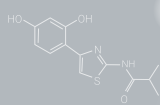
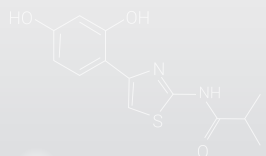


THIAMIDOL®

Targeted dermocosmetic solution
against hyperpigmentation

Study overview

2nd Edition, 2023



FOREWORD

Dear reader,

Hyperpigmentation of the skin is a major cosmetic problem and those affected by it often seek advice from their dermatologist. The current medical gold standard for the treatment is hydroquinone. However, hydroquinone can only be used for a limited period of time due to considerable adverse effects. As a consequence, dermo cosmetic solutions with comparable efficacy but without the known side effects are needed.

The most specific dermo cosmetic mechanism for the reduction of hyperpigmentation is the inhibition of the tyrosinase, which is the key enzyme for melanogenesis (Fig. 1 & 2). By inhibiting this enzyme, melanin synthesis cannot take place and pigment formation is stopped. This process is very efficient, as one single molecule of a tyrosinase inhibitor is enough per tyrosinase molecule to inhibit melanogenesis, whereas for other approaches (e.g. melanin precursor scavenging) more than hundred of molecules per tyrosinase are needed per second. Other depigmentation ingredients can remove superficial pigment (e.g. exfoliating agents) or disrupt melanin transfer (e.g. niacinamide), but only act when the pigment is already in the skin. And while antioxidants have an indirect effect via the reduction of free radicals and oxidative stress which aggravate hyperpigmentation, they do not directly interfere with melanin production.

Hundreds of tyrosinase inhibitors have been described and tested over the last decades, but Thiamidol is the only one developed and tested on human tyrosinase. At Beiersdorf, we have taken the very difficult path of producing recombinant human tyrosinase to screen for highly effective substances. Until recently, it was considered impossible to produce active human tyrosinase in cell culture, which is why mushroom tyrosinase was used for screening of active ingredients. However, together with leading international scientists, we have succeeded in producing human tyrosinase as recombinant protein, which has paved the way for the development of Thiamidol – the first true inhibitor of human tyrosinase.

This study book summarizes the scientific publications on Thiamidol. It is intended to provide you, dear reader, with a comprehensive overview while presenting take-home messages of the publications in a brief, concise and easy-to-understand manner.

Best regards!

Dr. Ludger Kolbe
Chief Scientist at Beiersdorf

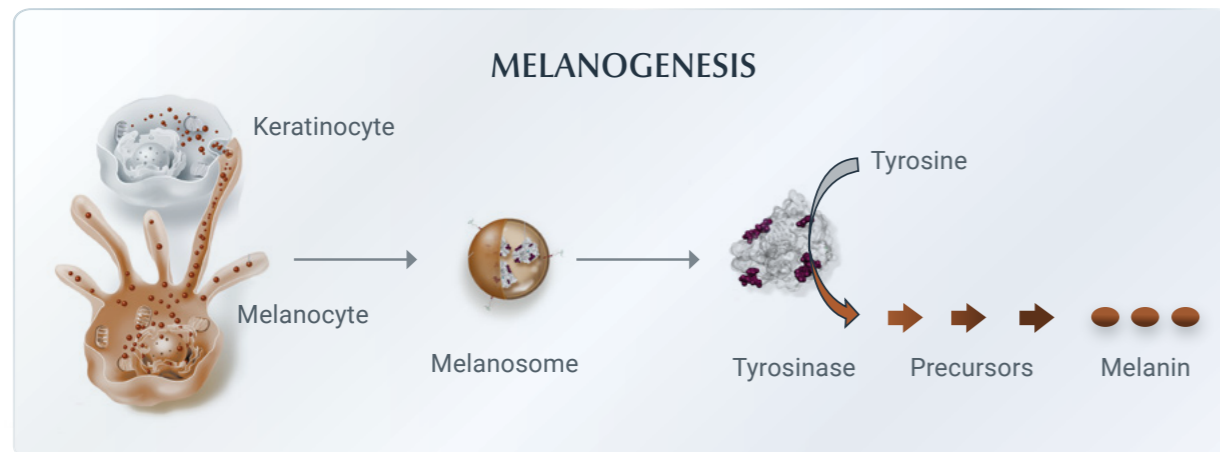


Fig 1: Tyrosinase is the key enzyme for melanogenesis.

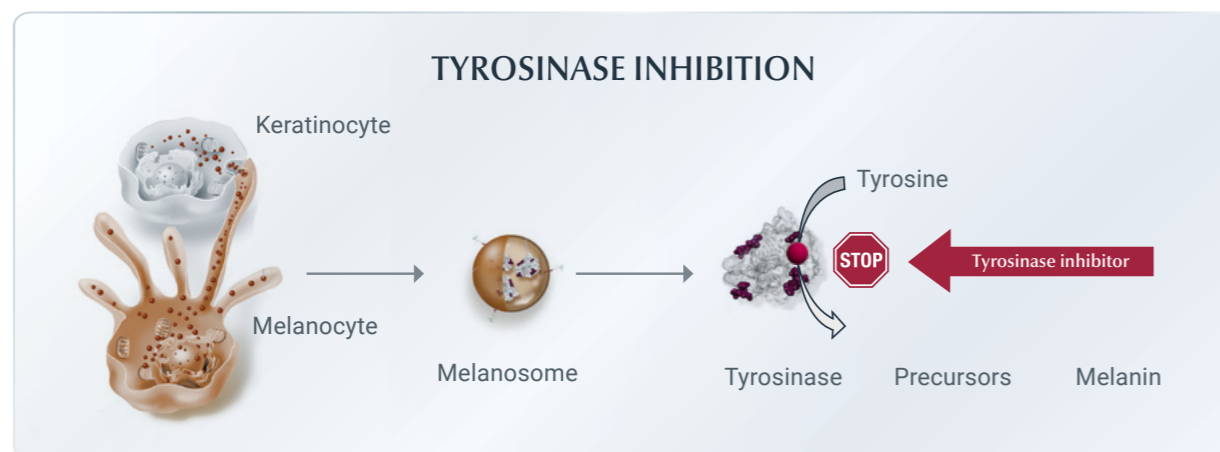


Fig 2: Tyrosinase inhibition stops melanin production. It is specific, safe, and effective.



STUDY OVERVIEW THIAMIDOL®

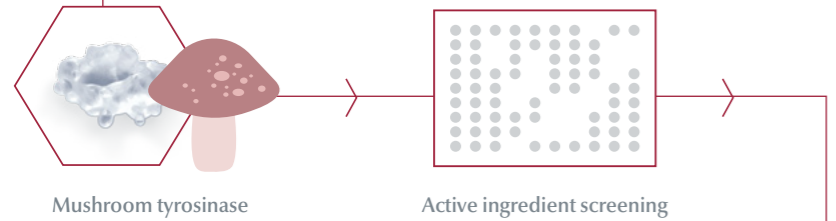
■ Foreword	2
■ Basic research	6
■ Hyperpigmentation	14
Hyperpigmentation on the face	18
Post-inflammatory hyperpigmentation	22
Hyperpigmentation & laser	23
Prevention of UV-induced hyperpigmentation	26
■ Hyperpigmentation on blemished skin	34
■ Hyperpigmentation on mature skin	42
■ Review articles, commentaries & other scientific articles	50
■ Sun protection	54



BASIC RESEARCH

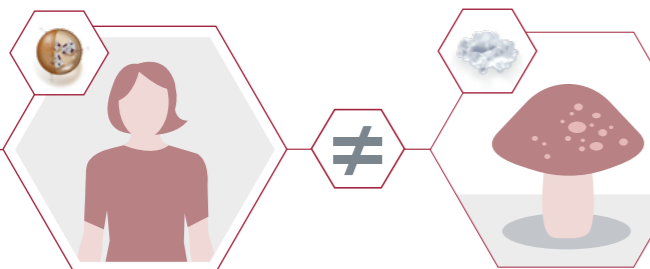
TYROSINASE IS THE KEY ENZYME FOR THE DEVELOPMENT OF HYPERPIGMENTATION

- Tyrosinase inhibition is the most targeted dermo cosmetic solution to reduce and prevent hyperpigmentation.
- Previously, it was not possible to isolate human tyrosinase in its active form. Research on tyrosinase inhibition was therefore tested using commercially available **mushroom tyrosinase**.



- Hydroquinone
- Butylresorcinol
- Phenylethyl resorcinol
- Hexylresorcinol

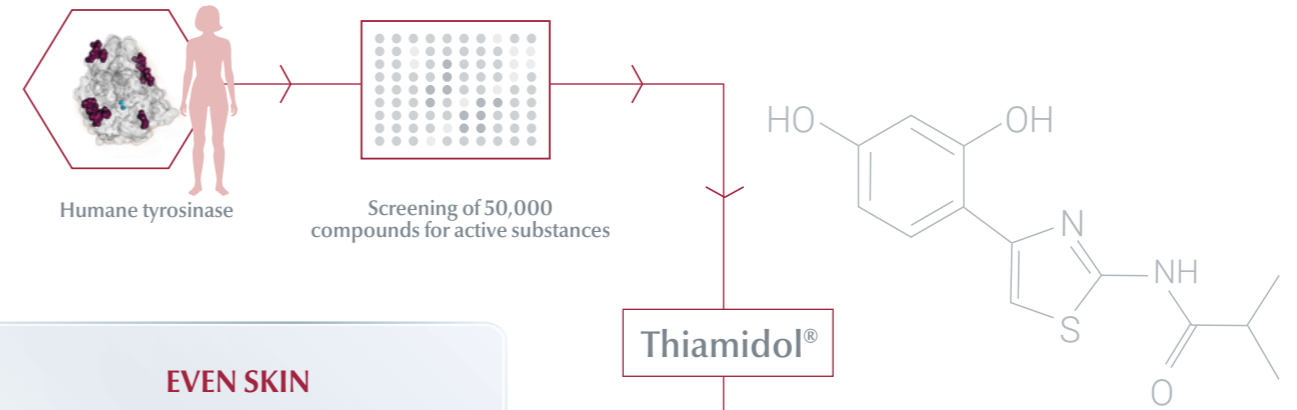
AFTER 10 YEARS OF RESEARCH, BEIERSDORF RESEARCHERS SUCCEEDED IN ISOLATING HUMAN TYROSINASE FOR THE FIRST TIME.¹



