JOURNAL LA MEDIHEALTICO

VOL. 06, ISSUE 02 (338-352), 2025
DOI: 10.37899/journallamedihealtico.v6i2.1923

Effectiveness of Topical Tranexamic Acid in the Treatment of Melasma

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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; Abdalla, 2021; Liu et al., 2023; Piętowska et al., 2022; Grimes & Alexis, 2019).

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 (Sillen & Declerck, 2021; Yatsenko et al., 2023; Plawinski et al., 2023). 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; Thawabteh et al., 2023). 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

ISSN 2721-1215 (Print), ISSN 2721-1231 (Online)

enzyme activity, modulation of blood vessels, anti-inflammatory properties, and the inhibition of mast cell activity (Yasnova et al., 2024; Ostadkarampour & Patnins, 2021; Abbas 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 authors applied systematic literature review methodology which follows the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guideline framework. The established guideline PRISMA delivers a systemized protocol that helps researchers conduct systematic reviews based on methodological transparency and replicability standards alongside reporting clarity. The systematic approach of PRISMA enables fair literature selection and analysis which strengthens both the analysis quality and the credibility of the synthesized information. The authors used this method to evaluate all existing clinical studies which examined topical tranexamic acid (TXA) treatment of melasma.

The research utilized two well-known academic databases to conduct the literature search which included Google Scholar and PubMed. The selected databases granted wide access to materials within biomedical and pharmaceutical and clinical research fields. The search centered on peer-reviewed articles that appeared in print from January 2019 until December 2024 because it emphasized recently published information regarding topical TXA therapies for melasma treatment. The study used particular key phrases that identified relevant publications regarding the research query. A combination of “Melasma” and “Tranexamic Acid” and “Topical” search terms tied with Boolean operators produced results that simultaneously focused on both ample scope of subject matter and precise findings.

Through the initial search 289 articles surfaced based on the Boolean combination of keywords applied between “Topical,” “Melasma” and “Tranexamic Acid.” The results included 200 records retrieved from Google Scholar and 89 from PubMed. A reference management tool was created to incorporate references before they entered the Covidence software platform which serves systematic review workflows. The automated duplicate detection system in Covidence allowed researchers to implement automated screening before manual verification of the possible duplicates occurred. The removal of sixty-five duplicate papers from the combined 289 records through both automatic (fifty-nine entries) and manual (six entries) elimination left a total of 224 available papers for screening.

A thorough examination of remaining studies took place through evaluation of their titles and abstracts during this phase. The evaluation procedure worked to remove studies that failed to contribute to the research goal. The screening step excluded studies that were non-English publications or inaccessible full-text documents or not focusing on specific melasma therapy with topical tranexamic acid treatment. The refinement process eliminated studies so that 74 articles remained available for full-text evaluation to establish their suitability for review inclusion.

The evaluation of complete research articles occurred through a system that used established requirements for study selection together with quality criteria for relevance, clinical practice and research quality assessments. The review included original studies that studied the use of topical tranexamic acid on melasma in human patients through either randomized controlled trials or cohort studies. All research must explicitly present outcomes which measure melasma

improvement using both the Melasma Area and Severity Index (MASI) score together with the melanin index. The selected studies performed their work exclusively within clinical facilities such as hospitals and dermatology clinics as well as aesthetic centers to guarantee that reported results match real-life clinical practices. Researchers removed studies which investigated TXA only through oral or intradermal routes and those using preclinical laboratory or animal models and those without measurable clinical results.

Thirty studies were selected through the completion of the evaluation process and became part of the final synthesis analysis. The included studies featured different research designs and sample sizes and lengths of TXA treatment and outcomes. The research featured multiple patient groups that used diverse treatments which created suitable conditions for an extensive description of their findings. The researchers thoroughly analyzed each chosen study to extract specific information such as participant numbers along with topical TXA formulation and dosage data, treatment duration and intervention type between monotherapy and combination therapy and the recorded clinical outcomes that included MASI scores and melanin index measurements and erythema index response data. The researchers gave special emphasis to evaluating safety aspects of treatments alongside evaluations of patient satisfaction and noted adverse effects for building an all-inclusive understanding of effects and tolerability. The diverse study design elements and intervention protocols and outcome assessment methods between included studies prevented a formal meta-analysis. Therefore the research team chose to perform data synthesis narratively through descriptive methods. Different therapy elements including formulation type and concentration and treatment duration and therapeutic effects were displayed through summary tables to enable effective comparison. Different topical TXA formulations ranging from creams to gels and solutions as well as liposomal serums delivered helpful information on its clinical utility for dermatology uses.

