JOURNAL LA MEDIHEALTICO

VOL. 06, ISSUE 02 (315-325), 2025
DOI: 10.37899/journallamedihealtico.v6i2.1923

Effectiveness of Topical Tranexamic Acid in the Treatment of Melasma

Siti Pandanwangi[1], Dedy Setriyadi[1], Hawa Dzulhijjah[1]

[1]*Fakultas farmasi universitas YPIB Majalengka*

**Corresponding Author: Hawa Dzulhijjah*
E-mail: dzulhijjahhawa@gmail.com

Article Info

Article history:
Received 13 January 2025
Received in revised form 23 February 2025
Accepted 9 March 2025

Keywords:
Tranexamic Acid
Topical
Melasma

Abstract

Melasma is a chronic skin hyperpigmentation condition that often occurs in women of reproductive age, especially in areas exposed to sunlight. One of the therapeutic agents that has attracted attention is tranexamic acid (TXA), which was originally used as an antifibrinolytic agent, but is now known to have an effective mechanism of action in reducing hyperpigmentation. TXA works through plasminogen inhibition, tyrosinase activity, and angiogenesis, as well as providing anti-inflammatory effects. This study uses the PRISMA systematic review method, involving the analysis of 30 relevant articles out of a total of 289 articles identified. The results showed that topical TXA in various formulations, such as creams, gels, or liposomal serums, provided a significant reduction in the Melasma Area and Severity Index (MASI) score. The combination of TXA with other modalities, such as microneedling, laser, and vitamin C, showed more effective results than monotherapy. Topical TXA is an effective and safe therapeutic agent for melasma, especially in the case of refractory or combination therapies. Further research is needed to evaluate the long-term effectiveness and innovation of new formulations in improving the penetration and efficacy of TXA.

Introduction

Melasma is a common skin condition that causes brown or gray-brown patches on the face. It is often triggered by sun exposure, hormonal changes, and certain medications (Asditya & Sukanto, 2017). Melasma is characterized by symmetrical hyperpigmentation of the skin, which mainly appears in the facial area. The condition has a significant prevalence rate, affecting 1%–50% of the population, especially in women and individuals with darker skin tones. Etiology-wise, the development of melasma is multifactorial, with exposure to sunlight, especially family history ultraviolet radiation, hormonal influences, medications, and metabolic factors playing an important role (Aghdam et al., 2024).

One of the agents that is now receiving attention is tranexamic acid (TA). Initially, TA was used as an antifibrinolytic agent to reduce bleeding. However, recent research shows that TA has an inhibitory effect on the activation of plasminogens into plasmin. Plasmin is known to play a role in triggering melanin production through the release of arachidonic acid and prostaglandins that induce tyrosinase activity in melanocytes (Maeda, 2022). With this mechanism, TA is considered to be able to reduce hyperpigmentation associated with melasma.

Tranexamic acid (TA) operates through multiple mechanisms in addressing melasma, targeting both the epidermal and dermal levels. These mechanisms include the suppression of tyrosinase enzyme activity, modulation of blood vessels, anti-inflammatory properties, and the inhibition of mast cell activity (Yasnova et al., 2024). Topical tranexamic acid functions by obstructing

the lysine binding site on plasminogen, thereby hindering the interaction between keratinocytes and plasminogen. Consequently, the UV-induced plasmin activity within keratinocytes is suppressed. This leads to a reduction in the production of prostaglandins and free arachidonic acid while also lowering tyrosinase activity in melanocytes. Additionally, TXA suppresses the release of prostaglandins (PGs) by human keratinocytes after exposure to UV light, which can reduce melanocyte and tyrosinase activity in melanocytes. These two mechanisms are believed to be how TXA works in reducing pigmentation in melasma patients (Sahu et al., 2021).

Methods

The approach employed in composing this literature article follows the "PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines". This method provides a structured framework designed to ensure transparency and consistency in conducting systematic reviews and meta-analyses. Search for articles in the PubMed database, and Google Scholar published from 2019 to 2024. The search keywords are as follows: "*Melasma*" and "*Tranexamic Acid*" and "Topical".

The articles obtained were 289 studies according to the keywords, then excluded after screening using covidence according to the title and abstract, 74 articles were obtained which were then assessed according to the inclusion and exclusion criteria. The inclusion criteria of this study are randomized *control trials* (RCTs), cohort studies, or observational studies that focus on topical therapy in melasma that are extracted, analyzed and discussed. The studies used in this study are studies in the community, beauty clinics and hospitals so that the results of 30 main articles used in this literature are obtained. Furthermore, a comprehensive analysis was carried out with descriptive analysis and displayed in the form of tables.