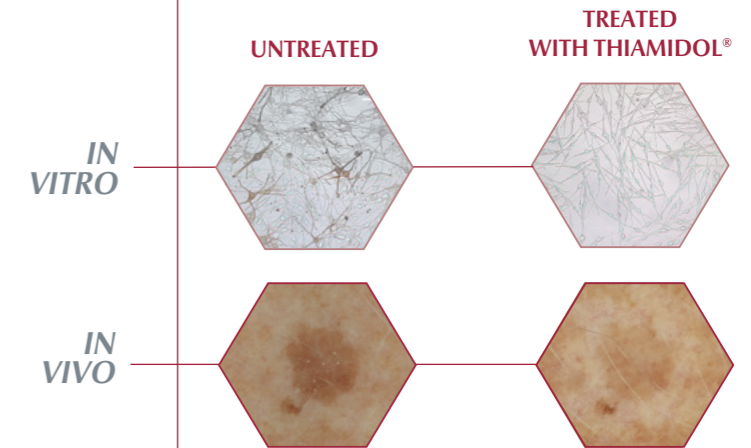
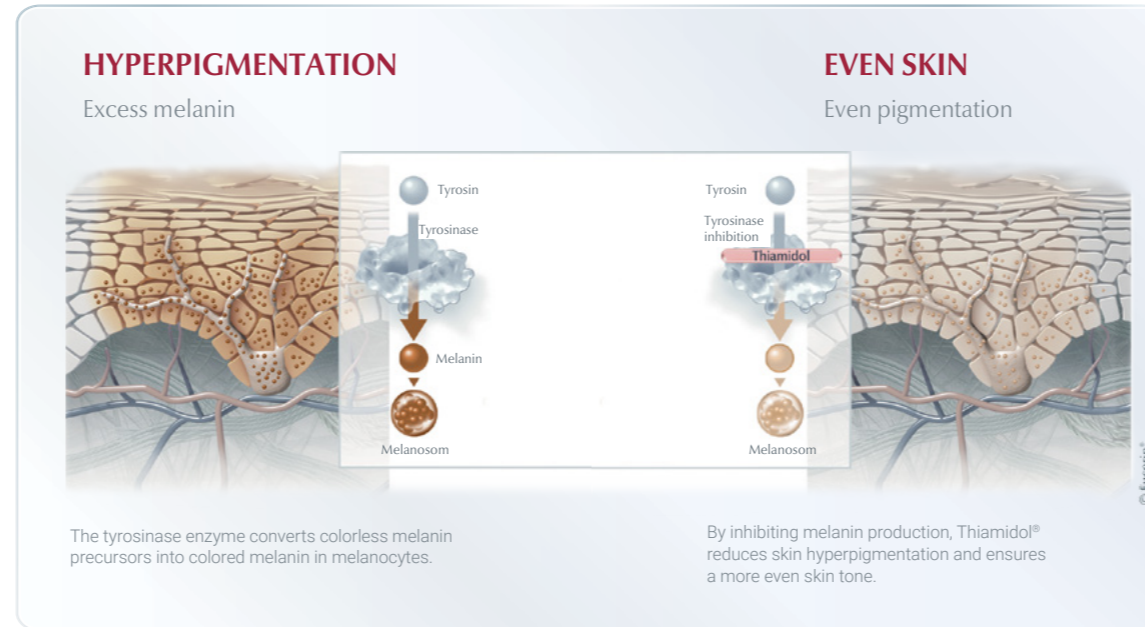
PEOPLE ARE NOT MUSHROOMS

It turns out there are fundamental differences between human tyrosinase and mushroom tyrosinase.²

THIAMIDOL® WAS IDENTIFIED AS THE MOST EFFECTIVE INHIBITOR OF HUMAN TYROSINASE²⁻⁵



Thiamidol® is a highly effective and reversible inhibitor of melanin production²



SUPERIOR EFFICACY ON THE HUMAN ENZYME

Conventional tyrosinase inhibitors have a good inhibitory effect on the mushroom enzyme, but are only weak inhibitors of the human enzyme. Thiamidol®, on the other hand, is a highly effective inhibitor of human tyrosinase.²



BASIC RESEARCH

ORIGINAL WORK

- 1 Cordes et al (2013). Expression in non-melanogenic systems and purification of soluble variants of human tyrosinase. *Biol Chem.* _____ 10
- 2 Mann et al (2018). Inhibition of human tyrosinase requires molecular motifs distinctively different from mushroom tyrosinase. *J Invest Dermatol.* _____ 11
- 3 Mann et al (2018). Structure-activity relationships of thiazolyl resorcinols, potent and selective inhibitors of human tyrosinase. *Int J Mol Sci.* _____ 12

SCIENTIFIC POSTER

- 4 Mann et al (2018). Isobutylamido thiazolyl resorcinol a highly effective inhibitor of human tyrosinase. 27th EADV Congress. _____ 13
- 5 Mann et al (2020). Efficacy of Thiamidol, niacinamide, tranexamic acid, cysteamine, azelaic acid on melanin production *in vitro*. 29th EADV Congress. _____ 13



BASIC RESEARCH

Original work

Expression in non-melanogenic systems and purification of soluble variants of human tyrosinase

P. Cordes, W. Sun, R. Wolber, L. Kolbe, G. Klebe, K.H. Röhme
Biol Chem. 2013; 394(5): 685-693.

The most important facts

HOW CAN HUMAN TYROSINASE BE ISOLATED IN ITS NATIVE FORM?

Tyrosinase is the key enzyme in melanogenesis. Previous research on tyrosinase inhibition was carried out on commercially available mushroom tyrosinase. **Beiersdorf researchers, in cooperation with leading enzyme researchers, have succeeded for the first time in isolating human tyrosinase in its active form and expressing it in cell cultures.** This laid the foundation for identification of Thiamidol® as the most effective available inhibitor of human tyrosinase.

ABSTRACT

Mammalian tyrosinases are key enzymes of melanin formation. Their native forms undergo complex maturation and sorting processes before being integrated into the melanosomal membrane, which greatly complicates their heterologous expression in other cell types.

In the present work, we constructed several differently truncated, soluble variants of human tyrosinase and studied their properties after expression in HEK 293 cells. In addition, we prepared two affinity-tagged forms of the enzyme for expression in the yeast *Kluyveromyces lactis* and HEK cells, respectively. A Strep-tagged variant was secreted by *K. lactis* in excellent yields but found to be inactive, whereas a His-tagged variant secreted by HEK 293 cells in an active state could be purified from cell supernatants to near homogeneity.

The resulting preparation consisted of an inactive, probably unglycosylated species of about 57 kDa and several glycosylated forms with masses between 63 and 75 kDa, as confirmed by activity staining, Western blotting and mass spectrometry. ■

BASIC RESEARCH

Original work

Inhibition of human tyrosinase requires molecular motifs distinctively different from mushroom tyrosinase

T. Mann, W. Gerwat, J. Batzer, K. Eggers, C. Scherner, H. Wenck, F. Stäb, V. Hearing, K. Röhme, L. Kolbe
J Invest Dermatol. 2018; 138(7): 1601–1608.

The most important facts

HOW CAN HUMAN TYROSINASE BE EFFECTIVELY INHIBITED?

Tyrosinase is the key enzyme in melanogenesis. The tyrosinase inhibitors available to date were identified using mushroom tyrosinase and showed limited clinical efficacy. **In this study, Thiamidol® was identified as the most effective inhibitor of human tyrosinase *in vitro* out of 50,000 compounds.** Thiamidol® reversibly inhibits melanin production.

For results on clinical efficacy in lentigines solares, see page 42.

ABSTRACT

Tyrosinase is the rate-limiting enzyme of melanin production and, accordingly, is the most prominent target for inhibiting hyperpigmentation. Numerous tyrosinase inhibitors have been identified, but most of those lack clinical efficacy because they were identified using mushroom tyrosinase as the target. Therefore, we used recombinant human tyrosinase to screen a library of 50,000 compounds and compared the active screening hits with well-known whitening ingredients.

Hydroquinone and its derivative arbutin only weakly inhibited human tyrosinase with a half-maximal inhibitory concentration (IC₅₀) in the millimolar range, and kojic acid showed a weak efficacy (IC₅₀ > 500 μmol/L). The most potent inhibitors of human tyrosinase identified in this screen were resorciny-thiazole derivatives, especially the newly identified Thiamidol (Beiers-

dorf AG, Hamburg, Germany) (isobutylamido thiazolyl resorcinol), which had an IC₅₀ of 1.1 μmol/L. In contrast, Thiamidol only weakly inhibited mushroom tyrosinase (IC₅₀ ¼ 108 μmol/L). In melanocyte cultures, Thiamidol strongly but reversibly inhibited melanin production (IC₅₀ ¼ 0.9 μmol/L), whereas hydroquinone irreversibly inhibited melanogenesis (IC₅₀ ¼ 16.3 μmol/L). Clinically, Thiamidol visibly reduced the appearance of age spots within 4 weeks, and after 12 weeks some age spots were indistinguishable from the normal adjacent skin. The full potential of Thiamidol to reduce hyperpigmentation of human skin needs to be explored in future studies. ■

BASIC RESEARCH

Original work

Structure-activity relationships of Thiazolyl resorcinols, potent and selective inhibitors of human tyrosinase

T. Mann, C. Scherner, K. Röhm, L. Kolbe
Int J Mol Sci. 2018; 19(3): 690.

The most important facts

HOW DO THIAZOLYL RESORCINOLS INTERACT WITH HUMAN TYROSINASE?

Thiazolyl resorcinols (4-thiazolyl resorcinol-2-amine and -amide), including Thiamidol®, selectively inhibit human tyrosinase *in vitro* and *in vivo*. This study investigates dose-response profiles of several thiazolyl resorcinols to better understand the molecular interactions with human tyrosinase. **By virtue of its structure, Thiamidol® binds perfectly to the active site of human tyrosinase.**

ABSTRACT

Tyrosinase inhibitors are of great clinical interest as agents for the treatment of hyperpigmentary disorders; however, most compounds described in the literature lack clinical efficiency due to insufficient inhibitory activity against human tyrosinase (hTyr). Recently, we reported that thiazolyl resorcinols (4-resorcinythiazol-2-amines and -amides) are both selective and efficacious inhibitors of hTyr *in vitro* and *in vivo*. Here, we measured dose-activity profiles of a large number of thiazolyl resorcinols and analogous compounds to better understand the molecular basis of their interaction with hTyr.

We show that both the resorcinylo moiety and the thiazole ring must be intact to allow efficient inhibition of hTyr, while the substituents at the thiazole 2-amino group confer additional inhibitory activity, depending on their size and polarity.

The results of molecular docking simulations were in excellent agreement with the experimental data, affording a rationale for the structural importance of either ring. We further propose that a special type of interaction between the thiazole sulfur and a conserved asparagine residue is partially responsible for the superior inhibitory activity of thiazolyl resorcinols against hTyr. ■

BASIC RESEARCH

Scientific poster

Isobutylamido thiazolyl resorcinol – a highly effective inhibitor of human tyrosinase

T. Mann, W. Gerwat, H. Wenck, K.H. Roehm, L. Kolbe
EADV Congress 2018.

The most important facts

Thiamidol® is a highly effective inhibitor of human tyrosinase and shows high clinical efficacy.

Full publication on page 11.

