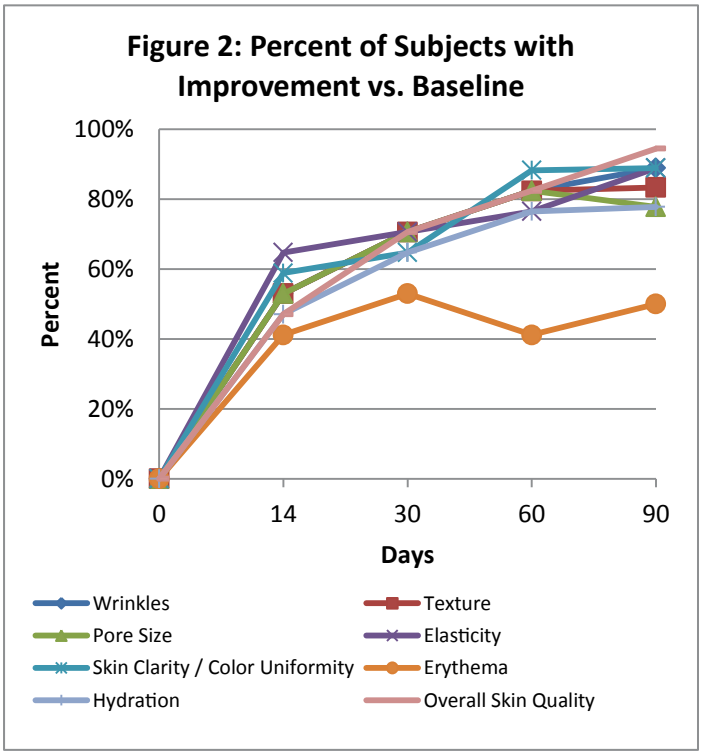
Improvement was rapid with significant improvement noted in all categories but erythema by week two. Results improved over the duration of the study with significant improvement in all categories at study completion (Table 2, Figure 1).

100% of individuals improved in 3 or more categories with an average improvement in 6.5 of the 8 measured categories. The average satisfaction score (range from -2 to 2) across all categories increased by 1.43 points from -0.85 pre to 0.58 post (Figure 1).

Figure 2 shows the percent of individuals with improvement vs. baseline by category across the duration of the study. 100% of subjects also improved by perceived change in skin in 3 or more categories each with 100% noting an improvement in overall skin quality and an average improvement in 6.7 of the eight categories (Figure 3). There were 0 cases of perceived reduction in skin quality in any recorded category.

Product attributes including smell, texture, feel and application were all rated as positive by 100% of study subjects. Further, there were 0 cases of subjects experiencing acclimation, tingling or burning reported in any follow-up assessment. Across all subjects and

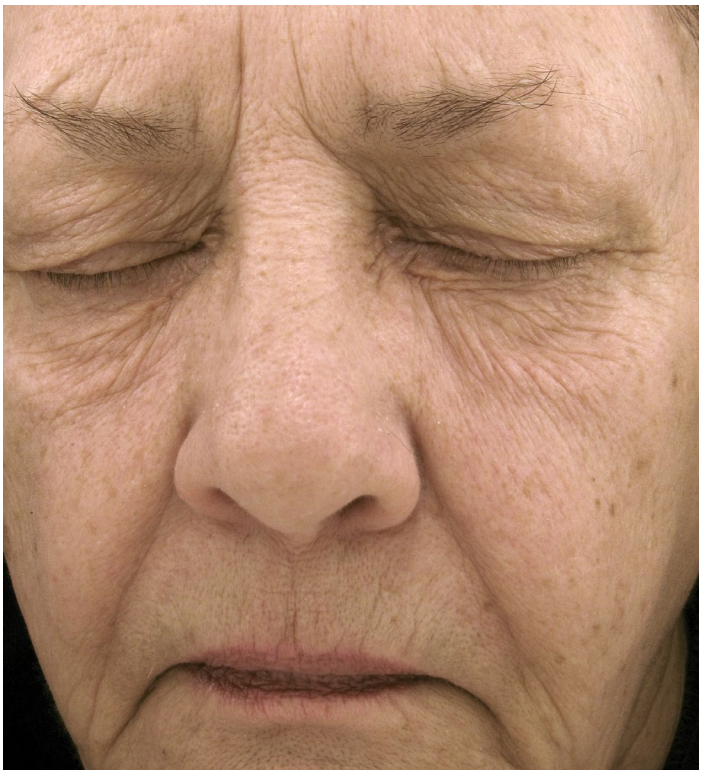




follow-up assessments there were a total of 4 reports of transient mild itching following application. No individual noted this for more than 2 of the 4 follow-up visits.

Satisfaction with the product was high with 100% of subjects indicating overall satisfaction with the product. Fourteen subjects indicated moderate to high satisfaction and 13 indicated that they would recommend the product to a family member or friend.

PHOTOGRAPHIC EVALUATIONS



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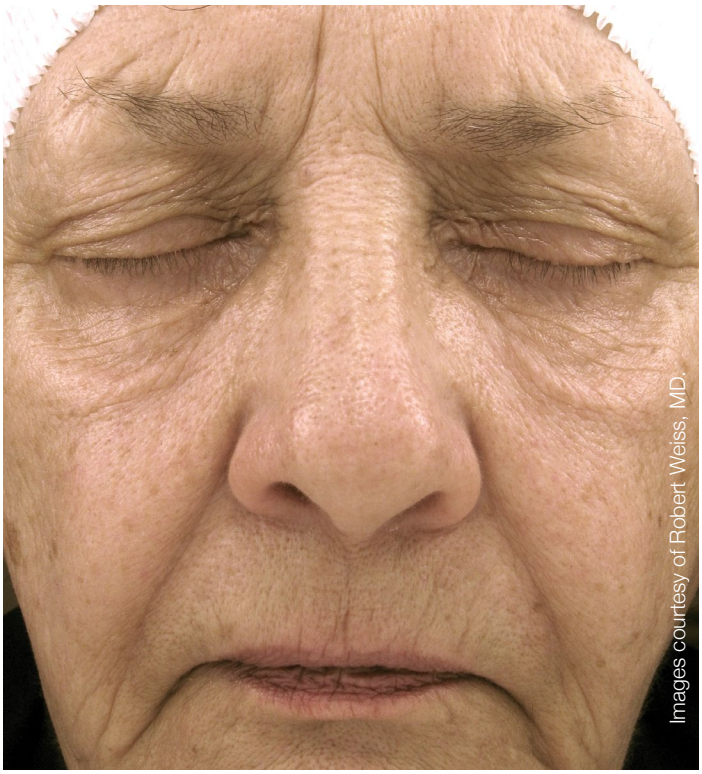
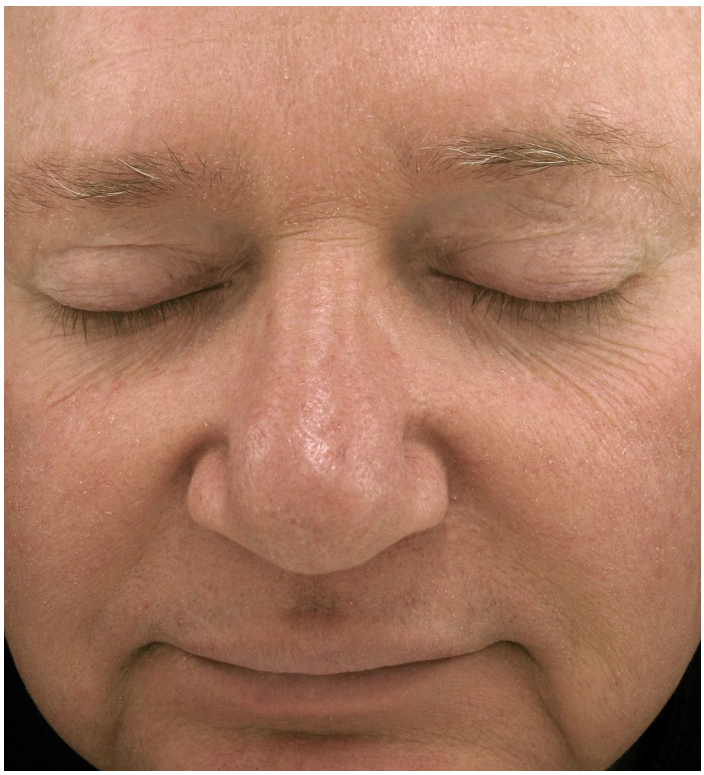


AFTER | 90 DAYS



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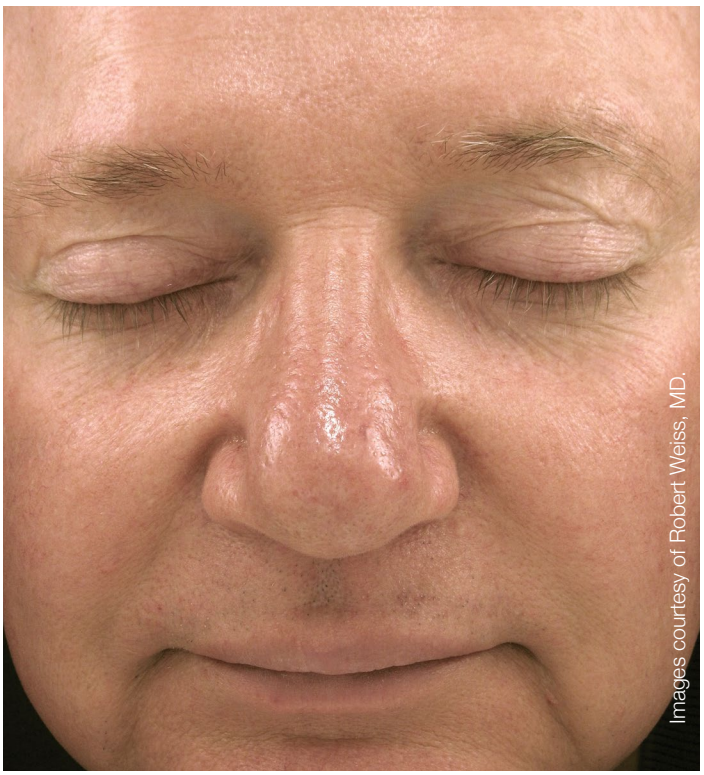
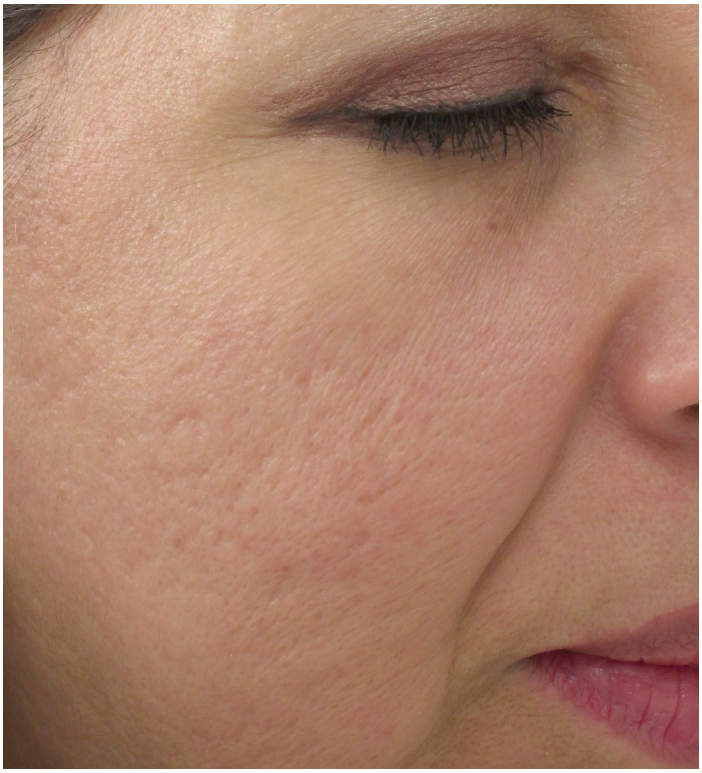


AFTER | 90 DAYS

PHOTOGRAPHIC EVALUATIONS



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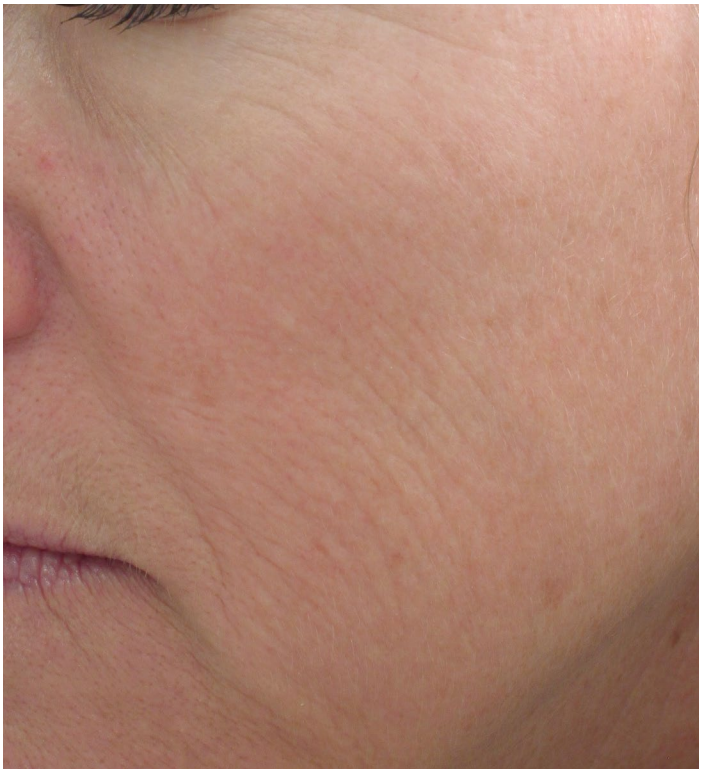