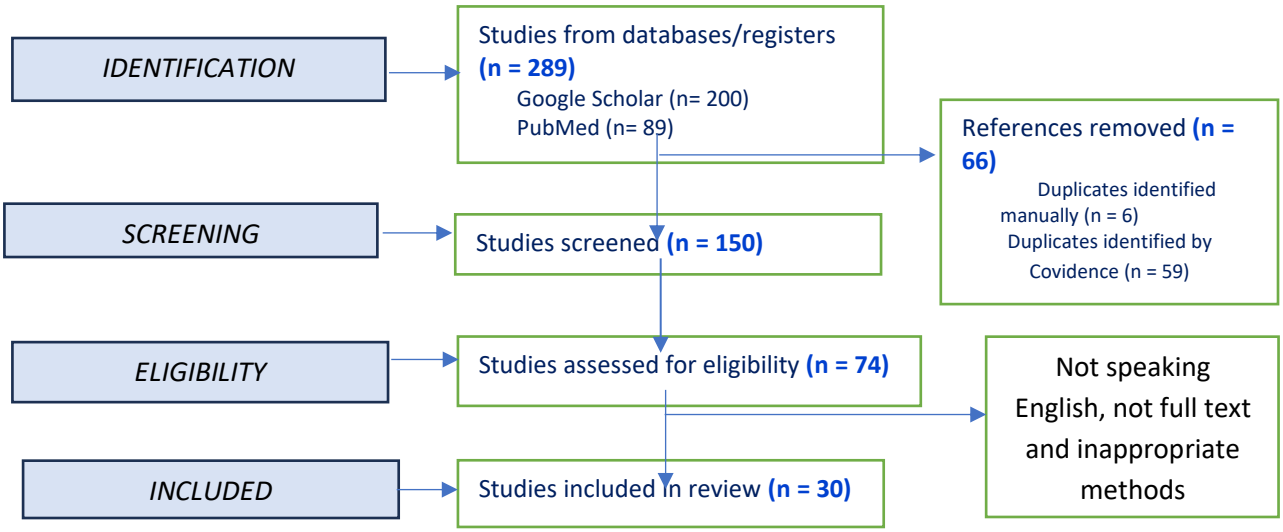

Figure 1. descriptive analysis and displayed

Result and Discussion

Initial search results resulted in 289 articles discussing various melasma therapies. After applying the inclusion and exclusion criteria, 30 studies were obtained that met these criteria (Figure 1). The selected studies focused on topical TXA therapy studies in melas.

Table 1. Summary of Studies on Tranexamic Acid (TXA) for Melasma Treatment

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
(Maeda, 2022)	30	3 months	Liposomal lotion 2% TXA	MASI Score	The use of pharmaceutical cosmetics (quasi-drugs) containing TXA, which has an antiplasmin effect, can help reduce the risk

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
					of hyperpigmentation. This mechanism works by inhibiting the uPA/plasminogen system located in the basal layer of the epidermis. The uPA/plasminogen system plays a role in the inflammatory process and melanin production, so its inhibition can reduce excess pigment formation that is often the cause of hyperpigmentation.
(Mushtaq et al., 2024)	200	6 months	5% Cream TXA vs 20% Azelic acid	MASI Score	Tranexamic acid 5% was shown to be more effective than azelic acid 20% in improving Melasma Area and Severity Index (MASI) scores in patients with melasma. These findings support the use of tranexamic acid as a superior treatment option for melasma, providing a potential alternative for patients who do not respond to conventional therapy.
(Agrawal et al., 2023)	84	12 months	5% TXA vs 250mg TXA oral	MASI Score	Based on these studies, melasma therapy with tranexamic acid (TXA), both topically and orally, has proven effective. However, comparative analysis showed that treatment outcomes were more optimal when tranexamic acid was used orally compared to topical application.
(Dawaud et al., 2023)	30	12 weeks	TXA 5% solution with daily topical night application of 5% TXA cream. TXA cream was prepared as: white soft paraffin (13.5 gm), cetyle alcohol (13 gm), tween 80 (10 gm), propylene glycol (8 gm), TXA (5 gm) and water to complete 100 gm.	mMASI Score	Topical tranexamic acid is a safe and relatively effective treatment option for facial melasma. The combination of TXA with fractional CO2 laser or *microneedling* (MN) provides significantly better improvements than using TXA alone. However, fractional CO2 lasers carry a risk of post-inflammatory hyperpigmentation in patients with skin types III and IV, making careful selection of candidates essential.
(Guo et al., 2024)	30	3 months	tranexamic acid essence 3% Iontophoresis treatment	MASI Score	The combination of essence containing the active substance TA and the Iontophoresis method shows great potential as a treatment for melasma. This combination is considered safe and effective in reducing dark spots on the skin. However, further research and clinical observations are needed to refine this method and ensure its optimal use in treating melasma.
(Yasnova et al., 2024)	20	4 weeks	3% TA cream and 4% HQ cream	MASI score and melanin index	An ointment containing 3% Tranexamic Acid (TA) has been shown to be effective in reducing dark spots on the face caused by melasma. The results showed that it was as effective as the commonly used drug hydroquinone (HQ), but had milder side effects. This means that 3% TA could be a

