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 ORIGINAL ARTICLE

Clinical Evaluation of Thiamidol-Containing Formulations for the Visual Management of Facial Hyperpigmentation

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ABSTRACT

Background: Cutaneous hyperpigmentation, which includes melasma, post-inflammatory hyperpigmentation, and solar lentigines, significantly impacts patients' quality of life. The overproduction of melanin is mediated by activation of the skin enzyme tyrosinase, leading to excess melanin deposition in the skin. Thiamidol (isobutylamido thiazolyl resorcinol) formulations have been previously shown to be effective in reducing the cutaneous pigmentation associated with this human skin enzyme.

Methods: A randomized study was performed with 90 subjects clinically presenting with facial hyperpigmentation (Thiamidol serum n=43; Thiamidol regimen n=47) as measured by colorimeter and individual typology angle (ITA^0) to assess the efficacy of a Thiamidol-based serum (2X daily application; morning/night) or a Thiamidol-based regimen (day lotion with SPF 30 + serum in morning; night cream + serum at night) for 12 weeks with a 6-week regression period.

Results: A significant visible reduction in facial hyperpigmentation, assessed by increases in L* and ITA° values, along with an increase in skin radiance and shine, were observed as early as week 2, with continued improvement through week 12 in both the treatment groups relative to baseline. At week 12, changes in radiance and shine were trending toward enhancement in the regimen group compared with the serum group.

Discussion: This study demonstrates the clinical effectiveness of Thiamidol-containing formulations in the visible improvement of facial hyperpigmentation and in overall skin radiance and shine.

Conclusion: These data support the use of Thiamidol-containing formulations as part of the overall management strategy for individuals affected by facial hyperpigmentation.

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INTRODUCTION

Pigmentary disorders, including melasma, post-inflammatory hyperpigmentation (PIH), solar lentigines, axillary hyperpigmentation, periorbital hyperpigmentation, and vitiligo, are some of the most commonly reported dermatological skin disorders, which significantly impact patients' quality of life.[1,2] In a recent survey of 48,000 individuals from 34 countries covering all continents, 50% of the subjects (average age 44 years) reported having at least one pigmentary disorder, with more women (59%) affected.[1] Amongst these disorders, hyperpigmentation-associated skin disorders, primarily melasma, PIH, and solar lentigo, accounted for the majority of the self-reported conditions.[1] Furthermore, in individuals with skin of color (SOC), particularly those with African, Asian, or Hispanic heritage, the incidence of reported PIH far exceeded that of the general population (15% vs ~1%).[1]

Hyperpigmentation is mediated by the overstimulation of the melanin production pathways in melanocytes, resulting in the deposition of excess melanin in the skin.[3,4] The key rate-limiting step in these complex pathways centers on the conversion of Tyrosine to L-Dopa, via the catalyzing enzyme tyrosinase, with eventual generation of the melanin end products eumelanin and pheomelanin.[5]

Recently, isobutylamido thiazolyl resorcinol (Thiamidol) has been identified from a library of 50,000 compounds as the most effective inhibitor of human tyrosinase with activity (half-maximal inhibition concentration, IC_{50} = 1.1 mmol/L). This far exceeds that of common anti-pigmentation ingredients, including hydroquinone and kojic acid,[6] making it a suitable ingredient for inclusion in over-the-counter (OTC) anti-pigmentation products.

Previous studies have demonstrated the reduction of hyperpigmentation mediated by melasma, post-inflammatory hyperpigmentation (acne-, UV-B-, and laser-induced), and solar lentigo via treatment with various Thiamidol-based formulations, both in a single product and in multi-product regimen protocols in both randomized controlled trials (RCTs) and real-world settings.[7-17] The objective of this research was to investigate the clinical efficacy of a novel cosmetic Thiamidol-containing serum and Thiamidol-containing regimen (day lotion with SPF 30, serum, and night cream) for the visible management of facial hyperpigmentation.

MATERIALS AND METHODS

Trial Design

This randomized study was conducted between August 2024 and January 2025 in a study center (Dermico, Broomall, Pennsylvania, USA). In the 12-week treatment phase, the subjects returned at weeks 2, 4, 8, and 12 for assessment and at week 18 after a 6-week treatment discontinuation (regression phase).

The study was conducted following International Conference on Harmonization Good Clinical Practice (ICH E6 (R2) GCP) guidelines, and in accordance with the ethical principles that have their origins in the Declaration of Helsinki. Prior to initiation of the study, 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.

Study Population and Treatment

Eligible for the trial were healthy male and female subjects aged 18 to 65 years with Fitzpatrick skin types (FST) I to VI, who had individual typology angles (ITA°) ranging from +65° to -31° and with an ITA° differences of >5 ITA units on their facial skin between the area of interest (AOI) and surrounding skin sites (SSS) as determined at the pre-study visit, who had used SPF-containing products in the past, who were able to read, understand, and sign the informed consent form (ICF), and who were willing and able to follow all study requirements and restrictions.