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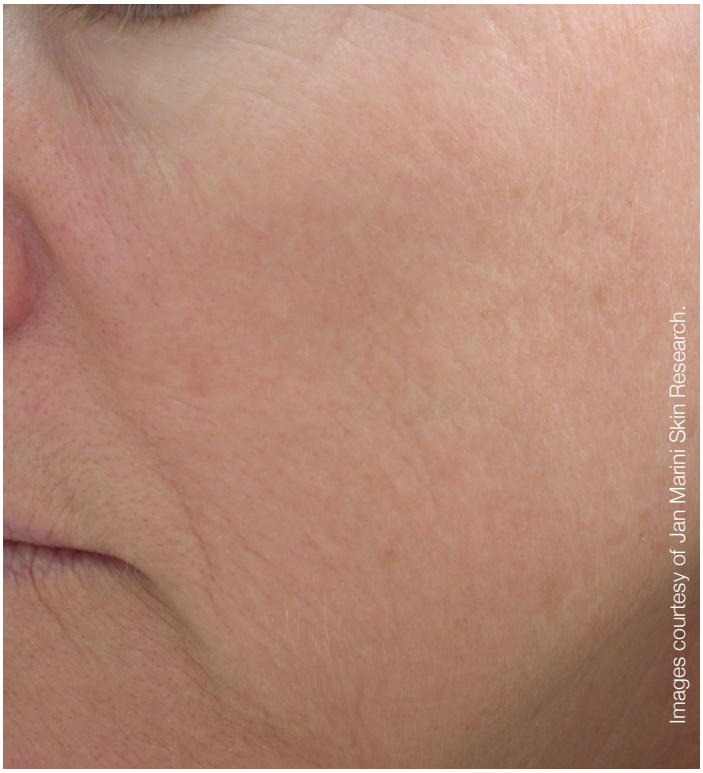


AFTER | 90 DAYS

The four subjects who did not indicate positive intent to recommend the product indicated a neutral or undecided intent to recommend. There were zero cases of dissatisfaction or intent not to recommend.

DISCUSSION

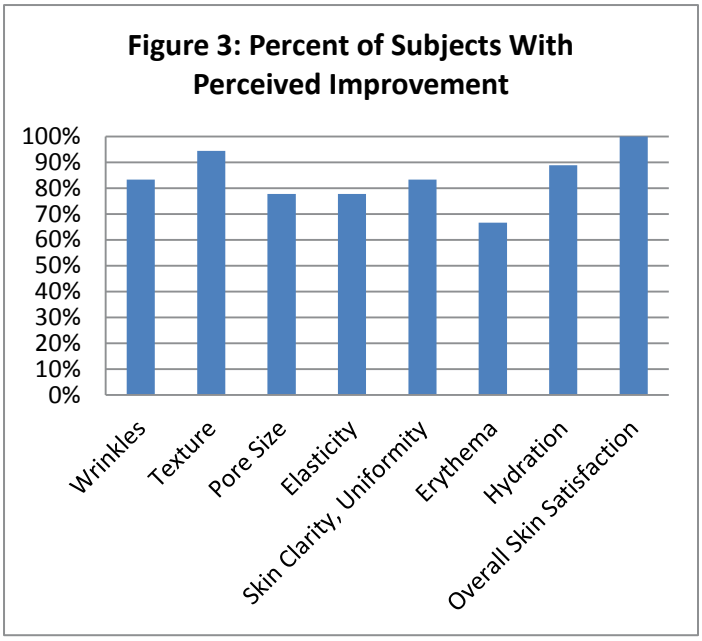
Anti-aging is the primary driver for the cosmetic industry and, now more than ever, adults in all age categories are seeking solutions to address the visible signs of aging.

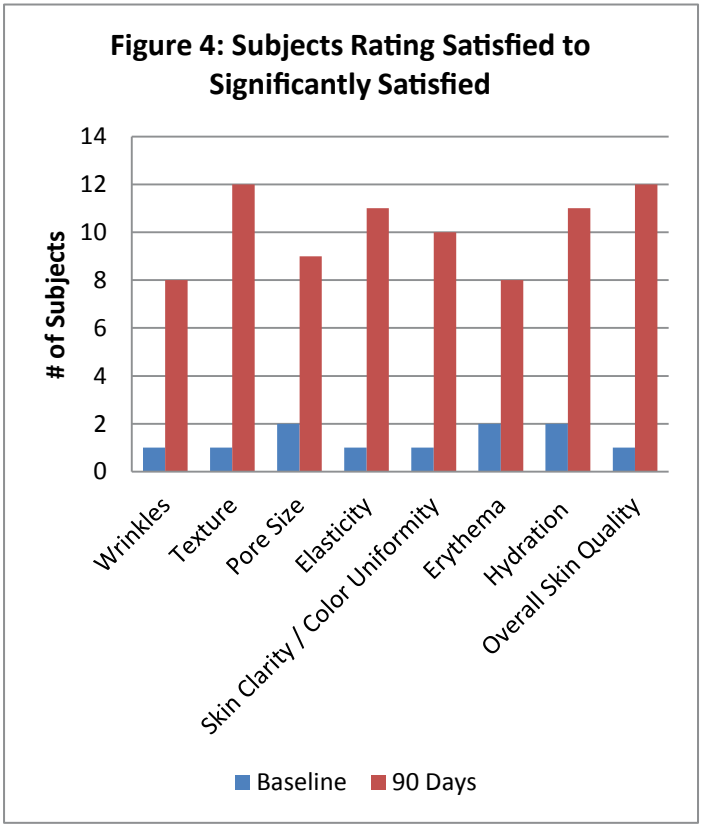
The tested sample provided rapid and significant improvement in the appearance of multiple common signs of aging with no sensitivity, irritation or acclimation. Subjects were able to use the product as directed from day one for optimal results. Improvement was rapid with individuals noting significant change at the initial 2 week visit in all categories except erythema, which was also significant at 90 days.

One notable point was the rapid response and broad degree of improvement in skin satisfaction. 100% of subjects improved by self-assessment from baseline to study completion in 3 or more categories. On average, subjects improved in 6.7 of the 8 categories with 100% noting improvement in overall skin quality (Figure 3). Further across all 144 individual assessments (18 subjects by 8 individual measured categories each), 117 (81%) of all assessments noted increased satisfaction from baseline while only 4 (0.03%) noted decreased satisfaction. Additionally, improvement in the visible signs of aging was not limited to those who completed the study. The two subjects lost to follow-up (not included in data) completed the study through the 60 day follow-up and showed improvement in 4 and 8 categories, respectively, with no decreased categories or adverse events.

While erythema reduction was not significant at 2 weeks, existence of erythema was not a criterion for enrollment so many individuals rated their satisfaction with erythema as Neutral to Significantly Satisfied at study baseline, leaving little room for improvement. For the subset of individuals (6 in total) that rated erythema as Significantly Dissatisfied or Dissatisfied, erythema decreased rapidly in the first 2 weeks of use from an average starting score of -1.3 (between significantly dissatisfied and dissatisfied) to +0.13 (between Neutral and Satisfied).

A good indicator of overall subject satisfaction is the increase in the number of subjects indicating satisfaction with skin post vs. pre study (Figure 4). The number of subjects indicating Satisfied to Significantly Satisfied per category increased significantly over the duration





of the study with an average increase of 8.75 individuals per category, ranging from a minimum increase of 6 individuals for erythema to a maximum increase of 11 individuals for texture and overall skin quality.

CONCLUSION

The tested product is a revolutionary new topical anti-aging product. It provides rapid and clinically proven

improvement for smoother, more uniform looking skin with marked reduction in the appearance of fine lines and wrinkles, erythema, skin color / clarity and pore size. 100% of subjects responded favorably with improvement in multiple areas of measurement. There were zero cases of even mild tingling or irritation with use allowing for immediate use with no acclimation period. Additionally, subjects noted improved elasticity and hydration with use. Finally, while this study is limited to a 90-day period, the rates of improvement indicate subjects should continue to notice further improvement in the visible signs of aging with continued use.

The benefits of rapid improvement with zero irritation lead to high subject satisfaction and compliance placing Regeneration Booster as a premier stand-alone topical product to address the visible signs of aging.

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Valenzuela H, F. T. (2009). Cycloastragenol extends T cell proliferation by increasing telomerase activity. *The Journal of Immunology,* 182:90.30.

100% OF SUBJECTS EXPERIENCED IMPROVEMENT IN 2 WEEKS.

GROWTH FACTORS

Improve the appearance of skin tone and texture.

ANTIOXIDANTS

Significantly improve the appearance of aging skin.

PEPTIDES

More polished skin with reduced appearance of pores.

PUBLISHED RESULTS

Study published in the “Journal of Drugs in Dermatology”.

Individual Results Will Vary

Jan MARINI SKIN RESEARCH®

NECK

Assessment of a Novel Anti-Aging Neck Cream

Leslie Baumann, MD

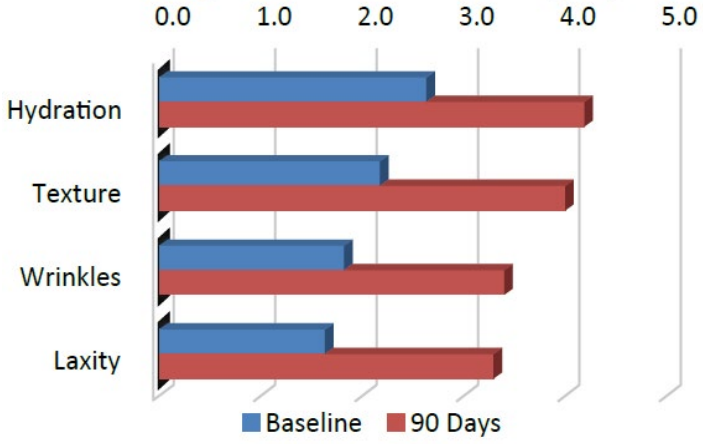
Method:

- 71 subjects ages 35-65 with moderate photo-aging of the neck
- 3-month study assessing improvement in texture, wrinkles, hydration and laxity
- Twice-daily application to the entire neck and jawline

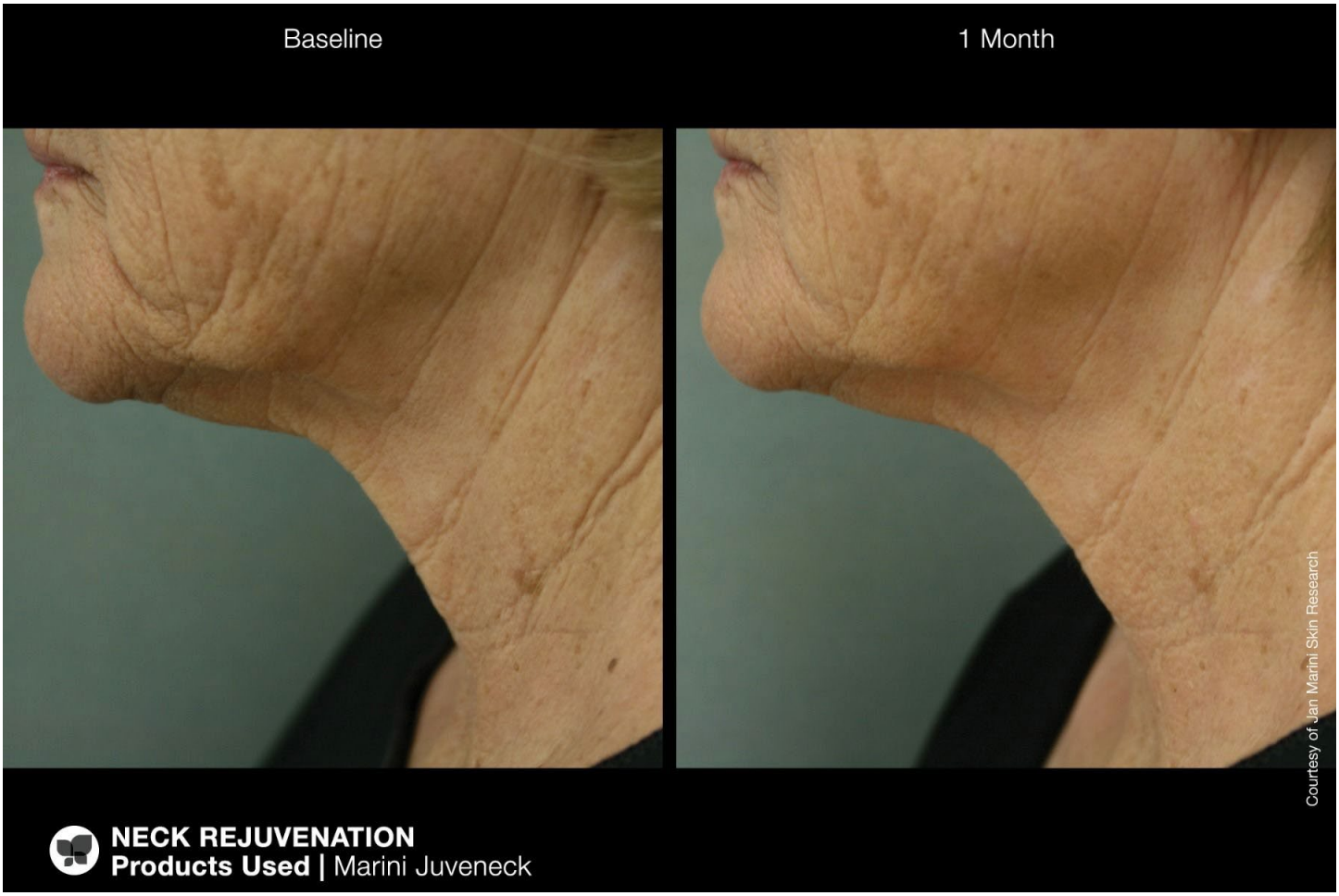
Study Summary:

- Extremely high satisfaction with 94% of subjects noting improvement in one or more categories
- Rapid improvement with changes noted at 2 days and continuing improvement over the 3-month period
- Statistically significant improvement in all measured categories ($p<1.0E-12$ or better)
- 100% of subjects liked the feel and application of the product
- 94x increase in the number of subjects rating "highly satisfied" with each of the measured categories

Figure 1:
Average Satisfaction by Category



This study was published in Volume 14 Issue 9 (September 2015) of JDD [Journal of Drugs in Dermatology].


