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Clinical Evaluation of a Thiamidol-Based Regimen With SPF Compared With SPF Alone for Facial Hyperpigmentation

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ABSTRACT

Background: Hyperpigmentation disorders are common skin concerns that negatively impact patient quality of life and self-perception. Hyperpigmentation results from the overproduction of melanin via a multi-step process with a rate-limiting step catalyzed by tyrosinase. Thiamidol, an effective human tyrosinase inhibitor, has recently been shown to reduce visible signs of hyperpigmentation and could provide additional benefits when combined with the standard of care treatment for hyperpigmentation: photoprotection, specifically sunscreens with sun protection factor (SPF).

Methods: A randomized study was performed with 95 subjects (n=47, Thiamidol regimen; n=48, standard SPF 30 lotion) aged 18–65 clinically presenting with facial hyperpigmentation (measured by colorimeter and individual typology angle [ITA°]) to assess the efficacy of the Thiamidol-containing regimen (Day Lotion with SPF 30 and Serum applied in the morning, Night Cream and Serum applied in the evening) compared with a standard SPF 30 lotion for 12 weeks, followed by a 6-week regression phase.

Results: Facial hyperpigmentation, measured by skin lightness, ITA° values, radiance, and shine, was significantly reduced relative to baseline for both groups as early as week 2, and significantly reduced for patients receiving the Thiamidol-containing regimen vs the standard SPF 30 lotion at weeks 8 and 12.

Discussion: This study demonstrates that while SPF alone can reduce the visible signs of hyperpigmentation, the addition of Thiamidol to a daily skin care regimen confers additional, durable benefits with regard to skin lightness, radiance, and shine.

Conclusion: These data support the integration of Thiamidol-containing formulations into existing skin regimens for individuals with facial hyperpigmentation.

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INTRODUCTION

Pigmentary disorders (particularly melasma, postinflammatory hyperpigmentation, and solar lentigines) are among the most common skin disorders, impacting patient quality of life, perception by others, and even self-perception.[1,2] Hyperpigmentation results from excess production of melanin induced by dysregulation of a multi-step synthesis process that converts tyrosine to L-DOPA via tyrosinase activity, eventually producing eumelanin and pheomelanin, which are deposited at the dermal and epidermal layers of skin.[3]

Excess melanin production may be initiated in response to skin injury, inflammation, certain medications, and sun exposure.[4] Melanin confers skin pigmentation and affords some protection to the skin from ultraviolet radiation.[5] Prolonged sun exposure stimulates melanogenesis, which generates superoxide and hydrogen peroxide, reactive oxygen species that can cause DNA damage and trigger inflammation, further upregulating melanogenesis.[6,7] Additionally, in patients with inflammatory skin conditions, the levels of antioxidants, which neutralize reactive oxygen species, can be lower than in patients with healthy skin.[8] As a result of the impact of prolonged sun exposure on excess melanin production, a fundamental aspect of hyperpigmentation management is the use of photoprotection (eg, photoprotective clothing, sunglasses, and topical application of sunscreen) to prevent worsening appearance of hyperpigmentation.[9] Specifically, the use of broad-spectrum sunscreens with SPF is recommended as the standard of care for arresting hyperpigmentation, particularly sunscreens that provide visible light protection using iron oxide and/or neutralize reactive oxygen species using antioxidants.[10-12] Common active treatments for hyperpigmentation (treatments that seek to reverse hyperpigmentation rather than just prevent further hyperpigmentation) include hydroquinone (often considered the most effective ingredient for hyperpigmentation), retinoids, kojic acid, chemical peels, laser therapy, and oral tranexamic acid, which have demonstrated some efficacy, but carry the risk of adverse effects and may not be as accessible as over-the-counter products due to price or the need for a doctor's visit or a prescription.[9]

Recently, isobutylamido thiazolyl resorcinol (Thiamidol) was identified as the most effective human tyrosinase inhibitor out of >50,000 screened compounds, with an affinity for human tyrosinase orders of magnitude better than common anti-hyperpigmentation ingredients such as hydroquinone and kojic acid (Thiamidol IC_{50}=1.1 µmol/L; hydroquinone IC_{50}>4000 µmol/L; kojic acid IC_{50}=500 µmol/L).[13] This high affinity makes Thiamidol a suitable ingredient for over-the-counter anti-hyperpigmentation skin care products, particularly in combination with SPF. The objective of this study was to evaluate the efficacy of a Thiamidol-containing regimen (Day Lotion with SPF 30 and Serum applied in the morning, Night Cream and Serum applied in the evening) at reducing the visible signs of hyperpigmentation compared with a vehicle control that includes the same ingredients as the Day Lotion with SPF 30 minus Thiamidol, thus allowing for evaluation of Thiamidol with SPF or SPF alone.

