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Effectiveness of Oral Tranexamic Acid in the Treatment of Melasma: A Systematic Review

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Abstract

Melasma is a skin condition characterized by hyperpigmented patches, generally appearing on facial areas such as the cheeks, forehead, and upper lip. This condition is more common in women, especially during pregnancy or when using hormonal contraceptives. The factors that cause melasma include sun exposure, hormonal changes, and genetic factors. The purpose of this study is to examine the effectiveness and safety of the use of oral Tranexamic acid (TXA) in the treatment of melasma based on recent studies. The method used by literature search in journals published between 2022–2024 used keywords related to oral TXA and melasma. Studies that met the inclusion criteria were evaluated to compare the outcomes of oral TXA therapy based on dose, duration, and side effects. The results showed that oral TXA was proven to be effective in reducing the Melasma Area Severity Index (MASI) score with a dose of 500–1500 mg/day for 8–12 weeks. A significant decrease in MASI scores was achieved at week 12, showing consistent results across multiple studies. The most commonly reported side effects are gastrointestinal disorders, such as nausea and abdominal pain. Oral TXA does not cause serious side effects at doses up to 4 g/day. Tranexamic acid (TXA) in oral form is an effective and safe therapy in managing melasma. However, further research is needed to determine the ideal duration of treatment and strategies in preventing melasma recurrence.

Introduction

Melasma is a skin condition characterized by hyperpigmented patches, generally appearing on facial areas such as the cheeks, forehead, and upper lip. This condition is more common in women, especially during pregnancy or when using hormonal contraceptives. The factors that cause melasma include sun exposure, hormonal changes, and genetic factors. Hyperpigmentation that occurs in the facial area can be a source of cosmetic concern for patients, negatively impacting the quality of life. Melasma in women has differences, namely in clinical aspects, etiology (Mustofa et al., 2021). According to Gupta et al. (2022), the prevalence of melasma can reach 50% among women of reproductive age, making it a significant dermatological problem. Melasma is a common dermatological condition, characterized by brown or brownish-gray patches on the face, more commonly affecting women, especially those with dark skin types (Mushtaq et al., 2024).

The clinical picture of melasma is hyperpigmented macula, irregular, symmetrical distribution on the face. The three main patterns of lesion distribution in melasma are centrfacial lesions on the cheeks, forehead, nose, above the lips and chin, which are the most common forms, dilarity on the cheeks and nose, and mandibles. The number of hyperpigmented maculae is single to

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multiple, and the distribution of lesions tends to be symmetrical (Asditya & Sukanto, 2017; Sandhu et al., 2021; Li & Tan, 2023; Das & Akhtar, 2023; Ankad et al., 2021; Zuniarto et al., 2025).

Treatment of melasma is generally difficult. Various treatment methods have been used, including topical treatments such as hydroquinone, either alone or in combination with retinoids and steroids, azelaic acid, as well as salicylic acid and topical glycolic acid. Other treatment options include chemical peels and lasers, but none show significant results. Because of this hard-to-overcome nature of melasma, more clinical trials of new therapeutic options are needed (Razman Faisal et al., 2023; Adebusoye & Srivastava, 2025; Nautiyal & Wairkar, 2021). The treatment of melasma has become a challenge in dermatological practice. Various therapies such as lightening creams, lasers, and chemical peels have been used, but the results are often unsatisfactory.

Tranexamic acid, known as an antifibrinolytic agent, has emerged as an interesting alternative in the treatment of melasma. Early research suggests that tranexamic acid may reduce melanin production by affecting the biological pathways involved in hyperpigmentation (Kim et al., 2017; Verma & Yadav, 2023; Widgerow et al., 2022). Tranexamic acid medication works by stopping skin cells from producing too much melanin pigment. It does this by interfering with the communication between skin cells and inhibiting certain processes within the cells. Transexamic acid also prevents induction from UV rays, plasmin activity, decreased activity of mast cells and can also inhibit fibroblast growth factors further decreased vascularization and the number of mast cells in the dermis (Wikurendra, 2018).

Tranexamic acid is considered a potential treatment for melasma. Although its oral use has shown good results, the effectiveness of topical use is still debated among researchers. The proposed mechanism is that tranexamic acid reduces melanin synthesis with its inhibitory effect on plasminogen-keratinocyte interactions which in turn lowers tyrosinase levels (Sawar, et al., 2023). The skin-lightening effect of tranexamic acid is associated with inhibition of plasmin-mediated prostaglandin production. These prostaglandins play a role in the activation of melanogenesis (Maeda, 2022; Latha, 2019). Tranexamic acid has a multitarget mechanism of action in melasma. In addition to inhibiting tyrosinase, it can also reduce fibroblast growth factor production, mast cell activity, and prevent angiogenesis through decreasing VEGF and endothelin-1.