Baseline
1 Month
Courtesy of Jan Marini Skin Research
NECK REJUVENATION
Products Used | Marini Juveneck


MARINI JUVENECK
Neck Cream/Crème Pour Le Cou
JANMARINI
MARINI JUVENECK
MARINI

Assessment of a Comprehensive Anti-Aging Neck Cream

Subhash J. Saxena PhD [(a)], Deysi Duque MS [(b)], and Michael J. Schirripa PhD [(b)]

[a] Jan Marini Skin Research, San Jose, CA
[b] Baumann Cosmetic & Research Institute, Miami FL

INTRODUCTION

The purpose of this study was to determine the tested neck cream's effect on self-reported signs of aging including skin hydration, texture, wrinkles and laxity. This study further investigates key user characteristics of the product including absorption, application, scent and feel as these product attributes are highly impactful toward consistent use and resultant efficacy.

METHODS

Subject screening was conducted via a virtual trial on 85 adult females ages 35-65 with Fitzpatrick skin types I through IV. Subjects applied the test neck cream (Marini Juveneck, Jan Marini Skin Research, San Jose, CA) and sunscreen (Antioxidant Daily Face Protectant SPF33, Jan Marini Skin Research, San Jose, CA) exclusively to the entire neck and jawline during the 3-month study period. Subjects rated satisfaction with skin using a 5 point scale from highly dissatisfied to highly satisfied in each of 4 categories including hydration, texture, wrinkles and laxity. Satisfaction with product attributes including application, feel and smell were also collected and assessed. Data collection was completed via online survey at Baseline, 2 days, 30 days, 60 days and 90 days.

RESULTS

71 of the initial 85 participants (84%) completed the final 90-day assessment. Improvement in satisfaction with skin was statistically significant from baseline scores for all measured categories (hydration, texture, wrinkles and laxity) with 78%-80% of individuals noting improvement in each individual assessment and 94% of study subjects noting improvement in at least one of the four categories. The quantity of subjects scoring "Satisfied" and "Highly Satisfied" across measured categories increased 8x from baseline with a 94x increase in the quantity of highly satisfied assessments. Satisfaction with product attributes was also high with 94-100% of subjects responding favorably to the product scent, application, absorption and feel. Overall, satisfaction was high with 94% of subjects responding positively to overall product satisfaction.

CONCLUSION

The results demonstrate that subject's belief that the neck cream product effectively improved the appearance of aging skin in the neck area. Based on subject assessment, it appears the neck cream product helped to significantly improve hydration and texture while significantly reducing the appearance of wrinkles and laxity along the jawline for more contoured skin. Results were rapid with continuing benefits over time. Future studies are recommended to determine the primary action mechanisms and to assess the degree of improvement by blinded physician assessment.

INTRODUCTION

While frequently discussed and associated with aging of the face, photo-aging also affects the delicate skin of the neck yet, while there are many anti-aging solutions for the face, there are few clinically proven solutions to address the range of photo-aging concerns to the neck. As such, there is significant growing media and consumer attention given to products and solutions for the neck. In the past three years there has been a significant increase in the number of devices and products indicated for or used on the neck yet

This study was published in Volume 14 Issue 9 (September 2015) of *JDD [Journal of Drugs in Dermatology]*.

there are few to no published studies on topical anti-aging solutions for this region.

Photo-aging is characterized by sagging and thinning of the skin, discoloration, fine lines, and skin fragility. Clinical signs of photo-aging are caused by loss of elastin, hyaluronic acid (HA), and collagen. Loss of elastin contributes to skin lax / sagging skin which, combined with aging downward pull of the platysmal muscle results in horizontal wrinkles commonly referred to as necklace lines. Loss of collagen in skin leads to fine lines, thinness, vertical lines, fragility and textural change. Loss of hyaluronic acid in skin results in decreased skin plumpness and fine lines.

Photo-aging of the neck share many if not all of the physiologic changes associated with aging skin on the face, the neck requires several unique considerations from solutions designed for the face. Skin off the face is dryer than skin on the face where sebaceous gland density is the highest with 400-900 glands / cm2. Off face, by comparison, densities drop significantly with both smaller glands and lower densities of only 100 glands / cm2 on the extremities.[1] Sebum naturally has a high content of Vitamin E and squalene. Because there are fewer sebaceous gland on the neck and other parts of the body as compared to the face, excretion of Vitamin E is 20x higher on the cheek and squalene is as much as 47X higher on the face than they are on the upper arm[2]. In addition, patients report that neck skin is more sensitive with an increased likelihood of redness and itching[3], minimizing the range of ingredient options. Laxity, discoloration and textural changes on the neck are harder to address with complimentary solutions like fillers and botulinum toxin. Finally, fat loss in the cheeks, fat deposits under the jawline, and shortening of the platysma muscle can exacerbate the appearance of laxity on an aging neck line.

The tested neck cream product contains multiple key ingredients designed to address hydration, improve texture, reduce wrinkles and improve skin tone and elasticity for a firmer, more lifted appearance. Key ingredients in the product include Rye Seed Extract, Oat Kernel Extract, Glaucine, Aminophylline, Acetyl Decapeptide 3, Dimethylethanolamine, Oligopeptide-24, Dipotassium Glycyrrhizate, alpha-Bisabolol, Tocopherol, Biotin, Panthenol and Sodium Hyaluronate.

HA, composed of repeated units of sugars (saccharides), is a humectant. When applied to the surface of the skin, it draws water into itself, which can increase and maintain skin hydration. HA has been shown to increase the penetration of other ingredients.[4] Panthenol, a form of vitamin B5, is also a humectant and is highly absorbed by the skin, making it a superior hydrating agent.[5] Studies have further shown that panthenol significantly reduces trans-epidermal water loss (TEWL) after 30 days of use.[5]

Biotin, another B vitamin and commonly referred to as vitamin H, is also shown to improve barrier function and reduce TEWL as well as reduce inflammation and sensitivity.

Alpha-bisabolol (bisabolol) is shown to have a broad range of benefits including anti-irritant and anti-inflammatory properties.[6] Bisabolol is also shown to possess anti-bacterial and anti-fungal properties as well as skin lightening characteristics associated with reduced inflammatory response.[7]

Vitamin E is one of the major naturally occurring antioxidants on the skin. The fact that there is less sebum production on the neck means that the neck has less natural protection to the sun and resulting free radicals. In addition to being a potent antioxidant, tocopherol (vitamin E) hydrates the skin and helps reduce inflammation, and inhibit UV-induced melanogenesis. Finally, dipotassium glycyrrhizate, the pure form of the active component in licorice root extract, is shown to inhibit tyrosinase (preventing the formation of melanin) resulting in evening of skin tone.

Anti-aging peptides and 2-dimethylaminoethanol (DMAE) are included to help reduce the appearance of wrinkles and help improve firming and contour. Although we do not know if these peptides are able to penetrate into the dermal layer of the skin, these advanced anti-aging peptides are engineered to encourage increased production of collagen and elastin by fibroblasts in the skin as well as increase hydration and cellular repair to minimize the appearance of fine lines and wrinkles. Their inclusion is based on in-vitro studies showing positive effect on these intended cells.[8, 9] Dimethylaminoethanol (DMAE) is shown to help improve skin tensile strength and reduce forehead lines and periorbital fine wrinkles.[10] Glaucine, Aminophylline, Rye Seed Extract and Oat Kernel extract are included in the formulation based on purported positive visible effects on skin tone, firmness contouring effect, though literature to prove these effects in-vivo is inconclusive or unavailable.

The intended combination of all these anti-aging, firming and hydrating technologies is to give the user the firmer, more contoured appearance. This prospective study investigates subject satisfaction using the neck cream product to determine its effect on self-reported signs of aging including skin hydration, texture, wrinkles and laxity. This study further investigates key user characteristics of the product including absorption, application, scent and feel as these product

attributes are highly impactful toward consistent use and resultant efficacy.

METHODS

Survey Subject Population

Subject screening was conducted via a virtual trial. Survey design consisted of an initial enrollment of 100 participants (of which 85 completed the baseline survey) to ensure a minimum of 25 participants at the three-month survey completion. All participants recruited for this online survey were females, Fitzpatrick skin types I through IV, between the ages of 35 and 65. All participants received 5 surveys at the following time points: Baseline, 2 days, 30 days, 60 days and 90 days.

The target population was selected from a self-reported set of individuals who met the following inclusion and exclusion criteria:

Inclusion Criteria

- Females between the ages of 35 to 65 with a loss of youthful elasticity, mild to moderate wrinkles and laxity on the neck. These include visible textural changes, mild laxity (up to 5mm under the chin) and fine to medium depth wrinkles.
- Participants who agree to limit their exposure to the sun and be willing to wear a sunscreen on their face and neck for the duration of the study.
- Females who are not pregnant, planning a pregnancy, or breast-feeding and are willing to use a consistent, medically effective method of birth control throughout the course of the study.
- Participants able to read, understand, and agree to participate in the online survey for three months

Exclusion Criteria

- Participants with excessive laxity, including deep lines and wrinkles along neck
- Use of any dedicated neck cream during the past 3 months
- Use of retinoids on the face or neck in the past 3 months (prescription or non-prescription)
- Use of topical medications on the neck for any skin condition (including acne)
- Any anti-aging resurfacing procedure (ablative or non-ablative laser or medium depth chemical) peel in the past 3 months that extended beyond the jawline
- Use of oral isotretinoin in the last 6 months
- Anyone who is pregnant, nursing, or planning a pregnancy
- Enrollment in any other clinical research study in the past 30 days (prior to enrollment)
- Anyone unwilling or unable to follow protocol and use products for the full study duration
- Anyone with known allergies /sensitivities to ingredients in either product
- Participants who smoke (more than an occasional cigarette at any time - past or present)

Survey Materials

Participants were instructed to apply the neck cream product, Marini Juveneck, (Jan Marini Skin Research, San Jose, CA), to the entire neck including under the chin, from the collarbone to the jawline and around both sides of the neck including behind the ears, twice daily in the morning and afternoon. Participants were also required to wear a broad spectrum SPF (Antioxidant Daily Face Protectant SPF 33, Jan Marini Skin Research, San Jose, CA). Study subjects received the neck cream products with home instructions to use throughout the three-month online survey period. The study was open-label, non-placebo controlled, with a generic product name “Neck Cream” given to the product.

Email notifications and reminders were provided to give instructions on how to fill out the 5 online surveys to determine the effectiveness and consumer preference of each of the products. Our detailed questionnaire allowed us to assess the participants’ responses regarding the improvement of the neck skin’s appearance at each time point as compared to baseline assessments. It also allows us to show the importance of their perception regarding the efficacy of the neck cream product.

Data Collection

Data was collected via online surveys at 5 time points – Day 0 (baseline) and days 2, 30, 60 and 90. Surveys were designed not to capture personal identifiable information. Online surveys were provided to all enrolled participants, ensuring confidentiality of their individual responses. All five surveys asked participants to assess their overall satisfaction with 4 categories of concern on their neck: a) hydration, b) texture, c) wrinkles, and d) laxity, along the neck and jowls. Follow-up surveys on days 2, 30, 60 and 90 also asked participants to assess their overall opinion of the neck cream, usage characteristics including feel, smell and texture, as well as overall perceived improvement in hydration, texture, quantity of wrinkles, depth of wrinkles, elasticity, jawline definition and tightening / lifting.

Statistical significance was determined using paired t-test comparing results at each time interval to baseline or prior time intervals.

RESULTS

Online survey participation was highly successful, with 85 participants completing the baseline questionnaire and 71 participants (84%) completing the final 90-day assessment. Of the 71 final online survey participants, 65 completed both the baseline and 90-day questionnaires. For averages, the full data set of participant's responses was used. For statistical significance, only the 65 participants with paired baseline and 90-day assessments were included.