Efficacy of Thiamidol, niacinamide, tranexamic acid, cysteamine, azelaic acid on melanin production *in vitro*

T. Mann, V. Welge, J. Weise, D. Roggenkamp, L. Kolbe
EADV Congress 2020.

The most important facts

Thiamidol® inhibits human tyrosinase more effectively than niacinamide, tranexamic acid, cysteamine & azelaic acid

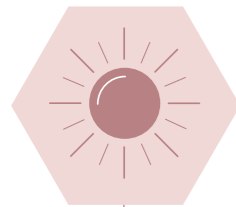
The inhibition efficiency of various tyrosinase inhibitors on human tyrosinase was measured *in vitro*. Thiamidol® showed the strongest inhibition efficiency compared to niacinamide, tranexamic acid, cysteamine & azelaic acid.

HYPERPIGMENTATION

HYPERPIGMENTATION CAN BE VERY STRESSFUL FOR THOSE AFFECTED

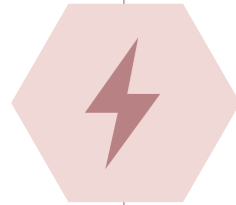
The long duration of therapy, a high risk of recurrence, as well as inadequate therapy options that are not well tolerated by the skin often make treatment challenging.

CONTRIBUTING FACTORS



Hyperpigmentation

- UV irradiation
- Age
- Hormones
- Genetic disposition



Post-inflammatory Hyperpigmentation

- Skin injuries
- Inflammatory skin diseases
- Cosmetic procedures

It is always there, on your face

It makes me feel self-conscious

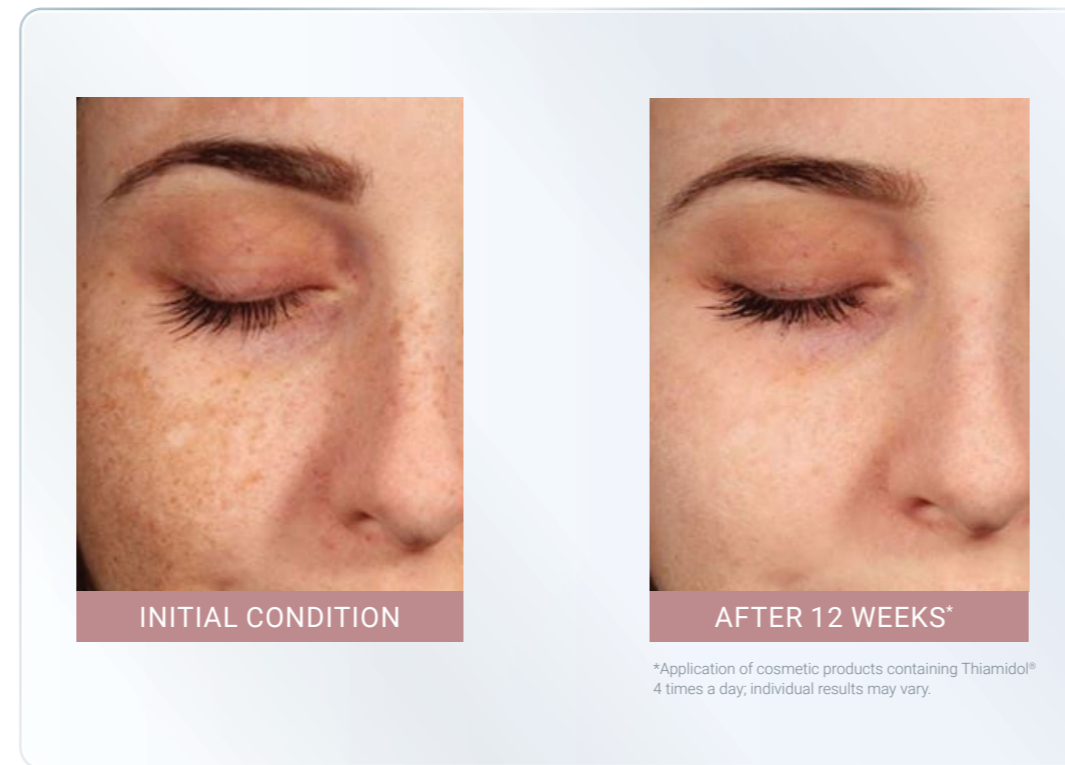


HYPERPIGMENTATION REDUCES THE QUALITY OF LIFE

Hyperpigmentation can be perceived as very bothersome, which impacts the quality of life of those affected.

THIAMIDOL® EFFECTIVELY REDUCES HYPERPIGMENTATION

Cosmetic application of skin care products containing Thiamidol® enables highly effective reduction of various types of hyperpigmentation and is well tolerated by the skin.



*Application of cosmetic products containing Thiamidol® 4 times a day; individual results may vary.

- ✓ **HYPERPIGMENTATION**^{6-10, 15-17, 19}
 - First visible results after just **2 weeks**^{6, 15}
 - Optimal results after using Thiamidol® **4x a day**^{7, 15}
 - Highly effective and well tolerated by the skin even when used for 6 months^{8, 19}
- ✓ **POST-INFLAMMATORY HYPERPIGMENTATION**¹¹
Effective reduction, both in the post-procedure model as well as in acne-induced hyperpigmentation
- ✓ **COMPLEMENTARY CARE FOR LASER TREATMENTS**^{12, 13}
Increased reduction in hyperpigmentation
- ✓ **PREVENTION OF UV-INDUCED HYPERPIGMENTATION**^{14, 18}



BETTER QUALITY OF LIFE THROUGH A MORE EVEN COMPLEXION¹⁹

Thiamidol® gradually fades pigment spots. The result is a more radiant, even complexion that noticeably improves the quality of life of those affected.

HYPERPIGMENTATION

ORIGINAL WORK

HYPERPIGMENTATION ON THE FACE

- 6** Arrowitz et al (2019). Effective tyrosinase inhibition by Thiamidol results in significant improvement of mild to Moderate melasma. *J Invest Dermatol.* _____ **18**
- 7** Philipp-Dormston et al (2020). Thiamidol containing treatment regimens in facial hyper-pigmentation: an inter-national multi-centre approach consisting of a double-blind, controlled, split-face study and of an open-label, real-world study. *Int J Cosmet Sci.* _____ **19**
- 8** Roggenkamp et al (2021). Thiamidol in moderate-to-severe melasma: 24-week, randomized, double-blind, vehicle-controlled clinical study with subsequent regression phase. *J Dermatol.* _____ **20**
- 9** Disphanurat et al (2021). 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-blinded trial. *J Cosmet Dermatol.* _____ **21**

POST-INFLAMMATORY HYPERPIGMENTATION

- 10** Roggenkamp et al (2021). Effective reduction of post-inflammatory hyperpigmentation with the tyrosinase inhibitor isobutylamido-thiazolyl-resorcinol (Thiamidol). *Int J Cosmet Sci.* _____ **22**

HYPERPIGMENTATION AND LASER THERAPY

- 11** Vachiramom et al (2020). 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.* _____ **23**
- 12** Nienstedt R, Rümmelein B (2021). Lentigo Solaris: Thiamidol-containing aftercare after laser treatment on the back of the hand. *Schweizer Zeitschrift für Dermatologie + Ästhetische Medizin [Swiss Journal of Dermatology + Cosmetic Medicine].* _____ **24**
- 13** Troilius Rubin A et al (2022). Treating post-inflammatory hyperpigmentation with a tyrosinase inhibitor. *PRIME.* _____ **25**

PREVENTION OF UV-INDUCED HYPERPIGMENTATION

- 14** Vachiramom V, Kositkuljorn C, Leerunyakul K, Chanprapaph K (2021). Isobutylamido thiazolyl resorcinol for prevention of UVB-induced hyperpigmentation. *J Cosmet Dermatol.* _____ **26**

SCIENTIFIC POSTER

- 15** Roggenkamp et al (2018). Efficacy of skin care formulations with Thiamidol in reducing facial hyperpigmentation. 27th EADV Congress. _____ **27**
- 16** Mann et al (2019). Isobutylamido thiazolyl resorcinol, a highly effective active for the treatment of facial hyperpigmentation. 24th WCD. _____ **27**
- 17** Roggenkamp et al (2019). Efficacy and tolerability of a skin care regimen with Thiamidol in patients with facial hyperpigmentation. 28th EADV Congress. _____ **28**
- 18** Mann et al (2019). Visible light-induced darkening of human skin can be reproduced by isobutylamido thiazolyl resorcinol (Thiamidol), an effective tyrosinase inhibitor. 28th EADV Congress. _____ **28**
- 19** Roggenkamp et al (2020). 24-week long-term efficacy and tolerability of a skin care regimen with Thiamidol in patients with moderate to severe facial hyperpigmentation. 29th EADV Congress. _____ **29**
- 20** Warnke et al (2022). Improving skin complexion for ultimate glow and radiant skin, combining liquid crystalline technology with an effective tyrosinase inhibitor. 31st EADV Congress. _____ **29**
- 21** Vendruscolo et al (2023). Challenge of managing hyperpigmentation in Latin American skin during the summer. *RADLA 2023.* _____ **30**
- 22** Vendruscolo et al (2023). Hyperpigmentation in oily skin: a constant challenge to maintain skincare routine. 25th WCD Congress. _____ **30**
- 23** Griffiths et al (2023). Real-World Evidence: Efficacy of a dermocosmetic regimen containing tyrosinase inhibitor Thiamidol to reduce hyperpigmentation. 32nd EADV Congress. _____ **31**
- 24** Warnke et al (2023). Eye-opening: combining an effective tyrosinase inhibitor with Oligopeptides and Hyaluronic Acid to tackle brown and blue under-eye circles. 32nd EADV Congress. _____ **31**
- 25** Sammain et al (2023): Tyrosinase Inhibition to prevent of iatrogenic, laser associated post inflammatory hyperpigmentation. 32nd EADV congress. _____ **32**
- 26** Warnke et al (2023). Targeting hyperpigmentation on friction areas with an effective tyrosinase inhibitor and skin renewal. 32nd EADV Congress. _____ **32**

HYPERPIGMENTATION

Original work

Effective tyrosinase inhibition by Thiamidol results in significant improvement of mild to moderate melasma

C. Arrowitz, A.M. Schoelermann, T. Mann, L.I. Jiang, T. Weber, L. Kolbe
J Invest Dermatol. 2019; 139(8): 1691-1698.e6.

The most important facts

HOW EFFECTIVE IS THIAMIDOL® FOR HYPERPIGMENTATION ON THE FACE?

The long duration of therapy, a high risk of recurrence, as well as inadequate therapy options thus far, make treatment of hyperpigmentation challenging. This randomized, split-face study investigated the efficacy of Thiamidol® in reducing hyperpigmentation on the face.

After 12 weeks, the use of Thiamidol® resulted in a 79% reduction in the Melasma Area and Severity (MASI) score.

ABSTRACT

Melasma is a pigmentary disorder characterized by hyperpigmented patchy skin in sun-exposed areas, especially the face. Treatment of melasma can be challenging because long-term therapy is required, reoccurrence is common and existing therapies are insufficient and unsatisfactory.

