**Introduction**

Pigmentation irregularities are a major concern for many ethnic skin populations spanning the globe. 1,2 Safe, effective, and aesthetically pleasing formulations that can even skin color, brighten skin tone, and reduce dark spots are requested by dermatology patients around the world. A new brightening skincare regimen was developed to improve the complexion of facial skin by targeting multiple steps and pathways that affect pigmentation. The regimen consists of a facial cleanser, serum, and lotion, which contain niacinamide plus a variety of other benefit ingredients to collectively whiten pigmented areas, reduce tyrosinase activity and melanin production, and deliver an overall pigmentation evening effect.

**Objective**

To evaluate the tolerability and lightening/brightening benefits of a high-strength twice-daily skincare regimen in normally pigmented and hyperpigmented skin in an ethnically diverse population of women with uneven facial pigmentation.

**Study Design**

Single-group, prospective skincare regimen use study with direct comparisons to baseline

**Population / Inclusion Criteria**

Women, 30–60 years old. Fitzpatrick skin type IV at enrollment, with areas of irregular hyperpigmentation on the face (confirmed by Wood’s Lamp), willing to limit sun exposure and not change procedures or routine use of antiaging or skin brightening topical medications.

**Exclusion Criteria**

- Procedures or routine use of antiaging or skin brightening topical medications, including prescription retinoids, vitamin A, retinol, hydroquinone, kojic acid, hydroxyacids, or other antiaging or lightening/brightening cosmetics within last 2 months; cosmetic procedures or serious use of bleaching or skin brightening topical medications, including prescription bleaching bleaching, vitamin A, retinol, hydroquinone, kojic acid, hydroxyacids, or other bleaching or skin brightening topical medications.
- Use of hydroquinone, kojic acid, hydroxyacids, or other bleaching or skin brightening topical medications.
- Allergies to skincare product ingredients.
- Use of hydroxyacids, retinol, hydroquinone, kojic acid, hydroxyacids, or other bleaching or skin brightening topical medications.
- Pregnancy or lactation.
- Use of bleaching or skin brightening topical medications.
- Diabetes mellitus.
- Acne vulgaris.
- Severe skin conditions that might interfere with the skin’s barrier function.
- Known photosensitivity.
- History of malignancy.
- Use of any other investigational drugs or devices.
- Use of color-correcting cosmetics.
- Use of any other investigational devices.
- Use of any other investigational drugs.
- Use of any other investigational devices.
- Use of any other investigational drugs or devices.

**Study Methods**

- **Study Initiation:** February 2010, completion: July 2010.
- **Study Design:** Single-group, prospective skincare regimen use study with direct comparisons to baseline.
- **Population / Inclusion Criteria:** Women, 30–60 years old. Fitzpatrick skin type IV at enrollment, with areas of irregular hyperpigmentation on the face (confirmed by Wood’s Lamp), willing to limit sun exposure and not change procedures or routine use of antiaging or skin brightening topical medications.
- **Exclusion Criteria:** Procedures or routine use of antiaging or skin brightening topical medications, including prescription retinoids, vitamin A, retinol, hydroquinone, kojic acid, hydroxyacids, or other antiaging or lightening/brightening cosmetics within last 2 months; cosmetic procedures or serious use of bleaching or skin brightening topical medications, including prescription bleaching bleaching, vitamin A, retinol, hydroquinone, kojic acid, hydroxyacids, or other bleaching or skin brightening topical medications.
- **Study Endpoints:** Week 0, 4, 8, 12, and 16.
- **Study Duration:** 16 weeks.
- **Study Regimen:** Twice a day use of the cleanser, serum, and lotion on the entire face (Fig. 1).