These mechanisms contribute to the decreased vascularization that is characteristic of melasma. Oral TXA has shown a good safety profile for up to 6 months of use in melasma therapy. Higher efficacy can be achieved with a synergistic approach, i.e. combining oral TXA with topical agents such as hydroquinone, kojiic acid, and energy-based therapeutic modalities. Tranexamic acid can be given orally or topically, but oral use has shown better effectiveness in some studies. In a study by (Bala et al., 2018), patients who received oral tranexamic acid showed a significant reduction in the intensity of melasma patches compared to a placebo. This opens up new opportunities in the management of melasma, especially for those who do not respond to conventional therapies. In melasma dermoscopy, light brown to dark brown globular structures will appear with a diffuse chocolate background (Chatterjee & Vasudevan, 2014).

An overview of epidermal lesions will show regular pigment networks with brownish homogeneous pigmentation, while dermal lesions will show irregular pigment networks with dark brown pseudoreticular pigmentation to diffuse bluish-gray pigmentation. Excess dermoscopy can detect chronic side effects of topical bleaching agent preparations - Exogenous Ochronosis (OE). OE abnormalities can occur in all skin color types but are increased in dark-skinned individuals (Fitzpatrick types IV and VI) and a history of high-concentration hydroquinone use of more than 1 year (Diah Tantri et al., 2024; Davis & Callender 2010).

So the researcher tries to formulate the problems that will be discussed in the research, which are as follows: How does the variability of response to oral tranexamic acid affect melasma treatment, what dose and duration of oral tranexamic acid treatment in melasma treatment, and What are the side effects that appear in the treatment of melasma with oral tranexamic acid.

Methods

A systematic review structure evaluated oraltranexamic acid (TXA) effects for melasma treatment along with its safety parameters. The systematic review followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 protocol that provides standardized methods to make results more transparent and easy to reproduce. The study's primary goal involved assessing oral TXA effectiveness by evaluating MASI score changes as well as studying its best treatment doses and duration lengths and measuring adverse reaction occurrence and frequencies. This research sought to construct an extensive evidence synthesis which included human-subject clinical trials and observational studies published during January 2022 to December 2024.

The search included biomedical databases where PubMed combined with Google Scholar to obtain results. The selected databases helped obtain both published scientific research from indexed journals while capturing non-peer-reviewed information. A time-span from January 1 2022 through December 31 2024 was selected as the search period for the literature review because it ensured the inclusion of current evidence about oral-transdermal TXA treatment for melasma. The Medical Subject Headings (MeSH) provided the basis for developing search terms which Boolean logic combined. The search utilized “tranexamic acid oral” with the “effectiveness” and “melasma” terms connected by “AND” and “OR” to boost the particularity and sensitivity of results. Further limits were installed during the search process which excluded both animal and non-English language research studies. The database search generated an initial outcome of 258 articles.

Covidence enabled the management and screening of systematic reviews by importing the retrieved articles. Duplicate records were detected and removed automatically by Covidence for accurate quality control while 131 articles got excluded following manual verification. Of these articles, 127 remained unique and were assessed through title and abstract review. The researchers eliminated studies that strayed from study topic or lacked relevance to oral TXA or absent data on melasma treatment. A total of sixty-six publications underwent complete text assessment following which the authors performed eligibility examination using defined criteria for retention and exclusion. A complete analysis of selected study full texts led researchers to select 37 studies for inclusion in their final evaluation. Figure 1 demonstrates the PRISMA flow diagram that showcases the identification screening eligibility and inclusion steps for the selection process.

Tranexamic acid studies received inclusion when they fulfilled four vital conditions: (1) randomized controlled trials (RCTs), prospective cohort studies, or observational studies format; (2) human subjects received oral tranexamic acid treatment; (3) the studies measured MASI score modifications or qualitative clinical results; and (4) they were accessible in full text and English language. The study inclusion criteria excluded trials which (1) studied exclusive topical or intradermal TXA use without oral TXA examination, (2) did not present a clear experimental design or procedural details, (3) published only abstract data instead of full text articles, and (4) were available only in languages other than English. The established criteria maintained the inclusion of methodologically sound studies which directly addressed therapeutic implementations.

