Use of a High-Strength Serum Containing N-Acetyl Tyrosinamide, the Polyhydroxy Acid Gluconolactone and LMW Hyaluronic Acid Improves Signs of Aging on the Face

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Introduction

Serums are used by consumers for their concentrated ingredients and targeted effects. They provide a desired product form which can be used alone or easily layered under products to boost everyday anti-aging regimens.

A high-strength serum was formulated with 1.25% N-acetyl tyrosinamide, a novel matrix-building amino acid derivative shown to provide firming effects in skin,[1] and 8% gluconolactone, a polyhydroxy acid (PHA) to gently exfoliate and promote an even skin tone.[2] The serum also contains low molecular weight (LMW) hyaluronic acid fragments, a key ingredient in skin known for its ability to retain water and provide hydration.[3]

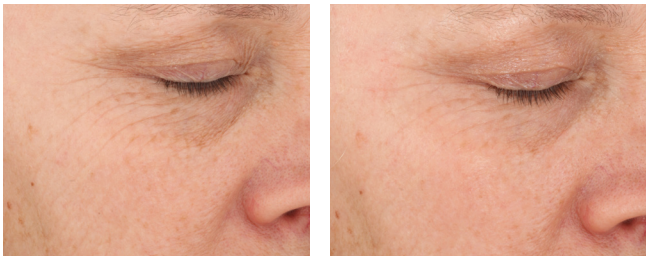
The poster presents a summary of an *in vitro* assessment of the effect of the combination of N-acetyl tyrosinamide and gluconolactone on anti-aging matrix markers as well as a 12-week *in vivo* clinical study to assess effectiveness and tolerability of the serum when used twice daily on an aging population.

Clinical Photography

Figure 1. Smoother Skin in Crow's Feet Area in Fitzpatrick Skin Type IV (Caucasian, Hispanic/Latino)

Week 0 Week 12

Figure 2. Volumizes Skin with Improvement in Under Eye and Cheek Wrinkles in Fitzpatrick Skin Type II (Caucasian)



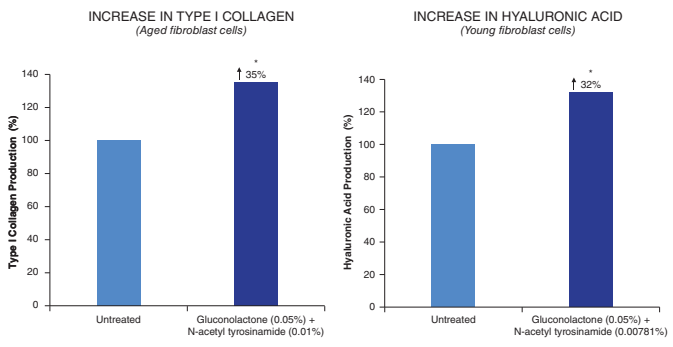
Week 0 Week 12

In vitro study: An *in vitro* assessment of the effect of the combination of N-acetyl tyrosinamide and gluconolactone on anti-aging matrix markers

Human fibroblasts were exposed in cell culture media to the combination of N-acetyl tyrosinamide and gluconolactone in roughly proportional ratios as formulated in the serum to assess changes in type I collagen and hyaluronic acid. Results show the combination of N-acetyl tyrosinamide and gluconolactone increased type I collagen (35%, p=0.01) and hyaluronic acid (32%, p=0.01) in human fibroblast cells. (Figure 3)

Based on these results a 12-week clinical study was conducted to determine the benefits of a serum containing N-acetyl tyrosinamide and gluconolactone *in vivo*.