**Results**

**Subject Demographics**

- **Subjects:** 60
- **Gender:** Female
- **Age, mean (range):** 50 (27–65)
- **Race/Ethnicity, n (%):**
  - Latin American: 14 (47%)
  - African American: 2 (7%)
  - Asian/Pacific Islander: 3 (10%)
  - Indian: 1 (3%)
  - Other: 6 (20%)

**Study Products**

- **Cleaner (NeoStrata® Enlighten Ultra Brightening Cleanser):** 4% N-Acetylglucosamine (NeoGlucosamine®), Swiss alpine plant extracts (GigaWhite®).
- **Serum (NeoStrata® Enlighten Illuminating Serum):** 4% N-Acetylglucosamine (NeoGlucosamine®), Swiss alpine plant extracts (GigaWhite®), Tetrahexyldecyl Ascorbate (Vitamin C), Oligopeptide-34, Swiss alpine plant extracts (GigaWhite®).
- **Lotions (NeoStrata® Enlighten Brightening Lotion):** 4% N-Acetylglucosamine (NeoGlucosamine®), Swiss alpine plant extracts (GigaWhite®), 1% Retinoic Acid, Tetrahexyldecyl Ascorbate (Vitamin C), Tetrahydroxyaloe butter (aloe vera analogue found naturally in aloe vera, SabiWhite®).

**Subject Self-Assessment**

- **Subjects reported brighter overall skin tone during regimen use:** >60% of subjects noticed an improvement as early as 2 weeks.
- **>90% of subjects rated excellent, very good or good improvement after 16 weeks.
- **Subjects reported more even pigmentation, less obvious brown spots, and improved clarity and radiance at each post-baseline visit (Fig. 2).**

**Tolerability**

- **Adverse reactions mild (n=3):** localized skin irritation, mostly within the first 2 weeks of use, and may have been due to twice-daily use of retinol without an acclimation phase. Reactions were qualitatively mild and resolved after use of a moisturizer.

**Clinical Photography**

- **Subjects photographed (Figs. 3, 4, and 5) show lighter and more even skin color, a brighter overall skin tone, and less apparent brown spots after regimen use (Fig. 6).**

**Summary**

A new multi-ingredient brightening skincare regimen was tested in an ethnically diverse sample of women with uneven facial pigmentation. Women applied the regimen to the entire face twice a day for 16 weeks.

**Visual Grading and clinical photographs:**

- **Lighter and more even skin color**
- **Brighter overall skin tone**
- **Reduced overall sallowness**
- **Lighter and less apparent brown spots**
- **Effects were observed in all ethnic groups**
- **Chromameter analyses of normally pigmented areas and brown spots showed:**
  - Normally pigmented areas brightened faster than brown spots
  - Reduced overall sallowness
  - Lighter and less apparent brown spots
  - Effects were observed in all ethnic groups

**References**

A Multi-Mechanism Skin Brightening Regimen Delivers Pigment Evening Benefits in an Ethnically Diverse Population

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21st Congress of the European Academy of Dermatology & Venereology
Prague, Czech Republic, 27-30 September, 2012
Introduction

Pigmentation irregularities are a major concern for many ethnic skin populations spanning the globe.1,2 Safe, effective, and aesthetically pleasing formulations that can even skin color, brighten skin tone, and reduce dark spots are requested by dermatology patients around the world.3 A new brightening skincare regimen was developed to improve the complexion of facial skin by targeting multiple steps and pathways that affect pigmentation. The regimen consists of a facial cleanser, serum, and lotion, which contain N-Acetylglucosamine4 plus a variety of other benefit ingredients to collectively exfoliate pigmented areas, reduce tyrosinase activity and melanin production, and deliver an overall pigment evening effect.

Objective

To evaluate the tolerability and lightening / brightening benefits of a high-strength twice-daily skincare regimen in normally pigmented and hyperpigmented skin in an ethnically diverse population of women with uneven facial pigmentation.

