

# Thiamidol: A Breakthrough Innovation in the Treatment of Hyperpigmentation

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## Abstract

Cutaneous hyperpigmentation, including melasma, solar lentigines, and post-inflammatory hyperpigmentation (PIH), results in a significant impact on patients' quality of life. Unfortunately, many currently available over-the-counter (OTC) options have been limited by efficacy, safety, and tolerability concerns. Melanogenesis is driven by a complex pathway resulting in the ultimate production and deposition of melanin in the skin. The major rate-limiting step of melanogenesis centers on the conversion of L-Dopa to the final melanin product mediated by a cellular tyrosinase, causing the overproduction of melanin clinically resulting in hyperpigmentation. Recently, isobutylamido thiazolyl resorcinol (Thiamidol) has been identified as the most effective inhibitor of human tyrosinase out of >50,000 compounds screened, and thus, a novel ingredient for inclusion in OTC products to address hyperpigmentation. The objective of this review was to describe and discuss the current pre-clinical and clinical safety and efficacy data of Thiamidol formulations aimed at educating the dermatology community on a safe and effective OTC option for use as part of the overall management of hyperpigmentation in patients.

## Introduction

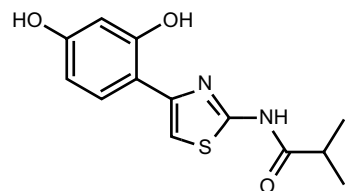
- Hyperpigmentation disorders, including melasma, post-inflammatory hyperpigmentation (PIH), dermal macular hyperpigmentation, seborrheic melanosis, and solar lentigines, represent a set of pigmentary disorders that are usually characterized by overstimulation of the melanin production pathway, resulting in deposition of excess melanin in the skin
- Recently, isobutylamido thiazolyl resorcinol (Thiamidol) was identified as the most effective inhibitor of human tyrosinase out of >50,000 compounds screened, and thus, a novel ingredient for inclusion in over-the-counter (OTC) hyperpigmentation products
- We review here the current pre-clinical and clinical studies on Thiamidol formulations aimed at educating the dermatology community on a safe and effective OTC option for use as part of the overall management of hyperpigmentation in patients

## Materials and Methods

A literature search was conducted in February 2025 on PubMed and Google Scholar databases using the search terms Thiamidol or isobutylamido thiazolyl resorcinol. This yielded a total of 21 articles which were evaluated for relevant information on the discovery and chemistry of Thiamidol, including *in vitro* analysis, as well as clinical studies investigating Thiamidol as a treatment or prophylaxis for hyperpigmentation.

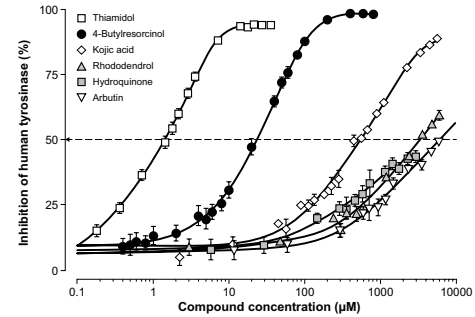
## Results

FIGURE 1. Chemical Structure of Thiamidol



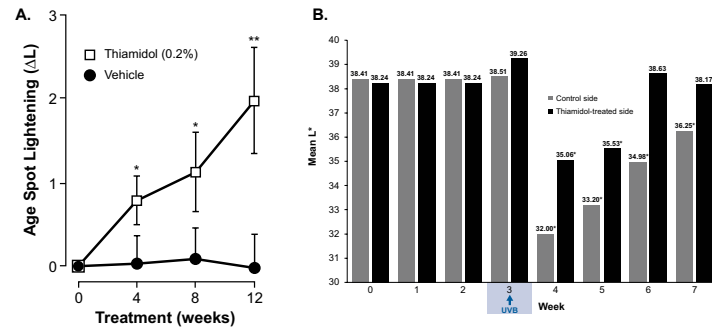
N-(4-(2,4-dihydroxyphenyl)thiazol-2-yl)isobutyramide  
Isobutylamido-Thiazolyl-Resorcinol  
**THIAMIDOL**

FIGURE 2. Inhibition of Human Tyrosinase by Thiamidol, 4-butylresorcinol, Kojic Acid, Rhododendrol, Hydroquinone, and Arbutin



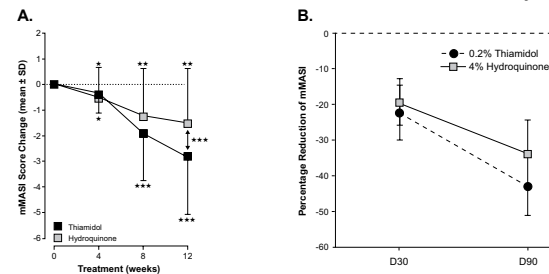
*In vitro* assays using purified hTyr in 50 mmol/L sodium phosphate buffer, pH 7.0, at a substrate (L-Dopa) concentration of 1 mmol/L and various concentrations of inhibitors as noted. Data represent the mean  $\pm$  standard deviation of three independent experiments. Kinetics of inhibition of hTyr by Thiamidol (Beiersdorf AG, Hamburg, Germany) at the concentrations noted. The experiment was performed in triplicate at pH 7.0. The data are plotted according to Lineweaver-Burk (with permission from Mann et al. 2018).