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
					safer and more convenient alternative to treat melasma.
(Sahu et al., 2021)	60	12 weeks	5% TA solution and 30% Glycolic acid peel. Topical solutions of 5% TXA was prepared by using 5 g of tranexamic acid (10 tablets of TXA of 500 mg each) crushed and dissolved in 10 cc ethanol and then distilled water was added to make it up to 100 cc.	MASI score	Combining TXA ointment with skin treatments using 30% glycolic acid (GA) is generally safe and does not cause major skin problems. Some patients do feel a slight burning, tingling, or itching sensation, but these reactions are mild and do not last long. Although these side effects were more common in the group that used the combination of the two treatments, overall, the combination was still relatively safe and did not cause any problems serious enough to stop treatment. These results are in line with previous studies which also show that the use of TXA ointment, either alone or in combination with other treatments, is generally safe and has minimal side effects.
(Aghdam et al., 2024)	50	4 months	4% and 10% TA solution, Kligman Formula	Melanin index and MASI score	Combining the microneedling method with topical application of 4% or 10% tranexamic acid (TA) and a modified Kligman formula showed superiority in producing better therapeutic outcomes when compared with conventional topical therapy.
(Saka et al., 2019)	40	12 weeks	10% TA cream	MASI Score	The study proved that topical tranexamic acid 10% as monotherapy is an effective and safe treatment option for melasma. This study recommends the use of topical tranexamic acid 10% as the first line of treatment for melasma in the Indian population.
(El Attar et al., 2022)	20	2 weeks	0.5 ml of topical tranexamic acid (kapron 500 mg in 5 ml, Amoun pharmaceutical Co.) VS d 0.5 ml of caps-cal vitamin C (cosmotech 5 ml vitamin C, Alpha medical cosmotech Yes.)	MASI Score	The study divided the face into two parts and administered different treatments to each. The results showed that the combination of microneedling followed by the use of tranexamic acid on the right side of the face gave better results in improving the small blood vessel problems that often appear in melasma.
(Patil & Deshmukh, 2019)	76	6 Months	Intradermal TA vs 3% TA cream vs triple combination (hydroquinone 2%, tretinoin 0.025%, fluocinolone acetonide 0.01%)	MASI Score	Tranexamic acid (TA) shows great potential as a new treatment for melasma. Studies show that TA is effective in reducing dark spots, safe to use, and affordable. TA's wide availability also makes it an attractive option.