Study Methodology

| Study Design | Single-group, prospective skincare regimen use study with direct comparisons to baseline |
| Population / Inclusion Criteria | Women, 30–60 years old, Fitzpatrick skin types I–IV, all ethnicities, with areas of mild to moderate facial hyperpigmentation (3–7 on a 10 cm visual analog scale), epidermal in nature (confirmed by Wood’s Lamp), willing to limit sun exposure and not change hormonal medications |
| Exclusion Criteria | Allergies to skincare product ingredients; use of hydroxyacids, retinol, hydroquinone, kojic acid and other antiaging or lightening/brightening cosmetics within last 2 months; cosmetic procedures or routine use of antiaging or skin brightening topical medications, including prescription retinoids, within last 6 months; planned or current pregnancy/breast-feeding |
| Study Duration | 16 weeks |
| Study Regimen | Twice a day use of the cleanser, serum, and lotion on the entire face (standard facial sunscreen provided for as needed use) |
| Evaluation Visits | Weeks 0, 4, 8, and 16 |
| Evaluation Tools | • Visual grading by a trained clinical grader using a 10 cm visual analog scale from extremely uneven skin tone (0) to even skin tone (10) |
| • Chromameter measurements of brightness (L*) and sallowness (yellow hue, b*) of normally pigmented and hyperpigmented areas (weeks 0, 8, and 16 only) |
| • Digital clinical photographs of the face |
| • Subjective | • Subject self-assessment questionnaires |
| • Objective | • Before and after treatment comparisons of visual grading scores and chromameter measurements using ANOVA followed by a Dunnet’s test at P<0.05 |
| • Subjective | • Chromameter change from baseline comparisons for hyperpigmented vs normally pigmented skin using paired t-tests at P<0.05 |
| • Tabulation of subject self-assessment scores |
| Safety | Observed and reported adverse events |

Study Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Key Benefit Ingredients</th>
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<tbody>
<tr>
<td>Cleanser (NeoStrata® Enlighten Ultra Brightening Cleanser)</td>
<td>• 4% N-Acetylglucosamine (NeoGlucosamine®)3,9</td>
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<tr>
<td></td>
<td>• Swiss alpine plant extracts (GigaWhite®)2,6</td>
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<tr>
<td></td>
<td>• 4% N-Acetylglucosamine (NeoGlucosamine®)3,9</td>
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<tr>
<td></td>
<td>• Swiss alpine plant extracts (GigaWhite®)2,6</td>
</tr>
<tr>
<td></td>
<td>• Oligopeptide-342,5</td>
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<tr>
<td></td>
<td>• Tetrahexyldecyl Ascorbate (Vitamin C)3,9</td>
</tr>
<tr>
<td></td>
<td>• Eucommia Ulmoides Leaf Extract (source of chlorogenic acid)7</td>
</tr>
<tr>
<td></td>
<td>• Licorice Extract6</td>
</tr>
<tr>
<td>Lotion (NeoStrata® Enlighten Pigment Controller)</td>
<td>• 6% N-Acetylglucosamine (NeoGlucosamine®)4,5</td>
</tr>
<tr>
<td></td>
<td>• Swiss alpine plant extracts (GigaWhite®)2,6</td>
</tr>
<tr>
<td></td>
<td>• 0.1% Retinol1,3</td>
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<tr>
<td></td>
<td>• Ascorbyl Glucoside (Vitamin C)2,5</td>
</tr>
<tr>
<td></td>
<td>• Tetrahydrodiferuloylmethane (curcumin analogue found naturally in turmeric, SabiWhite®)5,7</td>
</tr>
</tbody>
</table>

1. Exfoliant; 2. Tyrosinase Inhibitor; 3. Melanin Reducer
Results

Subject Demographics

<table>
<thead>
<tr>
<th>Subjects (n)</th>
<th>30</th>
</tr>
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<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
</tr>
<tr>
<td>Age, mean (range)</td>
<td>50 (37-60)</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
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<tr>
<td>Latin American</td>
<td>14 (47%)</td>
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<tr>
<td>Caucasian</td>
<td>10 (33%)</td>
</tr>
<tr>
<td>Pacific Rim Asian</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>African American</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Indian</td>
<td>1 (3%)</td>
</tr>
</tbody>
</table>

Visual Grading

- 93% of users achieved a more even skin tone after the first 4 weeks
- Significant improvement in evenness of skin tone was observed at every post-baseline visit (weeks 4, 8, and 16, \( P<0.0001 \))

Chromameter Measurements

- Normally pigmented skin and hyperpigmented skin (brown spots) showed significantly increased brightness and decreased sallowness (Fig. 1):
  - Brightness (\( L^* \)):
    - Normally pigmented skin achieved fast improvement in brightness (week 8, 16), \( P<0.01 \)
    - Hyperpigmented skin achieved strong improvement in brightness by week 16, \( P<0.01 \)
    - Normally pigmented skin and hyperpigmented skin achieved comparable increases in brightness by week 16
  - Sallowness (\( b^* \))
    - Normally pigmented skin was significantly less sallow at week 16, \( P<0.01 \)
    - Hyperpigmented skin was significantly less sallow at weeks 8 and 16, \( P<0.01 \)
    - Hyperpigmented skin achieved a significantly greater reduction in sallowness than normally pigmented skin at week 8, \( P<0.05 \)