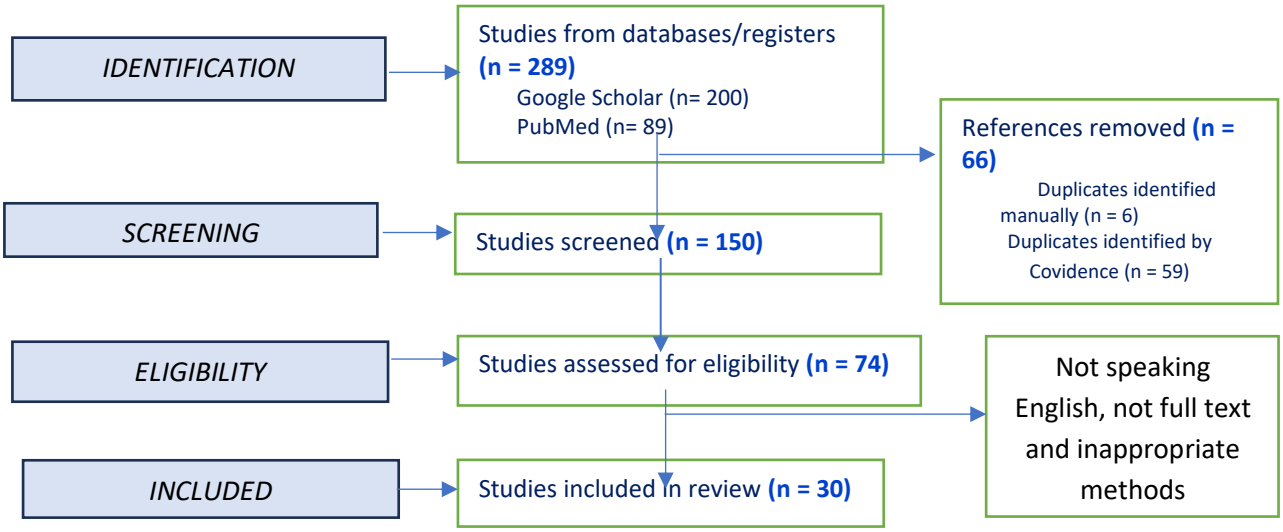

Figure 1. descriptive analysis and displayed

The PRISMA flow diagram documented all stages of the review from identification through inclusion of studies. Each step in the article selection process created a visual display that showed the total records examined as well as the number of screened and eligible studies and studies that made the final inclusion. Through its use of this flow diagram the review process achieved better methodological clarity while showing readers how the 30 selected studies emerged from the approximately 300 initial records. The methodical methodology strengthens both the evidence-based conclusions and the validity of recommending topical TXA for melasma treatment.

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 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

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
					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 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.

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
(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.
(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.

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
(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 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,

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
					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 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	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

Reserchers	Method				Conclusion
	N	Duration	Dose	Evaluasion	
			3% and microneedling		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.

Unmasking the Depths of Melasma Management

This systematic review demonstrates quantitative evidence that supports topical tranexamic acid (TXA) as a promising tool for fighting melasma yet the true meaning lies most strongly in the hidden patterns that exist between the studies though these patterns often exist involuntarily and subtly. As a product that initially functioned to control bleeding TXA has developed into an effective solution for controlling both skin color changes and vascular responses (Maeda, 2022; Guo et al., 2024). The use of TXA involves more than merely biochemical transactions. The interaction between pigment molecules and inflammation reactions depends on how people perceive the situation as well as how easily they can gain access to the subject. The scattered study elements regarding TXA must be examined in a comprehensive way to correctly position its therapeutic role in melasma treatment.

All analyzed studies agreed that TXA applied topically proved effective in minimizing hyperpigmentation treatment results either alone or with additional therapies (Akhtar et al, 2023, Marpaung et al, 2021, Patil & Deshmukh, 2019). A noticeable pattern remains across multiple clinical trials regarding topical TXA performance but specific changes occur between formulation types and dosage levels and treatment durations. Both clinical research and experimental studies demonstrate that TXA concentrations between 2%–10% in multiple delivery forms create non-linear improvements in hyperpigmentation (Saka et al., 2019; Gamea et al., 2022; Saleem et al., 2021). The studies concerning TXA concentrations for mixed-type or refractory melasma show promising results yet fail to confirm if these findings apply to all situations or remain specific to select conditions (Mawu et al., 2024; Aghdam et al., 2024). Outcomes from treatment with tranexamic acid appear to be shaped by patient factors such as Fitzpatrick skin type and lesion depth and vascular dominance and treatment history but these variables are not properly controlled or stratified in standard clinical protocols (Yasnova et al., 2024; Zhou et al., 2024).