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
(Da Silva Souza et al., 2021)	54	8 weeks	2% cetyl tranexa-mate mesylateserum TeraCeutic TXVector™,	Melanin index and Erythema index	Research shows that regular use of serums containing cetyl tranexamate mesylate can significantly improve the condition of facial skin. Both in terms of expert assessment and user perception, the serum proved effective in reducing dark spots, redness, and making skin tone more even. These results suggest that cetyl tranexamate mesylate has great potential as a safe and efficient skin lightening active ingredient.
(Shamsi Meymandi et al., 2020)	60	12 weeks	4% TA solution + microneedling and 4% HQ Cream	MASI Score and Melanin Index	This study compared the effectiveness of two types of treatments for melasma: a combination of microneedling and tranexamic acid, and the use of 4% hydroquinone. The results showed that both treatments had similar effectiveness. Although the combination treatment caused more significant redness initially, this side effect was temporary and would disappear within 3-5 days.
(Kaikati et al., 2023)	10	8 weeks	2% TA and 2% Vitamin C	MASI Score	A comparison between the use of single topical tranexamic acid and the combination of tranexamic acid and vitamin C showed that the group receiving the combination therapy had a statistically significant reduction in Melasma Area and Severity Index (MASI) scores at week 4. These findings are consistent with the literature showing lower effectiveness of tranexamic acid monotherapy.
(Zhou et al., 2024)	48	4 weeks	0.5–1 mL of 3% TA with Laser	MASI Score and Melanin Index	Topical tranexamic acid (TA) combined with laser therapy is an effective and safer treatment option for difficult-to-treat melasma. TA acts directly on melanin, helping to inhibit tyrosinase activity in epidermal melanocytes by blocking the plasminogen activator system in epidermal basal cells and keratinocytes. In addition, TA also affects mast cells and skin blood vessels by inhibiting angiogenesis through vascular endothelial growth factor.
(Qu et al., 2021)	90	4 weeks	TXA solution (30 mL, Yantai Xianse Trading Co., Ltd)	MASI Score	Analysis using a dermatoscope confirmed that topical TXA has a dual effect in the treatment of melasma. In addition to relieving pigmentation problems, TXA also helps repair damage to the outer layer of the skin and reduces the sensitivity of blood vessels, which is often the cause of melasma.
(Guo et al., 2023)	88	3 months	0.5% TA-loaded ethosomes andmoisturizers (moisturizers included hyaluronic acid, glyc-erol , and glycol propylene)	MASI Score	Face masks containing 0.5% tranexamic acid in ethosome form are highly effective in improving skin texture and reducing redness in melasma-prone skin, especially in Asians. In addition, this mask can also help brighten the skin gradually, without causing significant side effects.
(Ramzan et al., 2023)	100	12 weeks	5%tranexamic acid cream	MASI Score	To find out how effective 5% tranexamic acid cream is in removing dark spots on the

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
					face (melasma), researchers measured changes in melasma scores before and after treatment for 12 weeks. The results showed that the cream was effective, affordable and readily available to treat this often intractable skin problem.
(Debasmita et al., 2022)	60	2 months	QS Nd:YAG laser and topical 3% TA gel vs topical 3% TA gel and microneedling	MASI Score	Existing melasma treatment methods, such as a combination of three types of drugs, have significant side effects if used for a long period of time. To overcome this, researchers have developed a new treatment method. Studies show that both microneedling and laser, when combined with tranexamic acid cream, can be effective and safe options for treating melasma.
(Akhtar, 2023)	60	12 Weeks	TA Solution 5%	MASI Score	Research shows that the use of 5% tranexamic acid (TA) solution is effective for treating melasma skin problems in South Asians with dark skin. This finding provides a new option for doctors to treat melasma, especially in patients with darker skin tones. However, further studies in larger groups are needed to confirm the long-term safety and effectiveness of this treatment.
(Bijalwan et al., 2024)	60	30 – 90 days	3 % TA gel and 2 % glutathione gel	MASI Score	Both glutathione and tranexamic acid (TA) can be used to treat melasma. However, based on a 3-month study, glutathione applied directly to the skin (topical) was found to be more effective in reducing dark spots, safer, and made patients feel better compared to TA. However, more research needs to be done on many people over a longer period of time to confirm the long-term benefits of glutathione use.
(Saleem et al., 2021)	120	12 weeks	Topal 2% tranexamic acid (TXA)	MASI Score	Tranexamic acid 2% cream is becoming a popular choice in melasma treatment. It is proven to give good results quickly with very few side effects. The type of melasma with the most visible changes is the type that only affects the top layer of skin. However, further research is needed to determine the most appropriate dosage, long-term benefits, and possible combination with other treatments for more optimal results.
(Marpaung et al., 2021)	30	8 weeks	3% TA cream with 4% HQ cream	MASI Score and Melanin Index	The use of a cream containing 3% tranexamic acid (TA) and 4% hydroquinone (HQ) proved to be very effective in reducing dark spots on the face due to melasma, especially in the type of melasma that only affects the upper layers of the skin. The effectiveness of the cream was evident after 4 and 8 weeks of use. However, only two people experienced skin redness after using the hydroquinone cream.
(Mawu et al., 2024)	16	8 weeks	topical 10% TA and 5% TA	MASI Score	Tranexamic acid (TA) creams with 10% and 5% levels were shown to be effective in removing dark spots on the face (melasma) in women after being used for 4 to 8 weeks. The results showed that 5% is effective enough to treat melasma that only affects the