	AVERAGE SATISFACTION (TABLE 1)						
	Day 0	Day 2	Day 30	Day 60	Day 90	Delta	p value
Hydration	2.49	3.74	4.13	4.22	4.2	1.55	3.14E-13
Texture	2.11	3.52	3.81	3.95	3.99	1.83	5.68E-15
Wrinkles	1.84	2.78	3.17	3.32	3.41	1.58	1.42E-12
Laxity	1.6	2.76	3.19	3.25	3.32	1.66	5.09E-14

Improvement in satisfaction by category was determined by measuring satisfaction at baseline and comparing it against satisfaction at each follow-up visit. Subjects rated satisfaction n four key categories (Hydration, texture, wrinkles and laxity) using a 5-point grading scale: 1=Significantly Dissatisfied, 2=Dissatisfied, 3=Neutral, 4=Satisfied and 5=Very Satisfied. Participants noted significant improvement in satisfaction at all post-visits. Average satisfaction scores as well as statistical significance at day 90 are shown in Table 1.

Figure 1 also shows change in improvement from baseline to the 90-day visit. Figure 2 shows improvement changes at each follow-up visit.

PERCENT OF PARTICIPANTS WITH IMPROVEMENT FROM BASELINE (TABLE 2)	
Hydration	80%
Texture	78%
Wrinkles	77%
Laxity	78%
One or More Categories	94%

The online surveys indicated that rate of improvement was high with 94% of participants noting improvement in one or more categories vs. baseline – indicating that only 6% of respondents failed to note improvement. Table 2 shows improvement response rates by each individual category. Table 3 shows the total number of participants who rated

Figure 1:
Average Satisfaction by Category

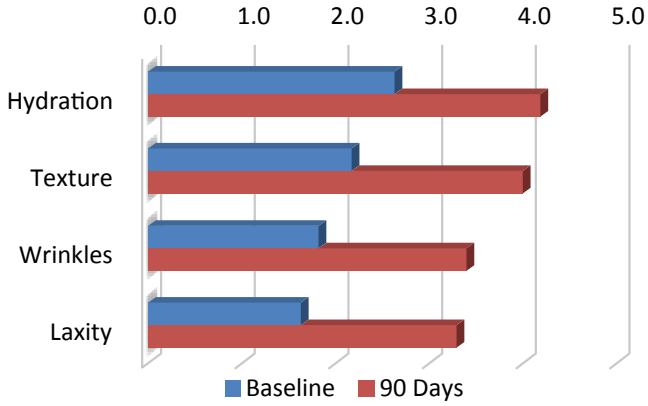
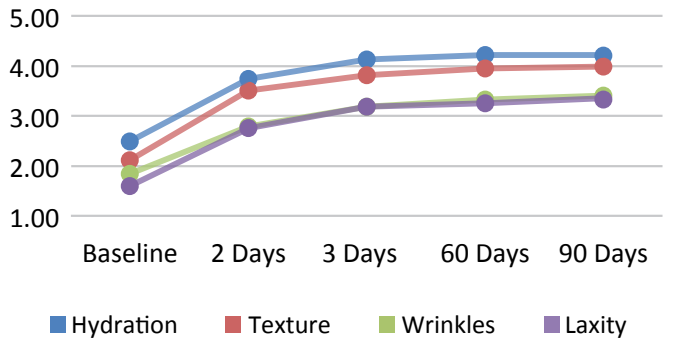


Figure 2:
Improvement in Average Satisfaction Over Time



themselves as "Satisfied" or "Highly Satisfied" with each of the categories on the baseline and 90-day surveys. The quantity of "Satisfied" and "Highly Satisfied" responses increased significantly with an 8x increase in overall satisfied assessments and a 94x increase in highly satisfied assessments.

NUMBER OF SATISFIED ASSESSMENTS PRE AND POST USE (TABLE 3)						
Concern	Baseline (n=85)			90 Days (n=71)		
	Satisfied	Highly Satisfied	Sum	Satisfied	Highly Satisfied	Sum
Hydration	10	1	11	18	40	58
Texture	9	0	9	27	28	55
Wrinkles	2	0	2	22	13	35
Laxity	0	0	0	20	13	33
% of Total	6.5%	0.3%	6.8%	31%	33%	64%

Attribute	PERCENT OF RESPONDENTS (TABLE 4)			
	Day 2 (89 Subjects)	Day 30 (86 Subjects)	Day 60 (79 Subjects)	Day 90 (71 Subjects)
Like the feel of the product	99%	99%	99%	100%
Like the application of the product	99%	99%	100%	100%
Like the absorption of the product	99%	100%	100%	99%
Like the scent of the product	91%	94%	97%	94%
Notice improved hydration	44%	67%	78%	72%
Notice improved texture	96%	99%	99%	94%
Notice reduced quantity of wrinkles	9%	42%	52%	46%
Notice reduced depth of wrinkles	16%	56%	59%	59%
Notice increased elasticity	19%	44%	46%	49%
Notice improved jawline definition	19%	56%	65%	59%
Notice tightening / lifting	21%	51%	63%	59%
Would recommend the product	72%	65%	78%	72%
Would use the product	97%	90%	85%	77%
Like the overall product	98%	99%	94%	94%

Wearability and overall perception of change was assessed at each interval (Table 4). Participants were asked to agree or disagree with a statement pertaining to product feel, application, absorption and scent. Example statement “I like the feel of the neck cream product” with two choices “Agree” or “Disagree”.The average satisfaction exceeded 90% for product attribute measurements at all follow-up surveys.

Subjects were also asked to assess their perception of improvement from the start of the study for a variety of attributes. Subjects were asked questions with 3 options – improved, remained the same, worsened i.e. “Compared to the start of the study, the number of wrinkles on my neck: “Reduced in Quantity”, “Remains the same” or “Increased in Quantity”. Of note, 0 respondents (0%) noted an increase in quantity of wrinkles, depth of wrinkles and laxity at 90 days.

Overall satisfaction with the neck cream product was high (Table 4) at each time interval with 94% - 99% of respondents reporting that they liked the overall results and feel of the product. Further, the majority of participants would both choose to use the product and recommend it to a friend or colleague.

DISCUSSION

This study was designed to target a representative sample of female subjects seeking improvement in their neckline. To assess improvement, the study enrolled subjects with self-reported mild-to-moderate aging of the neck. Self-reported aging is more representative of retail product usage in a practice setting but presents a greater challenge to showing statistical significance as outside cases with either greater or less significant aging may be enrolled in the study.

To ensure greater success, studies frequently narrow the inclusion criteria to those subjects most probable to show measurable results. As online surveys tend to have a higher drop-out rate than in-office procedure-based studies, an initial enrollment of approximately 100 subjects was deemed necessary to ensure a final population of 30 or more subjects.

Compliance was far higher than expected with a dropout rate of only 16% of subjects (71 of 85 baseline assessments completed the study) vs. the near 60-70% expected dropout rate. This high retention rate indicates the demand for and satisfaction with the neck cream product.

The results of the study were notable with significant improvement in all measured categories at every time interval and continued average improvement over time.

The observed improvement over time is particularly visible when comparing subject-perceived improvement for wrinkle depth, wrinkle quantity, elasticity, jawline definition and lifting / contouring from baseline to day 2 with the change from day 2 to day 30. As expected, the change from day 2 to day 30 was much more significant than the change from baseline to day 2.

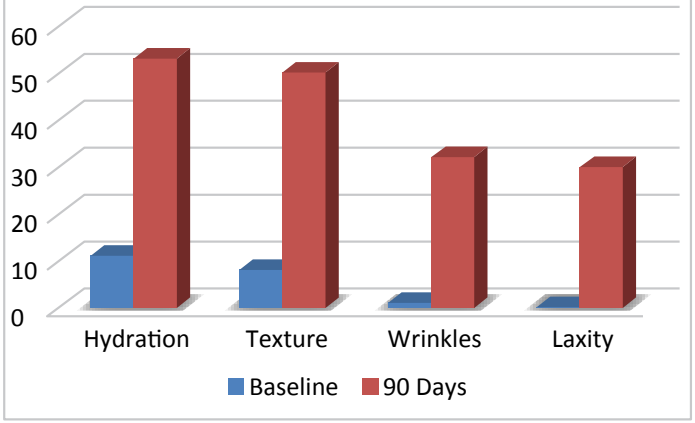
Overall improvement in satisfaction with skin on the neck was highly significant. 94% of total study subjects at Day 90 noted improvement in at least one category.

Further, out of the 65 paired baseline and 90-day assessments, there was an 8x increase in the number of subjects rating satisfied or significantly satisfied with any of the 4 measured attributes on the neck and a 94X increase in the number of highly satisfied assessments. Out of a total of 260 individual assessments (4 assessments by 65 paired subjects), there were only 21 total “satisfied” assessments and only 1 “highly satisfied” assessment at

baseline. By contrast, at day 90 there were 87 satisfied assessments and 94 highly satisfied assessments or 36.2% of total assessments were highly satisfied and 69.6% of assessments were satisfied or highly satisfied. Figure 3 and Table 3 show the total number of subjects rating satisfied or highly satisfied by category. The significant change from ratings of "Dissatisfied" to "Satisfied" shows the impact of the product on overall satisfaction with skin on the neck.

Equally significant to the observed increase in satisfaction was the decrease in dissatisfied assessments. 76% of all assessments were dissatisfied at baseline with 29% of total assessments rated as "highly dissatisfied".

Figure 3:
Number of Satisfied or Highly Satisfied Subjects by Category



By day 90, only 5% of assessments were rated as highly dissatisfied and only 19% of assessments were rated as dissatisfied. This indicates that the product worked across all individuals with varying degrees of aging skin and satisfaction at baseline.

In addition to creating a firmer, more contoured, less wrinkled appearance, subjects reported consistently high satisfaction with user attributes including product feel, application, absorption and scent. This is an important factor when assessing the probability of long-term use to achieve maximum efficacy and satisfaction. Our data show that, based on participant's satisfaction with the product attributes, perception of improvement and comparison to baseline assessments, the neck cream product creates an improved skin appearance in the neck area.

The overall participant's satisfaction, results and significant improvement compared to baseline assessments, high overall satisfaction and observed rate of improvement indicate indicates that the neck cream improves the appearance neck skin appearance. The high satisfaction ratings with product aesthetics including feel, application absorption, and scent indicate a high probable willingness for subjects to use the product long-term where they will observe best results.

It is important to remember that this is an open-label survey with the likelihood of a placebo effect. The placebo effect is enhanced by the fact that the data gathered was subjective. However, the high satisfaction rates and low drop-out rates suggest that the subjects were pleased with the effects and aesthetics of the product. This suggests that they would be compliant with the product and repurchase it - which would increase long term efficacy.

CONCLUSION

In conclusion, results from the participant's online survey assessments demonstrate that subjects believe that the neck cream product effectively improved the appearance of aging skin in the neck area. It appears that the neck cream product helped to significantly improve hydration and texture, while significantly reducing the appearance of wrinkles and laxity along the jawline for more contoured skin. Results were rapid with continuing benefits over time. Future studies are recommended to determine the primary action mechanisms and to assess the degree of improvement by blinded physician assessment.

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IMPROVE THE APPEARANCE OF AGING-SKIN IN THE NECK AREA.

SMOOTHING

Reduces the appearance of fine lines and wrinkles.

HYDRATING

Improves hydration and the appearance of texture.

BRIGHTENING

Corrects the appearance of discoloration and dark spots.

PUBLISHED RESULTS

Study published in the "Journal of Drugs in Dermatology".

Jan MARINI SKIN RESEARCH®

Individual Results Will Vary

ANTI-AGING HANDS

Assessment of a Novel Anti-Aging Hand Cream

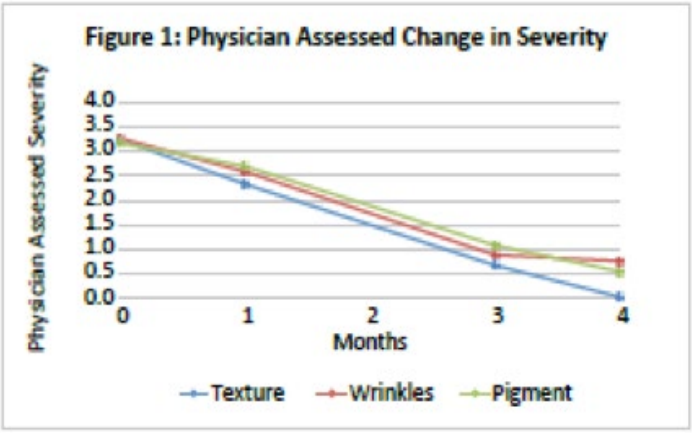
Joel Schlessinger, MD

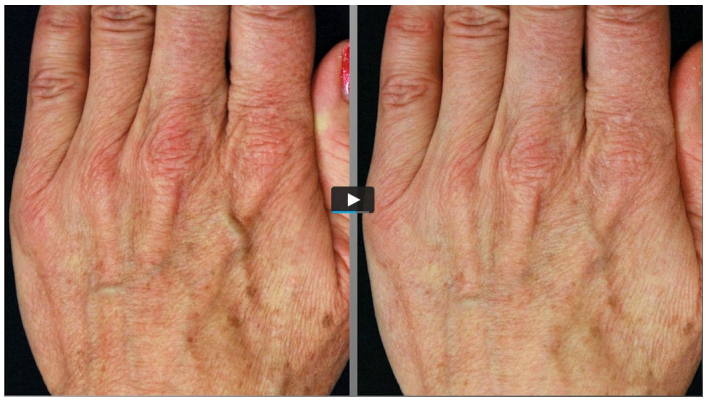
Method:

- 9 subjects with Fitzpatrick skin type I-IV between the ages of 30-65, with moderate sun-damage / photo-aging on the backs of the hands
- 4-month study from mid-December to late March in Omaha, NE
- AM/PM usage of Marini ReNu

