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High Concentration Retinol (0.3%) Serum Demonstrates Enhanced Bioactivity Without Added Irritation and Provides Clinical Benefits to Hyperpigmentation and Aging Skin in a Diverse Population for Everyday Use

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Introduction

- Retinol is widely used in skincare to treat skin conditions such as acne and to reduce the appearance of wrinkles, fine lines, and stretch marks.[1] However, retinoids can cause irritation and discomfort, thus restricting its use. The objective of this study was to produce a topical cosmetic formulation that provided increased retinoid activity with reduced retinoid irritation

Methods

- A unique cosmetic formulation was created combining a high concentration of retinol (0.3%) with beneficial ingredients of *Centella asiatica* leaf extract (nourishes and soothes), niacinamide (reduces the appearance of dark spots), sodium hyaluronate (provides hydration), and acetyl glucosamine (works synergistically with retinol to visibly fade skin discoloration[2])
- To validate the efficacy and tolerability of the high-strength formulation, gene expression of retinol-mediated beneficial genes was evaluated in a pre-clinical study. Additionally, a 12-week clinical study was conducted using the 0.3% retinol serum on a diverse population (Fitzpatrick Skin Types I-VI) to evaluate improvement in hyperpigmentation and aging parameters

Clinical Photography

- A face serum containing 0.3% retinol, *Centella asiatica* leaf extract, niacinamide, sodium hyaluronate, and acetyl glucosamine was used once daily for 12 weeks in a diverse population. Visible improvement in pigmentation and texture are shown as average to above average examples

Improved pigmentation, crow's feet, and fine lines

Asian, medium skin tone/color, Fitzpatrick Skin Type III

Baseline

Week 12

1. Oddos M et al. 2016. *Composition and Method of Treating Skin Conditions* (US Patent No. 9,387,160 B2). 2. Sayo T et al. *Skin Pharmacol Physiol.* 2004;17(2):77–83.

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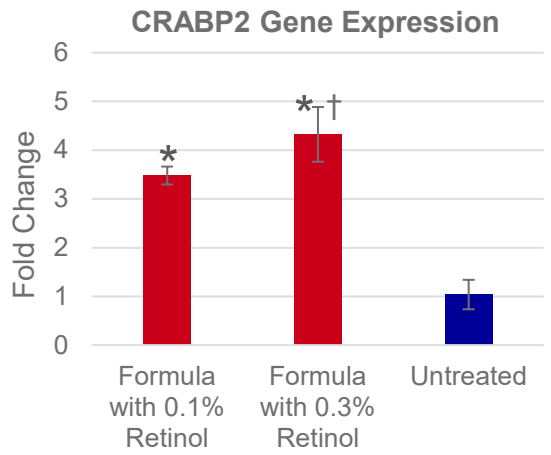
Pre-Clinical Study of Face Serum with 0.3% Retinol, *Centella asiatica*, and Niacinamide Demonstrates an Enhanced Bioactivity Without Added Irritation

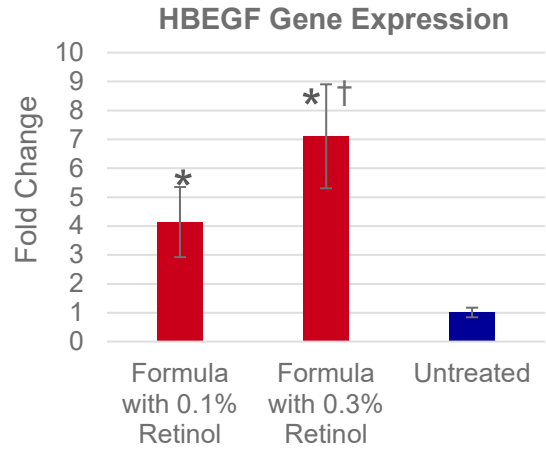
Preclinical Study Methodology

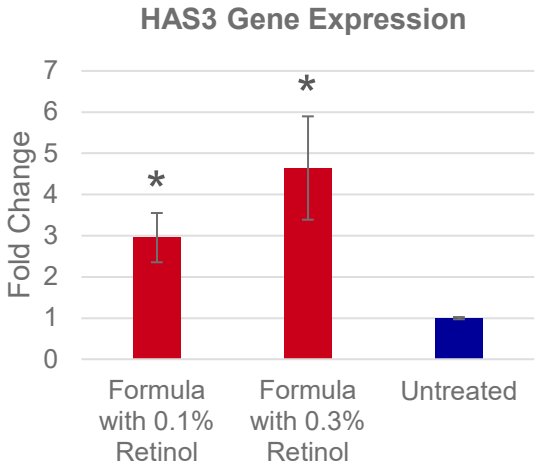
- Design: 48-hour, ex vivo study
- Retinol-mediated anti-aging benefits measured through expression of the following beneficial retinol-mediated genes:
  - CRABP2 (marker for retinol bioactivity)
  - HBEGF (marker for cell proliferation)
  - HAS3 (marker for hyaluronic acid synthesis)
  - IL-8 (marker for irritation)
- Test products were serum formulas containing 0.1% or 0.3% retinol combined with *Centella asiatica* leaf extract, niacinamide, sodium hyaluronate, and acetyl glucosamine
- For each treatment, gene expression fold change were compared to untreated using a *t* test; $p<0.05$. Treatments were also compared with each other using a *t* test; $p<0.05$