MATERIALS AND METHODS

Study Design

This randomized clinical study was conducted between August 2024 and January 2025 in a study center (Dermico, Broomall, PA). Subjects were assessed at baseline, weeks 2, 4, 8, and 12 of the 12-week treatment phase, and again at week 18 after a 6-week regression phase. The study was conducted following International Conference on Harmonization Good Clinical Practice guidelines, and in accordance with the Declaration of Helsinki. Prior to study initiation, the protocol, informed consent form, and product information were submitted and approved by the Sterling Investigational Review Board. Subject anonymity in the study documentation was maintained by coded entry.

Population and Treatment

Eligible subjects were aged 18–65 with Fitzpatrick Skin Types (FST) I-VI and individual typology angles (ITA°) ranging from +65° to -31° and with an ITA° difference of >5 ITA units on their facial skin between an area of interest and surrounding skin sites, as determined at the pre-study visit. Subjects must have been able to read, understand, and sign the Informed Consent Form, and been willing and able to follow the study requirements. Subjects were asked to discontinue the use of any topical products on their face and avoid sun exposure exceeding 15 minutes (including tanning) from 3 days prior to the study start and through the completion of the 12-week treatment period. Additionally, prior to the first 2 visits, activities that would raise body temperature or induce sweating were not allowed in the 2 hours before their visits. Facial cleansers without brightening or medical properties were permitted. The use of antiinflammatory medications, including topical corticosteroids, or antihistamines was not allowed in the 48-hour period before visits.

Subjects received either the Thiamidol-based regimen (Day Lotion with SPF 30 and Serum applied in the morning, Night Cream and Serum applied in the evening) or a standard SPF 30 lotion (applied 1–4 times daily as needed) for 12 weeks, followed by a 6-week regression phase. The standard SPF 30 lotion had the same formulation as the Day Lotion with SPF 30, but with no Thiamidol; neither the Day Lotion with SPF 30 nor the standard SPF 30 lotion contained visible light filters.

Assessments

The primary outcome of the study was the evaluation of the hyperpigmentation-reducing effect of the Thiamidol-regimen or standard SPF 30 lotion through skin pigmentation measurements (L*mean and ITA°), radiance, and shine at baseline, week 2, week 4, week 8, week 12, and after a 6-week regression (week 18). Briefly, Visible, cross-polarized (X-Pol), parallel-polarized (P-Pol) and UV fluorescence clinical images were acquired for each time point using a Visia-CR system (Canfield, Parsippany, NJ). X-Pol and P-Pol images were used to quantify skin tone, shine, and radiance. A standardized region of interest from each facial image was translated pixel by pixel from the native RGB values into the L*a*b* color space, then analyzed in terms of their image histogram parameters. Individual Topology Angle (ITA) was calculated from L* and b* values using the equation ITA = [arctan(L*-50)/b*)] *180/π. The mean of the L* value and ITA value were used to represent skin lightening, while a partial least squares regression model was employed to quantify perceived shine and radiance as a balance of skin surface and subsurface reflection components.[14,15]

Statistical Analysis

Statistical analyses of efficacy variables were based on the full analysis set consisting of all randomized subjects having completed the study without any major protocol deviation. Statistical significance amongst and between groups was determined using the Wilcoxon signed-rank test using the Statistical Analysis System (SAS Institute, Cary, NC) software package.

RESULTS

Study Demographics

A total of 95 subjects with facial hyperpigmentation enrolled between August 2024 and January 2025 and were randomized to receive either a Thiamidol-containing regimen (n=47) or a standard SPF 30 lotion (n=48). Demographics were well balanced between treatment groups (Table 1).