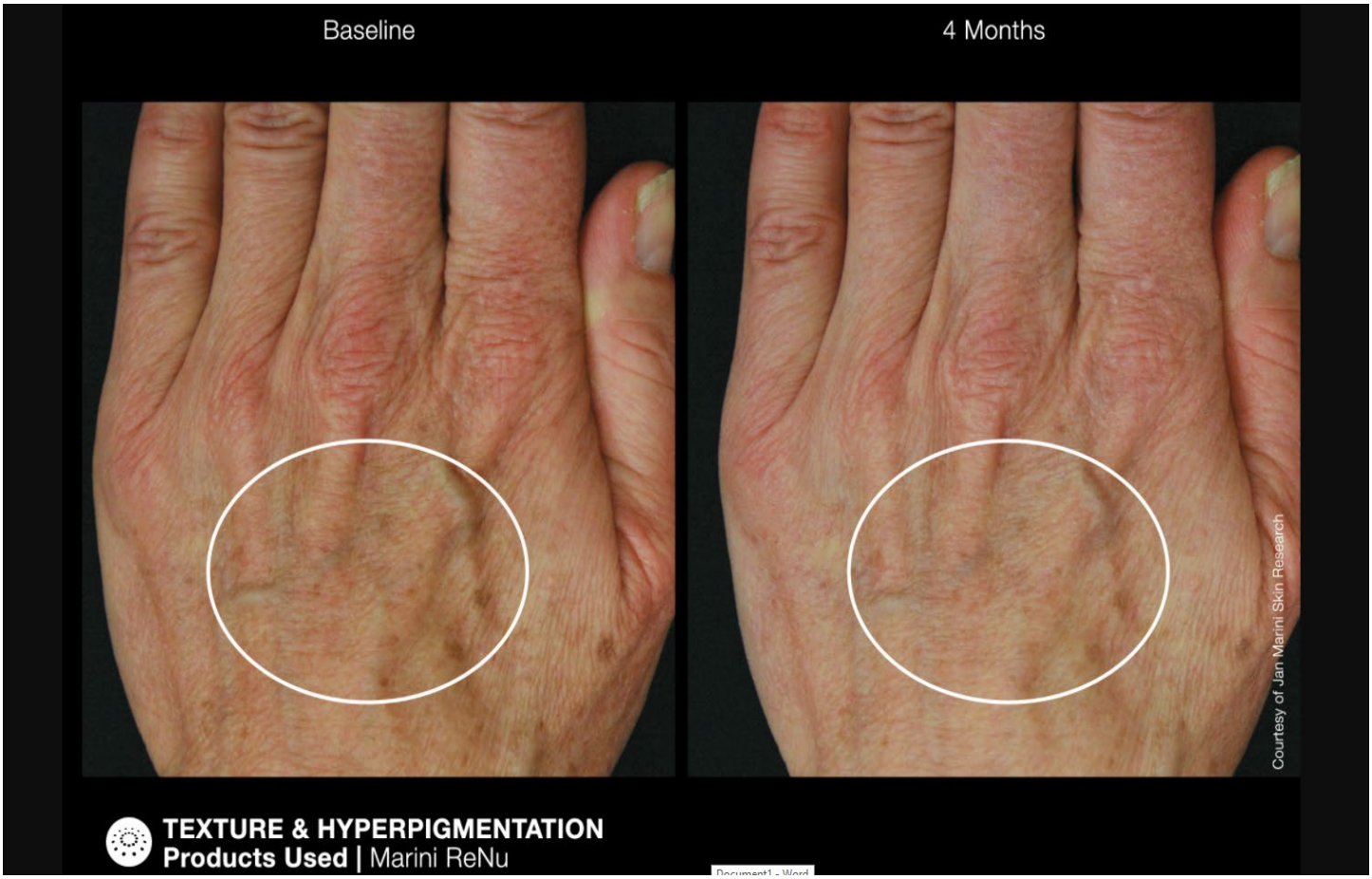
Study Summary:

- Significant improvement in physician-assessed appearance of texture, wrinkles and discoloration
- 100% of subjects noted increased satisfaction in at least 4 of 8 measured categories with 75% noting improvement in all measured categories
- 93%-96% of subjects rated improved satisfaction in texture, pigment, wrinkles and overall satisfaction with skin
- Significant improvement noted at 1 month with linear continuing improvement through study completion





This study was published in Volume 15 Issue 4 (April 2016) of JDD [Journal of Drugs in Dermatology].


Baseline
4 Months
Courtesy of Jan Marini Skin Research
TEXTURE & HYPERPIGMENTATION
Products Used | Marini ReNu


MARINI
ReNu
CORRECTIVE
HAND COMPLEX
JANMARINI
28 g / 1 oz.

Assessment of a Novel Anti-Aging Hand Cream

Joel Schlessinger, MD [(a)], Subhash Saxena, PhD [(b)], Stuart Mohr [(b)]

[a] Lovely Skin, Omaha, NE
[b] Jan Marini Skin Research, San Jose, CA

INTRODUCTION
With many advanced anti-aging creams developed and marketed for the face, attention is now turning to other visible areas of the body. There is growing interest in creams for aging skin on the hands, which receive high UV and environmental exposure. UV damage and secondary signs of aging[1, 2] on the hands make them one of the most obvious indicators of age outside the face. The past several years have seen a focus on and significant increase in the number of devices, procedures and injectables approved for the hands, yet a literature search for cosmeceutical topical solutions showed few to no published studies.

METHODS
29 subjects with Fitzpatrick skin type I-IV between the ages of 30-65 were enrolled in the study. To minimize the effect of seasonal sun exposure variation on lightening, participants in the 4-month study were enrolled from mid-December to late March in Omaha, Nebraska. Assessments were completed at Baseline, 1, 3 and 4 months. All subjects exhibited moderate sun-damage / photo-aging on the backs of the hands, characterized by visible pigmentation, textural changes and fine lines and wrinkles.

RESULTS
28 of the initial 29 subjects completed the study, with one subject lost to follow-up after baseline assessment. There were zero adverse events and zero reported cases of skin irritation or acclimation. Improvement vs. baseline was statistically significant in all categories and time intervals for both right and left hands (Table 3).

CONCLUSION
The Marini ReNu Corrective Hand Complex was judged highly effective by both physician assessment and subject self-assessment in reducing the visible signs of UV damage and aging, including loss of texture, wrinkles, pigmentation and loss of elasticity. Results were observed rapidly by both subjects and physicians, with statistically significant improvement noted at the very first follow-up visit after only 30 days of use.

INTRODUCTION

With many advanced anti-aging creams developed and marketed for the face, attention is now turning to other visible areas of the body. There is growing interest in creams for aging skin on the hands, which receive high UV and environmental exposure. UV damage and secondary signs of aging[1, 2] on the hands make them one of the most obvious indicators of age outside the face. The past several years have seen a focus on and significant increase in the number of devices, procedures and injectables approved for the hands, yet a literature search for cosmeceutical topical solutions showed few to no published studies.

Photo-aging is characterized by UV-induced epidermal and dermal changes, including textural changes, lentigines, actinic keratosis (AK) and seborrheic keratosis (SK). Dermal changes also play into visual aging, including sagging and thinning of the skin, loss of elasticity, increased fine lines and wrinkles, and increased skin fragility. Finally, a loss of subcutaneous fat due to both UV exposure and intrinsic aging leads to a loss of volume and increased visual prominence of vascular, tendon and bone structures.[3]

In-office procedures commonly used to help address the many visual manifestations of photo-aging include lasers (ablative and non-ablative), IPL, chemical peels, cryotherapy, electrodessication and photodynamic therapy (PDT). Options range from treating individual lesions to more comprehensive

This study was published in Volume 15 Issue 4 (April 2016) of *JDD [Journal of Drugs in Dermatology]*.

and aggressive full-surface treatments. For all in-office hand treatments, care needs to be taken when treating more aggressively due to longer recovery times and increased risk of scarring, hyperpigmentation or hypopigmentation on the hands (as compared to the face). Further, it is important to mitigate the risk of a line of demarcation between treated areas and the remainder of the arm.[3]

The final primary indicator of aging on the hands is increased visibility of vasculature, bone and tendon structures due to fat atrophy and thinning. Common office treatments for these issues include revolumizing through filler injections (especially with the newly approved Radiesse indication) and removal of vascularity via sclerosing or endovenous laser procedures.

With all treatment modalities, effective topical agents should be integrated to enhance and maintain procedure results. Marini ReNu Corrective Hand Complex (Jan Marini Skin Research) contains multiple key ingredients designed to address the visible signs of UV damage and photo-aging, including: textural changes, increased hyperpigmentation and discoloration, increased fine lines and wrinkles and decreased elasticity.

Primarily, these ingredients include Retinol, Alpha-Arbutin, Kojic Acid, Azelaic Acid, Hexylresorcinol, Licorice Root Extract, Dipotassium Glycyrrhizate and Vitamin C as well as multiple antioxidants and soothing agents to help hydrate the skin, reduce irritation and protect against further damage (Table 1).

Retinoids are vital to the maintenance of optimal skin health and are utilized extensively by dermatologists. They yield many benefits for the skin and are used to treat a variety of skin conditions, yet prescription-strength tretinoin is often too harsh or irritating and results in poor compliance or discontinuation by the patient. Many studies have show that retinoids provide significant anti-aging benefits by increasing skin thickness and cellular turnover, promoting healthier skin.[4]

The two most well-known retinoids are all-trans-retinol (retinol) and all-trans-retinoic acid (tretinoin). In a study investigating Type I collagen production in the skin (Type I accounts for 85% of total collagen), daily application of tretinoin was shown to reverse the loss of collagen in the papillary dermis of photo-damaged skin.[5] All-trans-retinol undergoes a conversion to tretinoin upon application to the skin, and studies confirm that results are equivalent for topically applied all-trans-retinol and all-trans-retinoic acid for multiple indications at differential concentrations of 10:1 of retinol to tretinoin.[6,7]

Alpha-Arbutin, Licorice Root Extract, Kojic Dipalmitate, Glycyrrhiza Glabra, Dipotassium Glycyrrhizate (a component of Licorice Root Extract) and Hexylresorcinol all function to inhibit tyrosinase formation, thereby preventing initiation of the melanin production cycle.[8] Alpha-Arbutin is a synthesized form of arbutin shown to inhibit tyrosinase much more strongly than classic beta-arbutin, derived from the bearberry leaves.[9] Licorice Root Extract is further shown to exhibit tyrosinase inhibition, with the potential to lighten skin.[10]

Table 1: Key Ingredients and Benefits

Retinol	Shown to increase cellular turnover and reduce pigmentation Stimulates collagen and increases skin firmness to improve texture and reduce the appearance of fine lines and wrinkles
Alpha-Arbutin	A non-Hydroquinone agent that reduces the appearance of pigmentation and age spots
Kojic Dipalmitate (stable form of Kojic Acid)	A non-Hydroquinone compound that reduces the appearance of pigmentation and age spots
Azelaic Acid	Helps reduce the appearance of redness and pigmentation
Hexylresorcinol	A non-Hydroquinone agent that reduces the appearance of pigmentation and age spots
Glycyrrhiza Glabra (Licorice Root Extract)	A natural extract that helps reduce the appearance of pigmentation and age spots
Dipotassium Glycyrrhizate	An active component of licorice extract that helps reduce the appearance of pigmentation and age spots
Ascorbyl Palmitate (stable form of Vitamin C)	A stable, oil-soluble form of Vitamin C that reduces the appearance of pigmentation and age spots
Glycerin	A humectant to increase hydration in the skin
Vitamin E	A powerful antioxidant with soothing properties that helps aid in the prevention of free-radical damage from UV exposure and helps to support cellular regeneration and skin repair
Sunflower Seed Oil	An antioxidant and effective emollient for softening the skin
Meadowfoam Seed Oil	A skin softening moisturizer
Pomegranate Extract	A powerful antioxidant with soothing properties that helps in the prevention of free-radical damage from UV exposure and helps to support cellular regeneration and skin repair
Cucumber Extract	A natural emollient with soothing properties

Additionally, Azelaic Acid, a non-phenolic dicarboxylic acid, is capable of oxidizing unsaturated fatty acids into dicarboxylic acids, which competitively inhibit tyrosinase. It has been shown to effectively reduce post-inflammatory

hyperpigmentation and hypermelanosis caused by abnormal proliferation of melanocytes.[11] Individually, each of these ingredients has been shown to provide effective reduction in the appearance of hyperpigmentation. In combination, these ingredients work together to increase the probability of success.

Antioxidants Vitamin C (ascorbyl palmitate) and Vitamin E (tocopherol) plus multiple plant-based antioxidants help to further reduce irritation and decrease oxidative damage and hyperpigmentation secondary to UV exposure.

This prospective study investigates both clinician-assessed and subject-perceived effects of a novel new multi-modal anti-aging and lightening hand cream on UV-damaged skin, including its effect on texture and the appearance of wrinkles and pigmentation.

METHODS

29 subjects with Fitzpatrick skin type I-IV between the ages of 30-65 were enrolled in the study. To minimize the effect of seasonal sun exposure variation on lightening, participants in the 4-month study were enrolled from mid-December to late March in Omaha, Nebraska. Assessments were completed at Baseline, 1, 3 and 4 months.

All subjects exhibited moderate sun-damage / photo-aging on the backs of the hands, characterized by visible pigmentation, textural changes and fine lines and wrinkles.

Subjects were excluded from study participation if any of the conditions below applied at the time of enrollment.

