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

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## 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.<sup>1</sup>

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<sup>2</sup> 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**

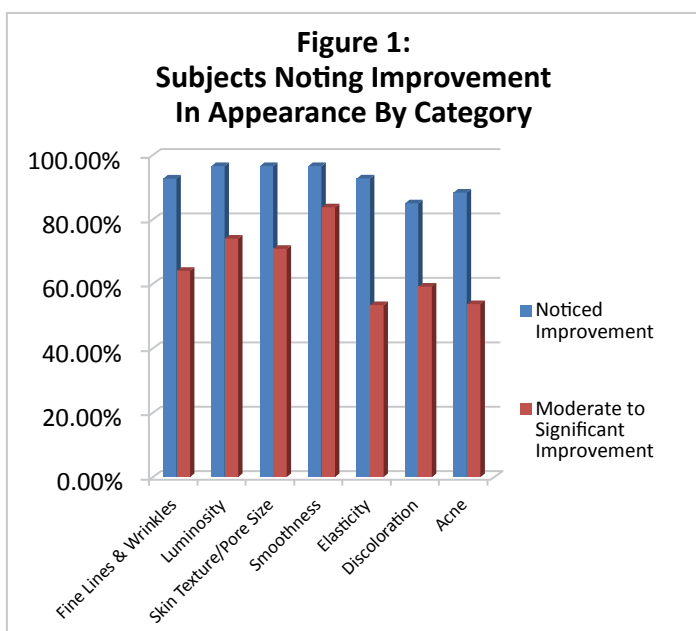
Age:	25-29	30-39	40-49	50-59	60+
Quantity:	4	5	12	8	3

**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	
<b>Total Subject Enrollment</b>		16	11	5	32	
<b>Fine Lines &amp; Wrinkles</b>	28	93%	100%	80%	92.9%	64.3%
<b>Luminosity</b>	30	100%	100%	80%	96.8%	74.2%
<b>Skin Texture/ Pore Size</b>	30	100%	100%	80%	96.8%	74.2%
<b>Smoothness</b>	30	100%	100%	80%	96.8%	83.9%
<b>Elasticity</b>	28	93%	100%	80%	92.9%	53.6%
<b>Discoloration</b>	27	75%	100%	80%	85.2%	59.3%
<b>Acne</b>	26	83%	100%	80%	88.5%	53.8%



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

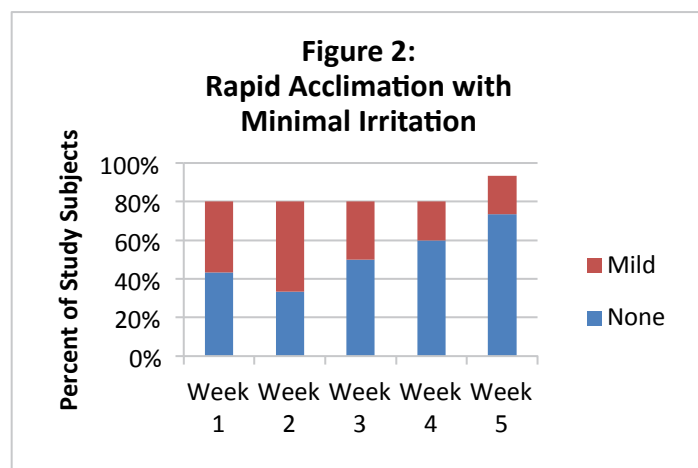
Subject satisfaction was high with 97% of subjects noticing overall improvement in skin and 84% of subjects stating they would purchase and/or recommend the tested product to a family member or friend.

## 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,

increase dermal thickness and reduce inflammation, abnormal pigmentation and diffuse redness.<sup>3,4,5</sup>

Table 4: Subject Experience vs. Other Anti-aging and Retinoid Product				
	"n"	Inferior	Equal	Superior
<b>Retinol Products (Non-Prescription)</b>	24	4.2%	8.3%	87.5%
<b>Prescription Retinoid</b>	23	4.3%	26.1%	69.6%
<b>Anti-Aging Products</b>	28	7.1%	14.3%	78.5%
<b>Acclimation vs. Prescription Retinoid</b>	23	13.0%	4.3%	82.6%



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,<sup>6</sup> 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



**BEFORE**



**AFTER | 1 MONTH**



**AFTER | 3 MONTHS**

Images courtesy of Jan Marini Skin Research



**BEFORE**



**AFTER | 3 MONTHS**

Images courtesy of Jan Marini Skin Research

# PHOTOGRAPHIC EVALUATIONS



**BEFORE**



**AFTER | 1 MONTH**

Images courtesy of Jan Marini Skin Research



**BEFORE**



**AFTER | 1 MONTH**



**AFTER | 3 MONTHS**

Images courtesy of Jan Marini Skin Research

acid for multiple indications.<sup>7</sup> 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.<sup>7</sup> 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<sup>8</sup> (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.<sup>9,10</sup>

The proven technologies combined in the tested product - multiple peptides, antioxidants and anti-inflammatories (green tea extract, chrysin, alpha-bisabolol, 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<sup>2</sup> and antioxidants are considered an essential component in helping to prevent many of the visible signs of aging.<sup>11</sup> 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.<sup>12,13,14</sup>

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.<sup>15,16</sup>

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



**BEFORE**



**AFTER | 1 MONTH | VISIBLE LIGHT**



**BEFORE**



**AFTER | 3 MONTHS | UV LIGHT**

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