To investigate new treatment options, we performed an exploratory double-blinded, randomized split-face study to assess the efficacy of the tyrosinase inhibitor Thiamidol compared to hydroquinone in women with mild to moderate melasma. After 12 weeks, modified Melasma Area and Severity Index scores significantly improved on both the Thiamidol-treated and the hydroquinone-treated sides of the face. Additionally, Thiamidol treatment improved modified Melasma Area and Severity Index scores significantly better than hydroquinone, and more subjects

improved following treatment with Thiamidol (79%) compared with hydroquinone (61%). During treatment, no subjects displayed worsening of modified Melasma Area and Severity Index scores on the Thiamidol-treated side, while approximately 10% of the subjects showed a worsening of modified Melasma Area and Severity Index scores on the hydroquinone-treated side.

All subjects routinely used sunscreens and consistent results were obtained in low and in high UV ambient conditions. Subjects rated the efficacy of the Thiamidol formulation significantly better with regard to overall decreased intensity of dark spots and their overall appearance throughout the study. Thiamidol was well tolerated and well perceived and represents an effective agent to reduce hyperpigmentation. ■

HYPERPIGMENTATION

Original work

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

W.G. Philipp-Dormston, A. Vila Echagüe, S.H. Pérez Damonte, J. Riedel, A. Filbry, K. Warnke, C. Lofrano, D. Roggenkamp, G. Nippel. | Int J Cosmet Sci. 2020; 42(4): 377-387.

The most important facts

HOW OFTEN SHOULD SKIN CARE PRODUCTS CONTAINING THIAMIDOL® BE USED TO REDUCE HYPERPIGMENTATION ON THE FACE?

Two studies compared the efficacy of a skin care regimen with Thiamidol® with application of skin care products containing Thiamidol® 2x vs. 4x a day. **Results showed superior efficacy with application 4x a day versus 2x a day, with the first visible results after 2 weeks.**

An open-label, real-world study subsequently confirmed that application of skin care products containing Thiamidol® 4x a day was **highly effective, very well tolerated, and easy to use.**

ABSTRACT

Objective:

Tyrosinase is the rate-limiting enzyme in melanogenesis. Thiamidol is the most potent inhibitor of human tyrosinase out of 50,000 tested compounds. In clinical studies, it was shown to improve facial hyperpigmentation, post-inflammatory hyperpigmentation and age spots significantly. To identify the optimal number of daily Thiamidol applications, we conducted a split-face study comparing the efficacy and tolerability of four-times with two-times daily application. Subsequently, we evaluated the efficacy and tolerability of a typical face care regimen containing Thiamidol in a real-world study.

Results:

In the split-face study (n = 34), hyperpigmentation, skin roughness and hMASI improved all significantly (P < 0.001) versus baseline, with first visible results after two weeks of twice-daily application. The four-times daily application led to significant

improvement versus the two-times daily application. In the real-world study (n = 83), all evaluated parameters, including skin condition and chromametry (n = 30), improved significantly (P < 0.001) in comparison with baseline and the corresponding preceding visits. The subjects judged the cosmetic properties of the products positively. In both studies, the products were well tolerated.

Conclusion:

Four-times daily Thiamidol improves facial hyperpigmentation significantly more than two-times daily and is well tolerated by the subjects. The real-world study with a typical face care regimen containing Thiamidol shows improvement of facial hyperpigmentation and confirms tolerability. Furthermore, the data provide evidence for the suitability of this three-product Thiamidol regimen for day-to-day life. ■

HYPERPIGMENTATION

Original work

Thiamidol® in moderate-to-severe melasma: 24-week, randomized, double-blind, vehicle-controlled clinical study with subsequent regression phase

D. Roggenkamp, A. Sammain, M. Fürstenau, M. Kausch, T. Passeron, L. Kolbe
J Dermatol. 2021; 48(12): 1871-1876.

The most important facts

HOW EFFECTIVE AND WELL TOLERATED IS A THIAMIDOL®-CONTAINING SKIN CARE REGIMEN FOR 6 MONTHS AND WHAT HAPPENS WHEN IT IS DISCONTINUED?

This double-blind, randomized, controlled clinical trial investigated the efficacy and tolerability of a skin care regimen with Thiamidol® for the reduction of hormonally induced hyperpigmentation for 6 months followed by a 3-month regression phase. **The skin care regimen with Thiamidol® was superior versus vehicle and the hyperpigmentation continuously improved (measured by MASI and clinical photographs) over 6 months.** After a 3-month regression phase, the MASI was still lower than at baseline, but the values for Thiamidol® vs. vehicle converged. The lightening effect of Thiamidol® is, therefore, reversible.

ABSTRACT

Thiamidol was the most potent inhibitor of human tyrosinase out of 50,000 screened substances. *In vivo*, it was well tolerated and improved melasma significantly. This was the first 24-week, randomized, double-blind, vehicle-controlled, cosmetic clinical study to assess the efficacy and tolerability of Thiamidol in moderate-to-severe melasma of phototype III-V subjects with subsequent regression phase. Females allocated to verum (n = 23), applied daily Dual Serum followed either by Day Care SPF30 in the morning or by Night Care in the evening, all containing Thiamidol.

The vehicle group (25 females) followed the same skin care routine, using the corresponding vehicle formulations. Subjects came back for a follow-up visit 13 to 20 weeks after treatment (regression phase). Assessments included clinical photography, Melasma Area and Severity Index (MASI), skin lightness, quality of life and tolerability. Baseline demographics and hyperpigmen-

tation were well balanced across the treatment groups. Clinical photography and MASI improved with Thiamidol significantly versus baseline ($p < 0.001$) and vehicle ($p < 0.001-0.043$) at all time points up to treatment end. At follow-up, the MASI was still significantly lower than at baseline but similar for verum and vehicle. Skin lightness and quality of life improved significantly versus baseline without significant differences between verum and vehicle. This study demonstrated that Thiamidol is well tolerated and superior in improving melasma compared to baseline and vehicle over a treatment period of 24 weeks. ■

HYPERPIGMENTATION

Original work

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

W. Disphanurat, B. Srisantithium
J Cosmet Dermatol. 2021; online ahead of print.

The most important facts

DOES USE OF HYALURONIC ACID IN COMBINATION WITH THIAMIDOL® INCREASE THE CLINICAL EFFICACY FOR MELASMA?

Hyaluronic acid is one of the most important skin moisturisers. Hyaluronic acid is found in many moisturizing skin care products as natural production declines with age. This study investigated a possible additional benefit of hyaluronic acid in combination with Thiamidol® in women with hormonally induced hyperpigmentation. **After 12 weeks, there was a significant improvement in hyperpigmentation (measured by MASI) in all Thiamidol® users.** Hyaluronic acid did not significantly increase the efficacy for reducing hyperpigmentation, but the **two ingredients can synergistically increase the homogeneity of hyperpigmentation.**

ABSTRACT

Background:

Melasma has a complex pathogenesis, and various aggravating factors contribute to its recalcitrance to treatments. A combination of isobutylamido thiazolyl resorcinol (ITR) and hyaluronic acid (HA) could increase melasma treatment efficacy.

Aims:

To compare the efficacy and safety of 0.15% ITR plus HA vs 0.15% ITR or HA alone in melasma treatment.

Methods:

Ninety-two patients received ITR 0.15% plus HA (n = 30), 0.15% ITR (n = 31), or HA (n = 31) along with broad-spectrum sunscreen application for 12 weeks. Treatment efficacy was determined using modified Melasma Area Severity Index (mMASI), average melanin and melanin variation with Antera3D, and safety based on transepidermal water loss.

Results:

Compared with the HA group, the ITR+HA group showed significantly reduced mMASI at weeks 4, 8 and 12 ($p = 0.026$, 0.015 and 0.001 , respectively), whereas the ITR group showed a significant reduction at week 12 ($p = 0.027$). There was no significant difference in the mMASI or average melanin level between the ITR+HA and ITR groups. Melanin variation was significantly lower in the ITR+HA group than in the ITR group at weeks 4, 8 and 12 ($p = 0.027$, 0.019 and 0.023 , respectively).

Conclusions:

The combination of 0.15% ITR and 0.15% ITR+HA effectively reduced melasma severity. HA could synergistically improve melasma homogeneity. ■

HYPERPIGMENTATION | PIH

Original work

Effective reduction of post-inflammatory hyperpigmentation with the tyrosinase inhibitor isobutylamido-thiazolyl-resorcinol (Thiamidol)

D. Roggenkamp, N. Dlova, T. Mann, J. Batzer, J. Riedel, M. Kausch, L. Kolbe
Int J Cosmet Sci. 2021; 43(3):292-301.

The most important facts

HOW EFFECTIVE IS THIAMIDOL® FOR POST-INFLAMMATORY HYPERPIGMENTATION?

Post-inflammatory hyperpigmentation (PIH) can be triggered by minimally invasive procedures. This study investigated the efficacy of a formulation containing Thiamidol® (used 2x a day for 12 weeks) in PIH caused by "suction blistering". **After just 2 weeks, there was significant lightening of the PIH (measured by spectroscopy) on the suction blister side treated with Thiamidol® compared to the side treated with vehicle.**

For results on the efficacy of acne-induced PIH, see page 38.

ABSTRACT

Objective:

Post-inflammatory hyperpigmentation (PIH) is a major cosmetic concern especially in individuals with darker skin complexion. Unfortunately, treatment with anti-inflammatory ingredients alone does not prevent the development of hyperpigmented spots. Recently, isobutylamido-thiazolyl-resorcinol (Thiamidol) was described as a very potent inhibitor of human tyrosinase. The objective of this research was to investigate the potential of this compound to prevent PIH induced by epidermal wounding (suction blister) and related to acne.

Methods:

Suction blister-induced PIH was treated with a formulation containing Thiamidol or a vehicle for 3 months and the changes in hyperpigmentation were monitored by spectroscopic measurements. The effect of skin care formulations containing Thiamidol on acne-related PIH was investigated in two studies: a vehicle-controlled, double-blinded, randomized clinical study

and a clinical observational study. Both studies had a duration of 3 months and included assessments such as clinical photography, clinical grading and melanin index measurements.

Results:

Already after 2 weeks of treatment, suction blister sites treated with Thiamidol were significantly lighter than control sites and improved throughout the treatment period. Subjects' self-grading demonstrated that Thiamidol significantly improved the visibility of acne-induced hyperpigmentation compared to the vehicle treatment. A skin care regimen with Thiamidol significantly improved acne-related PIH over 12 weeks shown by Mexameter measurements, expert grading, self-grading and clinical photography.