TXA differentiates from traditional skin-lightening drugs through its multiple action mechanisms of plasmin-mediated pathway blockage and tyrosinase suppression and prostaglandin reduction and inhibition of angiogenesis. Hydroquinone and kojic acid agents primarily affect melanin synthesis. (Maeda, 2022; Shamsi Meymandi et al., 2020; Guo et al., 2023) TXA shows multi-target action which matches the clinical characteristics of melasma because doctors now consider this skin condition an expression of combined vascular hormonal and inflammatory abnormalities (Debasmita et al., 2022; Malik et al., 2019; Sahu et al., 2021). TXA demonstrates exceptional effectiveness towards dermal melasma cases and telangiectatic components because of its blocking capability of the angiogenic cascade mediated by lowering vascular endothelial growth factor (VEGF) activity (Aghdam et al., 2024; Janney et al., 2019). The examination of vascular markers or patient stratification remained absent in most research despite being a common pattern in clinical dermatology to simplify complex dermatological issues by assessing pigment changes.

The majority of studies show that topical TXA causes minimal adverse reactions which mainly manifest as erythema, pruritus and temporary burning sensations (Ramzan et al., 2023; Saleh et al., 2019; El Attar et al., 2022). Patients favor TXA treatment because of its low-risk profile over hydroquinone as well as due to its suitability for sensitive skin patients or for people who have developed adverse reactions during long-term steroid or retinoid use (Kaikati et al., 2023; Bijalwan et al., 2024). Safety represents one part but not all aspects of acceptability. The

available trials failed to measure patient-reported quality of life indicators or skin confidence measurements together with social functioning which demonstrate strong links to how melasma affects skin appearance according to Asditya and Sukanto (2017) and Yasnova et al. (2024) most prominently in cultures where facial characteristics hold distinctive social value.

Trial performance shows significant differences from sustainable practices in actual clinical settings. Multiple therapy approaches incorporating TXA with microneedling and fractional CO_2 lasers as well as iontophoresis or glycolic acid peels have proven to generate better clinical results when used separately from TXA monotherapy (Dawaud et al., 2023; Debasmita et al., 2022; Zhou et al., 2024). The visible enhancements brought by these therapies require multiple factors to be factored in including procedural costs and equipment accessibility as well as clinician specialization and additional patient check-ups. Medical protocols based on multiple therapies tend to exist in theory only because they are not operational within resource-limited environments or among patients who lack access to aesthetic healthcare. True therapeutic value should be assessed by equity and accessibility instead of the commonly emphasized efficacy.

The weak evidence foundation emerges from different methods used in research studies. A weak statistical case exists for the research conclusions because some trials applied different study durations (two weeks to twelve months), numerous studies lacked blinding techniques and utilized non-standard MASI scoring criteria and worked with sample sizes less than 30 participants (Guo et al., 2023; Mawu et al., 2024; Kaur et al., 2020). The lasting effects of TXA remain unclear because most assessments stop when the treatment period ends thus creating uncertainty about its long-term efficacy. The condition of melasma persists as a long-term disease which repatterns repeatedly. The acceptance of an eight-week treatment yielding dramatic benefits initially while disappearing after three months will be limited by its recurring effect rates. The sustained effectiveness of Topical Tranexamic Acid needs additional examination through extended follow-up studies which last from six months to one year according to findings presented in Mushtaq et al. (2024) along with Agrawal et al. (2023).

Research into formulation science largely remains an underexplored area for skin disease management studies. The potential of liposomal TXA formulations with TXA-loaded ethosomes to improve skin penetration performance and therapeutic effect exists mostly in scholarly or limited commercial settings (Gamea et al., 2022; Guo et al., 2023). These innovative methods lack analysis of their industrial production capabilities and their required regulatory procedures. The efficacy of depigmenting agents in tightly controlled trials needs equal importance with understanding their formulation stability, storage conditions and real-life delivery under unregulated market and over-the-counter conditions.

The incorporation of TXA into therapeutic combinations presents fundamental inquiries about the approaching treatment design for melasma which will it be complex or straightforward. The medical goal should clinicians pursue is whether they need to create one perfect topical treatment or multiple combinations that focus on individual skin requirements. This review presents the opposition between therapeutic philosophies yet avoids concrete findings about why and how TXA works on pigmentation. This shows how the field of personalized medicine faces similar contradictions.

The most disturbing silence throughout this medical literature happens when patients are not allowed to narrate their experiences. The impact of TXA on skin pigmentation is known but there is no information describing how it affects how people perceive their faces or their identities when interacting with others. A MASI score reduction by 2 points establishes confidence during social interactions what kinds of improvements are required. People who use TXA for their skin pigmentation must continue treating their condition daily before their first appearance outside. The treatment effects of oral TXA fade because pigmentation returns alongside the fatigue from repeated tries. The scientific research provides no analysis of how

patients experience existential emotions during their treatment or after successful treatment completion.

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.

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