For 12 weeks, the subjects allocated to the Thiamidol-serum group applied twice daily (morning and night) on their face the Thiamidol-containing serum. Subjects were instructed to apply a standard SPF lotion to their face at least once in the morning after serum application. Subjects were allowed to apply SPF lotion up to 4 times daily as needed, with a minimum of 2 hours between applications. The subjects allocated to the Thiamidol-regimen group applied twice daily (morning and night) on their face the Thiamidol-containing serum followed by the Thiamidol-containing day lotion with SPF30 in the morning and the Thiamidol-containing night cream at night. Subjects were allowed to apply standard SPF lotion to their face as needed at least 2 hours after the day of lotion application.

Subjects were asked to stop the use of all topical products (lotions, creams, serums, sunscreens, etc.) on their face for the 3 days prior to the start of the study and until the completion of week 12. Subjects were allowed to continue using non-medicated and non-brightening facial cleansers. Subjects were asked to avoid sun exposure for over 15 minutes, including artificial sun, during the 3 days prior to the start of the study and for the duration of the study. Subjects had to refrain from any activities that would increase body temperature or induce sweating during the 2 hours before their first 2 visits. Subjects could not be taking and be willing to not take any anti-inflammatory medications starting 48 hours prior to their appointments.

Assessments

The primary outcome of the study was the evaluation of the hyperpigmentation-reducing effect of the Thiamidol-serum or Thiamidol-regimen (serum, day lotion with SPF 30, and night cream) through skin pigmentation measurements (L*Mean and ITA°), radiance, and shine at baseline, week 2, week 4, week 8, week 12, and post-regression phase (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 its 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.[21,22]

Statistical Analysis

Statistical analyses of efficacy variables were based on the full analysis set (FAS) consisting of all randomized subjects who had 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, North Carolina) software package.

RESULTS

Study Demographics

Between August 2024 and January 2025, 90 male and female subjects (n = 89 females; n = 1 male) between 18 and 64 years (mean: 50.61 + 10.83 years), with Fitzpatrick Skin Types

TABLE 1.

Study Demographics				
Characteristic	Thiamidol-serum group (n=43)		Thiamidol-regimen group (n=47)	
Gender	M	F	M	F
	1	42	0	47
Age, years + SD	27	51.59 (+ 9.71)	N/A	50.15 (+ 11.48)
Phototype, n				
FST I	0	2	N/A	3
FST II	0	13	N/A	13
FST III	0	15	N/A	14
FST IV	0	5	N/A	2
FST V	0	11	N/A	12
FST VI	1	1	N/A	3

FST, Fitzpatrick skin type; SD, standard deviation.

(FSTs) I-VI (FST I = 5; FST II = 26; FST III = 29; FST IV = 7; FST V = 23; FST VI = 4), and ITA° ranging from +65° to -31° with ITA° differences of >5 ITA units on their facial skin between and area of interest (AOI) and surrounding skin sites (SSS) as determined at their pre-study visit (PSV) were enrolled, of whom 43 were randomized to the Thiamidol-serum group and 47 were randomized to the Thiamidol-regimen group. The randomized subjects' demographics were balanced among the 2 treatment groups (Table 1).

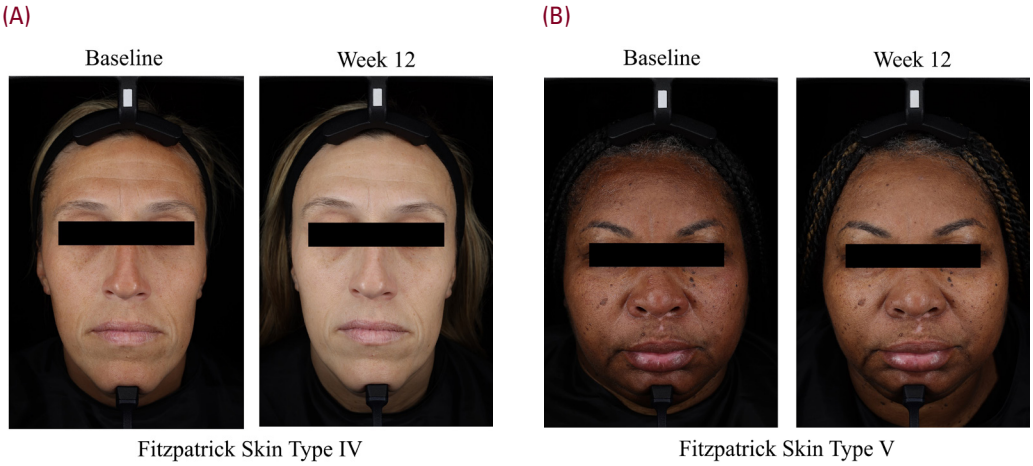
Efficacy, Clinical Photography

Clinical photographs demonstrated visible improvement of facial hyperpigmentation in subjects from both groups, Thiamidol-serum group (Figure 1) and Thiamidol-regimen group (Figure 2), and in multiple FSTs, including FST IV (Figure 1A) and FST V (Figure 1B) for the Thiamidol-serum groups and FST III (Figure 2A) and FST V (Figure 2B) for the Thiamidol-regimen group. Visible improvements of facial hyperpigmentation were observed in subjects from all FSTs included in both groups (full data not shown).

