Open-Label Evaluation of a Novel Skin Brightening System Containing 0.01% Decapeptide-12 in Combination With 20% Buffered Glycolic Acid for the Treatment of Mild to Moderate Facial Melasma

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ABSTRACT

Melasma is a cutaneous disorder that primarily affects females of Hispanic and Asian descent. Previous studies have shown that use of a brightening system comprised of 0.01% decapeptide-12 cream, an antioxidant cleanser, a 20% buffered glycolic acid lotion, and a broad spectrum SPF 30 sunscreen yields good clearance of mild-to-moderate melasma in Caucasian and Asian volunteers. The present open-label, prospective, and multicenter study sought to determine the tolerability and efficacy of the above-mentioned brightening system on mild-to-moderate melasma in 33 Hispanic females over 16 weeks. Clinical measures included self-assessment of tolerability, clinical grading, determination of Melasma Area and Severity Index (MASI) scores, and standardized clinical photography. Results showed that the system was well tolerated with no adverse events reported. Mean decreases of 36%, 46%, 54%, and 60% in MASI scores were observed at weeks 4, 8, 12, and 16, respectively, which were further corroborated by standardized photography. Results suggest that the brightening system consisting of 0.01% decapeptide-12 cream, an antioxidant cleanser, 20% buffered glycolic acid lotion, and broad spectrum SPF 30 sunscreen is safe and efficacious for the treatment of mild-to-moderate melasma in Hispanic females.


INTRODUCTION

Melasma is a common cutaneous disorder that presents as patches of darker pigmentation on the cheeks, forehead, upper lip, nose, and chin.¹ Melasma most commonly affects females of Asian and Hispanic descent having Fitzpatrick skin type (FST) of IV and higher, and only affects a very small percentage of men.² Moreover, pregnancy appears to be a contributing factor in bringing about the onset of melasma in females, supporting the proposed role of hormones in the regulation of melanogenesis in women.³⁴ Various skin lightening agents such as kojic acid, azelaic acid, ascorbic acid (and its derivatives), and hydroquinone (HQ) and its arbutin derivatives are currently used to treat melasma but are either efficacious and cytotoxic or are mildly efficacious and non-toxic.⁵ Although HQ is one of the most effective and popular skin lightening compounds, it has been shown to cause irritant contact dermatitis (in up to 70% of patients), pregnancy-induced hypertension, hypopigmentation, and allergic contact dermatitis.⁶ In 2006, the US Food and Drug Administration (FDA) proposed a new ruling that would ban HQ, and any ingredients with “skin bleaching” claims, from all cosmetics (currently HQ is allowed in the United States at concentrations of 2% or less) and require a new drug application for products containing higher concentrations of HQ. The FDA proposed such a ban on the basis of (1) suspected high absorption rates, (2) reports of exogenous ochronosis in humans, and (3) murine hepatic adenomas, renal adenomas, and leukemia after large doses over an extended period.³ Although the FDA has not yet taken further action, it is clear that there is a need for novel compounds that strike a balance between skin lightening efficacy and dermal/systemic toxicity.

Tyrosinase is a key enzyme involved in producing melanin and other pigments in plants and animals. It has been previously demonstrated that a novel synthetic oligopeptide (decrapep-
tide-12) competitively inhibits both mushroom and human tyrosinase enzymes more potently than HQ. Moreover, cell culture studies with human melanocytes confirmed that decapptide-12 also inhibited intracellular tyrosinase more potently than HQ and that this effect was without cytotoxicity. A subsequent double-blinded, randomized, and placebo-controlled clinical study consisting of 5 female volunteers of Asian and Hispanic descent with FST IV and moderate recalcitrant melasma showed that a cream containing 0.01% decapptide-12 was well tolerated and reduced the appearance of melasma significantly better than the placebo cream after 16 weeks of twice-daily topical use. Another study consisting of 15 female volunteers of Caucasian and Asian descent, with FSTs I to IV and moderate to severe melasma or solar lentigines showed that twice-daily application of an antioxidant cleanser, twice-daily application of a 0.01% decapptide-12 cream, and daily or alternate day application of a 20% buffered glycolic acid exfoliating lotion, as well as daily application of a broad-spectrum SPF 30 sunscreen significantly reduced the appearance of hyperpigmentation in all study volunteers. A recently published case report with 3 female volunteers of Caucasian descent and one male volunteer of Hispanic descent, between the ages of 30 and 47 with FST III and mild to moderate facial hyperpigmentation, also reported significant visual improvement in the appearance of melasma after 12 to 24 weeks of using this treatment regimen in a similar manner. Given the prevalence of hyperpigmentation in Hispanic women, the aim of the present study was to further characterize the tolerability and efficacy of this product regimen in 33 Hispanic women over 16 weeks.