FIGURE 3. Impact of Thiamidol on UVB-induced Hyperpigmentation



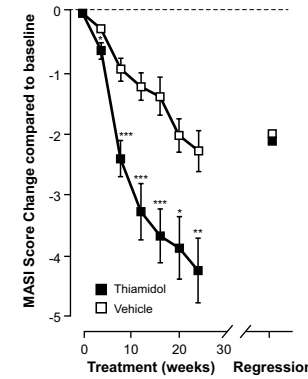
(A) Solar lentigines on the volar forearms of each subject were treated twice daily for 12 weeks with 0.2% Thiamidol (Beiersdorf AG, Hamburg, Germany) or with the vehicle only as a control using a spot applicator. Efficacy was evaluated after 4, 8, and 12 weeks. Data represent the mean  $\pm$  standard error of the mean of 17 subjects. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ; statistically significant versus the control (with permission from Mann et al. 2018). (B) Mean lightness index (L\*) of Thiamidol treated side and control side compared to baseline compared at each visit. \*Significant difference compared with baseline,  $P < 0.05$  (adapted from Vachiramon et al. 2021).

FIGURE 4. Mean mMASI Scores Before and After Treatment with Thiamidol or Hydroquinone



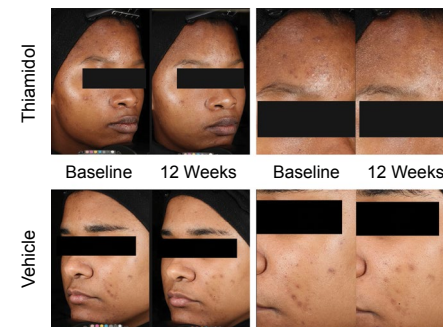
(A) Time course of mMASI score changes compared to the baseline. Scores were assessed after 4, 8, and 12 weeks of treatment. Data are reported as means  $\pm$  SD. Significant differences as marked in comparison to baseline and hydroquinone (\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ). mMASI, modified Melasma Area and Severity Index; SD, standard deviation. (B) Mean (CI 95%) percentage reduction of modified Melasma Area and Severity Index (mMASI) scores at D30 and D90 for the 0.2% Thiamidol and 4% hydroquinone groups (with permission from Arrowsitz and Lima).

FIGURE 5. Changes in Melasma Area and Severity Index (MASI) Score versus Baseline After Treatment with Thiamidol or Vehicle Control in Patients with Moderate-Severe Melasma



Significant improvement in comparison to baseline for Thiamidol and vehicle at all points in time. Significant differences between Thiamidol and vehicle as indicated (\* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ ). After 13 to 20 weeks of cessation of all treatment (regression), including sunscreen use, there was a significant difference for both treatments compared to baseline ( $P < 0.005$ ) (with permission from Roggenkamp).

FIGURE 6. Treatment of Acne-induced PIH in Dark-skinned Individuals



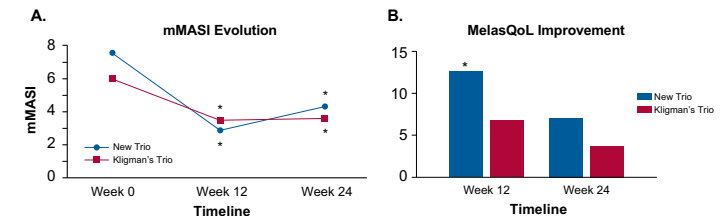
Representative images of subjects with acne-induced PIH at baseline and after 12 weeks of treatment with the Thiamidol-containing regimen or the vehicle (with permission from Roggenkamp et al. 2020).

FIGURE 7. Treatment with a Skin Care Regimen of Three Thiamidol-containing Products



(A) Representative images of a subject at baseline and after 4, 8, and 12 weeks of treatment with the Thiamidol-containing skin care regimen (day lotion with SPF 30, night cream, and dual serum). (B) Melanin index scores of lesional and perilesional skin after 4, 8, and 12 weeks of treatment. Data are depicted as mean  $\pm$  SD. Significant differences are marked in comparison to the baseline (\*\* $P < 0.001$ ) (with permission from Roggenkamp).

FIGURE 8. Clinical Evaluation of Thiamidol Trio vs Kligman's Trio in Melasma



(A) Evolution of the modified Melasma Area Severity Index (mMASI) score. Ordinate represents the mean mMASI score of the subjects of each treatment arm in points. mMASI values range from 0 to 24. \* $P < 0.05$ . (B) Improvement of the melasQoL score. Ordinate represents the mean melasQoL score improvement of the subjects of each treatment arm in points. MelasQoL values range from 0 to 70. \* $P < 0.05$  (with permission from Bertold et al).

## Study Limitations

This review is limited by studies conducted primarily on female participants, without full demographic information regarding race, ethnicity, or Fitzpatrick Skin Types for several studies, and with limited information on efficacy, safety, and tolerability in men. Additionally, many of the studies were conducted and/or sponsored by Beiersdorf AG, the developers of Thiamidol; thus, independent clinical studies would be beneficial.

## Conclusions

- Skin hyperpigmentation, including melasma, solar lentigines, and post-inflammatory hyperpigmentation, results in a significant impact on patients' quality of life
- The major rate-limiting step of melanogenesis centers on tyrosinase enzyme activity within melanocytes resulting in overproduction of melanin
- Thiamidol, isobutylamido thiazolyl resorcinol, has been identified as an effective inhibitor of human tyrosinase and melanin production with an  $IC_{50} = 1.4$  mmol/L
- Thiamidol has been shown to reduce hyperpigmentation in solar lentigines, mild-to-severe melasma, and acne-induced hyperpigmentation
- Additionally, Thiamidol has been shown to work as well as Kligman's formula when used in combination with tretinoin and dexamethasone acetate
- From these results, Thiamidol appears to be a safe and effective ingredient that should be considered as part of the overall treatment regimen for patients with hyperpigmentation

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