Efficacy, Skin Lightening (L*Mean, ITA°)

Two methods were used to measure the efficacy (skin lightening) of the Thiamidol-serum and Thiamidol-regimen treated subjects, L*Mean and ITA°. L*Mean uses a 3-dimensional color model (CIELAB Color Space), to objectively measure the lightness or darkness of skin on a scale of 0 (pure black/darkest) to 100 (pure white/lightness), with increases in L*Mean after anti-pigmentation treatment demonstrating overall skin lightening.[18,19] ITA° is an objective measure of skin color and

FIGURE 1. Representative clinical photography of subjects. Improvement in facial hyperpigmentation following treatment with Thiamidol formulated serum (12 weeks). (A) FST IV subject; (B) FST V subject.

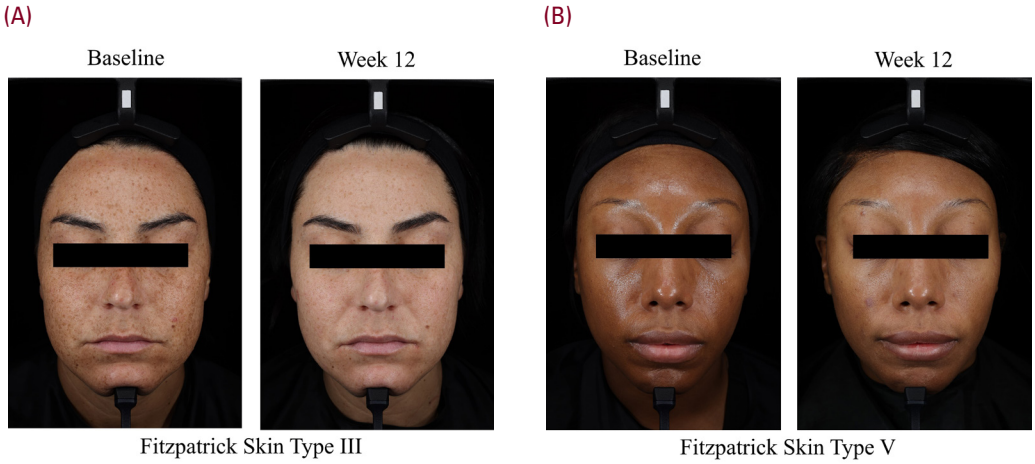


FST, Fitzpatrick skin type.

overall skin pigmentation and is derived from both lightness of skin (L*Mean) and the yellow and blue color of skin.[20] Statistically significant (P<0.05) increases in L*Mean were observed as early as week 2 relative to baseline for both the Thiamidol-serum and Thiamidol-regimen groups, with continued increases in skin lightening measured (L*M) through week 12 (Figure 3). Skin lightening was maintained through the end of the study (week 18), which included a 6-week regression phase (no application of product) (Figure 3).

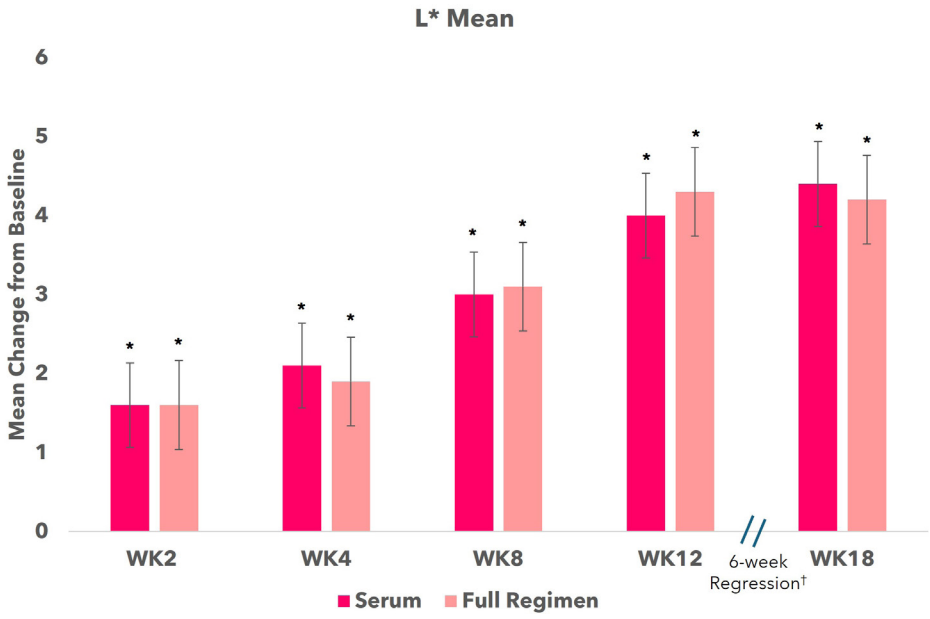
Similar to L*Mean, a statistically significant (P<0.05) increase in ITA° mean was measured relative to baseline as early as week 2, with an ~4 mean ITA unit increase in both the Thiamidol-serum and Thiamidol-regimen groups, with continued increases observed through week 12 (Thiamidol-serum = Mean 11.3 ITA units increase; Thiamidol-regimen = Mean 11.8 ITA units) and sustained efficacy through week 18 (6 week regression phase) (Figure 4).