Figure 1. Improvement in Brightness and Sallowness of Normally Pigmented and Hyperpigmented Skin

Subject Self-Assessment

- Subjects reported brighter overall skin tone during regimen use:
  - 60% of subjects noticed an improvement as early as 2 weeks
  - 90% of subjects rated excellent, very good or good improvement after 16 weeks
- Subjects reported more even pigmentation, less obvious brown spots, and improved clarity and radiance at each post-baseline visit (Fig. 2)
A Multi-Mechanism Skin Brightening Regimen Delivers Pigment Evening Benefits in an Ethnically Diverse Population

Objective

- Hyperpigmented skin achieved a significantly greater reduction in sallowness than normally pigmented skin and hyperpigmented skin (brown spots) showed significantly increased brightness and decreased sallowness (Fig. 1):
  - Baseline Week 8 Week 16
  - Normally pigmented skin and hyperpigmented skin (brown spots) showed significantly increased brightness and decreased sallowness (Fig. 1):
  - Hyperpigmented skin achieved strong improvement in brightness by week 16,
  - Normally pigmented skin and hyperpigmented skin achieved comparable increases in brightness and sallowness by week 16
  - Lighter and more even skin color, and less apparent brown spots after regimen use.

Criteria

- Reduced overall sallowness
- Lighter and less apparent brown spots
- Subjects reported brighter overall skin tone during regimen use:
  - 60% of subjects noticed an improvement as early as 2 weeks
  - Visual grading and clinical photographs showed:
    - Significant improvement in evenness of skin tone was observed at every post-baseline visit (Fig. 2)
    - Increased brightness and decreased sallowness (Fig. 1)

Evaluation Tools

- Visual grading by a trained clinical grader using a 10 cm visual analog scale from
- Tabulation of subject self-assessment scores
- Chromameter change from baseline comparisons for hyperpigmented vs normally pigmented skin using paired t-tests at <0.05

Study Methodology

- Women, 30–60 years old, Fitzpatrick skin types I-IV, all ethnicities, with areas of mild to moderate hyperpigmentation
- Hyperpigmented areas, reduce tyrosinase activity and melanin production, and deliver an overall improvement
- Twice a day use of the cleanser, serum, and lotion on the entire face
- 16 weeks

Subject Demographics

- Subjects reported more even pigmentation, less obvious brown spots, and improved clarity and radiance at each post-baseline visit (Fig. 2)

Tolerability

- The high-strength regimen was well-tolerated. Adverse reactions were mild (n=3) to moderate (n=3) localized skin irritation, mostly within the first 2 weeks of use, and may have been due to twice-daily use of retinol without an acclimation phase. Reactions were distributed across ethnicities.

Clinical Photography

- Subject photographs (Figs. 3, 4, and 5) show lighter and more even skin color, a brighter overall skin tone, and less apparent brown spots after regimen use.

Figure 2. Subject Self-Assessment of Improvement in Skin Pigmentation

Figure 3.

Figure 4.

Figure 5.
A new multi-ingredient brightening skincare regimen was tested in an ethnically diverse sample of women with uneven facial pigmentation. Women applied the regimen to the entire face twice a day for 16 weeks.

**Visual grading and clinical photographs showed:**
- Lighter and more even skin color
- Brighter overall skin tone
- Reduced overall sallowness
- Lighter and less apparent brown spots
- Effects were observed in all ethnic groups

**Chromameter analyses of normally pigmented areas and brown spots showed that:**
- Both normally pigmented areas and brown spots became brighter and less sallow
- Normally pigmented areas brightened faster than brown spots
- Brown spots improved in sallowness faster and to a greater degree than normally pigmented areas

**Self-assessment questionnaires** confirmed that subjects noticed brighter skin tone, more even pigmentation, and less apparent brown spots

**References**