Figure 3. *In vitro:* Assessments of Anti-Aging Matrix Markers



*Statistically significant increase, p=0.01

In Vivo Study Methodology

Design	• A 12-week, single center, prospective clinical study with direct comparison to baseline condition
Population	***Key Inclusion*** • Women, ages 40-60 years • Fitzpatrick skin type II-IV • Clinically graded moderate global facial lines and wrinkles and/or moderate facial mottled hyperpigmentation (score of 4-6 on modified Griffith's scale) ***Key Exclusion*** • Known allergies to facial skin care products • Routine use of anti-aging topical products, including: – Prescription retinoid or retinol over 0.1% within 6 months; – Hydroxyacids, retinol and another anti-aging cosmetics within 8 weeks; – Cosmetic procedures (e.g. peels, laser treatments, microdermabrasion) within 6 months – Pregnant, nursing, or planning to become pregnant
Evaluations Tools	• Weeks 0, 4, 8 and 12 ***Clinical Measures*** – Visual grading by an expert grader at each visit • Eye area fine lines, eye area wrinkles, cheek wrinkles, mottled and discrete hyperpigmentation, clarity/brightness, visual and tactile firmness, evenness of skin tone/redness, visual skin smoothness, tactile roughness, and pore size (modified Griffith's scale: 0 (none) to 9 (severe) with half point increments) • Irritation/tolerability including dryness, erythema, burning, stinging, itching, tightness (0 (none) - 3 (severe) scale) • Pinch recoil as a measure of firmness/elasticity. Skin in the right sub-orbital area was pinched, held for approximately 2 seconds, released, and the time to return to original conformation was recorded to the nearest hundredth of a second. Measurements were taken in triplicate. ***Subjective Measures*** – Self-Assessment questionnaires were completed by subjects • Self-assessed subject grading scores were captured via questionnaire for the signs of aging using a 7-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe with half point increments) at baseline and weeks 4, 8, and 12 • Subjects also assessed product aesthetics and perceived benefits to skin at weeks 4, 8 and/or 12 ***Digital photography*** at weeks 0 & 12 ***Safety*** – Adverse events were recorded and tabulated
Statistics	• Clinical grading scores were compared to baseline condition for each subject at each visit using Wilcoxon signed-rank test ($p<0.05$). Percent change from baseline calculated from mean delta scores are presented.

Test Products

The Serum was applied twice daily to the entire face. A bland moisturizer SPF 35 was provided for facial use, up to twice daily, to provide sun protection.

Serum *(NeoStrata® Tri-Therapy Lifting Serum)*

- 1.25% N-acetyl tyrosinamide, a patented amino acid compound to target hyaluronic acid and collagen, to help volumize and firm skin
- 8% PHA, Gluconolactone to help build skin barrier function, gently exfoliate, provide antioxidant/chelating properties and help even skin tone/coloration
- LMW Hyaluronic Acid, penetrates skin's surface to attract moisture, providing hydration to visibly improve skin texture

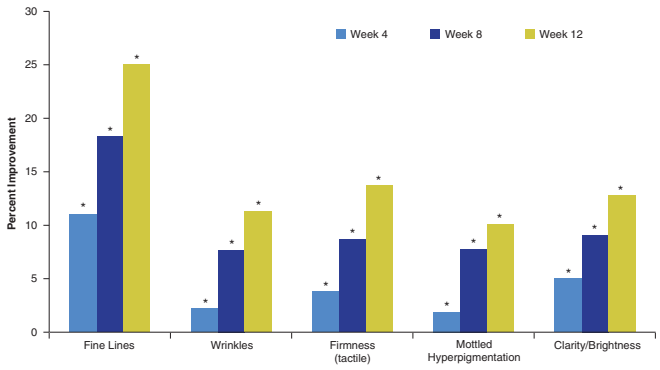
Results

Thirty-eight women completed the study.

Clinical Grading

- All clinically graded parameters were significantly improved from baseline at weeks 8 & 12, $p<0.05$ (Figure 4 and Table 1)
- Most parameters were significantly improved by Week 4 including fine lines, wrinkles, mottled pigmentation, clarity/brightness, visual and tactile firmness, lack of blotchiness, skin smoothness and tactile roughness, $p<0.05$ (Table 1)
- Pinch recoil (firmness/elasticity) was significantly improved at all visits, $p<0.05$

Figure 4. Improvement to Firmness, More Even Tone, and Skin Smoothness



*Statistically significant improvement, $p<0.05$

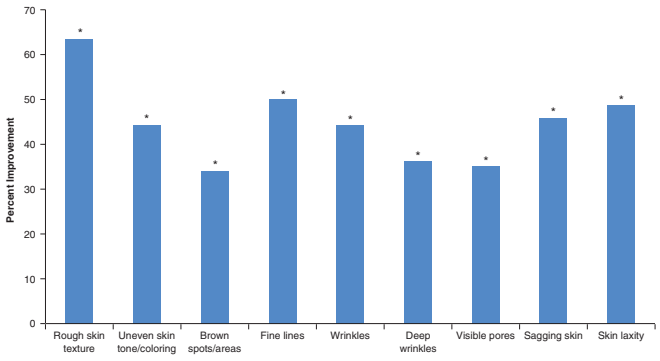
Table 1. Timepoints Achieving Significant Improvement for all Anti-Aging parameters