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
					top layer of the skin, so there is no need to use higher levels.
(Gamea et al., 2022)	40	12 Weeks	5% tranexamic acid in liposome based cream	MASI Score	The study proved that 5% tranexamic acid cream encapsulated in liposomes is a good treatment option for melasma. The use of liposomes makes the cream more easily absorbed into the skin. The combination of this cream with PRP, which is a component of one's own blood, can increase the effectiveness of the treatment. As a result, dark spots on the face can disappear faster.
(Malik et al., 2019)	100	6 months	oral tranexamic acid (250 mg twice daily) with topical 3% tranexamic acid (twice daily) vs cases had oral tranexamic acid (250 mg twice daily) with topical 20% azelaic acid (daily).	MASI score and melanin index	The use of 3% tranexamic acid cream directly on the skin, combined with taking tranexamic acid medication, gives much better results in removing dark spots on the face (melasma) than the combination of taking tranexamic acid medication with 20% azelaic acid cream.
(Saleh et al., 2019)	42	2 weeks	TXA solution (Kapron ampoules 100 mg/ 1 ml; Sunny Pharmaceutical, Amoun, Egypt) with microneedling	MASI Score	Microneedling is already effective for brightening the skin. However, if this treatment is combined with the use of tranexamic acid cream, the results will be more optimal and satisfying.
(Janney et al., 2019)	100	12 weeks	5% TA solution with 3% HQ cream	MASI Score	A comparison between topical tranexamic acid solution 5% and hydroquinone cream 3% in the treatment of melasma showed equivalent efficacy. However, 5% tranexamic acid solution was associated with a better safety profile, characterized by a lower incidence of adverse events and higher patient satisfaction.
(Irfanti et al., 2021)	23	12 weeks	combination of topical cream of tranexamic acid 3%, nicotinamide 3% and microneedling	MASI score and melanin index	Combination therapy of 3% tranexamic acid cream, 3% nicotinamide, and microneedling was shown to be effective in reducing the MASI (Melasma Area and Severity Index) score and melanin index in melasma patients. This indicates that this combination therapy can be a good adjuvant in melasma management.
(Kaur et al., 2020)	40	8 weeks	10% TA solution	MASI Score	Topical tranexamic acid, especially when combined with microneedling, has great potential as a therapy for melasma. This combination has shown effectiveness in reducing skin pigmentation.

The management of melasma requires a comprehensive approach, including protection against sun exposure, the use of topical agents, procedural therapy, and combination therapy. Sun protection is a key component, with the use of broad-spectrum sunscreens that contain high

SPF to prevent ultraviolet exposure that worsens melasma. Topical therapy involves brightening agents such as hydroquinone, tranexamic acid (topical or intradermal injection), azelaic acid, tretinoin, and combinations of agents (e.g., combinations of three agents such as hydroquinone, tretinoin, and corticosteroids). Transexamic acid (TXA) is an effective plasmin inhibitor by inhibiting activity *Urokinase-type plasminogen activator* (uPA). TXA works by preventing the conversion of plasminogens to plasmin in the basal layer of the epidermis. This inhibited plasmin activity decreases the secretion of inflammatory mediators from keratinocytes, such as prostaglandin E2, which can stimulate melanogenesis. This effect helps reduce excessive melanin production and prevents hyperpigmentation (Maeda, 2022).

The exploration of tranexamic acid (TXA), both in topical and injectable form, is a significant advance in the management of melasma. TXA has been shown to be effective in addressing the pigment and vascular components of melasma, potentially offering a dual-action approach in treatment. Transexamic acid (TXA), a plasmin inhibitor with anti-inflammatory and bleaching properties, has emerged as a promising option for the treatment of melasma (Guo et al., 2024). Topically applied tranexamic acid (TXA) shows penetration especially in the epidermal and dermisal layers. In pharmacokinetic studies, TXA is distributed to the basal layer of the epidermis, where melanogenesis occurs. This has a direct effect on the decrease in activity *urokinase plasminogen activator* (uPA) in keratinocytes, which decreases melanin production (Maeda, 2022). Studies show that topical TXA with a concentration of 2% can provide a significant depigmentation effect without severe side effects, such as irritation or sensibilization, which often occur in other depigmentation therapies. BPOM sets the maximum level of tranexamic acid in topical preparations at 3%.