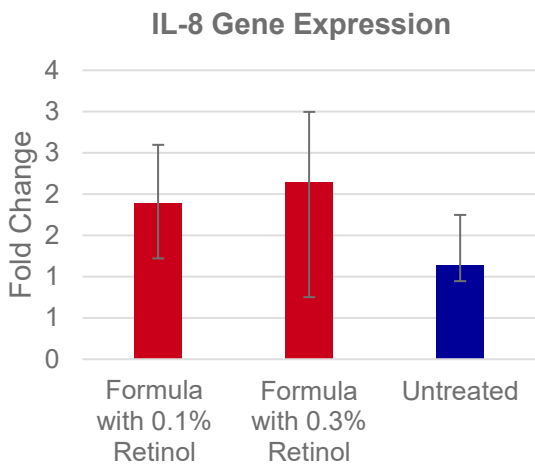
Results

- All treatments showed significant gene expression induction in CRABP2, HBEGF, and HAS3 compared with untreated
- The bioactivities of the retinol-mediated beneficial genes (CRABP2 and HBEGF) were significantly increased for 0.3% retinol vs 0.1% retinol
- No significant increase in irritation, measured by IL-8 gene expression, for the 0.3% retinol vs the 0.1% retinol dosage was observed









* $p<0.05$ vs untreated
† $p<0.05$ vs formula with 0.1% retinol

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Clinical Study of Face Serum with 0.3% Retinol, *Centella asiatica*, and Niacinamide Provides Benefits to Hyperpigmentation and Aging Skin for Everyday Use Across All Skin Tones

Clinical Study Methodology

- Design: 12-week, institutional review board-approved, single-center, prospective clinical study with direct comparison to baseline condition
- Population
  - Women, ages 30-65 years with Fitzpatrick Skin Types I-VI
  - Key inclusion criteria: mild to moderate pigmentation confirmed with a Wood's lamp to be epidermal in nature and mild to moderate fine lines or wrinkles (modified Griffith's scale)
- Test product: face serum containing 0.3% retinol, *Centella asiatica* leaf extract, niacinamide, sodium hyaluronate, and acetyl glucosamine was used once daily; bland day SPF 35 and night moisturizers were provided to standardize the regimen
- Clinical grading for pigmentation, textural attributes, and tolerability were collected as well as self-assessment questionnaires and digital photography
- Clinical grading scores were compared to baseline scores for each subject at each visit using a Wilcoxon signed-rank test; $p<0.05$. Percent change from baseline calculated from mean delta scores are presented. Self-assessment scores were tabulated

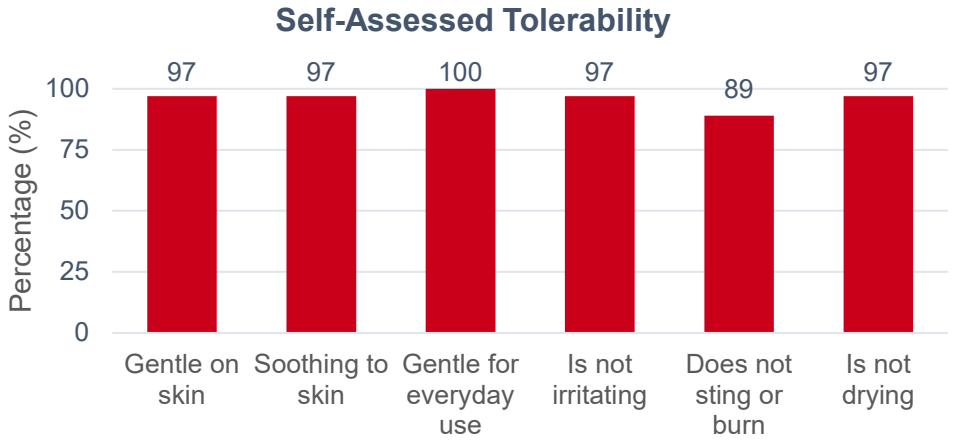
Results

- 40 women with diverse races, ethnicities, and skin tones/color completed
  - Race: 30% Black/African American, 8% Asian, 60% Caucasian, 2% Other
  - Ethnicity: 25% Hispanic/Latino
  - Self-identified skin tones/color:* 25% darker, 43% middle/medium, and 32% lighter

* 6 descriptors from light/white to dark brown or black

Tolerability

- Serum was well tolerated, with less than mild scores on average for edema, erythema, dryness, burning, stinging, itching, tightness
- Three adverse events (possibly/very likely related) for moderate dryness/peeling, burning, itching, and or erythema were reported, and participants discontinued the study



Consumer Perception

- 95% noticed skin instantly feels soft and nourished
- After 12 weeks
  - 97% dark spots fading
  - 97% skin is firmer
  - 97% skin is brighter, more luminous
  - 97% skin tone/color is more even
  - 95% fine lines are improved
  - 95% calms the look of skin

