
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, electrodesiccation and photodynamic therapy (PDT). Options range from treating individual lesions to more comprehensive

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 shown 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).

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.

		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						

	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

	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%

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



BEFORE



AFTER | 4 MONTHS

Images courtesy of Joel Schlessinger, MD

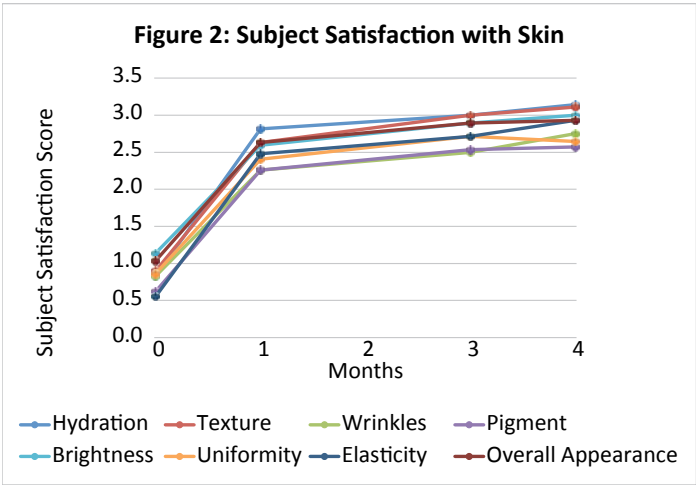
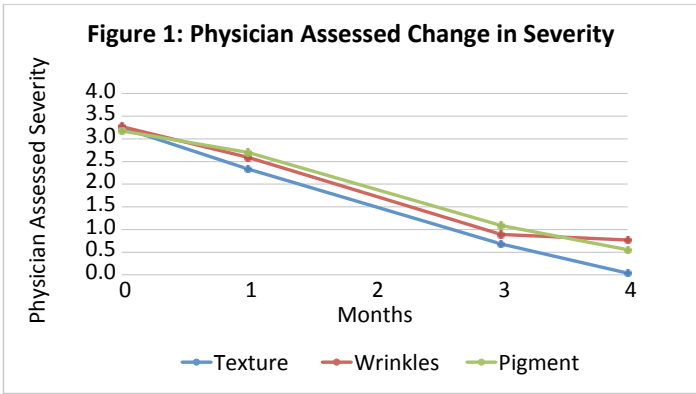


BEFORE



AFTER | 4 MONTHS

Images courtesy of Joel Schlessinger, MD



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

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

days, however, both subject satisfaction assessments and physician assessed scores showed a high degree of correlation.

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.

REFERENCES

- ¹ Fisher GJ, Kang S, Varani J, et al. Mechanisms of photoaging and chronological skin aging. Arch. Dermatol. 2002 Nov. 138(11) 1462-70.
- ² Kligman AM. Early Destructive Effect of Sunlight on Human Skin. JAMA. 1969; 210(13):2377-2380.
- ³ Shamban AT. Combination Hand Rejuvenation Procedures. Aesthetic Surg. J. 2009; Sept-Oct; 29(5) 409-413.
- ⁴ Stefanaki C SAKA. Topical retinoids in the treatment of photoaging. J Cosmet Dermatol. 2005; June; 4(2).
- ⁵ Griffiths CEM, Russman AN, Majmudar G, et al. Restoration of Collagen Formation in Photodamaged Human Skin by Tretinoin (Retinoic Acid). New England J. of Med. 1993; August 530-535.
- ⁶ Kligman LH GE. Re-emergence of topical retinol in dermatology. J. of Dermatological Treatment. 2000: p. 47-52.
- ⁷ Babcock M, Mehta RC, et al. A Randomized, Double-blind, Split Face Study Comparing the Efficacy and Tolerability of Three Retinol-based Products vs. Three Tretinoin-based Products in Subjects with Moderate to Severe Facial Photodamage. J. of Drugs in Derm. 2015; (1)14 24-30.
- ⁸ Zhu W, Gao J. The use of Botanical Extracts as Topical Skin-Lightening Agents for the Improvement of Skin Pigmentation Disorders. Journal of Investigative Dermatology Symposium Proceedings. 2008; 13: 20-28.
- ⁹ Sugimoto K, Nishimura T, Nomura K, et. al. Syntheses of Arbutin-a-glycosides and a Comparison of Their Inhibitory Effects with Those of a-Arbutin and Arbutin on Human Tyrosinase. Chem. Pharm. Bull. 2003; 51.7: 798-801.
- ¹⁰ Nerya O, Vaya J, Musa R, et.al Glabrene and isoliquiritigenin as tyrosinase inhibitors from licorice roots. J. Agric. Food Chem. 2003; 51(5) 1201-7.
- ¹¹ Halder RM, Richards GM. Topical agents used in the management of hyperpigmentation. Skin Therapy Lett. 2004; June 9(6): 1-3.

DO YOUR HANDS SHOW YOUR AGE?



BASELINE



4 MONTHS

Image courtesy of Jan Marini Skin Research

Product Used: Marini ReNu Corrective Hand Complex



BASELINE



2 MONTHS

Image courtesy of Jan Marini Skin Research

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®