FIGURE 2. Representative clinical photography of subjects. Improvement in facial hyperpigmentation following treatment with Thiamidol formulated full regimen (serum, day lotion, and night cream) (12 weeks). (A) FST III subject; (B) FST V subject.



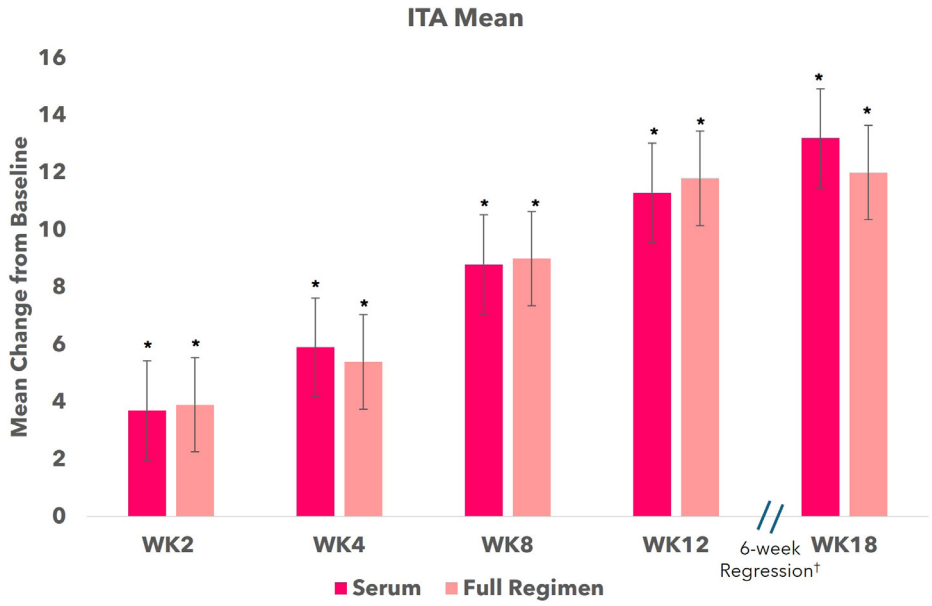
FST, Fitzpatrick skin type.

FIGURE 3. L* Mean (skin lightness) following treatment with Thiamidol formulated serum or Thiamidol formulated full product regimen (serum, day lotion, and night cream) compared with baseline at all time points assessed.



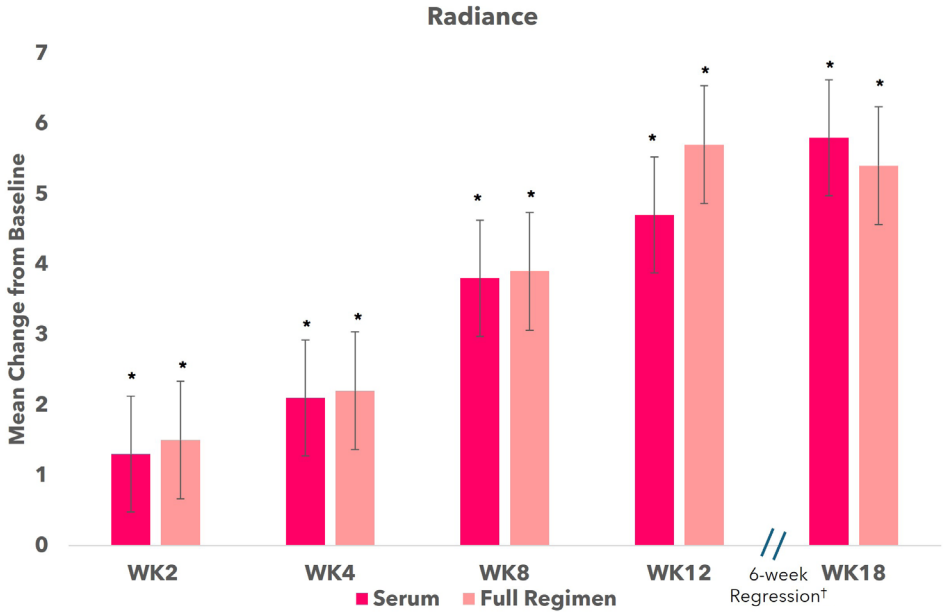
Significant differences between treatment groups and baseline as indicated (*P<0.05).
†Subjects did not use any Thiamidol products during regression phase.

FIGURE 4. Mean Individual Typology Angle (ITA°) following treatment with Thiamidol formulated serum or thiamidol formulated full product regimen (serum, day lotion, and night cream) compared with baseline at all time points assessed.