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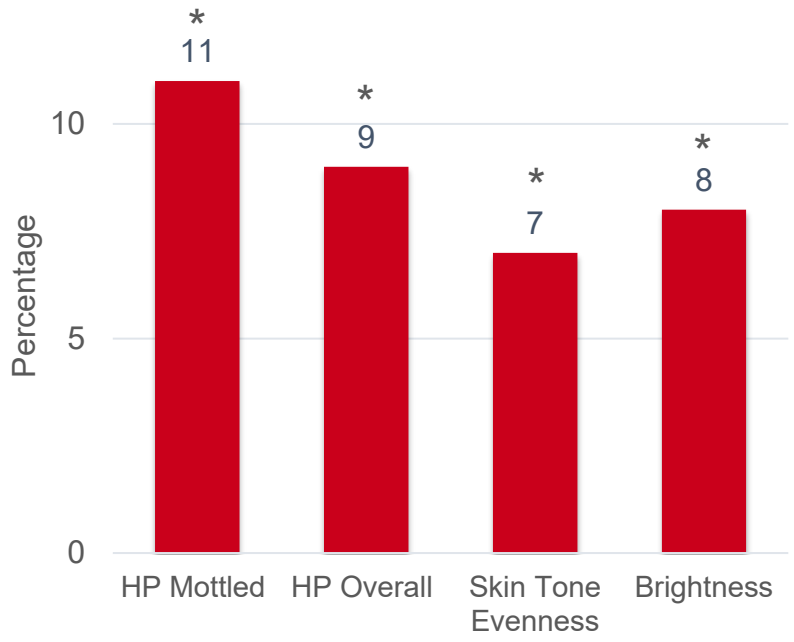
Clinical Grading

- All 13 clinically graded parameters showed significant improvement at Week 12; $p \leq 0.05$
- More than half of the parameters were significantly improved as early as Week 4, with 12 of the 13 parameters significantly improved by Week 8; $p \leq 0.05$

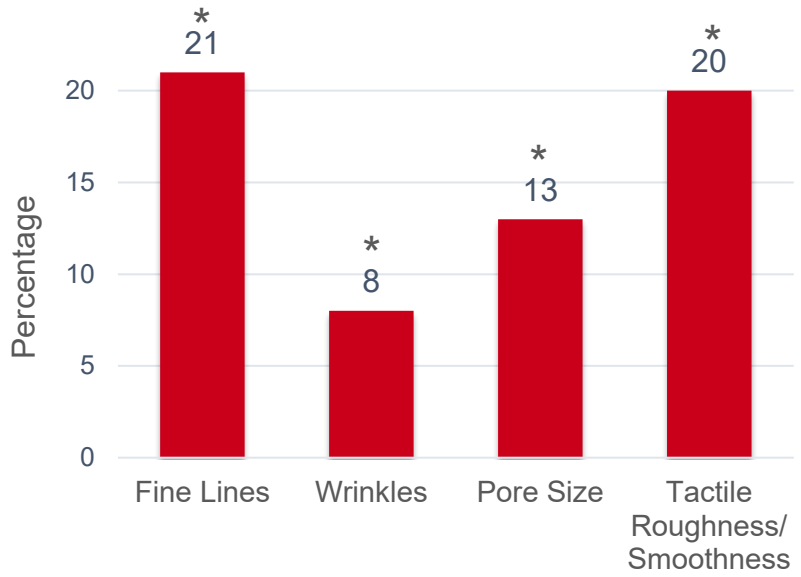
Clinical Improvement in Pigmentation at Week 12



HP, hyperpigmentation

*$p \leq 0.05$

Clinical Improvement in Textural Parameters at Week 12



Clinical Improvement in Additional Anti-Aging Parameters

Parameter	Week 12
Laxity/Lack of firmness	8%*
Global Lift	6%*
Clarity	8%*
Overall photodamage	8%*
Pinch Recoil (elasticity)	7%*

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Clinical Photography

- Obvious improvements to hyperpigmentation along with benefits to brightness and overall tone provide visual support for the clinical and consumer-perceived benefits

Improved pigmentation, brightness, and overall tone

Black/African American, medium skin tone/color, Fitzpatrick Skin Type V

Baseline | Week 12

Improved pigmentation

Caucasian, lighter skin tone/color, Fitzpatrick Skin Type II

Baseline | Week 12

Conclusions

- A holistic formulation was developed with synergistic ingredients[1,2] to **reduce hyperpigmentation**, **even skin tone,** and **reduce textural fine lines**
- The higher-strength 0.3% retinol serum delivered **enhanced bioavailability with a low irritation profile**, providing significantly increased retinol-mediated beneficial gene bioactivity **without increased irritation vs the 0.1% formulation**
- The higher-strength **0.3% retinol formulation with *Centella asiatica* and niacinamide,** formulated to provide **effective pigment-evening and retinol-mediated anti-aging benefits,** delivered clinical and consumer-perceivable benefits **in a diverse population**

1. Sayo T et al. *Skin Pharmacol Physiol.* 2004;17(2):77–83. 2. Green B et al. *J Am Acad Dermatol.* 2007;56(2; Suppl 2):AB19.

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