Conclusion:

Thiamidol represents a safe and effective ingredient for cosmetic products against post-inflammatory hyperpigmentation. ■

HYPERPIGMENTATION | LASER

Original work

Combined isobutylamido thiazolyl resorcinol and low-fluence Q-switched Nd: YAG laser for the treatment of facial hyperpigmentation: A randomized, split-face study

V. Vachiramon, K. Leerunyakul, C. Kositkuljorn, P. Chayavichitsilp
J Cosmet Dermatol. 2021; 20(6):1724-1731.

The most important facts

DOES USE OF THIAMIDOL® AS A COMPLEMENTARY CARE PRODUCT INCREASE THE THERAPEUTIC SUCCESS OF LASER TREATMENTS FOR THE REDUCTION OF HYPERPIGMENTATION ON THE FACE?

A variety of types of hyperpigmentation are often treated with laser therapy in dermatological practice. This split-face study investigated whether use of Thiamidol® as complementary care (applied 2x a day for 12 weeks, starting with the first laser session) can increase the therapeutic success of a five-week laser therapy (one session per week). **After the last laser treatment, there was superior lightening on the half of the face treated with Thiamidol® compared to the half of the face treated with vehicle.** The use of Thiamidol® as complementary care for laser therapy was also well tolerated.

ABSTRACT

Background:

Isobutylamido thiazolyl resorcinol (ITR) is a novel anti-tyrosinase recently shown to be effective in the treatment of hyperpigmentation. Low-fluence Q-switched Nd:YAG 1064-nm laser (LFQS) has proven to be effective for various hyperpigmentary conditions. However, there is no study on the efficacy and safety of combined ITR and LFQS treatment.

Objectives:

To compare the efficacy and safety of combined ITR and LFQS with LFQS monotherapy for facial hyperpigmentation.

Materials and Methods:

Patients with symmetrical facial hyperpigmentation were treated with five sessions of once weekly LFQS on the whole face. One side was randomly treated with ITR and the other side received a placebo cream for 12 weeks. Patients were followed for 8 weeks after the last laser treatment. Relative lightness index (RL*1), Facial Hyperpigmentation

Severity Score on the malar area (FHSSm), patient satisfaction, recurrence and adverse events were recorded.

Results:

Twenty-four patients completed the study. Both sides demonstrated significant reductions of mean RL*1 and mean FHSSm from baseline ($p < 0.01$). At the 4th week, the ITR-treated side showed more improvement of mean RL*1 than the placebo-treated side (62.5% vs 47.3% improvement, $P < .05$). The mean FHSSm on the ITR-treated was reduced at a significantly higher percentage than the placebo-treated side (54.4% vs 40.2% reduction, $p < 0.05$). Partial recurrence was observed on both sides. No serious side effects were noted.

Conclusion:

Combined ITR and LFQS therapy was more superior than LFQS mono-therapy in the treatment of facial hyperpigmentation. ITR may serve as adjuvant for patients with such a condition. ■

HYPERPIGMENTATION | LASER

Original work

Lentigo solaris: Thiamidol-containing aftercare following laser treatment on the back of the hand

R. Nienstedt, B. Rümmelein
Schweizer Zeitschrift für Dermatologie + Ästhetische Medizin [Swiss Journal of Dermatology + Cosmetic Medicine].

The most important facts

DOES USE OF THIAMIDOL® AS COMPLEMENTARY CARE INCREASE THE THERAPEUTIC SUCCESS OF LASER TREATMENTS FOR THE REDUCTION OF LENTIGO SOLARIS IN DIFFICULT THERAPEUTIC INITIAL CONDITIONS?

This double-blind study investigated whether applying an SPF50+ formulation and Thiamidol® 4 times a day after laser treatment to reduce lentigo solaris on the back of the hand leads to increased treatment success compared to applying an SPF50+ formulation 4 times a day. All subjects had a difficult therapeutic initial condition (e.g. actinic damage, strong predisposition to post-inflammatory hyperpigmentation). **After applying SPF 50+ and Thiamidol® to one hand for 8 weeks and SPF 50+ to the other, 69% of the subjects showed superior lightening on the back of the hand treated with Thiamidol®.** The lack of success in the remaining subjects could partly be attributed to application errors.

HYPERPIGMENTATION | LASER

Original work

Treating Post-Inflammatory Hyperpigmentation with A Tyrosinase Inhibitor

A. Troilius Rubin, Z. Tsaknakis, A. Sammain, L. Schmidt
PRIME 2022; 12(1): 29-32.

The most important facts

CAN THIAMIDOL HELP TO REDUCE POST-INFLAMMATORY HYPERPIGMENTATION CAUSED BY LASER TREATMENTS?

Post-inflammatory hyperpigmentation (PIH) is a common side-effect after ablative treatments of the skin, especially in Skin type III-IV but also after sunburn or inflammatory acne. This study aimed to evaluate the efficacy and safety of a skin care regimen containing Thiamidol to improve PIH due to ablative laser treatment, acne or sunburns.

Thiamidol demonstrated effective improvement of epidermal PIH without severe side-effects as well as a high patient satisfaction rate after 1 month of treatment.

ABSTRACT

Background:

Post-inflammatory hyperpigmentation (PIH) is a common side-effect after ablative treatments of the skin, especially in Skin type III-IV but also after sunburn or inflammatory acne. Isobutylamido thiazolyl resorcinol (ITR, Thiamidol®) has been proposed as a potent tyrosinase inhibitor to improve PIH.

Objectives:

This study aimed to evaluate the efficacy and safety of an ITR-containing regimen (Eucerin AntiPigment Range) to improve melasma or PIH due to ablative laser treatment, acne or sunburns.

Materials and methods:

A single centre post-laser study was performed to evaluate the reduction of PIH and Melasma in healthy participants by using two formulations containing ITR in the morning (Eucerin® AntiPigment Day Care SPF 30 and Eucerin® AntiPigment Dual Serum) and two formulations containing ITR in the evening (Eucerin® AntiPigment Night Care and Eucerin® AntiPigment

Dual Serum) for 12 consecutive weeks. Clinical photography (Canfield Visia Skin Analysis system of brown spot and UV spot count and intensity) and patient self-assessment were performed at 0, 4, and 12 weeks.

Results:

30 patients were included in this study and 3 patients were lost to follow up. In the remaining 27 patients, a statistically significant improvement on both brown spot count and intensity, as well as UV-spot count and intensity, was noted after 4 and 12 weeks of treatment (p-value <0,001).

Conclusion:

Thiamidol demonstrated effective improvement of epidermal PIH without severe side-effects as well as a high patient satisfaction rate after 1 month of treatment. ■

HYPERPIGMENTATION | PREVENTION

Original work

Isobutylamido thiazolyl resorcinol for prevention of UVB-induced hyperpigmentation

V. Vachiramon, C. Kositkuljorn, K. Leerunyakul, K. Chanprapaph
J Cosmet Dermatol. 2021; 20(3): 987-992.

The most important facts

CAN THIAMIDOL® PREVENT UVB-INDUCED HYPERPIGMENTATION?

UV irradiation is one of the most common causes of hyperpigmentation. This study investigated whether treatment with Thiamidol® can prevent UVB-induced hyperpigmentation. After application of Thiamidol® 2 times a day for 3 weeks, **significantly less pronounced hyperpigmentation (measured via colorimeter)** was observed on the treated upper arm compared to the untreated upper arm after bilateral irradiation with UVB. **Furthermore, the discoloration on the treated upper arm faded more quickly;** after just 3 weeks it was no longer visible.

ABSTRACT

Background:

Isobutylamido thiazolyl resorcinol (ITR, Thiamidol®) has been proposed as a potent tyrosinase inhibitor. A formulation containing ITR has recently showed promising efficacy for the treatment of some hyperpigmentary conditions.

Objectives:

This study aimed to evaluate the efficacy and safety of ITR in the prevention of ultraviolet (UV)-induced hyperpigmentation in human skin.

Materials and Methods:

We performed a randomized, single-blinded, pilot study in 30 healthy participants. One arm was randomly assigned to receive an ITR-containing product for 3 weeks. Three hyperpigmented spots were induced by UVB irradiation on both arms after 3 weeks of ITR application. Outcome evaluations included measuring mean lightness index (*L) obtained by colorimeter, hyperpigmentation scores by visual analog scale (VAS) and adverse effects.

Results:

Both experimental sides showed no significant difference in terms of skin lightening after ITR application. However, the ITR-treated sides showed a statistically significant lower mean lightness index compared to control after an induction with UVB. In addition, the ITR-treated sides had an earlier improvement and resumed the normal skin color after 3 weeks post-UVB induction. A clinical evaluation by a blinded nontreating physician and subjects was more favorable on the ITR-treated side than the control side ($p < 0.05$). No significant side effect was noted.

Conclusions:

ITR is an effective agent in the prevention of pigmentary change from UVB irradiation and may serve as a promising agent for preventing other hyperpigmentary conditions. ■

Efficacy of skin care formulations with Thiamidol in reducing facial hyperpigmentation

D. Roggenkamp, J. Riedel, G-M. Warnke, L. Kolbe, A. Filbry
EADV Congress 2018.

The most important facts

The application of Thiamidol® 4 times a day in a skin care regimen (consisting of serum and day care) showed a clearly superior efficacy in treatment of hyperpigmentation compared to application of Thiamidol® 2 times a day (day care).

See full publication on page 19.

HYPERPIGMENTATION

Scientific poster

Isobutylamido thiazolyl resorcinol, a highly effective active for the treatment of facial hyperpigmentation

T. Mann, G. Arrowitz, W. Gerwat, T. Weber, L. Kolbe
World Congress of Dermatology WCD 2019.

The most important facts

Thiamidol® is a reversible inhibitor of human tyrosinase and, thus, effectively prevents formation of hyperpigmentation on the face.

See full publication on page 16.

HYPERPIGMENTATION

Scientific poster

Efficacy and tolerability of a skin care regimen with Thiamidol in patients with facial hyperpigmentation

D. Roggenkamp, G. Neufang, C. Lofrano, S. Damonte Perez, A. Vila Echagüe
EADV Congress 2019.

The most important facts

A Thiamidol®-containing skin care regimen significantly reduces mild to moderate hyperpigmentation on the face.

Full publication on page 16.

Visible light-induced darkening of human skin can be reduced by isobutylamido thiazolyl resorcinol (Thiamidol), an effective tyrosinase inhibitor

T. Mann, K. Eggers, J. Riedel, M. Luettkens, L. Hemprich, L. Kolbe
EADV Congress 2019.

The most important facts

Thiamidol® reduces hyperpigmentation on the face caused by visible light.

In this study, irradiation with visible light resulted in darkening of the skin, which was visible for up to 24 hours on skin areas that were already hyperpigmented. The darkening was more pronounced on areas of hyperpigmented skin than on normal skin areas. Daily application of Thiamidol® reduced the hyperpigmentation caused by visible light.

HYPERPIGMENTATION

Scientific poster

24-week long-term efficacy and tolerability of a skin care regimen with Thiamidol in patients with moderate to severe facial hyperpigmentation

D. Roggenkamp, M. Fürstenau, M. Kausch, A. Sammain, L. Kolbe
EADV Congress 2020.

The most important facts

A Thiamidol®-containing skin care regimen, when used for 6 months, resulted in continuous improvement of hyperpigmentation for the entire study duration and an increase in the subjects' quality of life.