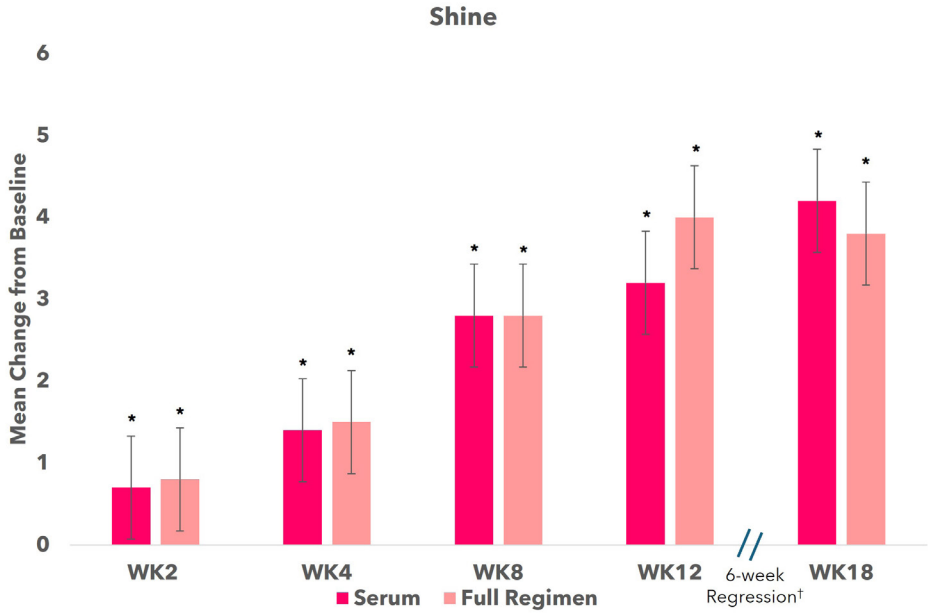
Significant differences compared with baseline as indicated (*$P<0.05$).
†Subjects did not use any Thiamidol products during regression phase.

FIGURE 5. Mean radiance measured following treatment with Thiamidol formulated serum or Thiamidol formulated full product regimen (serum, day lotion, and night cream) compared with baseline at all time points assessed.



Significant differences compared with baseline as indicated (*$P<0.05$).
†Subjects did not use any Thiamidol products during regression phase.

FIGURE 6. Mean shine measured following treatment with Thiamidol formulated serum or Thiamidol formulated full product regimen (serum, day lotion, and night cream) compared with baseline all time points assessed.



Significant differences compared with baseline as indicated (*P<0.05).
†Subjects did not use any Thiamidol products during regression phase.

Efficacy, Radiance, and Shine

Efforts to better evaluate the efficacy of anti-pigmentation products beyond skin lightening have expanded into the objective quantitative measurement of skin's radiance and shine. Both skin radiance and shine center on the skin's interaction with light, more specifically, the amount of light reflected at the skin surface and resulting optical characteristics of skin, giving the appearance of younger, brighter, glossier, even-toned skin.[21,22] Subject's full-face images were captured using a Visia-CR imaging system, with subsequent measurement and quantitation of radiance and shine.

On hyperpigmented skin, both radiance and shine improved statistically significantly (P<0.05) compared with baseline in both the Thiamidol-serum and Thiamidol-regimen groups starting at week 2 and increasing at every time point through week 12, and maintained through the 6-week regression phase, week 18 (Figures 5 and 6). While not reaching statistical significance, changes in radiance and shine trended in favor of the Thiamidol-regimen group compared with the Thiamidol-serum group at week 12 (Figures 5 and 6).

DISCUSSION

Pigmentary disorders, particularly those associated with hyperpigmentation (eg, melasma, PIH, solar lentigines, etc.), remain one of the most common dermatologic diagnoses, especially in individuals with skin of color (SOC).[23-25] The prevalence of PIH, melasma, and solar lentigo has been reported to be as high as 15%, 50%, and 90%, respectively.[4,26,27]

Hyperpigmentation occurs when excess melanin is deposited in the skin, most commonly due to overstimulation of melanin synthesis within the melanocyte.[4,28,29] The key rate-limiting step in this complex pathway centers on the conversion of the amino acid tyrosine to L-Dopa, mediated by the cellular enzyme, tyrosinase, leading to a cascade of reactions culminating with the production of the 2 melanin products, eumelanin (brown/black pigment) and pheomelanin (light red-yellow pigment).[5,30]

Therapeutic approaches to treat hyperpigmentation center on agents that reduce melanin synthesis or enhance dispersion and removal of melanin once formed.[24,31] The removal of 2% hydroquinone from the market, following the passing of the CARES Act of September 2023, created a critical gap in over-the-counter anti-pigmentation options, particularly for patients with access to care issues.[24,31] Recently, isobutylamido thiazolyl resorcinol (Thiamidol) has been identified as an effective inhibitor of human tyrosinase and melanin production, with an IC50 = 1.1 mmol/L and near 100% inhibition of human tyrosinase at 10 mmol/L, as compared with 4-butylresorcinol's IC_{50} = 21 mmol/L and hydroquinone's IC_{50} > 4000 mmol/L.[6] Thiamidol-based formulations have been studied in multiple clinical studies worldwide targeting hyperpigmentation associated with mild-to-severe melasma, acne-induced PIH, laser-induced PIH, and solar lentigines in both randomized controlled, vehicle-controlled, head-to-head, combination/adjunctive treatment, and real-world studies.[6,7,10,12-17]