Two independent examiners used a standardized data extraction sheet to retrieve data from the 37 included studies in order to eliminate bias. The study data extraction process gathered information about the authors, publication year, research design, sample number, treatment

dosage and length of exposure, MASI score reduction results and adverse effects and concluding statements. The reviewers settled their differing points through either discussions between them or by using a third-party adjudicator. This research considered a descriptive synthesis approach instead of performing a meta-analysis due to the multiple design variations and inconsistent outcome information. The research data received a detailed organizing structure that enabled comparison among different studies. The researchers conducted thematic analysis of medication effectiveness patterns along with reaction times and side effects frequency data. The researchers used narrative synthesis to create practical guidance for practice and determine what questions demand future study.

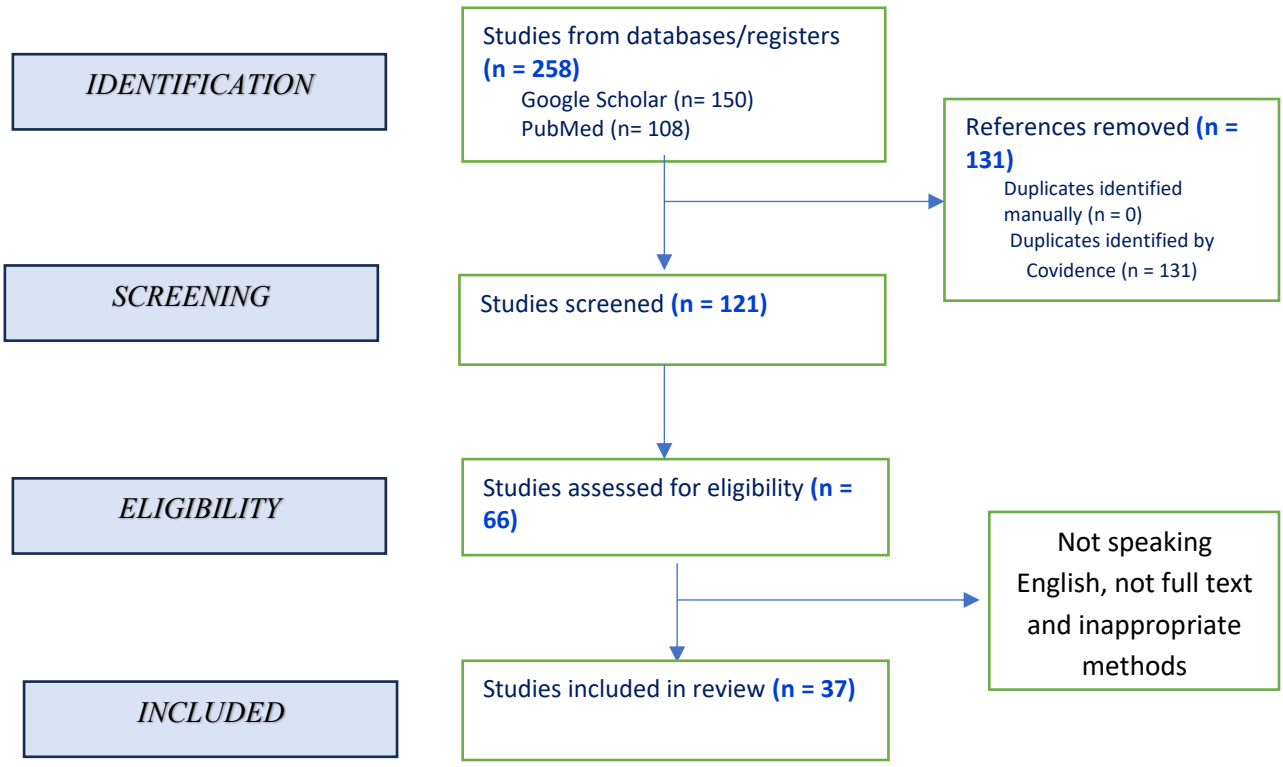

Figure 1. descriptive analysis and displayed

This review examined research that occurred in different healthcare settings including community health centers together with dermatology clinics and hospital outpatient departments as well as aesthetic institutions thus providing diverse insights about practical implementation. Studies analyzed participant samples who differed because of their ethnic backgrounds together with their Fitzpatrick skin types and melasma stage severity. Although study participants received oral TXA doses between 250 mg and 1500 mg per day they took their medication in two or more portions during 2 weeks to 6 months. The study design incorporated differing treatment protocols to examine various outpatient care settings and disease predicaments. The review provides a holistic evaluation of oral TXA effectiveness and tolerability, contributing valuable insight for dermatologists and clinicians involved in pigmentary disorder management.