- Smoker
- Pregnant or nursing
- Use of any prescription products on the treatment area
- Use of retinoids or tyrosinase inhibitors on the hands in the past 3 months
- Any significant hormonal changes in the past 3 months (change of birth control, menopause, etc.)
- Inability to adhere to study protocols
- Any condition that, in the treating physician's professional opinion, might delay or complicate results

Participants were instructed to apply the hand cream (Marini ReNu Corrective Hand Complex, Jan Marini Skin Research, San Jose, CA) to the entire back of both hands twice daily. Following AM application, participants applied a broad spectrum SPF (Antioxidant Daily Face Protectant SPF 33, Jan Marini Skin Research, San Jose, CA), following directions for sunscreen application based on US Food and Drug Administration OTC Monograph for Sunscreens. Subjects were instructed to limit washing or scrubbing hands for at least 2 hours post-application.

Assessment was performed by direct physician assessment and subject self-assessment. Physician assessment rated three primary indicators on each hand: skin texture, the appearance of wrinkles and overall pigmentation / contrast. Assessment for each category was based on a 5-point (0-4) increasing severity assessment scale (Table 2).

Table 2: Physician Assessment Grading Scale

Score	Texture	Wrinkles	Discoloration
0	Smooth, even texture	No wrinkles	No discoloration
1	Mild textural loss, few fine wrinkles	Minimal wrinkles, high elasticity	Average contrast is low (light pigment compared to skin)
2	Rough texture, multiple fine wrinkles	Moderate wrinkles, moderate elasticity	Average contrast is moderate (moderate pigment compared to skin)
3	Rough texture, multiple fine wrinkles, few moderate wrinkles	Marked wrinkles, minimal elasticity	Average contrast is high (dark pigment compared to skin)
4	Rough texture, multiple fine wrinkles, multiple moderate wrinkles	Significant wrinkles, very little elasticity	Average contrast is very high (very dark pigment, compared to skin)

Subject self-assessment was performed two separate ways, measuring Hydration, Texture, Wrinkles, Pigmentation, Brightness, Uniformity of Color, Elasticity and Overall Appearance. To assess a change vs. a baseline score, subjects were asked at baseline and at each follow-up visit to rate their overall satisfaction with each measured category based on an ascending 5-point scale: 0=Highly Dissatisfied, 1=Dissatisfied, 2=Neutral, 3=Satisfied, 4=Highly Satisfied.

Separately, subjects were asked via a Yes / No question: if they believe they noticed an improvement from baseline in each measured category. This question required the subject to recall a baseline reference (vs. comparing current assessments to recorded baseline assessments).

Data was collected in-office via physician and subject self-assessment at Days 0 (baseline), 30, 90 and 120. Statistical significance was determined using a paired t-test comparing results at each time interval to baseline or prior time intervals.

RESULTS

28 of the initial 29 subjects completed the study, with one subject lost to follow-up after baseline assessment. There were zero adverse events and zero reported cases of skin irritation or acclimation. Improvement vs. baseline was statistically significant in all categories and time intervals for both right and left hands (Table 3).

For the physician-based assessment, left and right hand assessments were not significantly different at any time interval and therefore are grouped into a single combined

average for further data. Improvement was approximately linear over the course of the study as seen in Figure 1.

Table 3: Change in Physician-Assessed Severity by Category

		Base	30 Days	90 Days	120 Days	p*
Texture	R	3.25	2.33	0.68	0.04	<0.001
	L	3.25	2.33	0.68	0.04	<0.001
Wrinkles	R	3.25	2.59	0.89	0.79	<0.001
	L	3.29	2.59	0.89	0.75	<0.001
Pigment	R	3.18	2.70	1.11	0.54	<0.001
	L	3.18	2.70	1.07	0.57	<0.001

***p value, 120 days vs. baseline**

Table 4: Improvement in Satisfaction with Skin

	Base	30 Days	90 Days	120 Days
Hydration	0.83	2.81	3.00	3.14
Texture	0.90	2.63	3.00	3.11
Wrinkles	0.83	2.26	2.50	2.75
Pigment	0.62	2.26	2.54	2.57
Brightness	1.14	2.59	2.89	3.00
Uniformity	0.86	2.41	2.71	2.64
Elasticity	0.55	2.48	2.71	2.93
Overall Appearance	1.03	2.63	2.89	2.93

Table 6: Percent of Subjects with Perceived Improvement

	30 Days	90 Days	120 Days
Texture Improved	74%	89%	89%
Wrinkles Improved	48%	57%	75%
Skin is Brighter	74%	82%	86%
Discoloration is Reduced	48%	71%	64%
Pigment is Lighter	52%	68%	64%

Table 6: Percent of Subjects with Perceived Improvement

Looks and Feels Healthier	78%	86%	86%

The rate of change and significance was highest with improvement in texture. Improvement in wrinkles appeared to reach a limit between 3-4 months, while improvement in discoloration was significant at every time interval after the 1-month measurement.

For the subject self-assessment part of the study, improvement from baseline was statistically significant for all measured categories (Table 4, Figure 2). 100% of subject assessments yielded increased satisfaction in 4 or more of the 8 measured categories and 75% of subjects showed improvement in every measured category. The total percent of subjects rating higher satisfaction at day 120 vs. baseline satisfaction scores are shown in Table 5.

When subjects were questioned as to whether they noticed an improvement from baseline, response rates ranged from 64% to 89% by category (Table 6) with 90% of subjects observing improvement in one or more categories and 76% of subjects noting improvement in 3 or more categories.

DISCUSSION

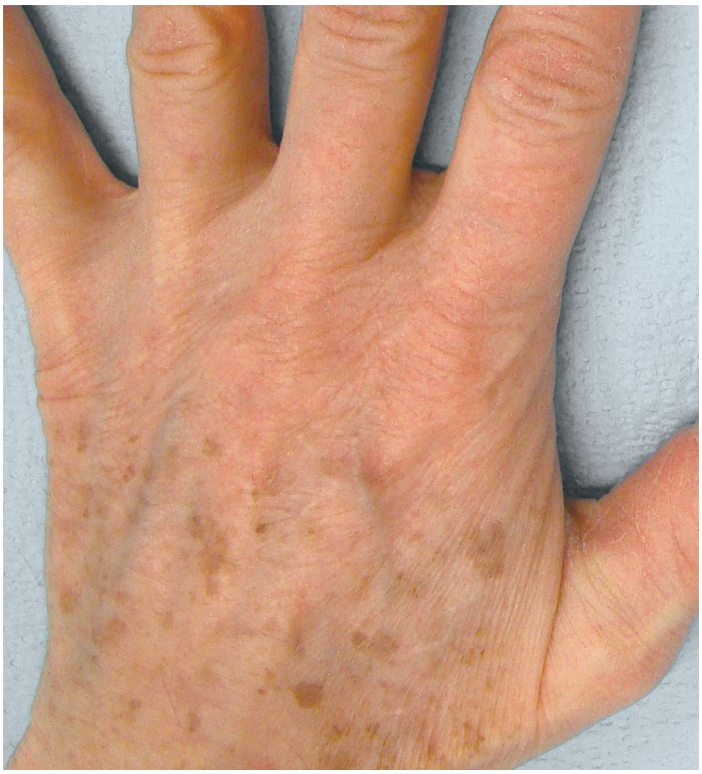
This study was designed to assess a new comprehensive anti-aging hand cream developed to improve skin texture and reduce the appearance of wrinkles and hyperpigmentation.

The product under investigation contains significant concentrations of multiple ingredients shown to reduce the visible signs of aging and cumulative sun exposure, including retinol, azelaic acid and multiple independently-proven tyrosinase inhibitors. With use of any concentrated retinoid and lightening ingredients, there is the potential to irritate or sensitize skin. In this study, there were zero cases of stated irritation, and 28 of the 29 subjects completed the study, which is a significant result in itself.

To fully assess the hand cream, two separate assessments were used: assessment by a dermatologist and subject self-assessment. The two methods used for evaluation (physician and self-assessment) are consistent with the real-world and medical aspects that relate to most retail cosmeceutical products, which should deliver not only meaningful results per independent physician assessment, but also produce meaningful results from a consumer self-perception.

The positive results via physician-assessed improvement (in all metrics) including texture, appearance of wrinkles and pigment / discoloration are notable. Furthermore, the continual improvement following a relatively linear progression over the 4-month period of the study could leave room for even more improvement over continued use (Figure 1). Longer term improvement such as pigmentation

PHOTOGRAPHIC EVALUATIONS



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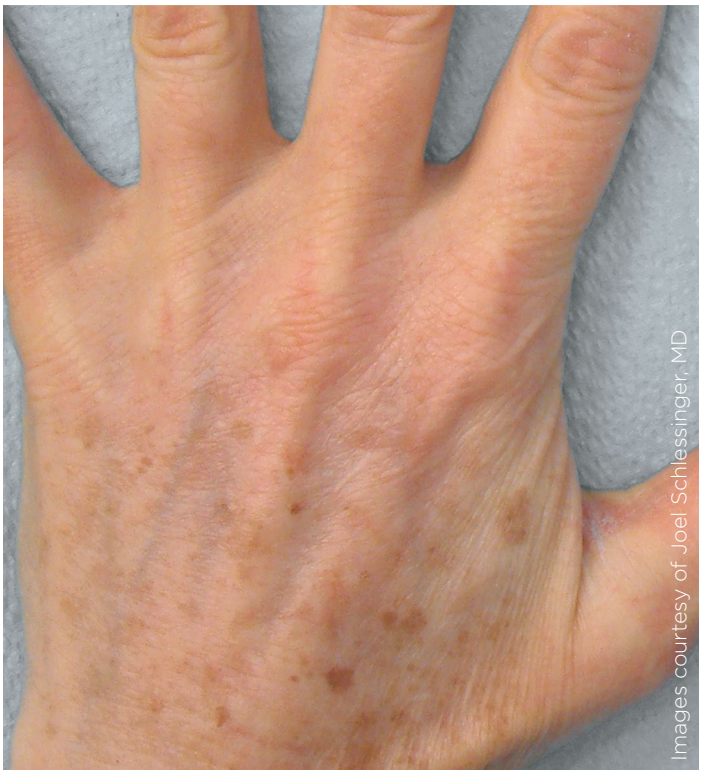
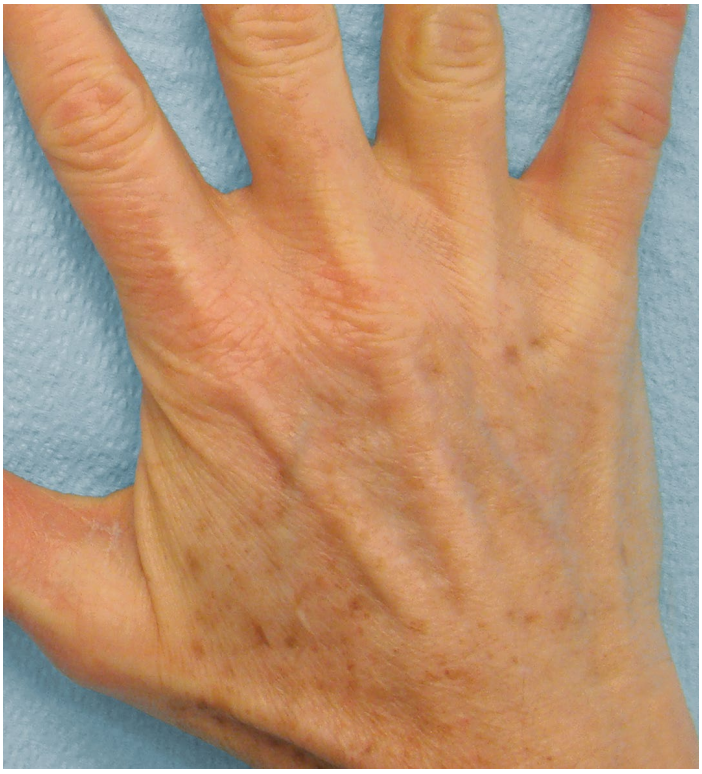


AFTER | 4 MONTHS



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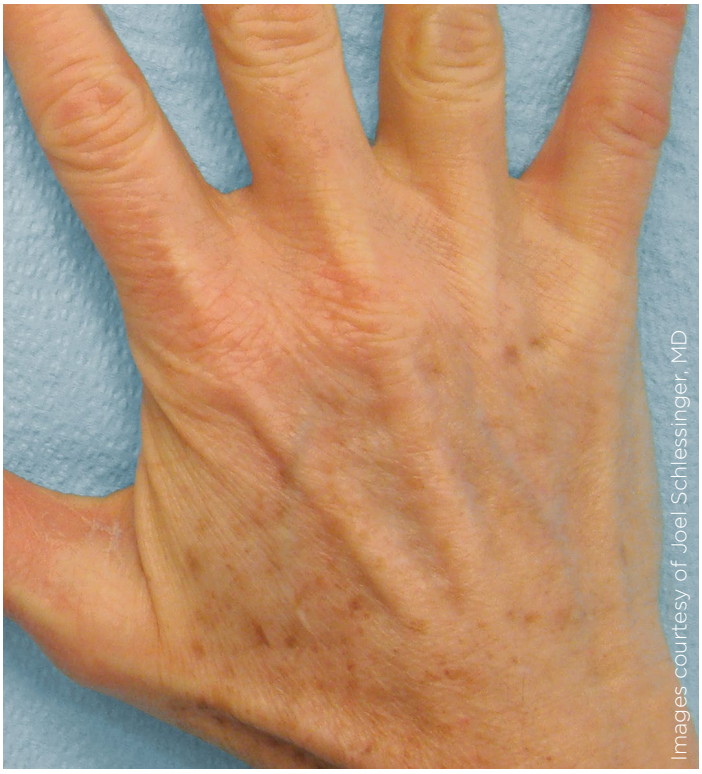