TXA decreases vascularization of the dermis by reducing angiogenic activity, which is often increased in melasma patients. Excessive angiogenic activity can trigger chronic inflammation and favor the formation of new pigments. By suppressing angiogenesis, TXA contributes to the stabilization of the basal membrane and reduces the production of melanin associated with excessive blood vessels (Maeda 2022). Various tranexamic acid (TA) formulations, such as 3%-10% creams, solutions, gels, and liposomal serums, showed a significant decrease in *Melasma Area and Severity Index* (MASI) scores over a period of 4-12 weeks. Liposomal-based formulations, such as in the study of Gamea et al. (2022), increase TA penetration and reduce the risk of irritation. A 5% TA has been shown to be effective in most studies for epidermal-type melasma, while a concentration of 10% is more suitable for mixed or refractory melasma. Topical tranexamic acid is generally safe to use with minimal side effects such as mild erythema, burning sensation, or itching. These side effects are often temporary and do not require discontinuation of therapy.

Compared to hydroquinone (HQ) of 4%, topical TA has similar effectiveness but with lower side effects, thereby increasing patient satisfaction (Janney et al., 2019). Topical TA combined with vitamin C provides better results in reducing MASI scores than TA alone (Kaikati et al., 2023). Combination with other modalities, such as microneedling, fractional CO2 laser, iontophoresis, or azelaic acid, increases the effectiveness of therapy compared to TA monotherapy. The combination gives better results than single topical use, especially for cases of refractory melasma. Long-term studies with larger sample sizes are needed to confirm the benefits of topical TA in combination therapy, such as with *platelet-rich plasma (PRP)* or glutathione, which also show promising potential.

Conclusion

Based on the studies that have been conducted, topical tranexamic acid (TXA) has been proven to be an effective and safe therapeutic agent for the treatment of melasma. Its mechanisms of action include inhibition of the plasminogen system, reduction of angiogenic activity, and inhibition of tyrosinase, which contribute to reducing melanin production and stabilization of

the basal membrane. Liposomal-based formulations have shown increased penetration and efficacy, with minimal risk of irritation. The combination of TXA with other modalities, such as microneedling, fractional CO2 laser, and vitamin C, provides better results than monotherapy, especially in cases of refractory melasma. Research shows that topical TXA is well tolerated by patients, with mild side effects and higher levels of satisfaction compared to hydroquinone. Long-term studies with larger sample sizes are needed to confirm the long-term efficacy and safety of topical TXA, including its benefits in preventing melasma recurrence. Innovative formulations, such as the combination of TXA with other depigmenting agents, or with technologies such as laser-assisted drug delivery (LADD), need to be further explored to improve the effectiveness of therapy.

References

Aghdam, S. B., Mohammad, A. P., Hosseini-Baharanchi, F. S., Atefi, N., Roohaninasab, M., Kahjoogh, H. A., Yazdanian, N., & Goodarzi, A. (2024). Efficacy, safety, tolerability, and treatment durability of microneedling plus topical tranexamic acid in combination with topical modified Kligman lightening formula for melasma: A four-arm assessor and analyst blinded randomized controlled clinical trial. *Journal of Cosmetic Dermatology, 23*(11), 3585–3597. https://doi.org/10.1111/jocd.16464

Agrawal, M., Varma, K., Kumar, U., Bhargava, S., Mahadik, A., & Agrawal, V. (2023). Comparison of oral versus topical tranexamic acid for treatment of melasma. *International Journal of Clinical and Experimental Dermatology, 30*, 28. https://doi.org/10.18231/j.ijced.2023.015

Akhtar, N., Shah, R. R., Waqas, N., Jasti, S., Sharif, S., Shah, A., & Rao, B. (2023). Assessment of the efficacy of tranexamic acid solution 5% in the treatment of melasma in patients of South Asian descent. *Cutis, 112*(4), 187–191. https://doi.org/10.12788/cutis.0869

Asditya, A., & Sukanto, H. (2017). Studi retrospektif: Profil pasien melasma. *Jurnal Dermatologi Indonesia, 29*(3). https://doi.org/10.20473/bikk.V29.3.2017.220-228

Bijalwan, S., Randhawa, G. K., & Kaur, T. (2024). A prospective, randomized, and open-label study to compare efficacy, safety, and quality of life impact of topical glutathione (2%) in comparison to topical tranexamic acid (3%) in adult melasma patients. *JK Science: Journal of Medical Education & Research, 26*(3), 149–154. https://journal.jkscience.org/index.php/JK-Science/article/view/270

da Silva Souza, I. D., Lampe, L., & Winn, D. (2021). New topical tranexamic acid derivative for the improvement of hyperpigmentation and inflammation in the sun-damaged skin. *Journal of Cosmetic Dermatology, 20*(2), 561–565. https://doi.org/10.1111/jocd.13545