Result and Discussion

Initial search results resulted in 258 articles discussing various melasma therapies. After applying the inclusion and exclusion criteria, 37 studies were obtained that met these criteria (Figure 1). The selected studies focused on oral therapy studies

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

Researchers	Method			Side effects	Conclusion
	N	Duration	Dose		
(Liu et al., 2024)	Rats: 20 animals divided into 4 groups (5 animals per group). Human skin explantation: Taken from 3 healthy female patients undergoing blepharoplasty surgery.	In animal experiments, twice a day for one month (topical). Human skin explant culture was carried out for 48 hours with the administration of TXA.	In rats: 750 mg/kg/day for intragastric administration, or 3% TXA for topical application. In human cells: 3 mM TXA for 48 hours.	No direct side effects were mentioned in the study	Oral administration of TXA is more effective than topical for reducing UVB-induced hyperpigmentation in the skin, mainly through a mechanism of decreased expression of endothelin-1 (ET-1) in the microvascular endothelial cells of the dermis. TXA also inhibits melanocyte proliferation and melanin production.
Mehta Dr.Neha, et al 2024	100	3 months.	250 mg	No serious side effects	TXA drugs are proven to be effective and do not cause serious side effects in treating melasma.
Sohila et al,2024	40	twice a day, for three months.	250 mg	No direct side effects were mentioned in the study	Oral intake of TA is a safe and effective method for the treatment of melasma, without the risk of PIH, thrombotic tendencies or bleeding.
(Zhang et al., 2022)	80 patients	3 months	250 mg	No direct side effects were mentioned in the study	PRP in combination with TXA in treatment Melasma may improve treatment outcomes by safely regulating VEGF, ET-1 and MSH levels and reducing the rate of recurrence.
(Tawanwongsri et al., 2024)	26 patients (13 for PRP + acid tranexamamy, 13 for PRP only).	3 months	Oral: 500 mg of acid tranexamic acid per day. PRP: Intradermal injection of 0.1 ml/cm² every 4 weeks for 3 sessions.	15.4% of patients reported erythema and mild swelling that disappeared within a few hours. 7.7% of patients reported mild gastrointestinal discomfort after the first week of oral use of tranexamic acid.	The combination of PRP injections into the skin and taking TXA medication is very effective in removing dark spots (melasma), even for patients who have difficulty healing. In addition, this combination is also safe and does not cause any harmful side effects.
Singh et al. 2023	59 patients	4 weeks	500 mg	No serious side effects	Studies show that the combination of oral tranexamic acid with a modified Kligman formula has superiority in treating melasma compared to azelaic acid. Patients in this treatment group showed faster improvement and longer duration of response,

					resulting in an overall shorter treatment time.
(Prathyoosha et al., 2024)	90 patients	3 months	250 mg	No direct side effects were mentioned in the study	Oral TXA may be considered a better option for moderate to severe melasma.
(Agrawal et al., 2023)	84 patients	4 weeks – 3 months	250 mg	abdominal pain, nausea, and oligomenogenesis	The use of tranexamic acid in oral form gives better results in the treatment of melasma compared to topical use. Although oral use may cause gastrointestinal distress, patient compliance with oral treatment tends to be higher. This makes oral tranexamic acid a promising treatment option for melasma.
(Sarwar et al., 2023)	80 patients	3 months	250 mg	No serious side effects	Oral administration of tranexamic acid is an effective and safe therapeutic approach for patients with moderate to severe melasma. The drug is generally well tolerated by patients.
(Akl, 2022)	50 patients	3 months	250 mg	Gastrointestinal	The combination of 20% liposomal azelic acid topical therapy and tranexamic acid oral therapy showed synergistic effectiveness in treating melasma. This combination provides satisfactory results with a good safety profile.
(Batra et al., 2022)	40 patients	3 months	250 mg	No direct side effects were mentioned in the study	Oral and transepidermal TXA appear to be equally effective, which suggests that The efficacy of TXA may not depend on the route of its administration. Oral therapy is comfortable for patients.
(Botsali et al., 2022)	33 patients	5 months	250 mg	No direct side effects were mentioned in the study	Laser therapy combined with oral tranexamic acid (TA) therapy is an effective approach in managing melasma in patients with Mediterranean ancestry. The addition of oral TA substantially improves the effectiveness of treatment.
Hee Jeong Han, et al 2024	15 patients	8 months	250 mg	No serious side effects	Conventional Melasma Therapy which showed the protective effect of

