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

Brenda L. Edison BA, Barbara A. Green RPh, MS, Lisa Buckley BA, Irina Brouda MA, Peter N. Konish MS, Yaling Lee PhD, Ronni L. Weinkauf PhD
NeoStrata Company, Inc., Princeton, NJ, USA

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-Acetylglucosamine[4] 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	
• **Objective**	– 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
Statistics	– Before and after treatment comparisons of visual grading scores and chromameter measurements using ANOVA followed by a Dunnett's test at $P<0.05$ – 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

Product	Key Benefit Ingredients
Cleanser (NeoStrata® Enlighten Ultra Brightening Cleanser)	• 4% N-Acetylglucosamine (NeoGlucosamine®)[a,b] • Swiss alpine plant extracts (GigaWhite®)[b,c]
Serum (NeoStrata® Enlighten Illuminating Serum)	• 4% N-Acetylglucosamine (NeoGlucosamine)[a,b] • Swiss alpine plant extracts (GigaWhite)[b,c] • Oligopeptide-34[b,c] • Tetrahexyldecyl Ascorbate (Vitamin C)[b,c] • Eucommia Ulmoides Leaf Extract (source of chlorogenic acid)[c] • Licorice Extract[b]
Lotion (NeoStrata® Enlighten Pigment Controller)	• 6% N-Acetylglucosamine (NeoGlucosamine)[a,b] • Swiss alpine plant extracts (GigaWhite)[b,c] • 0.1% Retinol[b,c] • Ascorbyl Glucoside (Vitamin C)[b,c] • Tetrahydrodiferuloylmethane (curcumin analogue found naturally in tumeric, SabiWhite®)[b,c]

[a]Exfoliant; [b]Tyrosinase Inhibitor; [c]Melanin Reducer

Results

Subject Demographics

Subjects (n)	30
Gender	Female
Age, mean (range)	50 (37–60)
Race/Ethnicity, n (%)	
Latin American	14 (47%)
Caucasian	10 (33%)
Pacific Rim Asian	3 (10%)
African American	2 (7%)
Indian	1 (3%)

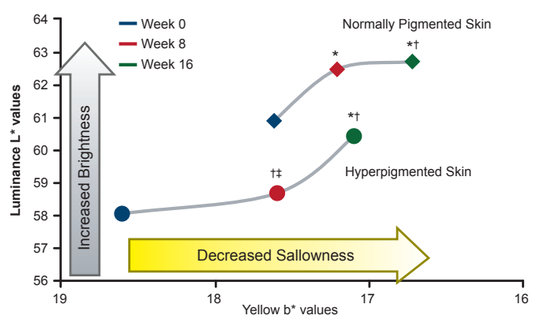
Visual Grading

- 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, $P<0.05$

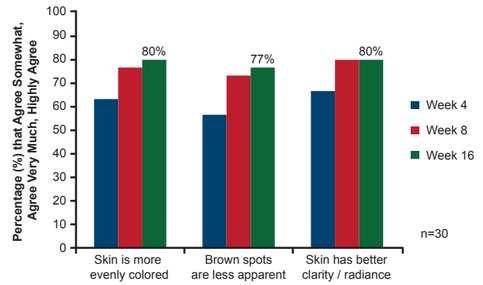
Figure 1. Improvement in Brightness and Sallowness of Normally Pigmented and Hyperpigmented Skin



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)

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



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.

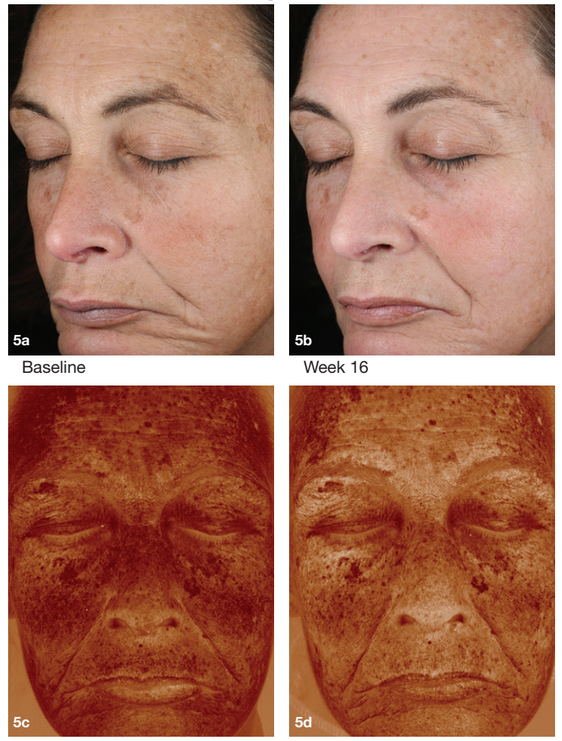
Clinical Photography

- 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 3.