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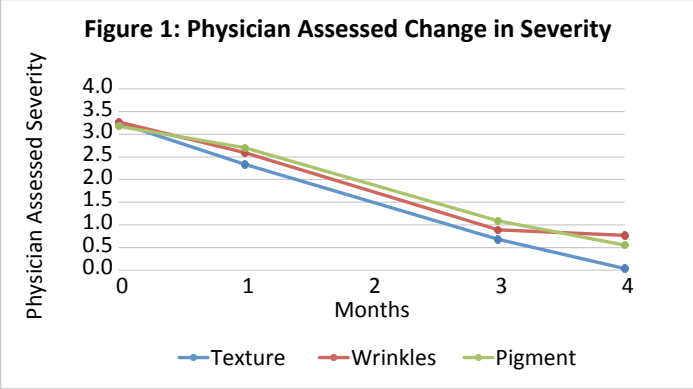

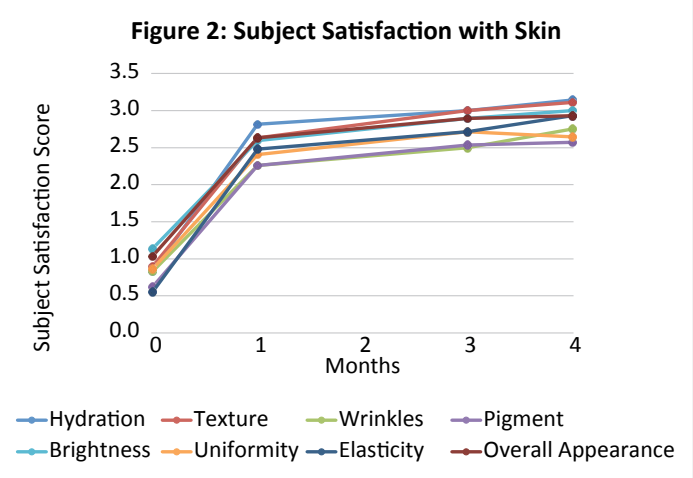

and discoloration was noted at 3 and 4 months, but is consistent with cellular turnover characteristics.

Retinol and azelaic acid help to brighten the skin via exfoliation early on via increased cellular turnover during the first month, while tyrosinase inhibitors take a longer period of time to meaningfully reduce the overall level of discoloration.

The most significant area of improvement noted by physicians was skin texture.

There was a definite improvement based on patient self-assessment. Improvement in self-assessed satisfaction was highly significant in all categories, with an average improvement in satisfaction observed in 7.5 of the 8 measured categories. 100% of subjects reported higher satisfaction in 4 or more measured categories and 75% of subjects reported improvement in all measured categories. This is highly unusual to see in a study setting.

Subject assessment of improvement vs. a recalled baseline varies slightly from actual satisfaction scores, which could relate to the challenge of recalling a baseline (Table 7). Additionally, subtle changes such as depth of a wrinkle, are somewhat more difficult for a non-medical professional to assess over time without pictures or guides, which were not part of the design of this study.

Subject self-assessed satisfaction scores showed a much more rapid response, with significantly higher assessed changes at 30 days than observed by physician assessment, which is also interesting. This could be due to certain innate clues that aren't obvious to the physician observer. By 120 days, however, both subject satisfaction assessments and physician assessed scores showed a high degree of correlation.

Table 7: Increased Satisfaction vs. Perceived Improvement

	Increased Satisfaction Score	Perceived Improvement from Baseline
Texture	96%	89%
Wrinkles	93%	75%
Pigment	93%	64%
Brightness	93%	86%
Overall Appearance	96%	86%

CONCLUSION

The Marini ReNu Corrective Hand Complex was judged highly effective by both physician assessment and subject self-assessment in reducing the visible signs of UV damage and aging, including loss of texture, wrinkles, pigmentation and loss of elasticity. Results were observed rapidly by both subjects and physicians, with statistically significant improvement noted at the very first follow-up visit after only 30 days of use.

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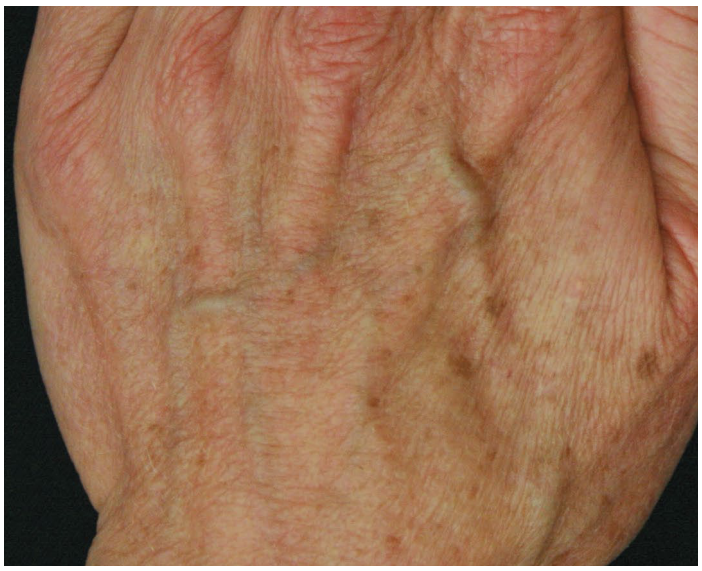
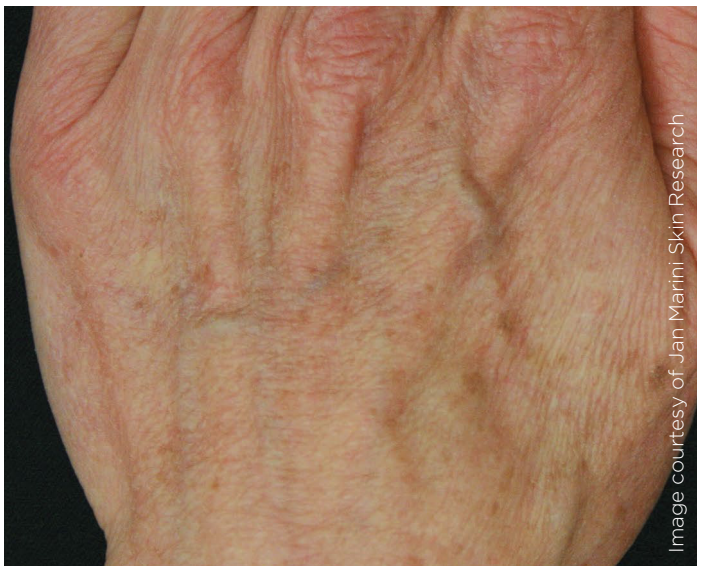
DO YOUR HANDS SHOW YOUR AGE?

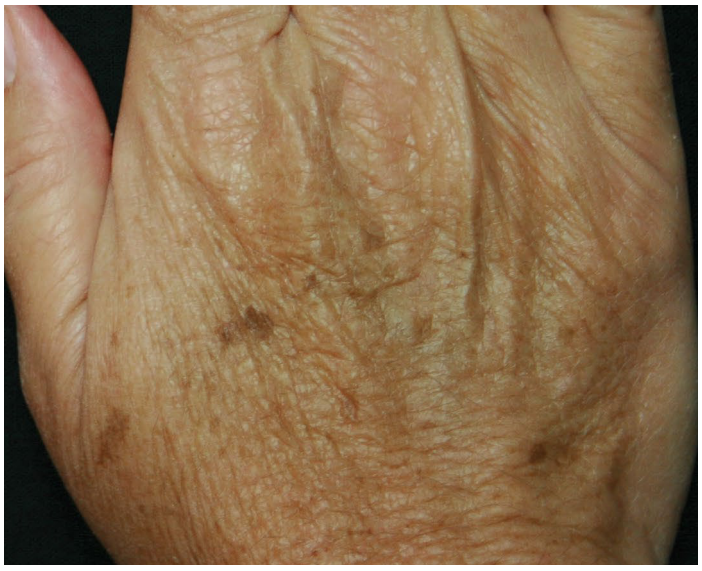


BASELINE

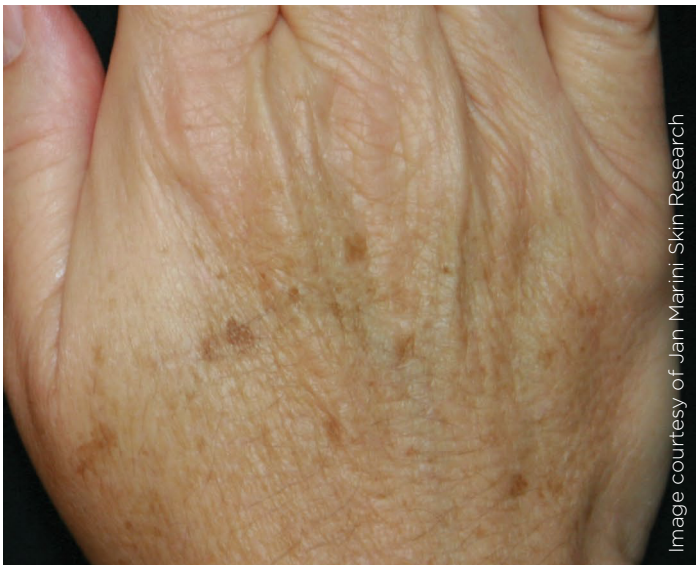


4 MONTHS

Product Used: Marini ReNu Corrective Hand Complex



BASELINE



2 MONTHS

Products Used: Marini ReNu Corrective Hand Complex with a 40% glycolic peel and Retinol Plus Mask.

Marini ReNu Corrective Hand Complex

Marini ReNu Corrective Hand Complex is an exciting new patent-pending, multi-functional solution shown to brighten overall skin tone and decrease the appearance of wrinkles, uneven texture, and discoloration on the hands!

Jan MARINI SKIN RESEARCH®

Marini Peel System Case Study

by Brian Biesman, MD & Tammy Holton, RN | Nashville, TN

STUDY INTENT: This prospective study evaluates the efficacy of the Marini Peel System in conjunction with an integrated homecare solution on improving the visible signs of photo-aging, including hyperpigmentation, fine lines and wrinkles, texture and overall skin quality.

STUDY POPULATION: 11 subjects ages 28-73 with moderate photo-aging and hyperpigmentation

PRODUCTS USED: Marini Peel System: Transform Peel, Marini BioShield Rapid Recovery Complex, Skin Care Management System™ and Age Intervention® Retinol Plus by Jan Marini Skin Research.

STUDY DESIGN: This was a 15 week study with photographic assessment at baseline and 1 month post final peel. Three peels were performed on a 4-week interval starting on week 3. Homecare products were integrated at baseline, 3 weeks prior to the first peel, and used for the duration of the study. The study concluded on week 15, 4 weeks after the final peel. Homecare products were suspended the day of treatment and reintegrated 3-7 days post-peel, as tolerated. Marini BioShield and included sunscreen were used exclusively during the immediate recovery period.

OBSERVATIONS: All of the subjects attained improvement in the visible signs of photo-aging as determined by visual assessment of standardized photography by study investigators (see photographs). In addition, all subjects indicated they were highly satisfied with the results. The products were well tolerated by study subjects with no reported acclimation issues or adverse events.