Full publication on page 18.

Improving skin complexion for ultimate glow and radiant skin, combining liquid crystalline technology with an effective tyrosinase inhibitor

K. Warnke, U. Meiring, M. Meyer, M. Fuerstenau, G. Muhr, S. Keyhanian
EADV Congress 2022.

The most important facts

Significant improvements in facial evenness and radiant skin using an innovative approach combining tyrosinase inhibitor Thiamidol, hyaluronic acid and glycerin.

In an *in vivo* study 120 volunteers were treated with a new formula technology based on a liquid crystalline structure combined with tyrosinase inhibitor Thiamidol, hyaluronic acid and glycerin. After 12 weeks, 84% of the volunteers experienced improvements in radiance, and 73% showed an improvement in overall skin appearance. Results of corneometry indicated a significant increase in hydration after one single application.

HYPERPIGMENTATION

Scientific poster

Challenge of managing hyperpigmentation in Latin American skin during the summer – with the use of Thiamidol®

C. W. Vendruscolo, D. Griffiths, A Sammain, P Pitta, L Guerra
RADLA Brasil 2023.

The most important facts

During the summer months in Brazil, Thiamidol demonstrated efficacy and safety, controlling the hyperpigmentation process, avoiding the worsening of the condition.

Hyperpigmentation in oily skin: a constant challenge to maintain skincare routine

C. W. Vendruscolo, D. Griffiths, F. Addor
25th World Congress of Dermatology 2023.

The most important facts

Ultralight formula with Thiamidols is suitable for oily skin.

In a single-blind clinical study with 23 participants with oily skin, an ultralight formula containing Thiamidol showed the ability to control skin oiliness for 10 hours and demonstrated suitability for use in oily skin.

HYPERPIGMENTATION

Scientific poster

Real-World Evidence: Efficacy of a dermocosmetic regimen containing tyrosinase inhibitor Thiamidol to reduce hyperpigmentation

D. Griffiths, Warnke K, Drescher P, Radenkovic S, Schuster B.
32nd EADV Congress 2023.

The most important facts

Dermatologists and patients confirm efficacy and tolerability of skin care regimen containing Thiamidol for the reduction of facial hyperpigmentation.

In a large multi-center study with 629 participants with hyperpigmentation from 11 European countries, participants and dermatologists confirmed tolerability and efficacy of a daily skin care routine to significantly reduce mild-to-moderate facial hyperpigmentation.

Eye-opening: combining an effective tyrosinase inhibitor with Oligopeptides and Hyaluronic Acid to tackle brown and blue under-eye circles

K. Warnke, U. Meiring, N. Kurz, G. Muhr, P. Drescher, D. Griffiths
32nd EADV Congress 2023.

The most important facts

An eye cream combining Thiamidol with the skin strengthening actives Oligopeptides and Hyaluronic Acid significantly reduced all types of under-eye circles (vascular, pigmented and mixed).

The results of a clinical split-face study showed a significant improvement for all types of dark circles (vascular, pigmented and mixed) after 12 weeks with first visible results after 2 weeks. Another clinical study confirmed very good tolerability proven by dermatological and ophthalmological assessment.

HYPERPIGMENTATION

Scientific poster

Tyrosinase Inhibition to prevent of iatrogenic, laser associated post inflammatory hyperpigmentation

A. Sammain, B. Ruemmelein, A. Troilius Rubin, V. Vachiramou
32nd EADV Congress 2023.

The most important facts

Adjunctive or post-treatment application of Thiamidol improves treatment outcomes of laser treatments and reduces PIH

This poster summarized findings from three studies which explored potential benefits of adjunctive use of Thiamidol for ablative and non-ablative laser treatments as well as the efficacy in reducing laser associated PIH. The results show that Thiamidol may serve as adjuvant for patients with hyperpigmentation undergoing ablative laser treatments and an effective improvement of PIH without side effects and very high patient satisfaction.

Targeting hyperpigmentation on friction areas with an effective tyrosinase inhibitor and skin renewal

K. Warnke, U. Meiring, A. Waerncke, G. Muhr, M. Fuerstenau, D. Griffiths
32nd EADV Congress 2023.

The most important facts

A body cream containing Thiamidol, Lactic Acid and Dexpanthenol effectively reduced hyperpigmentation and discoloration on friction areas on knees and elbows

This poster combines data from three clinical studies which demonstrate the effectiveness and tolerability of a body cream containing Thiamidol, lactic acid and dexpanthenol for use on friction areas on knees and elbows. The results show a significant improvement of hyperpigmentation and skin smoothness, as well as very good tolerability on all skin types including sensitive skin and all phototypes.



HYPERPIGMENTATION ON BLEMISHED SKIN

ACNE LEAVES A MARK...



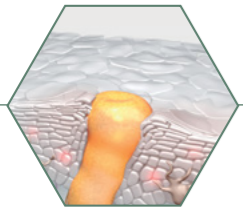
... emotionally

Acne can be very stressful for those affected and can severely impact self-esteem.

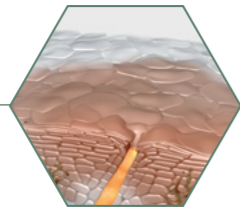


... physically

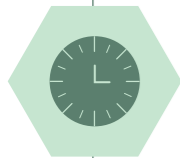
When acne finally disappears, post-inflammatory hyperpigmentation often remains, commonly called pimple marks.



Inflammatory mediators stimulate melanocytes, which produce more melanin.



The resulting hyperpigmentation remains even after the acne has subsided and only fades slowly.



POST-ACNE MARKS PROLONG THE PSYCHOLOGICAL STRESS OF ACNE

Back when I had acne, I suffered a lot due to my appearance

Now the acne is finally gone, but I still have dark spots on my face



PEOPLE WITH POST-ACNE MARKS ARE STIGMATIZED

People with post-acne marks are seen as less self-confident, less happy and less successful.

Schuster et al. Br J Dermatol. 2023;188(5):682-684.

THIAMIDOL® IS HIGHLY EFFECTIVE AT REDUCING POST-ACNE MARKS²²⁻²⁴

The special skin needs of acne-prone skin must not be ignored. Skin care products tailored to this do not only reduce post-acne marks, but also skin impurities and shine:²³⁻²⁴



INITIAL CONDITION

AFTER 12 WEEKS*

*Application 2 times a day of Thiamidol®-containing skin care with salicylic acid and licochalcone A; individual results may vary.



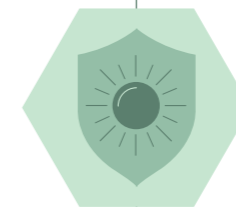
POST-ACNE MARKS
THIAMIDOL® INHIBITS MELANOGENESIS



SKIN BLEMISHES
SALICYLIC ACID HAS A KERATOLYTIC EFFECT. LICOCHALCONE A HAS AN ANTI-INFLAMMATORY EFFECT



SHINE
SEBUM-REGULATING TECHNOLOGY



DON'T FORGET SUNSCREEN IF YOU HAVE ACNE!

To prevent acne from worsening, always use a sunscreen specifically designed for blemished skin.

The combination of sunscreen and Thiamidol® reduces post-acne marks particularly effectively.²⁴



THE RESULT: BETTER QUALITY OF LIFE DUE TO A MORE EVEN COMPLEXION²³

92% of users report an improvement in their quality of life (DLQI)

HYPERPIGMENTATION ON BLEMISHED SKIN

ORIGINAL WORK

- 27** Roggenkamp et al. (2021). Effective reduction of post-inflammatory hyperpigmentation with the tyrosinase inhibitor isobutylamido-thiazolyl-resorcinol (Thiamidol). *Int J Cosmet Sci.* _____ 38

SCIENTIFIC POSTER

- 28** Mann et al (2019). Effective treatment of post-inflammatory hyperpigmentation (PIH) with the tyrosinase inhibitor Thiamidol. 28th EADV Congress. _____ 39
- 29** Roggenkamp et al (2019). A skin care regimen with Thiamidol effectively reduces post-inflammatory hyperpigmentation in patients with resolved acne. 28th EADV Congress. _____ 39
- 30** Gallinger et al (2021). Addressing an unmet cosmetic need: Effective solution to reduce both blemishes and acne-related post-inflammatory hyperpigmentation with a novel skin care formulation tailored for acne-prone skin containing the tyrosinase inhibitor Thiamidol. 30th EADV Congress. _____ 40
- 31** Gallinger et al (2021). When 2 become 1: Effective reduction and prevention of blemishes and acne-related post-inflammatory hyperpigmentation by two new formulations tailored for acne-prone skin combining Thiamidol efficacy, UV protection and antibacterial effect for improved quality of life. 30th EADV Congress. _____ 40
- 32** Pitta et al (2023): New multifunctional formula has anti blemish efficacy, improves post-inflammatory hyperpigmentation and reduces sebum content in acne prone skin. 29th WCD Congress. _____ 41
- 33** Gallinger et al (2023): Tolerance and efficacy of a skincare regimen tailored for acne-prone skin to reduce blemishes and post-acne marks and improve quality of life. 29th WCD Congress. _____ 41



HYPERPIGMENTATION ON BLEMISHED SKIN

Original work

Effective reduction of post-inflammatory hyperpigmentation with the tyrosinase inhibitor isobutylamido-thiazolyl-resorcinol (Thiamidol)

D. Roggenkamp, N. Dlova, T. Mann, J. Batzer, J. Riedel, M. Kausch, L. Kolbe
Int J Cosmet Sci. 2021; 43(3):292-301.

The most important facts

DOES THIAMIDOL® ALSO WORK FOR ACNE-INDUCED POST-INFLAMMATORY HYPERPIGMENTATION?

Acne is a common cause of post-inflammatory hyperpigmentation (PIH). In a controlled, randomized clinical trial and an observational study, **3-month use of a Thiamidol®-containing skin care regimen was shown to effectively reduce acne-induced PIH.**

For results on the reduction of PIH after minimally invasive surgery, see page 23.

ABSTRACT

Objective:

Post-inflammatory hyperpigmentation (PIH) is a major cosmetic concern especially in individuals with darker skin complexion. Unfortunately, treatment with anti-inflammatory ingredients alone does not prevent the development of hyperpigmented spots. Recently, isobutylamido-thiazolyl-resorcinol (Thiamidol) was described as a very potent inhibitor of human tyrosinase. The objective of this research was to investigate the potential of this compound to prevent PIH induced by epidermal wounding (suction blister) and related to acne.

Methods:

Suction blister-induced PIH was treated with a formulation containing Thiamidol or a vehicle for 3 months and the changes in hyperpigmentation were monitored by spectroscopic measurements. The effect of skin care formulations containing Thiamidol on acne-related PIH was investigated in two studies, a vehicle-controlled, double-blinded, randomized clinical study and a clinical observational study. Both studies had a duration of 3 months and included assessments such as clinical photogra-

phy, clinical grading and melanin index measurements.