**MATERIALS AND METHODS**

**Study Design**

An open-label, prospective, and multi-center study (6 clinical sites located in the city of Medellin, Colombia) was conducted to assess the ability of the Lumixyl Topical Brightening System (Envy Medical Inc, Westlake Village, CA, USA) to diminish the appearance of facial melasma (hyperpigmentation). The test regimen consists of a cream containing 0.01% decapptide-12 (a cosmetic skin brightening peptide under the trade name, Lumixyl	extsuperscript{TM}), an antioxidant cleanser, a 20% glycolic acid lotion (buffered to pH 3.4), and a broad spectrum SPF 30 sunscreen containing 8.4% titanium dioxide. The secondary objective of the study was to determine the tolerability of the test regimen when used as described in the present study. This study was approved by the local institutional review board and was conducted following the guidelines of the Declaration of Helsinki.

**Inclusion/Exclusion Criteria**

Thirty-three healthy females were enrolled in the study. Volunteers eligible for inclusion in the study were between the ages of 25 and 50, with FSTs III to V and mild-to-moderate melasma. Melasma severity was determined using the visual grading scale by Pandya et al. Grounds for exclusion included pregnancy, overly sensitive skin, use of oral or topical retinoids in the past 3 months, use of HQ or other prescription skin lightening products in the past 3 months, having received a chemical peel, microdermabrasion, or laser resurfacing in the past 3 months, use of corticosteroids or immunosuppressive prescription drugs in the past 6 months, and pre-existing dermatologic condition(s) that would interfere with the conduct of this study.

**Treatment Regimen**

Consent was obtained from all study volunteers prior to participation in the study. In the morning, volunteers were instructed to cleanse their face with an antioxidant cleanser, apply a 0.01% decapptide-12 cream, and then apply a 20% buffered glycolic acid lotion, as directed, followed by application of a broad spectrum SPF 30 sunscreen. In the evening, volunteers were instructed to cleanse their face with an antioxidant cleanser, apply a 0.01% decapptide-12 cream, and then apply a 20% buffered glycolic acid lotion, as directed. The 20% buffered glycolic acid lotion was applied with varying frequency throughout the study. Volunteers were instructed to apply the 20% buffered glycolic acid lotion once every other morning from week 0 to week 4, then every morning from week 5 to week 8, then every morning and every other evening from week 9 to week 12, and finally twice daily from week 13 to week 16.

**Measures of Clinical Efficacy and Safety**

Volunteers were clinically evaluated for melasma severity at weeks 0, 4, 8, 12, and 16. Clinical evaluation of melasma severity was conducted according to the modified Melasma Area and Severity Index (MASI) proposed by Pandya and coworkers. Very briefly, area of involvement (A) of melasma for the forehead (f), left malar (lm), right malar (rm), and chin (c) areas was graded as 0 (absent), 1 (<10%), 2 (10% -29%), 3 (30% -49%), 4 (50% -69%), 5 (70% -89%), and 6 (90% -100%). Darkness (D) of melasma for the forehead (f), left malar (lm), right malar (rm), and chin (c) areas was graded as 0 (absent), 1 (slight), 2 (mild), 3 (marked), and 4 (severe). A MASI score was then calculated using this equation:

\[
\text{Modified MASI Score} = 0.3 \times A(f) \times D(f) + 0.3 \times A(lm) \times D(lm) + 0.3 \times A(rm) \times D(rm) + 0.1 \times A(c) \times D(c)
\]

Melasma severity was also documented through the use of standardized digital photography taken by the same professional photographer at all study sites. Standardized photos of each volunteer were taken at weeks 0 and 16. Photos were not re-touched other than being cropped and assembled into before and after photo composites.

Tolerability toward the treatment regimen was also evaluated at weeks 4, 8, 12, and 16. Tolerability was evaluated via volunteer self-assessment grading using the tolerability scale described by...
RESULTS
Thirty-three healthy females were enrolled in the study, with a mean age of 42 years, and 26 volunteers completed the study. One volunteer dropped out due to pregnancy, 3 discontinued the study due to severe irritation within the first 2 weeks of the study, presumably caused by the 20% buffered glycolic acid lotion, and 3 volunteers were lost to follow-up for reasons unrelated to the study. Data for those volunteers who discontinued the study were omitted from subsequent tolerability and MASI analyses reported herein. Fifty-five percent of the volunteers had FST III, 33% had FST IV, and 12% had FST V. As for sebum production, 30.3% of volunteers had combination skin, 30.3% of the volunteers had oily skin, 27.3% had normal skin, and 12.1% had dry skin.

The treatment regimen was generally well tolerated with no serious adverse events reported. Self-assessment of tolerability showed that the majority of study volunteers experienced no or mild stinging/burning, erythema, dryness, and pruritus over the duration of the study (Figure 1). Very mild desquamation was observed only in volunteers with dry skin types.