Parameter	Week 4	Week 8	Week 12
Fine Lines	✓	✓	✓
Wrinkles	✓	✓	✓
Cheek Wrinkles		✓	✓
Mottled Pigmentation	✓	✓	✓
Discrete Pigmentation		✓	✓
Clarity/brightness	✓	✓	✓
Visual Firmness	✓	✓	✓
Tactile Firmness	✓	✓	✓
Lack of blotchiness	✓	✓	✓
Skin smoothness	✓	✓	✓
Tactile roughness	✓	✓	✓
Pore Size		✓	✓

Self-Assessment

- Self-assessment supports clinical grading showing improvements in fine lines, wrinkles, skin tone, skin texture, sagging skin and skin laxity at Week 12 (Figure 5 and Table 2)

Figure 5. Self-Assessed Subject Grading of the Signs of Aging –Percent Improvement from Baseline Condition at Week 12



*Statistically significant improvement, $p<0.05$

Table 2. Mean Scores for Self-Assessed Subject Grading

Visit	Week 0	Week 12
Rough skin texture	1.3	0.5
Uneven skin tone/coloring	1.8	1.0
Brown spots/areas	1.7	1.1
Fine lines	2.0	1.0
Wrinkles	2.0	1.1
Deep wrinkles	1.7	1.1
Visible pores	1.4	0.9
Sagging skin	1.6	0.9
Skin laxity	1.6	0.8

Grading Scale: 0 = none, 1 = mild, 2 = moderate, 3 = severe with half point increments

- In addition, a high percentage of subjects noticed improvement in their skin after 12 weeks including fine lines diminished (95%), wrinkles diminished (92%), firmness increased (100%), skin is plumper and volumized (97%), skin brighter/more luminous (100%) and skin tone is more even (92%)
- The aesthetics of the serum were positive with subjects noticing absorbs easily (97%) and feels lightweight (100%)

Tolerability

- **The serum was well tolerated with less than mild irritation reported on average**
  - Mean objective and subjective tolerability evaluations were on average less than mild in severity at baseline and throughout the study
  - Five subjects reported product related adverse events of mild to moderate irritation; of those, four subjects completed the study and one subject discontinued

Clinical Photography

- Benefits to skin volume, more even tone and smoother skin are shown in Figures 1 - 2 and 6 - 7

Figure 6. Improvement in Eye Area Smoothness and Clarity in Fitzpatrick Skin Type II (Caucasian)

Week 0 | Week 12

Figure 7. Renews Tone for a More Even Appearance in Fitzpatrick Skin Type II (Caucasian)

Week 0 | Week 12

Conclusions

- The combination of **N-acetyl tryrosinamide and gluconolactone** contained in the serum demonstrated **increases in collagen and hyaluronic acid *in vitro***
- **The high-strength serum provided clinical benefits to skin volume, more even tone and skin smoothness**
  - Significant improvements to all clinically graded parameters, $p<0.05$
  - Significant improvements in firmness/elasticity via pinch recoil, $p<0.05$
  - Self-Assessment and clinical photography support the clinical grading
- **The serum was well tolerated** with less than mild irritation reported on average
- The serum provides **clinically proven and consumer perceivable benefits to firming, skin smoothing and evening of skin tone** with a **triple anti-aging complex of N-acetyl tyrosinamide, PHA, and LMW hyaluronic acid**

References

1. Farris PK, Edison BL, Weinkauf RL, and Green BA. A Novel, Volumizing Cosmetic Formulation Significantly Improves the Appearance of Target Glabellar Lines, Nasolabial Folds, and Crow's Feet in a Double–blind, Vehicle Controlled Clinical Trial. *J Drugs Dermatol.* 2014;13(1):41-46.
2. Green BA, Sabherwal Y. Antiaging benefit ingredients: AHAs, PHAs, and Bionic Acids in Draelos ZD, ed. *Cosmeceuticals*. 3rd ed. London: Elsevier; 2016:99-116.
3. Papakonstantinou E, Roth M, Karakiulakis G. Hyaluronic acid: A key molecule in skin aging. *Dermatoendocrinol*. 2012;4(3):253-258.

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