Results:

Already after 2 weeks of treatment, suction blister sites treated with Thiamidol were significantly lighter than control sites and improved throughout the treatment period. Subjects' self-grading demonstrated that Thiamidol significantly improved the visibility of acne-induced hyperpigmentation compared to the vehicle treatment. A skin care regimen with Thiamidol significantly improved acne-related PIH over 12 weeks shown by Mexameter measurements, expert grading, self-grading and clinical photography.

Conclusion:

Thiamidol represents a safe and effective ingredient for cosmetic products against post-inflammatory hyperpigmentation. ■

HYPERPIGMENTATION ON BLEMISHED SKIN

Scientific poster

Effective treatment of post-inflammatory hyperpigmentation (PIH) with the tyrosinase inhibitor Thiamidol

T. Mann, U. Wensorra, J. Batzer, L. Kolbe
EADV Congress 2019.

The most important facts

In a randomized, controlled study, a superior reduction in acne-induced post-inflammatory hyperpigmentation was demonstrated with use of a Thiamidol®-containing skin care regimen compared to treatment with vehicle.

Full publication on page 40.

A skin care regimen with Thiamidol effectively reduces post-inflammatory hyperpigmentation in patients with resolved acne

D. Roggenkamp, G. Neufang, A. Pillay, I. Zoric, M. Kausch, N.C. Dlova
EADV Congress 2019.

The most important facts

An observational study showed an effective reduction of acne-induced post-inflammatory hyperpigmentation after application of a Thiamidol®-containing skin care regimen for 3 months.

See full publication on page 40.

HYPERPIGMENTATION ON BLEMISHED SKIN

Scientific poster

Addressing an unmet cosmetical need: Effective solution to reduce both blemishes and acne-related post-inflammatory hyperpigmentation with a novel skin care formulation tailored for acne-prone skin containing the tyrosinase inhibitor Thiamidol

J. Gallinger, C. Rauscher, A. Kuhn, R. Dippe, S. Dorsch, A. Buerger
EADV Congress 2021.

The most important facts

Use of a serum with Thiamidol®, salicylic acid and licochalcone A tailored to acne-prone skin effectively reduces blemishes and post-inflammatory hyperpigmentation and improves the quality of life of those affected.

In a clinical study, treatment with a serum containing Thiamidol®, salicylic acid and licochalcone A showed a continuous reduction in pimple marks (post-inflammatory hyperpigmentation) and skin blemishes over 12 weeks, with the first results seen after only 4 weeks. Furthermore, 92% of the subjects with impaired quality of life (DLQI ≥ 2) showed an improvement in quality of life after 8 weeks.

When 2 become 1: Effective reduction and prevention of blemishes and acne-related post-inflammatory hyperpigmentation by two new formulations tailored for acne-prone skin combining Thiamidol efficacy, UV protection and antibacterial effect for improved quality of life

J. Gallinger, C. Rauscher, A. Kuhn, R. Dippe, A. Noelter, S. Baumann, S. Dorsch, A. Buerger
EADV Congress 2021.

The most important facts

Combined use of a serum with Thiamidol®, salicylic acid and licochalcone A, and day care with decandiol and SPF 30 reduced both skin blemishes and post-inflammatory hyperpigmentation more effectively than use of day care alone.

In a randomized, controlled, split-face study, combined use of both products showed a significant reduction in pimple marks and skin blemishes and superior efficacy compared to use of day care alone after only 4 weeks.

HYPERPIGMENTATION ON BLEMISHED SKIN

Scientific poster

New multifunctional formula has anti blemish efficacy, improves post-inflammatory hyperpigmentation and reduces sebum content in acne prone skin: Evidence supported by clinical, instrumental, and subjective methodologies

P. Pitta, C.W. Vendruscolo, J. Gallinger, F. Addor
29th World Congress of Dermatology 2023.

The most important facts

Combining Thiamidol with Salicylic Acid and Licochalcone A in a multifunctional formula helps to reduce erythema, edema, post-inflammatory hyperpigmentation and shine in patients with acne.

In this blind non-comparative clinical study, a formulation with Thiamidol, Salicylic Acid and Licochalcone A showed good efficacy in reducing acne-related edema and erythema after 3 and 7 days as well as dark spot lightening and sebum reduction after 28 days.

Tolerance and efficacy of a skincare regimen tailored for acne-prone skin to reduce blemishes and post-acne marks and improve quality of life: Real-world-evidence on acne-prone skin in Latin America

J. Gallinger, C.W. Vendruscolo, S. Perez Damonte, C. De La Cruz, J. Orbegón, R. Alas Carbajal, S. Scarano, A. Piegari Felui, M. Dominquez, M.V. Vagnoni, V. Tosi, C. Lofrano, A. Sammain
29th World Congress of Dermatology 2023.

The most important facts

Real-world-data from Latin America confirms efficacy and tolerability of a Thiamidol containing skin care regimen for acne-prone skin and demonstrates improvement in quality of life and happiness.

In this 12-week multicenter study with 244 patients from Latin America, a Thiamidol-containing skin care regimen for acne-prone skin effectively reduced acne IGA as well as both post-inflammatory hyperpigmentation and erythema. Additionally, a significant increase in quality of life (CAD) and happiness was observed.

HYPERPIGMENTATION ON MATURE SKIN

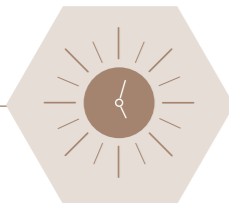
AGE SPOTS ARE THE NEW WRINKLES

Age spots are a form of hyperpigmentation that occur with increasing age

- More than 90% of people over 50 are affected.

Skin ageing affects us at all ages:

- From the age of 25, the decrease in elastin and collagen levels results in a loss of elasticity.
- The decline in the skin's own hyaluronic acid production with increasing age leads to a decrease in skin moisture and elasticity.



AGE SPOTS ARE MAINLY CAUSED BY MANY YEARS OF UV EXPOSURE.

UV irradiation increases the activity of melanocytes, which produce more melanin as a result. Over the years, dark-colored skin spots develops on the hands and face – the areas that are most frequently exposed to the sun.



AGE SPOTS MAKE PEOPLE THINK THAT THEY ARE MUCH OLDER THAN THEY REALLY ARE.

THIAMIDOL® IS HIGHLY EFFECTIVE AT REDUCING AGE SPOTS²⁵⁻²⁸

In terms of skin ageing, development of age spots is accompanied by the appearance of wrinkles and a decrease in the elasticity of the skin. Anti-age skin care tailored to these needs can reduce these signs of skin ageing.²⁷



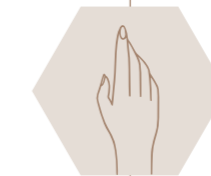
AGE SPOTS
THIAMIDOL® INHIBITS MELANOGENESIS



LOSS OF ELASTICITY
ARCTIIN STIMULATES COLLAGEN PRODUCTION

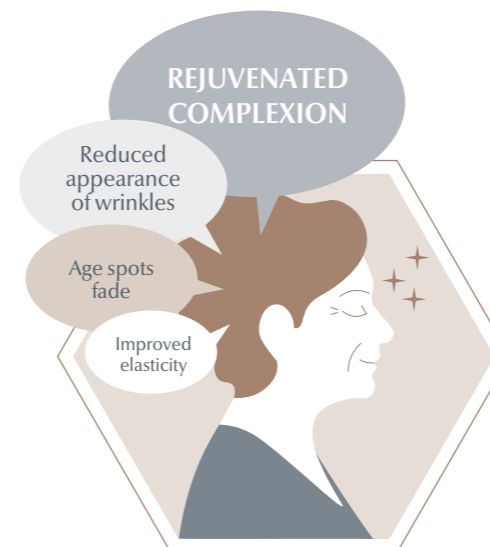


WRINKLES
LONG- AND SHORT-CHAIN HYALURONIC ACID MOISTURIZES AND PLUMPS UP WRINKLES



ALSO FOR AGE SPOTS ON THE HANDS

Application two times a day of a hand cream containing Thiamidol® effectively reduced age spots on the hands.²⁸



100% OF USERS CONFIRMED A REJUVENATED COMPLEXION AFTER 4 WEEKS²⁷

Fink, Grammer & Matts (2006) Evolution and Human Behavior; 27:433-422;



HYPERPIGMENTATION ON MATURE SKIN

ORIGINAL WORK

34 Mann et al (2018). Inhibition of human tyrosinase requires molecular motifs distinctively different from mushroom tyrosinase. *J Invest Dermatol.* _____ 46

SCIENTIFIC POSTER

35 Mann et al (2018). Isobutylamido thiazolyl resorcinol, a highly effective inhibitor of human tyrosinase. 27th EADV Congress. _____ 47

36 Schmidt et al (2020). Closing the need gap – Effective anti-age care targeting age spots for more skin evenness. 29th EADV Congress. _____ 47

37 Schmidt et al (2021). Closing a need gap – Effective dermocosmetic hand care targeting photoaging including lentigines solares with first visible results after 2 weeks. 30th EADV Congress. _____ 47

38 van Geloven et al (2022). A novel topical approach for mature aging skin to improve all 4 skin quality EPCs for younger looking skin. 31st EADV Congress. _____ 48

ANTI-AGE

Original work

Inhibition of human tyrosinase requires molecular motifs distinctively different from mushroom tyrosinase

T. Mann, W. Gerwat, J. Batzer, K. Eggers, C. Scherner, H. Wenck, F. Stäb, V. Hearing, K. Röhm, L. Kolbe
J Invest Dermatol. 2018; 138(7): 1601–1608.

The most important facts

IS THE HIGH *IN VITRO* INHIBITION EFFICIENCY OF THIAMIDOL® CLINICALLY REFLECTED IN THE LIGHTENING OF AGE SPOTS?

Thiamidol® was identified as the most effective *in vitro* inhibitor of human tyrosinase. A controlled clinical study subsequently showed **that application of Thiamidol® twice a day *in vivo* led to a visible lightening of the age spots after just 4 weeks and that the spots faded continuously over the study duration of 12 weeks.**

For more information on the *in vitro* tests, see page 11.

ABSTRACT

Tyrosinase is the rate-limiting enzyme of melanin production and, accordingly, is the most prominent target for inhibiting hyperpigmentation. Numerous tyrosinase inhibitors have been identified, but most of those lack clinical efficacy because they were identified using mushroom tyrosinase as the target. Therefore, we used recombinant human tyrosinase to screen a library of 50,000 compounds and compared the active screening hits with well-known whitening ingredients.