Based on these studies, a randomized study was conducted to investigate the clinical efficacy of a novel cosmetic Thiamidol-containing serum and a Thiamidol-containing regimen consisting of a Thiamidol-containing day lotion with SPF 30, the Thiamidol-containing serum, and a Thiamidol-containing night cream for the visible management of facial hyperpigmentation as assessed by various objective assays (colorimetric and photographic image analysis), including L*Mean, ITA°, Radiance, and Shine. While other investigators have included L*Mean and ITA° as part of the clinical assessment of Thiamidol-containing formulation, this is the first reported study to include Radiance and Shine as key endpoints objectively measured, rather than subjectively by the investigator or patient questionnaire.

In this study, changes in hyperpigmentation as measured by 2 objective skin lightening measurements (L*Mean and ITA°) were observed as early as week 2 posttreatment initiation in both the Thiamidol-serum and Thiamidol-regimen groups compared with baseline levels. This improvement continued to increase at each assessment time point (week 4, week 8) through the end of the treatment phase of the study (week 12), with skin lightening maintained through the 6-week regression phase (no treatment), suggesting sustained inhibition of tyrosinase activity and melanin production, with enhancement of prolonged sustainment of melanin inhibition trending in favor of the Thiamidol-serum group compared with the Thiamidol-regiment group (statistical significance not reached), which warrants longer term studies to evaluate further.

It should be noted that Thiamidol mediated inhibition of melanin synthesis is reversible, with viability of human cultured melanocytes post treatment as demonstrated by Mann et al.[6] The increases in ITA° observed in this study are consistent with data reported by Roggenkamp et al, for subjects using a similar regimen of Thiamidol-containing products (day lotion with SPF, serum, and night cream) for 24 weeks for treatment of moderate-to-severe melasma.[13] Additionally, the observed increases in L*Mean are consistent with those reported by Vachiramon et al following twice-daily application of a Thiamidol-containing formulation for treatment of laser-induced PIH for 8 weeks.[16]

While reduction of melanin deposition in skin is the key attribute for any anti-pigmentation therapeutic, efforts to address the overall skin's appearance, including commercially appealing attributes like radiance and shine are highly desirable.[32] The visual perception of skin's radiance and shine is mediated by interactions of light and skin resulting in surface and subsurface reflections yielding what consumers commonly describe as "an internal glow".[21,22,32] Efforts to improve overall skin appearance by improving radiance and shine, in addition to reducing hyperpigmentation, could lend to overall patient satisfaction with skin appearance and patient adherence.

To evaluate the impact of treatment with both the Thiamidol-serum and Thiamidol-regimen, radiance and shine were measured at weeks 2, 4, 8, 12, and after the 6-week regression period (week 18). Subject photographs were taken using a Visia-CR imaging system, and images were graded for radiance and shine according to methods developed by Matsubara et al.[21,22] Increases in both parameters (relative to baseline) were observed starting at week 2, increasing at each time point through week 12 with sustainment through the 6-week regression period. Changes in radiance and shine trended to enhancement in the Thiamidol-regimen group compared with the Thiamidol-serum group at 12; however, statistical significance was not achieved. Additional studies beyond 12 weeks would be beneficial to evaluate any additional benefits of the full treatment regimen compared with serum alone on the improvement of skin radiance and shine. The increases in both of these parameters over time suggest that reduction of hyperpigmentation by Thiamidol-containing products/regimen treatment may result in optical characteristics of the skin, yielding a perception of brighter, more radiant skin.

This study has several strengths, including the inclusion of varied skin types representing the general population dealing with hyperpigmentation, spanning FST I to VI. Additionally, the inclusion of both a Thiamidol regimen and a Thiamidol-serum-alone group is in accordance with real-world settings in which individuals often using an array of treatment products for the management of hyperpigmentation or lean towards serums alone to complement their overall skin health regimen. Lastly, the inclusion of the 2-objective measure of optical reflection of skin resulting in the visual perception of radiance and shine is a novel approach to assessing anti-pigmentation products and treatment approaches. Limitations of the study are the monocentric study approach, relatively low number of patients, and lack of a vehicle control group, which should be addressed in future studies.

CONCLUSION

This study demonstrates the clinical effectiveness of Thiamidol-containing formulations in the visible improvement of facial hyperpigmentation and in overall skin radiance and shine. Use of the Thiamidol containing either the serum twice daily or the full regimen (day lotion with SPF 30, serum, and night cream) resulted in a significant visible improvement of facial hyperpigmentation as early as week 2, while use of the full regimen trended towards enhanced efficacy of radiance and shine. Therefore, these data support the use of Thiamidol-containing formulations as part of the overall management strategy for individuals affected by facial hyperpigmentation.