Skin Pigmentation Efficacy

The skin lightening efficacy of the Thiamidol regimen and standard SPF 30 lotion was assessed using L*mean and ITA°. Subjects receiving the Thiamidol regimen had a greater change from baseline in L* mean than did patients receiving standard SPF 30 lotion, with significant changes between the treatment groups at weeks 8 and 12 (P<0.05); both treatment groups experienced significant changes from baseline starting at week

TABLE 1.

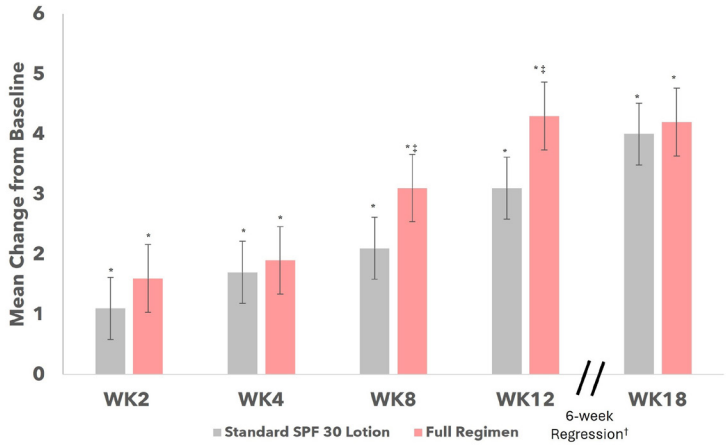
Study Demographics		
Characteristic	**Thiamidol Regimen Group (n=47)**	**Standard SPF 30 Lotion Group (n=48)**
Sex, n (%)		
Female	47 (100)	44 (91.7)
Male	0 (0)	4 (8.3)
Age, years (SD)	50.15 (11.48)	53.40 (9.92)
Phototype, n (%)		
FST I	3 (6.4)	1 (2.1)
FST II	13 (27.7)	13 (27.1)
FST III	14 (29.8)	17 (35.4)
FST IV	2 (4.3)	4 (8.3)
FST V	12 (25.5)	12 (25.0)
FST VI	3 (6.4)	1 (2.1)

2 and through week 18 (P<0.05; Figure 1). Similarly, subjects receiving the Thiamidol regimen had statistically significant improvements from baseline in ITA° compared with subjects receiving the standard SPF 30 lotion at weeks 2, 8, and 12 (P<0.05), while both treatment groups again had significantly improved ITA° compared with baseline from week 2 and through week 18 (P<0.05; Figure 2).

Radiance and Shine Efficacy

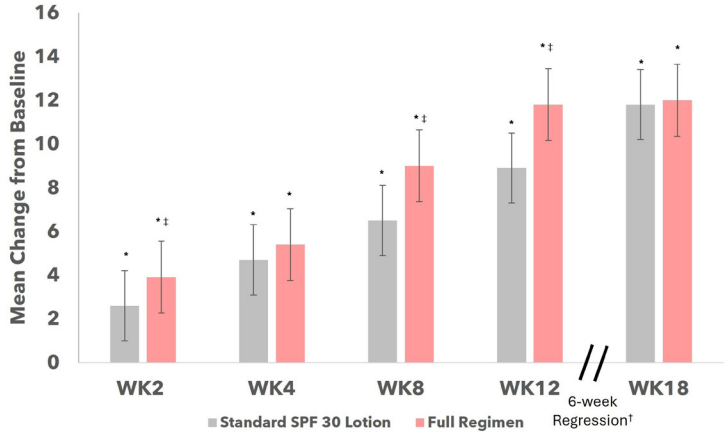
While skin lightening remains an effective measure of anti-hyperpigmentation, radiance and shine, which confer the appearance of brighter, even-toned, and youthful skin have become objective assessments in their own right.[14,15] For both radiance and shine, subjects receiving the Thiamidol regimen had significant improvements compared with subjects receiving the standard SPF 30 lotion at weeks 8 and 12 (P<0.05); both treatment groups experienced significant improvements compared with baseline at all time points (P<0.05; Figures 3 and 4).

FIGURE 1. L* mean following treatment with Thiamidol-formulated full product regimen (serum, day lotion, and night cream) or standard SPF 30 lotion compared with baseline.