Hydroquinone and its derivative arbutin only weakly inhibited human tyrosinase with a half-maximal inhibitory concentration (IC50) in the millimolar range, and kojic acid showed a weak efficacy (IC50 > 500 mmol/L). The most potent inhibitors of human tyrosinase identified in this screen were resorcinyl-thiazole derivatives, especially the newly identified Thiamidol (Beiersdorf AG, Hamburg, Germany) (isobutylamido thiazolyl resorcinol), which had an IC50 of 1.1 mmol/L. In contrast, Thiamidol only weakly inhibited mushroom tyrosinase (IC50

¼ 108 mmol/L). In melanocyte cultures, Thiamidol strongly but reversibly inhibited melanin production (IC50 ¼ 0.9 mmol/L), whereas hydroquinone irreversibly inhibited melanogenesis (IC50 ¼ 16.3 mmol/L). Clinically,

Thiamidol visibly reduced the appearance of age spots within 4 weeks, and after 12 weeks some age spots were indistinguishable from the normal adjacent skin. The full potential of Thiamidol to reduce hyperpigmentation of human skin needs to be explored in future studies. ■

ANTI-AGE

Scientific poster

Isobutylamido thiazolyl resorcinol – a highly effective inhibitor of human tyrosinase

T. Mann, W. Gerwat, H. Wenck, K.H. Roehm, L. Kolbe | EADV Congress 2018.

The most important facts

The newly identified tyrosinase inhibitor, Thiamidol® shows high clinical efficacy in reducing age spots.

Full publication on page 48.

Closing the need gap – Effective anti-age care targeting age spots for more skin evenness

L. Schmidt, A. van Geloven, S. Harbig, M. Fürstenau, G. Muhr, R. Dippe, K. Wamke | EADV Congress 2020.

The most important facts

In a 12-week, randomized, split-face study, a skin care serum containing hyaluronic acid, arctiin and Thiamidol® resulted in a measurable reduction in both age spots and wrinkles and increased the elasticity of mature skin.

Closing a need gap – Effective dermocosmetic hand care targeting photoaging including lentigines solares with first visible results after 2 weeks

L. Schmidt, U. Meiring, J. Djamil, D. Kuschel, P. Drescher, R. Dippe, K. Warnke | EADV Congress 2021.

The most important facts

A combination of Thiamidol®, arctiin, hyaluronic acid and a wide range of UV filters visibly reduces age spots on the hands and makes them look significantly younger after just 2 out of 12 weeks of use.

ANTI-AGE

Scientific poster

A novel topical approach for mature aging skin to improve all 4 skin quality EPCs for younger looking skin

A. van Geloven, S. Harbig, A. Stuhr, J. Dunkel, G. Muhr, M. Fürstenau, C. Rauscher, K. Warnke
EADV Congress 2022.

The most important facts

The innovative formulation containing a combination of highly active ingredients targeting all 4 EPCs and top needs of mature skin.

This user survey investigated the effect of a new formulation on the 4 EPCs: skin tone evenness, skin surface evenness, skin firmness and skin glow. The formulation significantly improved all EPCs, and out of the 120 volunteers more than 75% confirmed improvement of overall skin quality accompanied by improvement of radiance and youthful appearance.



REVIEW ARTICLES, COMMENTARIES & OTHER SCIENTIFIC ARTICLES

Thiamidol® has been discussed in numerous review articles and commentaries as an innovative active substance for the reduction of hyperpigmentation:

Next time, save mushrooms for the pizza!

T.J. Hornyak | J Invest Dermatol. 2018; 138(7): 1470-1472.

Key statement on Thiamidol®

Commentary on the discovery of Thiamidol® as the most effective inhibitor of human tyrosinase.

Chemical peeling in dermatology

W.G. Philipp-Dormston | Dermatologist. 2019; 70(7): 535-546.

Key statement on Thiamidol®

Preventive use of Thiamidol® may reduce the risk of post-inflammatory hyperpigmentation resulting from deep chemical peels.

The top 10 cosmeceuticals for facial hyperpigmentation

T. Searle, F. Al-Niimi, F.R. Ali | Dermatol Ther. 2020; 33(6):e14095.

Key statement on Thiamidol®

Review articles on the top 10 cosmetic active substances that reduce hyperpigmentation on the face. Thiamidol® was found to be the most potent and effective inhibitor of human tyrosinase.

REVIEW ARTICLES, COMMENTARIES & OTHER SCIENTIFIC ARTICLES

Actualidades en el tratamiento de melasma

A. Guadalupe Dagdug Villegas, C.G. Hernandez, I. Arellano Mendoza
Dermatologica CMQ 2020.

Key statement on Thiamidol®

Review article on the treatment options for melasma. Thiamidol® is described as a potent tyrosinase inhibitor with high clinical efficacy in reducing hyperpigmentation in melasma.

New insight into the interaction of arbutin with mushroom tyrosinase

N.S. Ghofrani, M. Sheikhi, J.Z. Amirzakaria, S. Hassandi, S. Aminzadeh, K. Haghbeen
Protein J. 2021; online ahead of print.

Key statement on Thiamidol®

Review article on the interaction of arbutin with mushroom tyrosinase. Arbutin has been shown to be a weak inhibitor of human tyrosinase compared to Thiamidol®.

REVIEW ARTICLES, COMMENTARIES & OTHER SCIENTIFIC ARTICLES

Melasma treatment: a systematic review

M. Neagu, C. Conforti, M. Agozzino, G.F. Marangi, S.H. Morariu, G. Pellacani, P. Persichetti, D. Piccolo, F. Segreto, I. Zalaudek, C. Dianzani | J Dermatolog Treat. 2021; 1-39; online ahead of print.

Key statement on Thiamidol®

Systematic review article on the treatment options for melasma. Thiamidol® is listed as an effective skin care active substance.

Recent advances in the design and discovery of synthetic tyrosinase inhibitors

J. Li, L. Feng, L. Liu, F. Wang, L. Ouyang, L. Zhang, X. Hu, G. Wang
Eur J Med Chem. 2021; 3224: 113744; online ahead of print.

Key statement on Thiamidol®

Review article on synthetic tyrosinase inhibitors. Thiamidol® has proven to be the most effective inhibitor of human tyrosinase.

Hyperpigmentation: Looking beyond hydroquinone

N. A. Charoo
J Cosmet Dermatol. 2022 Oct;21(10):4133-4145

Key statement on Thiamidol®

Review providing an overview of treatment options for facial hyperpigmentation beyond hydroquinone. Thiamidol is listed as new treatment with high potential for the reduction of hyperpigmentation as well as the prevention of UV-induced hyperpigmentation.

REVIEW ARTICLES, COMMENTARIES & OTHER SCIENTIFIC ARTICLES

Topical treatment for postinflammatory hyperpigmentation: a systematic review

M. G. Tan, W. B. Kim, C. E. Jo, K. Nabieva, C. Kirshen, A. E. Ortiz
J Dermatolog Treat. 2022;33(5):2518-2526.

Key statement on Thiamidol®

Review article on the topical treatment of post-inflammatory hyperpigmentation (PIH). Thiamidol is discussed as an effective topical agent for the reduction of PIH with high-quality scientific evidence.

Structural dynamics and susceptibility of isobutylamido thiazolyl resorcinol (Thiamidol™) against human and mushroom tyrosinases

P. Mahalapbutr, N. Nuramrum, T. Rungrotmongkol, N. Kongtaworn, S. Sabuakham
J Biomol Struct Dyn 2023: 16; 1-8.

Key statement on Thiamidol®

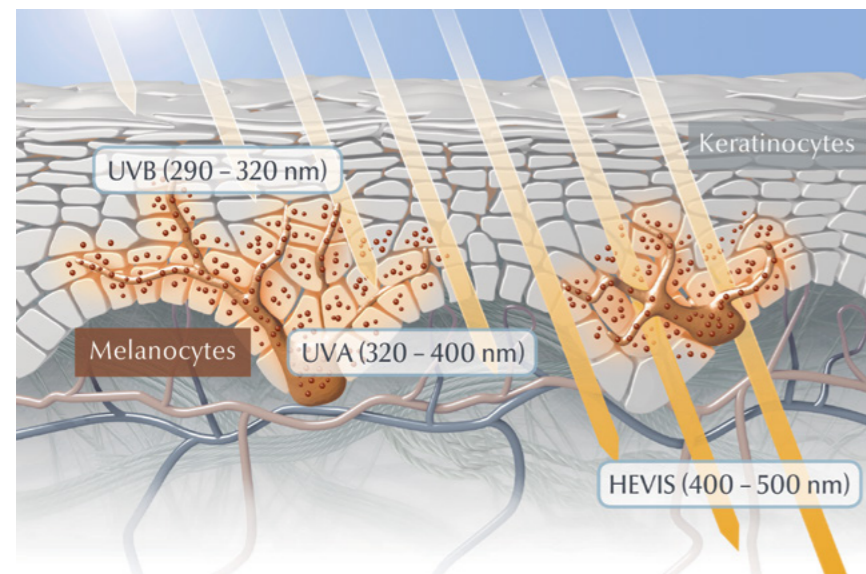
Original research exploring the structural dynamics and susceptibility of Thiamidol against human and mushroom tyrosinase. The findings confirm strong inhibitory efficacy of Thiamidol on human tyrosinase.

SUN PROTECTION

THE NUMBER ONE CAUSE FOR DEVELOPMENT OF HYPERPIGMENTATION IS UV RAYS.

The number one cause for development of hyperpigmentation is UV rays. Sunlight activates production of melanin in the melanocytes of the skin. The dye reaches the surrounding skin cells via cell extensions of the melanocytes. There, it covers the cell nucleus like a protective cap, absorbing damaging UV rays and, thus, protects the cell nucleus. This protection becomes visible as an even pigmentation or skin tan. However, this is not a manifestation of healthy skin – it is already associated with UV-induced skin damage.

In combination with other factors, this UV-induced pigmentation can be disruptive and thus darker pigmented areas of skin may develop. The pigment spots formed in this way, visible as freckles, age spots, melasma or as post-inflammatory hyperpigmentation, can become even darker if they continue to be exposed to the sun without protection.



KERATINOCYTE



MELANOCYTE

Staying in the sun for as short a time as possible, wearing protective clothing and using sunscreen products with a high sun protection factor can reduce the risk of developing pigment spots and prevent spots that have already developed from becoming even darker. Even when using Thiamidol® to reduce and prevent hyperpigmentation, care should therefore always be taken to use a high or very high sun protection factor.

SUN PROTECTION

Scientific poster

Licochalcone A efficiently protects against HEVIS-induced hyperpigmentation

J. Weise, N. Möller, U. Wensorra, T. Mann, K. Eggers, K. Warnke, L. Kolbe
EADV Congress 2022.

The most important facts

Licochalcone A effectively inhibits melanin production and reactive oxygen species after HEVIS stress.

In this *in vitro* study the impact of active licochalcone A was demonstrated to have an anti-pigment and antioxidative effect. When melanocytes were pre-treated with licochalcone A, HEVIS-induced melanin production was inhibited. Pre-treatment with licochalcone A in HEVIS-stressed fibroblasts similarly prevented the induction of reactive oxygen species.

Please contact your local medical representative for a copy of this study poster



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