Figure 4.

Figure 5.



For the subject in Figure 5 above, note improvement in pigmentation in standard lighting photographs (5a, 5b) and in cross-polarized photographs with melanin imaging applied to visualize hyperpigmented areas (5c, 5d).

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 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

1. Cole PD, Hatef DA, Taylor S, Bullocks JM. Skin care in ethnic populations. *Semin Plast Surg*. 2009 Aug;23(3):168-72.
2. Grimes PE. Management of hyperpigmentation in darker racial ethnic groups. *Semin Cutan Med Surg*. 2009 Jun;28(2):77-85.
3. Taylor SC. Cosmetic problems in skin of color. *Skin Pharmacol Appl Skin Physiol*. 1999 May-Jun;12(3):139-43.
4. Hwang JS, Lee HY, Lim TY, Kim MY, Yoon TJ. Disruption of tyrosinase glycosylation by N-acetylglucosamine and its depigmenting effects in guinea pig skin and in human skin. *J Dermatol Sci*. 2011 Sep;63(3):199-201.

Poster presented at the 21st *Congress of the European Academy of Dermatology & Venereology*, Prague, Czech Republic, 27–30 September, 2012
Study sponsored by NeoStrata Company, Inc., Princeton, NJ, USA

P248

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

Brenda L. Edison BA
Barbara A. Green RPh, MS
Lisa Buckley BA
Irina Brouda MA
Peter N. Konish MS
Yaling Lee PhD
Ronni L. Weinkauf PhD

NeoStrata Company, Inc., Princeton, NJ, USA

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-Acetylglucosamine[4] 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	
• **Objective**	– 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
Statistics	– Before and after treatment comparisons of visual grading scores and chromameter measurements using ANOVA followed by a Dunnett's test at $P<0.05$ – 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

Product	Key Benefit Ingredients
Cleanser (NeoStrata® Enlighten Ultra Brightening Cleanser)	• 4% N-Acetylglucosamine (NeoGlucosamine®)[a,b] • Swiss alpine plant extracts (GigaWhite®)[b,c]
Serum (NeoStrata® Enlighten Illuminating Serum)	• 4% N-Acetylglucosamine (NeoGlucosamine)[a,b] • Swiss alpine plant extracts (GigaWhite)[b,c] • Oligopeptide-34[b,c] • Tetrahexyldecyl Ascorbate (Vitamin C)[b,c] • Eucommia Ulmoides Leaf Extract (source of chlorogenic acid)[c] • Licorice Extract[b]
Lotion (NeoStrata® Enlighten Pigment Controller)	• 6% N-Acetylglucosamine (NeoGlucosamine)[a,b] • Swiss alpine plant extracts (GigaWhite)[b,c] • 0.1% Retinol[b,c] • Ascorbyl Glucoside (Vitamin C)[b,c] • Tetrahydrodiferuloylmethane (curcumin analogue found naturally in tumeric, SabiWhite®)[b,c]

[a]Exfoliant; [b]Tyrosinase Inhibitor; [c]Melanin Reducer

Results

Subject Demographics

Subjects (n)	30
Gender	Female
Age, mean (range)	50 (37–60)
Race/Ethnicity, n (%)	
Latin American	14 (47%)
Caucasian	10 (33%)
Pacific Rim Asian	3 (10%)
African American	2 (7%)
Indian	1 (3%)