					dermal targeting therapy in the development of melasma.
(AbdElrahman et al., 2023)	The number of regimens in this study was not mentioned	6 months	500-1500 mg	Gastrointestinal	TA has been investigated for melasma treatment in a variety of formulations, which include topical, intradermal (ID), and oral administration, with oral formulations showing the highest benefit although temporary.
Carolina jessica, et al 2022	44 patients	2 months	325 mg	No serious side effects	The combined use of tranexamic acid (TA) oral therapy and f-TCC light therapy showed superiority in the treatment of severe melasma in the Hispanic population compared to single oral TA therapy.
Behrani agam, et al 2022	40 patients	2 minngu	250 mg	Gastrointestinal	Combination treatment methods can be the right choice for Middle Eastern patients. The oral method is more tolerable to the patient, it may have systemic side effects.
Simpsons js, jordan et al 2022	42 patients	The duration of treatment in this study was not mentioned	625 mg	headaches, malaise and nausea, gastrointestinal disorders, congestion, numbness in the legs, hypomenorrhea, and hypermenorrhea	Oral TXA is a safe and effective treatment option for patients with persistent melasma.
(Cassiano et al., 2022)	64 patients	2 months	250 mg	Headache	Oral tranexamic acid works synergistically with topical therapy of melasma by inhibiting stem cell growth factors, thereby reducing melanocyte proliferation and activity, and ultimately decreasing melanin production.
Official, sarkar et al 2024	25 patients	6 months	250 mg	No direct side effects were mentioned in the study	Taking tranexamic acid medication is helpful in treating dark spots (melasma). To maintain good results, medication usually needs to be taken regularly. In addition, patients who are prone to blood clots need to be closely monitored while on this medication.

Singh, ridima et al 2023	19 patients	2 months	500 mg	No direct side effects were mentioned in the study	The study concluded that a therapeutic regimen combining oral tranexamic acid with a modified Kligman formula was significantly more effective in reducing the severity of melasma compared to a combination of oral tranexamic acid with 15% azelaic acid.
Bala, H 2022	61 patients	3 months	250 mg	No direct side effects were mentioned in the study	Oral TA 250 mg twice daily used for 12 weeks appears to be effective in treating moderate to severe melasma with minimal side effects in Australia's diverse ethnic population.
Bhattacharjee, Rajsmita et al 2023	50 patients	3 months	250 mg and 500 mg	No side effects were observed in either group.	The dosing regimens studied showed comparable efficiency in lowering MASI scores at week 12, and significant clinical improvement was maintained throughout the 12-week post-treatment follow-up period, with minimal relapse rates.
Elkamshoushi MD, Abdelaal M et al 2022	20 patients	9 months	250 mg	No side effects were observed in either group.	Oral TA is an effective and tolerable treatment modality for melasma. Combining 4% hydroquinone with oral TA was associated with relatively earlier and better cosmetic results.
Zining Xu, et al 2024	70 patients	2 months	500 mg	No side effects	The addition of oral TXA to traditional therapies can result in rapid and effective improvements in PPR, which may be due to improved skin barrier function.
Do, michael fos et al 2022	4 patients	6 months	325 mg	No side effects	the effectiveness and safety of the use of oral TXA to treat stubborn melasma and highlight the possibility of dosage regimens that could be used for such new therapies.
(Guo et al., 2024)	30 patients	3 months	500 mg	No side effects	The combination of tranexamic acid and iontophoresis was significantly more effective in reducing melasma severity and improving skin brightness compared to placebo, as

					shown by the decrease in MASI score.
Samina Islam, Dr. Syeda 2024	60 patients	3 months	500 mg	No direct side effects were mentioned in the study	Oral tranexamic acid combined with fluosinolone-based triple combination cream was significantly more effective in treating facial melasma than cream alone.
Behrangi MD, Elham et al 2022	40 patients	2 weeks	750 mg	No direct side effects were mentioned in the study	Combination treatment methods can be the right choice for Middle Eastern patients with melasma disorders, and tranexamic acid appears to be an effective and safe treatment for melasma
Pratama, lucky et al 2022	74 patients	6 months	250 mg	No direct side effects were mentioned in the study	Tranexamic acid shows results which is promising in melasma.
Rajashekar TS MD, et al 2022	70 patients	3 months	500 mg	No direct side effects were mentioned in the study	Oral tranexamic acid is a promising candidate for melasma therapy. However, further studies with larger sample sizes and longer observation periods are needed to determine its long-term safety and efficacy profile.