MASI scores indicated that melasma severity was significantly reduced from baseline values at weeks 4, 8, 12, and 16 (Figure 2). Normalized (percentage change from baseline scores) MASI data indicate an average 36%, 46%, 54%, and 60% reduction in melasma area and severity at weeks 4, 8, 12, and 16 (Table 1). Moreover, standardized before and after photos also demonstrated a marked reduction in the appearance of melasma at week 16 (Figures 3, 4, and 5).

DISCUSSION
An extensive literature review by Pawaskar and coworkers of articles published in English and Spanish over 15 years (1991-2006) revealed that melasma severely affects social life, emotional well-being, physical health, and money matters in Hispanic women. First-line therapy for treating melasma in Hispanic and Latin-American patients typically involves the use of effective topical therapies including HQ or a fixed triple combination of HQ, retinoic acid, and fluocinolone acetonide. It is important to note, however, that products or

Statistical Method(s)
All statistical data is presented as mean (± standard deviation). Statistical difference (P≤.05, two-tailed) between MASI scores at weeks 4, 8, 12, and 16 compared with baseline MASI values was determined using one-way analysis of variance with a Dunnet’s post-test. Statistical significance (P≤.05, two-tailed) for percentage change in MASI scores from baseline was determined using a Wilcoxon Signed Rank Test. All evaluations were performed using the Prism 5 (Graphpad Software Inc, La Jolla, CA) statistical software suite.

Tanghetti and coworkers. Volunteers graded stinging/burning, erythema, skin dryness, and pruritus as 0 (none), 1 (mild), 2 (moderate), and 3 (severe) at each clinical visit.

TABLE 1.
Mean Percentage Change in MASI Scores from Baseline Over Time

<table>
<thead>
<tr>
<th>Week</th>
<th>n</th>
<th>Mean % Change in MASI from Baseline (± Standard Deviation)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>26</td>
<td>-35.58 (± 22.25)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>8</td>
<td>26</td>
<td>-46.24 (± 31.84)</td>
<td>.0001</td>
</tr>
<tr>
<td>12</td>
<td>26</td>
<td>-53.58 (± 26.99)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>16</td>
<td>26</td>
<td>-60.45 (± 32.73)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

MASI, Melasma Area and Severity Index.
Results suggest that the tested skin care regimen consisting of an antioxidant cleanser, a 0.01% decapptide-12 cream, a 20% buffered glycolic acid lotion, and a broad-spectrum SPF 30 sunscreen is well tolerated by Hispanic females, with the majority of study volunteers experiencing no to mild stinging/burning, erythema, dry skin, and pruritus. However, 3 study volunteers discontinued their participation in the study within the first 2 weeks due to excessive irritation presumably caused by the 20% buffered glycolic acid lotion. Results of previously conducted Repeated Insult Patch Testing (data not shown) conducted by the manufacturer of the Lumixyl Topical Brightening System on 200 study volunteers confirmed that the tested antioxidant cleanser, 0.01% decapptide-12 cream, and SPF 30 sunscreen did not cause visible irritation or allergic reaction in any of the study volunteers. However, results showed that the 20% buffered glycolic acid lotion caused mild irritation in 10% of study volunteers, confirming that it is capable of causing irritation in skin. Only those study volunteers with dry skin presented mild desquamation, also presumably due to the use of the 20% buffered glycolic acid lotion. No cases of ochronosis have been reported thus far with the use of decapptide-12, which supports its potential use in long-term treatment of hyperpigmentary dyschromias and maintenance thereof.

The efficacy of the skin care regimen, tested in the present study, on volunteers of Caucasian and Asian descent over 24 weeks has recently been reported by Kassim and coworkers. Results showed that 85% of volunteers who presented with moderate to severe facial hyperpigmentation at baseline presented with mild or completely cleared hyperpigmentation at 24 weeks. The present study quantitatively demonstrates that 85% of study volunteers experienced greater than 50% reduction in melasma area and severity, with 35% of all volunteers experiencing greater than 80% reduction, after using the test regimen for 16 weeks. The study population as a whole experienced a mean reduction in melasma area and severity of 60%. Standardized photos further corroborate the efficacy of the test regimen by showing a visible reduction in the intensity of the hyperpigmented spots as well as a reduction in their overall size, similar to results reported by Kassim and coworkers in volunteers of Caucasian and Asian descent who used the skin care regimen tested in the present study.
CONCLUSION

Results of the study described herein suggest that the Lumixyl Topical Brightening System, consisting of an antioxidant cleanser, a 0.01% decapeptide-12 cream, a 20% buffered glycolic acid lotion, and a broad spectrum SPF 30 sunscreen, is an effective new treatment regimen for mild to moderate melasma that is generally safe for use in women of Hispanic descent. The limitations of this study are that it was uncontrolled and that the study population was very small. Controlled studies, with a larger, more representative study population, are necessary to confirm these findings.

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DISCLOSURES

Estelena S.A provided financial support for this study. The authors have no conflicts of interest to report.

REFERENCES