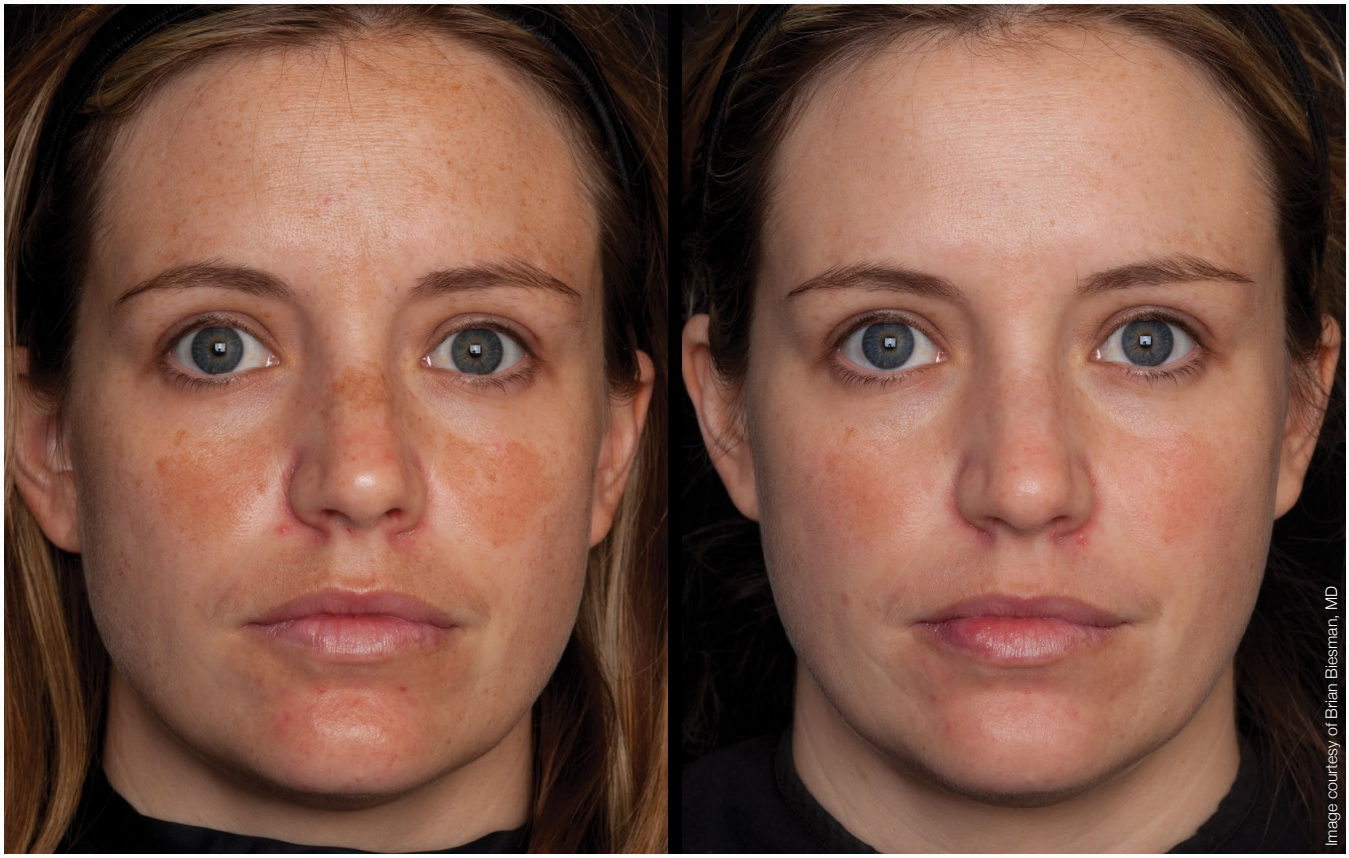


Image courtesy of Brian Biesman, MD

Uncover Your Skin's Full Potential

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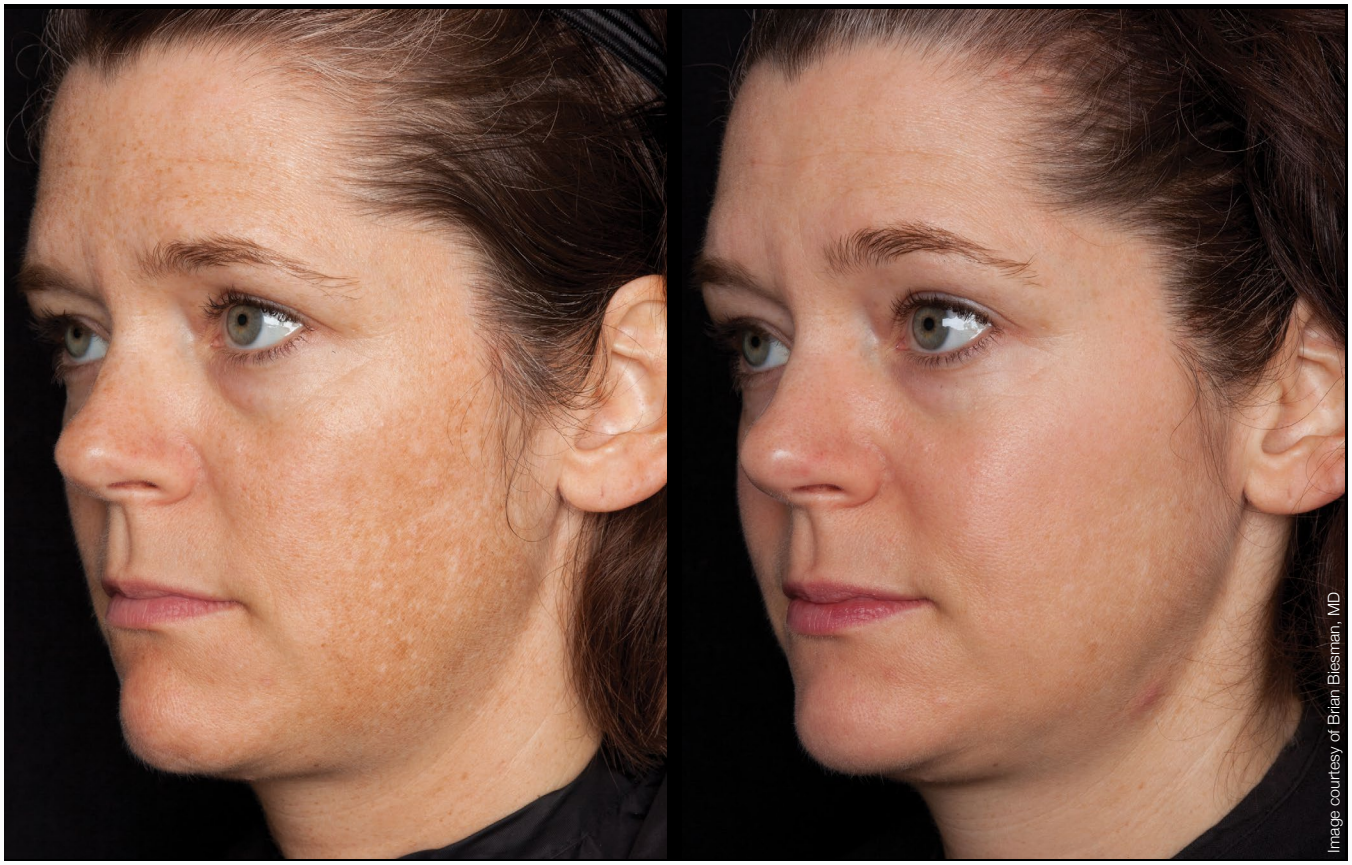


Maximize and control results with Jan Marini Skin Research’s professional peels, homecare and post-procedure solutions

MARINI PEEL SYSTEM | PEEL:

This advanced two-step peel includes all you need for dramatic results. A multi-acid combination exfoliates the skin. A second, leave on, 1% retinol activator peel with anti-aging peptides and antioxidants enhances results and kick-starts the healing process. Available in three formulations for optimal results on varying skin types and concerns.

MARINI BIOSHIELD | POST-PROCEDURE CARE:

Give your patients superior results with reduced downtime. Immediately post-procedure, soothe the skin and create an environment for optimal recovery. This silicone based post-procedure complex combines TGF Beta 1, Epidermal Growth Factor and Keratinocyte Growth factor with multiple anti-aging and anti-inflammatory peptides for optimal results and recovery.

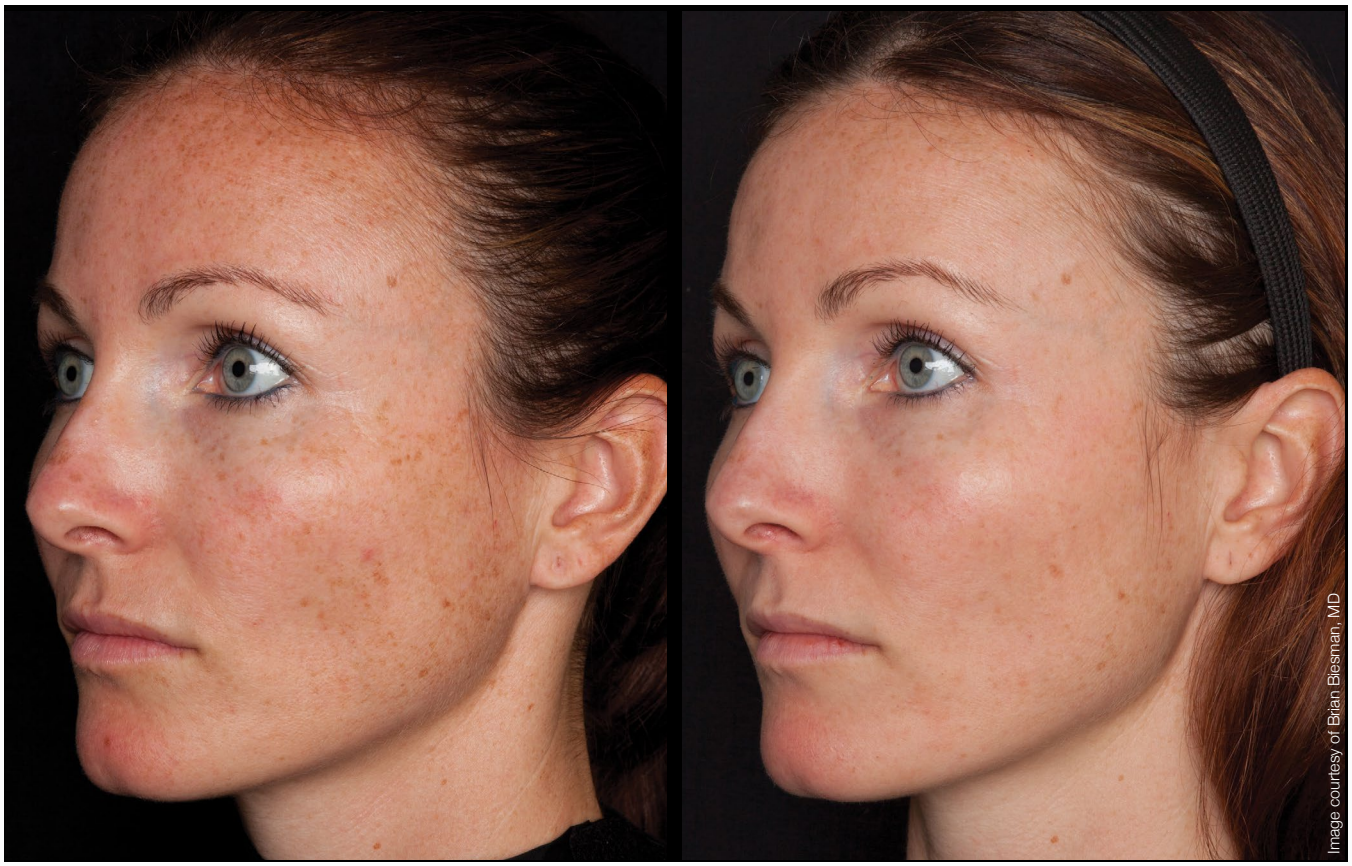
SKIN CARE MANAGEMENT SYSTEM™:

Maximize results and control homecare variables with this award-winning skincare system. The System includes a cleanser, vitamin C, combination exfoliator, advanced hydrator with growth factors and peptides, and a broad spectrum SPF. Great for pre-treating the skin and maximizing results following any office procedure.

AGE INTERVENTION® RETINOL PLUS:

Amplify your results with targeted retinol accelerators. Age Intervention® Retinol Plus combines highly concentrated retinol with multiple anti-aging peptides for maximum anti-aging benefits. Anti-inflammatory agents, antioxidants and hydrators simultaneously soothe the skin for superior wear. Great for pre-treating the skin and maximizing results following any anti-aging procedure.

Dramatic results from the first peel.



INVESTIGATOR TESTIMONIALS

"The peels and skincare were easy to administer and well tolerated by patients, compliance with the protocol and homecare solutions was very high and the results attained for individuals with sun-damage and photo-aging undeniably speak for themselves. As is true with any treatment, patient selection, clinical technique and subject compliance are fundamental to success."

– Brian Biesman, MD

"The peel is very consistent with excellent results. My patients are thrilled with the dramatic changes visible after just one peel. I am amazed at the improvement achieved with this protocol in discoloration, texture and wrinkles. This is a great stand-alone solution or adjunct to lasers and other procedures. I have worked with many similar downtime peels and have never seen results that compare with the Marini Peel System."

– Tammy Holton, RN

PATIENT TESTIMONIALS

"My skin looks the best it's ever been!! How exciting! And I had two people at church last week tell me that my skin looked amazing. Even my son commented that my skin looked really good. You have me hooked and I am Jan Marini's biggest fan! I'm planning on getting the second peel in the next week or so."

– Jodie Richfield, professional clinical study photographer (After 1 Peel)

"I'd never had any kind of peel before and only a few facials in my life before the chemical peel study. Finally, I have skin like I've always wanted, skin I thought you had to be born with! I get compliments all the time and I feel more satisfied with how I look with or without make-up."

– Study Subject

"I had never had a peel before so I did not know what to expect. It was much easier than I thought. I thought my skin was in fairly good shape. Yes, I had a few brown spots but I didn't think they were that noticeable. I was astounded at how much better my skin looked. The Jan Marini products prepared my face for the peel and the peel produced results far above what I could imagine. My friends at work still tell me how beautiful my complexion looks."

– Study Subject

Images courtesy of Brian Biesman, MD. Clinical Study Photographs by Jodie Richfield Photography

FINANCIAL OPPORTUNITY:
Based on Transform Peel

DON'T LEAVE RESULTS TO CHANCE!
Enhance results and control recovery following any procedure with professional homecare solutions from Jan Marini Skin Research.

RECOMMENDED PROMOTION:
"Buy a complete package and save $300! Package includes 3 peels plus our recommended homecare solution for maximum results."
> Package promotions increase revenue, results and satisfaction by rewarding adoption of the full solution for best results.

PROMOTION / PAYMENT IDEA:
Increase package buy-in with payment options! Book all three peels but only charge for the initial peel and skincare. Give the consumer 2 coupons for $150 off each of the future peels. Set the coupons to expire after 6 months to ensure the peels are completed in a reasonable time.

REVENUE:
> 3 Transform Peels: $750
> Home Care Solution: $375
> Post Procedure Recovery: $130
> Total Value: $1330
> Consumer Promotion: ($300 savings)
= Revenue Per Package: $1030

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