The use of tranexamic acid in melasma therapy was first reported in 1979 by Nijo in Japan as a result of an accidental observation in a patient with chronic urticaria. Since that initial report, a number of cases have supported the use of tranexamic acid as an effective therapeutic agent for melasma. For melasma, a low dose of 250 mg twice a day is generally used, it can also be topically and intradermal. *Trans-4-aminomethylcyclohexanecarboxylic* acid (TXA) is a synthetic *lysine* analogue that has an antifibrinolytic effect through the reversible blockade of the lysin-binding part of the plasminogen molecule. Tranexamic acid has been used for the treatment of menoragia since 1970 at doses of 2.0-4.5 g/day during a cycle; Increasing doses to 4.0-4.5 g/day is reported to cause no serious side effects. Oral tranexamic acid prophylaxis for 8 to 34 months successfully prevents hereditary angioedema without serious side effects or abnormal blood fibrinolytic activity (Triyanti, 2022; Fijen et al., 2021). Tranexamic acid can be a promising therapeutic modality, especially for melasma patients who are difficult to treat with other methods. The combination of the use of tranexamic acid with other approaches such as microneedling also yielded significant results (Rao et al., 2022).

The dose of tranexamic acid for melasma is 500-1500 mg per day, usually 250 mg, taken 2 times a day, for 8-12 weeks. This dose is in stark contrast to the dose of tranexamic acid for menorrhagia therapy which is 3.9-4 g for 5 days once in 1 month. Doses of tranexamic acid 4-4.5 g/day did not show serious side effects; however, the determination of the optimal daily dose and duration of tranexamic acid therapy requires further research. The use of tranexamic acid is not recommended in patients with renal impairment, cancer, heart and vascular disease, and lung disease. In addition, patients who are on blood-thinning medication or have a history of blood clots such as DVT (deep vein thrombosis), pulmonary embolism, stroke, or cerebral hemorrhage should also avoid tranexamic acid. Other risk factors such as pregnancy, use of

hormonal contraceptives, and smoking may increase the risk of blood clots, which should be considered before starting tranexamic acid therapy (Wulandari, 2021).

In a study of 84 melasma patients, there was a significant reduction in MASI scores after 12 weeks of treatment in both the group receiving oral tranexamic acid (mean MASI score = 7.93) and the group receiving topical tranexamic acid (mean MASI score = 9.45). The very small p value (p=0.000) in both groups indicated the statistical significance of the results. These findings are consistent with a previous study by Vinod K. Khurana et al. who reported a decrease in the mean MASI score to 3.18±1.93 at week 12 with the use of oral tranexamic acid. 14 The study conducted by Bahareh Ebrahimi et al. reported a mean MASI score reduction of 10.76±9.43 at week 12 in the group of patients using topical tranexamic acid. Although both treatment modalities (oral and topical) were effective in reducing melasma severity, comparative analysis showed superiority of oral tranexamic acid compared to topical tranexamic acid. Research shows that patients are more compliant with taking tranexamic acid in its oral form. However, oral use is more often associated with side effects on the gastrointestinal tract such as abdominal pain, nausea, and changes in the menstrual cycle. On the other hand, topical (applied) use of tranexamic acid at a concentration of 5% may cause local side effects such as redness, irritation, and dry skin (Agrawal et al., 2023).

A study was conducted on 64 women with melasma. The participants were randomly divided into groups. Each group was given a different treatment for 2 months. Some only used creams, some were supplemented with microneedling, some were given medication (tranexamic acid), and some received a combination of treatments. The researchers who assessed the treatment results did not know which group received which treatment (blind-evaluator) to make the assessment more objective. The aim of this study is to find out which combination of treatments is most effective for melasma. Participants underwent biopsy of the melasma-affected area on day 1 and day 60 from inclusion. The primary outcomes of the study involved changes (day 1 compared to day 60) in several variables, viz: The thickness of the epidermis and stratum corneum, the degree of compaction of the stratum corneum, the degree of elastosis due to sun exposure; the density of melanin in the epidermis and upper dermis; the ratio between intact and incomplete basement membrane zones; the number of mast cells in the upper dermis; the number of melanocytes in the basal layer, the number of melanocytes in the pendulum, and the area of melanocytes; and the intensity of immunohistochemical staining for vascular endothelial growth factor, stem cell factor, and keratinocyte growth factor.