DISCLOSURES

SRD has served as an investigator and/or consultant for multiple entities in the past, including Beiersdorf. He has also held multiple leadership positions in organized medicine. EL has

served as an investigator, speaker, advisor, and/or consultant for AbbVie, Almirall, Amgen, Arcutis, Bausch, Beiersdorf, Bristol-Myers Squibb, Cassiopeia, Cellceutix, Dermavant, Eli Lilly, Galderma, GSK, Incyte, Kenvue, LEO, L'Oreal, Novartis, Pfizer, Pierre Fabre, Regeneron, Sanofi, Sun Pharma, Takeda, UCB Pharma, and Vyne. NE has served as an investigator for Pfizer and as a speaker and/or advisory board member for AbbVie, Allergan, Avita, Beiersdorf, Canfield, Dior, Galderma, Incyte, Janssen, L'Oreal, La Roche-Posay, Lilly, McGraw-Hill, Medscape, Pfizer, Sanofi, Takeda, and VisualDx. She has also received royalties from McGraw-Hill and has stock options in VisualDx. CF is an investigator affiliated with Novartis. Additionally, she serves as a consultant or advisor for Galderma, Sun Pharma, Avita, Procter & Gamble, Regeneron, Aerolase, Benev, L'Oreal, La Mer, Avene, Kenvue, Bristol Myers Squibb, Nutrafol, Acclaro, Beiersdorf, Primus, Johnson & Johnson, Crown Aesthetics, and AbbVie. PG 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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REFERENCES