Dawaud, S. M. K., Hegab, D. S., El Maghraby, G. M., & El-Ashmawy, A. A. (2023). Efficacy and safety of topical tranexamic acid alone or in combination with either fractional carbon dioxide laser or microneedling for the treatment of melasma. *Dermatology Practical & Conceptual, 13*(3). https://doi.org/10.5826/dpc.1303a195

Debasmita, B., Raj, C., Ishan, A., & Ipsita, D. (2022). A prospective randomized controlled trial of Q-switched Nd: YAG laser with topical 3% tranexamic acid (TA) versus microneedling with topical 3% tranexamic acid (TA) in treatment of melasma. *Journal of Cosmetic Dermatology, 21*(7), 2801–2807. https://doi.org/10.1111/jocd.14532

El Attar, Y., Doghaim, N., El Far, N., El Hedody, S., & Hawwam, S. A. (2022). Efficacy and safety of tranexamic acid versus vitamin C after microneedling in treatment of melasma: Clinical and dermoscopic study. *Journal of Cosmetic Dermatology, 21*(7),

2817–2825. https://doi.org/10.1111/jocd.14538

Gamea, M. M., Kamal, D. A., Donia, A. A., & Hegab, D. S. (2022). Comparative study between topical tranexamic acid alone versus its combination with autologous platelet-rich plasma for treatment of melasma. *Journal of Dermatological Treatment, 33*(2), 798–804. https://doi.org/10.1080/09546634.2020.1781755

Guo, L., Liu, X., Liu, Q., Xie, X., & Jiang, X. (2024). Treatment of melasma with tranexamic acid essence combined with iontophoresis: A randomized, double-blind, placebo-controlled clinical trial. *Drug Design, Development and Therapy, 18*, 3659–3666. https://doi.org/10.2147/DDDT.S472922

Guo, Q., Hu, D., Pei, Q., Wang, S., Yan, M., Dong, J., & Yao, M. (2023). Effects of masks containing 0.5% tranexamic acid-loaded ethosomes on melasma in Asian skin: A randomized controlled clinical trial. *Dermatologic Therapy, 2023*(1), 1917453. https://doi.org/10.1155/2023/1917453

Irfanti, R. T., Damayanti, W., Dewi, P. F., Oktriana, P., Mulianto, N., & Mawardi, P. (2021). Terapi topikal kombinasi krim asam traneksamat 3%, nikotinamid 3%, dan microneedling pada melasma (Pilot study). *Jurnal Kedokteran Indonesia, 48*(3).

Janney, M., Subramaniyan, R., Dabas, R., Lal, S., Das, N., & Godara, S. (2019). A randomized controlled study comparing the efficacy of topical 5% tranexamic acid solution versus 3% hydroquinone cream in melasma. *Journal of Cutaneous and Aesthetic Surgery, 12*(1), 63. https://doi.org/10.4103/JCAS.JCAS_40_18

Kaikati, J., El Bcherawi, N., Abou Khater, J., Dib, S. M., Kechichian, E., & Helou, J. (2023). Combination of topical tranexamic acid and vitamin C for the treatment of refractory melasma. *The Journal of Clinical and Aesthetic Dermatology, 16*(7), 63. https://pubmed.ncbi.nlm.nih.gov/37560507/

Kaur, A., Bhalla, M., Pal Thami, G., & Sandhu, J. (2020). Clinical efficacy of topical tranexamic acid with microneedling in melasma. *Dermatologic Surgery, 46*(11), e96–e101. https://doi.org/10.1097/DSS.0000000000002520

Maeda, K. (2022). Mechanism of action of topical tranexamic acid in the treatment of melasma and sun-induced skin hyperpigmentation. *Cosmetics, 9*(5), 108. https://doi.org/10.3390/cosmetics9050108

Malik, F., Hanif, M., & Mustafa, G. (2019). Combination of oral tranexamic acid with topical 3% tranexamic acid versus oral tranexamic acid with topical 20% azelaic acid in the treatment of melasma. *Journal of the College of Physicians and Surgeons Pakistan, 29*(6), 502–504. https://doi.org/10.29271/jcpsp.2019.06.502

Marpaung, H. K., Toruan, T. L., & Kurniawati, Y. (2021). Comparison of the effectiveness of 3% tranexamic acid cream versus 4% hydroquinone cream for treatment of epidermal type melasma. *Bioscientia Medicina: Journal of Biomedicine and Translational Research, 5*(3), 340-347. https://doi.org/10.32539/bsm.v5i2.221