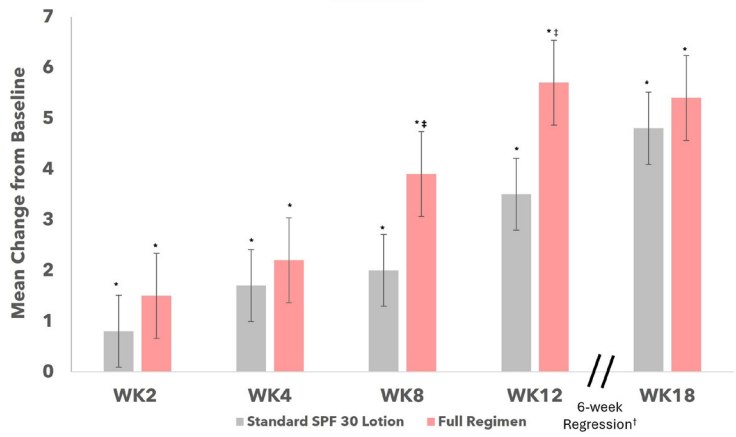
Significant difference between treatment groups and baseline as indicated (*P<0.05). Significant difference between full regimen and standard SPF 30 lotion as indicated (‡P<0.05).
†Subjects did not use any Thiamidol-containing products during the regression phase.

FIGURE 2. Mean Individual Typology Angle (ITA°) following treatment with Thiamidol-formulated full product regimen or standard SPF 30 lotion compared with baseline.



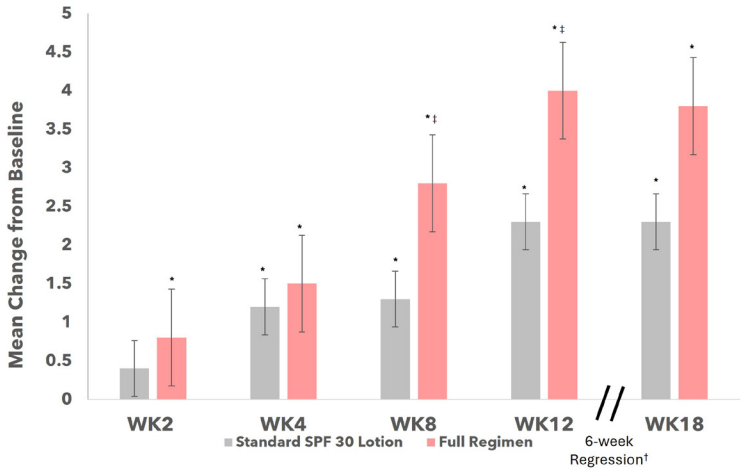
Significant difference between treatment groups and baseline as indicated (*P<0.05). Significant difference between full regimen and standard SPF 30 lotion as indicated (‡P<0.05).
†Subjects did not use any Thiamidol-containing products during the regression phase.

FIGURE 3. Mean radiance measured following treatment with Thiamidol-formulated full product regimen or standard SPF 30 lotion compared with baseline.



Significant difference between treatment groups and baseline as indicated (*P< 0.05). Significant difference between full regimen and standard SPF 30 lotion as indicated (‡P<0.05). †Subjects did not use any Thiamidol-containing products during the regression phase.

FIGURE 4. Mean shine measured following treatment with Thiamidol-formulated full product regimen or standard SPF 30 lotion compared with baseline



Significant difference between treatment groups and baseline as indicated (*P<0.05). Significant difference between full regimen and standard SPF 30 lotion as indicated (‡P<0.05). †Subjects did not use any Thiamidol-containing products during the regression phase.

Clinical Photography

In addition to objective measurements of skin lightening, radiance, and shine, subjects receiving the Thiamidol regimen (Figure 5A-B) had reductions in the visible appearance of hyperpigmentation, as did subjects receiving the standard SPF 30 lotion (Figure 5C-D) in clinical photographs taken at baseline and at week 12. Importantly, the use of the Thiamidol-containing regimen lightened hyperpigmented skin, without whitening the surrounding, unaffected skin. The generally lighter appearance of the subjects' skin tones in the week 12 photographs may be due to the combination of limited sun exposure (protocol-mandated limit of 15 minutes of sun exposure at a time) and subject compliance with sunscreen application during the study period. Photograph lighting and exposure were consistent across timepoints.