One participant from the group receiving tranexamic acid therapy discontinued the drug due to persistent headaches. In addition, in three patients, herpes simplex infection occurred after the microneedling procedure. This group recorded a 24% reduction in melanin density in the epidermis (95% confidence interval: 17-35%; $P < 0.01$), indicating a statistically significant reduction. However, no change was found in melanin density in the dermis or the size of the melanocyte area after treatment. An overall decrease in the number of pendulum melanocytes by 25% (95% confidence interval: 7-42%; $P < 0.01$) was also reported. This reduction was most pronounced in the group that received the combination of microneedling and tranexamic acid, with a reduction of up to 41% (95% confidence interval: 7-73%; $P < 0.01$). After treatment, the proportion of non-intact basement membrane compared with intact basement membrane decreased, especially in the group that underwent microneedling as well as the group that received the combination of microneedling and tranexamic acid. In these groups, there was a 13% increase in epidermal thickness (95% confidence interval: 5-21%; $P = 0.02$) and a 6% decrease in stratum corneum thickness (95% confidence interval: 0-22%; $P = 0.04$). In addition, all groups showed increased compaction in the stratum corneum. However, improvement in solar elastosis was only found in the microneedling group as well as the combination group of microneedling and tranexamic acid. In that group, vascular endothelial growth factor immunostaining increased by 14% (95% confidence interval: 4-24%; $P = 0.03$),

while stem cell factor only showed an increase in the group that received microneedling. No significant changes were found in mast cell count, cluster of differentiation 34 (CD34) expression, or keratinocyte growth factor levels based on immunoassay results. Greater epidermal thickness appeared to be associated with melasma whitening. However, melanin levels in the skin do not affect the prognosis of melasma. It is important to avoid damage to the skin barrier and stimulation of angiogenesis during melasma treatment (Cassiano et al., 2022; Wang et al., 2021; Cassiano et al., 2022).

Both oral and transepidermal administration of TXA showed equally good results in treating melasma. This means that the way the drug is administered does not really affect its effectiveness. Oral administration is more comfortable for patients. Meanwhile, skin administration is more localized and thus has fewer side effects, but the procedure can be a bit painful and requires several sessions. In addition, melasma tends to recur so treatment needs to be done periodically (Batra et al., 2022). Oral administration of TXA has been shown to be superior in treating skin hyperpigmentation compared to topical administration. The mechanism that may underlie this difference in effectiveness is the ability of oral TXA to suppress the production of endothelin-1, a vasoconstrictor that plays a role in pigment regulation in skin microvascular endothelial cells (Liu et al., 2024).

Combination therapy of oral TXA and PRP shows better results in treating melasma compared to the use of TXA alone. PRP, with its growth factor content, can increase the effectiveness of TXA in inhibiting melanin formation and accelerating skin regeneration (Zhang et al., 2022). Transexamic acid and vitamin C are effective therapies for melasma in addition to microneedling (Raza et al., 2022; Santos et al., 2021).

Clinical Realities and Concealed Implications

Study results display without doubt that oral tranexamic acid (TXA) shows therapeutic potential as a treatment for melasma. All studies examined by Bala et al. (2018), Bhattacharjee et al. (2023), Prathyoosha et al. (2024) and Agrawal et al. (2023) showed significant MASI score reduction at week 8 to week 12 of the treatment period. Patients who want to see quick results from depigmentation treatment find the fast results especially attractive. Visible improvement from oral tranexamic acid treatment does not necessarily represent permanent resolution since it simplifies a condition that needs complex management. The evidence appearing strong by itself includes blind spots along with ethical questions and various contradictions requiring further analysis.

The recurrent nature of this condition exists as one of the most noticeable yet unnoticed problems because science still lacks proper long-term data on relapse patterns. Success results from interventions undertaken at week 8 or week 12 per the findings by Singh et al. (2023) and Zhang et al. (2022) nevertheless limited long-term follow-ups exceeded 16 weeks according to research by Cassiano et al. (2022), Hee Jeong Han et al. (2024) and AbdElrahman et al. (2023). The skin condition that is melasma acts as a recurrent dermatosis that stems from both sunlight exposure and hormonal as well as inflammatory triggers. As per Mushtaq et al (2024) and Wulandari (2021) and Maeda (2022) the efficacy assessment of treatment becomes incomplete when relying only on three-month protocols that do not explore remission durability. Studies which omit the information about relapse rates after treatment create a philosophical gap in their assessment of treatment success because they only report skin-lightening results instead of maintaining long-term skin health.