1. Kerob DK, Passeron T, Alexis A, et al. Prevalance of post-inflammatory hyperpigmentation, impact on quality of life and social stigmatization: results of the first large international survey. *J Am Acad Dermatol.* 2024;91(3)(AB73)
2. Maymone MBC, Neamah HH, Wirya SA, et al. The impact of skin hyperpigmentation and hyperchromia on quality of life: A cross-sectional study. *J Am Acad Dermatol.* 2017;77(4):775-778. doi:10.1016/j.jaad.2017.05.009
3. Wang G, Li J, Xiao-Li P, et al. Discovery of tyrosinase inhibitors: structure-based virtual screening and biological evaluation. *Pharmaceut Fronts.* 2022;4(1):e1-e8.
4. Kaufman BP, Aman T, Alexis AF. Postinflammatory hyperpigmentation: epidemiology, clinical presentation, pathogenesis, and treatment. *Am J Clin Dermatol.* 2018;19(4):489-503.
5. Qian W, Liu W, Zhu D, et al. Natural skin-whitening compounds for the treatment of melanogenesis (Review). *Exp Ther Med.* 2020;20(1):173-185. doi:10.3892/etm.2020.8687
6. Mann T, Gerwat W, Batzer J, et al. Inhibition of human tyrosinase requires molecular motifs distinctively different from mushroom tyrosinase. *J Invest Dermatol.* 2018;138(7):1601-1608. doi:10.1016/j.jid.2018.01.019
7. Arrowitz C, Schoelermann AM, Mann T, et al. Effective tyrosinase inhibition by thiamidol results in significant improvement of mild to moderate melasma. *J Invest Dermatol.* 2019;139(8):1691-1698.e6. doi:10.1016/j.jid.2019.02.013
8. Bertold C, Fontas E, Singh T, et al. Efficacy and safety of a novel triple combination cream compared with Kligman's trio for melasma: a 24-week double-blind prospective randomized controlled trial. *J Eur Acad Dermatol Venereol.* 2023;37(12):2601-2607. doi:10.1111/jdv.19455
9. Disphanurat W, Srisantithum B. Efficacy and safety of 0.15% isobutylamido thiazolyl resorcinol combined with hyaluronic acid vs 0.15% isobutylamido thiazolyl resorcinol or hyaluronic acid alone in melasma treatment: a randomized evaluator-blind trial. *J Cosmet Dermatol.* 2021;20(11):3563-3572. doi:10.1111/jocd.14031
10. Lima PB, Dias JAF, Cassiano DP, et al. Efficacy and safety of topical isobutylamido thiazolyl resorcinol (Thiamidol) vs 4% hydroquinone cream for facial melasma: an evaluator-blinded, randomized controlled trial. *J Eur Acad Dermatol Venereol.* 2021;35(9):1881-1887. doi:10.1111/jdv.17344
11. Philipp-Dormston WG, Vila Echague A, Perez Damonte SH, et al. Thiamidol containing treatment regimens in facial hyperpigmentation: an international multi-centre approach consisting of a double-blind, controlled, split-face study and of an open-label, real-world study. *Int J Cosmet Sci.* 2020;42(4):377-387. doi:10.1111/ics.12626
12. Roggenkamp D, Dlova N, Mann T, et al. Effective reduction of post-inflammatory hyperpigmentation with the tyrosinase inhibitor isobutylamido-thiazolyl-resorcinol (Thiamidol). *Int J Cosmet Sci.* 2021;43(3):292-301. doi:10.1111/ics.12694
13. Roggenkamp D, Sammain A, Furstenau M, et al. Thiamidol((R)) in moderate-to-severe melasma: 24-week, randomized, double-blind, vehicle-controlled clinical study with subsequent regression phase. *J Dermatol.* 2021;48(12):1871-1876. doi:10.1111/1346-8138.16080
14. Vachiramon V, Kositkuljorn C, Leerunyakul K, et al. Isobutylamido thiazolyl resorcinol for prevention of UVB-induced hyperpigmentation. *J Cosmet Dermatol.* 2021;20(3):987-992. doi:10.1111/jocd.13615
15. Vachiramon V, Leerunyakul K, Kositkuljorn C, et al. Combined isobutylamido thiazolyl resorcinol and low-fluence Q-switched Nd: YAG laser for the treatment of facial hyperpigmentation: a randomized, split-face study. *J Cosmet Dermatol.* 2021;20(6):1724-1731. doi:10.1111/jocd.13790
16. Vachiramon V, Sakpuwadol N, Yongpisarn T, et al. Efficacy of isobutylamido thiazolyl resorcinol for prevention of laser-induced post-inflammatory hyperpigmentation: a randomized, controlled trial. *J Cosmet Dermatol.* 2024;23(7):2450-2457. doi:10.1111/jocd.16287
17. Griffiths D, Warnke K, Drescher P, et al. Real-World Evidence: Efficacy of a dermocosmetic regimen containing tryosinase inhibitor Thiamidol to reduce hyperpigmentation. Presented at the European Academy of Dermatology and Venereology 32nd Congress, 2023.
18. Daniel LC, Heckman CJ, Kloss JD, et al. Comparing alternative methods of measuring skin color and damage. *Cancer Cause Control.* 2009;20(3):313-321.
19. Boo YC, Jo DJ, Oh CM, et al. The first human clinical trial on the skin depigmentation effiacacy of glycinamide hydrochloride. *Biomedicines.* 2020;8(8):257.
20. Chardon A, Cretois I, Hourseau C. Skin colour typology and suntanning pathways. *Int J Cosmet Sci.* 1991;13(4):191-208. doi:10.1111/j.1467-2494.1991.tb00561.x
21. Matsubara A, Liang Z, Sato Y, et al. Analysis of human perception of facial skin radiance by means of image histogram parameters of surface and subsurface reflections from the skin. *Skin Res Technol.* 2012;18(3):265-271. doi:10.1111/j.1600-0846.2011.00570.x
22. Matsubara A. Differences in the surface and subsurface reflection characteristics of facial skin by age group. *Skin Res Technol.* 2012;18(1):29-35. doi:10.1111/j.1600-0846.2011.00537.x
23. Davis EC, Callender VD. Postinflammatory hyperpigmentation: a review of the epidemiology, clinical features, and treatment options in skin of color. *J Clin Aesthet Dermatol.* 2010;3(7):20-31.
24. Frey C, Grimes P, Callender VD, et al. Thiamidol: a breakthrough innovation in the treatment of hyperpigmentation. *J Drugs Dermatol.* 2025;24(6):608-616. doi:10.36849/JDD.9093
25. Dlova NC, Akintilo LO, Taylor SC. Prevalence of pigmentary disorders: a cross-sectional study in public hospitals in Durban, South Africa. *Int J Womens Dermatol.* 2019;5(5):345-348. doi:10.1016/j.ijwd.2019.07.002
26. Kerob D, Passeron T, Alexis A, et al. 54772 Pigmentary disorders, prevalence, impact on quality of life and social stigmatization: results of the first large international survey. *J Am Acad Dermatol.* 2024;91(3):AB280.
27. Ogbechie-Godec OA, Elbuluk N. Melasma: an up-to-date comprehensive review. *Dermatol Ther (Heidelb).* 2017;7(3):305-318. doi:10.1007/s13555-017-0194-1
28. Wang RF, Ko D, Friedman BJ, Lim HW, Mohammad TF. Disorders of hyperpigmentation. Part I. Pathogenesis and clinical features of common pigmentary disorders. *J Am Acad Dermatol.* 2023;88(2):271-288.
29. Syder NC, Quarshie C, Elbuluk N. Disorders of facial hyperpigmentation. *Dermatol Clin.* 2023;41(3):393-405.
30. Ito S, Wakamatsu K. Quantitative analysis of eumelanin and pheomelanin in humans, mice, and other animals: a comparative review. *Pigment Cell Res.* 2003;16(5):523-31.
31. Ko D, Wang RF, Ozog D, Lim HW, Mohammad TF. Disorders of hyperpigmentation. Part II. Review of management and treatment options for hyperpigmentation. *J Am Acad Dermatol.* 2023;88(2):291-320. doi:10.1016/j.jaad.2021.12.065
32. Haeri M, Phamduy T, Cafone N, Turkileri K, Velkov D. Novel digital image analysis using fractal dimension for assessment of skin radiance. *Skin Res Technol.* 2018;25:564-571.

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