Mawu, F. O., Kapantow, M. G., Pandaleke, H. E. J., Cahyadi, A. I., Togelang, L., Tampi, J. A., & Christopher, P. M. (2024). Comparative efficacy of topical 10% versus 5% tranexamic acid in treatment of women with melasma: A double-blind randomized controlled trial. *Universa Medicina, 43*(2), 213–219. https://doi.org/10.18051/UnivMed.2024.v43.213-219

Mushtaq, F., Marwat, R. K., Saleem, M., Khan, A., Khan, S., & Imran, H. (2024). Comparison of efficacy of 5% tranexamic acid vs 20% azelaic acid in patients with melasma. *Journal of Health and Rehabilitation Research, 4*(1), 591-595.

https://doi.org/10.61919/jhrr.v4i1.465

Patil, S. S., & Deshmukh, A. R. (2019). Comparative study of efficacy of intradermal tranexamic acid versus topical tranexamic acid versus triple combination in melasma. *Pigment International*, *6*(2), 84-95. https://doi.org/10.4103/Pigmentinternational.Pigmentinternational_

Qu, Y., Wang, F., Liu, J., & Xia, X. (2021). Clinical observation and dermoscopy evaluation of fractional CO_2 laser combined with topical tranexamic acid in melasma treatments. *Journal of Cosmetic Dermatology*, *20*(4), 1110-1116. https://doi.org/10.1111/jocd.13992

Ramzan, F., Malik, K., Bashir, B., Naseer, Z., Shehzad, A., Malik, L., & Rashid, T. (2023). Efficacy of 5% tranexamic acid in melasma. *Journal of Pakistan Association of Dermatologists*, *33*(4), 1257-1262. https://www.jpad.com.pk/index.php/jpad/article/view/2449

Sahu, P., Dayal, S., & Bhardwaj, N. (2021). Topical 5% tranexamic acid with 30% glycolic acid peel: A useful combination for accelerating the improvement in melasma. *Dermatologic Therapy*, *34*(6), e15107. https://doi.org/10.1111/dth.15107

Shamsi Meymandi, S., Mozayyeni, A., Shamsi Meymandi, M., & Aflatoonian, M. (2020). Efficacy of microneedling plus topical 4% tranexamic acid solution vs 4% hydroquinone in the treatment of melasma: A single-blind randomized clinical trial. *Journal of Cosmetic Dermatology*, *19*(11), 2906-2911. https://doi.org/10.1111/jocd.13392

Saka, S., Rao, G. R. R., Komaram, R. B., Kotha, S., Tatavarthi, R., & Chitturi, L. P. (2019). Efficacy of 10% topical tranexamic acid in melasma: A randomized placebo-controlled split-face study. *International Journal of Pharmaceutical Sciences and Research, 10*(5), 2583-2586. https://doi.org/10.13040/IJPSR.0975-8232.10(5).2583-86

Saleem, D. Z., Shehzad, D. A., Abeer, D., Tahir, D. K., Siddiqui, D. S., & Amin, D. U. A. (2021). Effectiveness of topical 2% tranexamic acid in the management of melasma. *Journal of Pakistan Association of Dermatologists*, *31*(3), 479-483. https://www.jpad.com.pk/index.php/jpad/article/view/1761

Saleh, F., Abdel-Azim, E., Ragaie, M., & Guendy, M. (2019). Topical tranexamic acid with microneedling versus microneedling alone in treatment of melasma: Clinical, histopathologic, and immunohistochemical study. *Journal of the Egyptian Women's Dermatologic Society*, *16*(2), 89. https://doi.org/10.4103/JEWD.JEWD_25_19

Yasnova, N., Sirait, S. P., & Rahmayunita, G. (2024). The effectiveness and safety of 3% tranexamic acid cream vs. 4% hydroquinone cream for mixed-type melasma in skin of color: A double-blind, split-face, randomized controlled trial. *Acta Dermatovenerologica Alpina, Pannonica et Adriatica*, *33*(2). https://doi.org/10.15570/actaapa.2024.16

Zhou, N., Tao, J., Yi, Z., Wu, L., Liu, Z., & Yang, B. (2024). Safety and efficacy of a picosecond 755-nm alexandrite laser combined with topical tranexamic acid in the treatment of melasma. *Journal of Cosmetic Dermatology, 23*(11), 3579-3584. https://doi.org/10.1111/jocd.16432