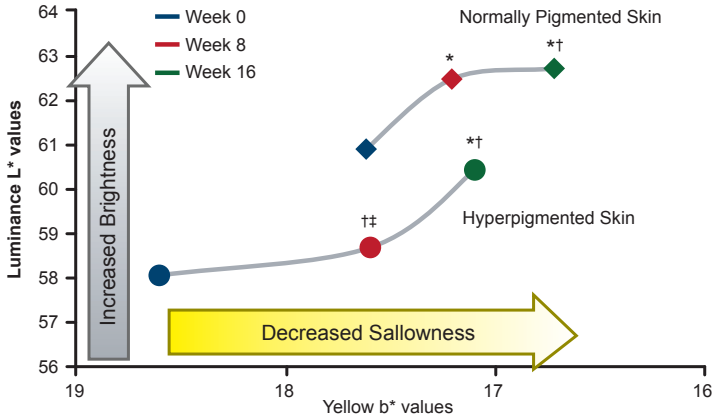
Visual Grading

- 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, $P<0.05$

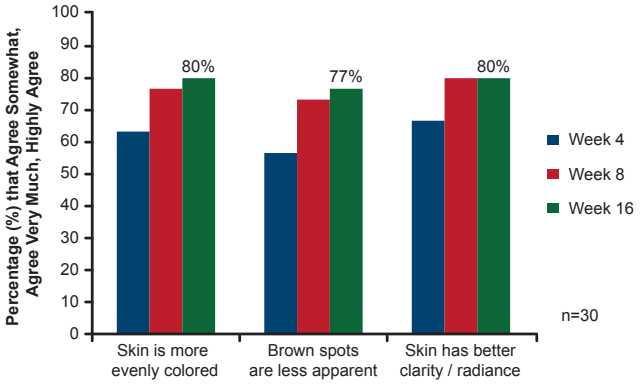
Figure 1. Improvement in Brightness and Sallowness of Normally Pigmented and Hyperpigmented Skin



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)

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



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.

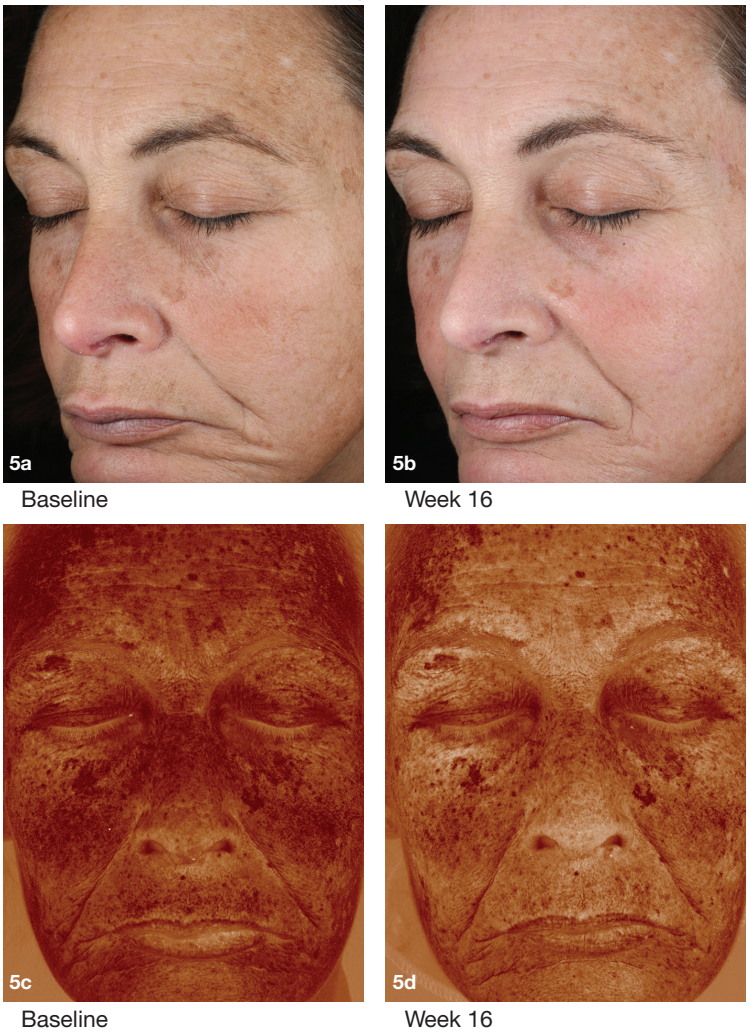
Figure 3.

Baseline Week 16

Figure 4.

Baseline Week 16

Figure 5.



For the subject in Figure 5 above, note improvement in pigmentation in standard lighting photographs (5a, 5b) and in cross-polarized photographs with melanin imaging applied to visualize hyperpigmented areas (5c, 5d).

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 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

1. Cole PD, Hatef DA, Taylor S, Bullocks JM. Skin care in ethnic populations. *Semin Plast Surg*. 2009 Aug;23(3):168-72.
2. Grimes PE. Management of hyperpigmentation in darker racial ethnic groups. *Semin Cutan Med Surg*. 2009 Jun;28(2):77-85.
3. Taylor SC. Cosmetic problems in skin of color. *Skin Pharmacol Appl Skin Physiol*. 1999 May-Jun;12(3):139-43.
4. Hwang JS, Lee HY, Lim TY, Kim MY, Yoon TJ. Disruption of tyrosinase glycosylation by N-acetylglucosamine and its depigmenting effects in guinea pig skin and in human skin. *J Dermatol Sci*. 2011 Sep;63(3):199-201.

Poster presented at the 21st *Congress of the European Academy of Dermatology & Venereology*, Prague, Czech Republic, 27–30 September, 2012
Study sponsored by NeoStrata Company, Inc., Princeton, NJ, USA