DISCUSSION

The standard of care treatment for facial hyperpigmentation is consistent application of broad-spectrum sunscreen with SPF. In this study, the efficacy of skin care regimens utilizing sunscreen with SPF in the visible reduction of facial hyperpigmentation was demonstrated, with both treatment groups experiencing significant improvements in skin lightness, radiance, and shine compared with baseline. The use of the Thiamidol-containing skin care regimen consisting of the Day Lotion with SPF 30 and Serum applied in the morning and Night Cream and Serum applied in the evening, conferred additional benefits to skin lightness, radiance, and shine compared with SPF sunscreen alone. Notably, both the regimen and standard SPF 30 lotion treatment groups retained statistically significant improvements in skin lightness, radiance, and shine compared with baseline

FIGURE 5. Representative clinical photography of subjects showing change in facial hyperpigmentation following treatment with Thiamidol-formulated full regimen (A-B) or standard SPF 30 lotion (C-D).

following the 6-week regression phase, indicating a durable anti hyperpigmentation response; this durable response is consistent with that seen in a previous 24-week study of Thiamidol in subjects with moderate-to-severe melasma and a 13–20 week regression phase.[16] The inhibition of melanin synthesis by Thiamidol was demonstrated to be reversible in human cultured melanocytes, by Mann et al; following the initial treatment with Thiamidol, melanocytes restarted melanin production and eventually reached pre-treatment levels when cultivated without Thiamidol.[13] Clinical photography of subjects in both treatment groups showed marked improvements in the appearance of facial hyperpigmentation from baseline to week 12. The subjects' overall skin tone appears lighter in the week 12 photographs, likely due to protocol-mandated limited sun exposure (<15 minutes at a time) and regimented SPF moisturizer use; lighting and exposure were consistent for the baseline and week 12 photographs.

Previous studies have demonstrated the efficacy of Thiamidol-containing formulations at reducing the visible signs of facial hyperpigmentation resulting from mild-to-severe melasma, acne-induced post-inflammatory hyperpigmentation, laser-induced post-inflammatory hyperpigmentation, and solar lentigines in randomized, controlled trials and real-world studies, either in conjunction with other topical treatments or alone.[13,16-22] The results of the current study are consistent with the improvements demonstrated in these previous studies.

The strengths of this study include the representation of subjects of all FSTs and the novel approach of using objective measures to describe skin radiance and shine. Limitations of this study include the lack of ethnicity data on the subjects, relatively low sample size, and lack of a true vehicle control (full regimen with no Thiamidol rather than just the day lotion), which may limit the generalizability of these findings. Future studies may benefit from the collection of more extensive demographic data and the use of a full regimen vehicle control.

In conclusion, while photoprotection via sunscreens with SPF alone can reduce the visible signs of hyperpigmentation, the addition of Thiamidol to a daily skin care regimen utilizing SPF can confer additional benefits, particularly skin lightness, radiance, and shine. These data support the integration of Thiamidol-containing formulations into the dermatologist's armamentarium and existing skin care regimens for individuals with facial hyperpigmentation.

DISCLOSURES

ST has served as an investigator for Allergan Aesthetics, Concert Pharmaceuticals, Croma-Pharm GmbH, Lilly, and Pfizer; as a consultant for Arcutis, Armis, Avita Medical, Beiersdorf, Biorez Inc, BMS, Cara Therapeutics, Dior, EPI Health, Estee Lauder, Evolus Inc, Galderma, GloGetter, Hugel America, Incyte, Johnson & Johnson, L'Oreal, Lilly, Medscape, Pfizer, Piction Health, Sanofi, Scientis US, UCB, Vichy Laboratories; as a speaker for Beiersdorf, Catalyst Medical Education, CME Outfitters, DermSquared, HMP Global, LearnSkin, Medscape, and MJH Lifesciences; and as an editorial board member for Archives in Dermatologic Research, Cutis, and Practical Dermatology. She has also received royalties from McGraw-Hill. PEG has served as an investigator and/or consultant for Allergan, BOD Clinuvel, Clinuvel, Incyte, Johnson & Johnson, L'Oreal, Merck, Pfizer, SkinBetterScience, and Versicolor Technologies.

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