The problem of heterogeneous study designs creates major challenges for making valid comparisons which results in broken-down conclusions. TXA was used as an individual treatment in studies conducted by Sohila et al. (2024) and Singh et al. (2023) but also appeared in combination with hydroquinone, topical azelaic acid and PRP in different trials (Zhang et al., 2022; Akl, 2022; Sarwar et al., 2023; Botsali et al., 2022). The current trial uses polytherapy

approaches which both mimic actual treatment but simultaneously obscures the effects of individual drugs. MASI score calculations show subjectivity and visual grading in their assessment process because this methodology allows for observer bias when assessment occurs without blinded protocols (Cassiano et al, 2022; Prathyoosha et al, 2024). The studies show inconsistent dosage ranges from 250 mg once-daily to 1500 mg/day and duration lengths from 2 weeks to 9 months which leads to more complications in this issue (AbdElrahman et al., 2023; Behrangi et al., 2022; Rajashekar et al., 2022).

The pharmacological advantages of TXA appear unable to match the limited degree of enzymological analysis performed in these research studies. TXA inhibits plasminogen activation to block melanocyte-stimulating pathways through endothelin-1 and VEGF and prostaglandins according to Kim et al. (2017) and Liu et al. (2024) and Maeda (2022). The human body exhibits evidence showing that TXA suppresses melanocyte activity according to Zining Xu et al. (2024) and Do et al. (2022). Very few studies analyzed both molecular and tissue markers after treatment was completed. TXA revealed a decrease in epidermal melanin while showing no effect on dermal melanin or angiogenesis according to Cassiano et al. (2022). Thus TXA manages the symptoms yet fails to address the core issues of this pathology. The research indicates that TXA works primarily as a surface treatment by reducing appearance of tumors but not addressing persistent pathological issues.

The reports about adverse effects commonly underestimate their frequency along with their severity levels. Studies by Agrawal et al. (2023) along with Tawanwongsri et al. (2024) noted gastrointestinal discomfort as the primary adverse effect but failed to detail the extent of discomfort or number of discontinued treatments. A systemic drug known to carry thromboembolic risks (Wulandari, 2021; Triyanti, 2022) necessitates deep examination of safety data which this study has failed to deliver efficiently. Two research articles provided both patient risk selection and coagulation monitoring (Simpsons et al., 2022; AbdElrahman et al., 2023). Research studies showed a trend whereby they selected efficacy outcomes over safety considerations as minor notes which unfavorably compared pharmacological assumptions to clinical wisdom.

Patient experience along with patient perception stands as an important but underresearched theme. Empirical research demonstrates that oral TXA administration receives frequent positive praise because of how easily patients can take it and achieve high compliance rates (Batra et al., 2022; Rajashekar et al., 2022) but such studies rarely incorporated quality-of-life assessments for domains exceeding pigmentation outcomes. Successful treatment of melasma should encompass changes in MASI scores together with emotional relief and improved self-image and reduction of associated stigma in communities where patients face psychosocial burdens because of their condition. Only subjective quality features tend to disappear from quantitative-based trials that prioritize numeric measurement systems. This review of TXA treatment for melasma reveals an unexpected effect which grants equal care opportunities. TXA offers an accessible treatment option since it comes with low cost and can be taken by mouth while requiring no expert administration or expensive equipment like laser or microneedling therapies. TXA emerges as a desirable treatment solution because it functions well in communities that lack specialized dermatological care facilities (Do et al., 2022; Behrani et al., 2022; Singh et al., 2023). The extensive availability of Theraminol requires medical professionals to both understand proper use limitations and teach patients responsible medication usage and doctors to protect patients from illicit drug use because this application uses the drug outside its prescribed purpose.

Several analyzed studies fail to match concepts since they treat melasma exclusively as pigmentary skin issue. The visible aspect of melasma consists of pigmentation but under the skin this condition produces multiple cutaneous disturbances between inflammation and hormonal signaling and vascular growth and skin damage from sun exposure (Mustofa et al.,

2021; Mushtaq et al., 2024). A therapeutic approach to treat it demands more than skin-whitening solutions because it needs restoration of the cutaneous homeostasis state. The singular use of TXA achieves dimension reduction of the visible disease symptoms yet full remission needs multi-component skin treatment that tackles both ecological elements and color variations.

Conclusion

The research shows that oral tranexamic acid (TXA) achieves satisfactory results for melasma treatment by producing significant MASI score reductions across multiple short to medium-term clinical studies while remaining well received by patients. The drug delivers easy administration through oral routes with good acceptance from patients and broad suitability for various clinical settings. The positive treatment results remain limited because they represent only one aspect of therapeutic improvement. This review demonstrates major weaknesses in available research data because it fails to provide robust data about long-term effects combined with recurrence tracking and safety evaluations as well as patient outcome assessments. Research success reports exist alongside minimal or absent descriptions of adverse events as well as untreated relapse indicators throughout numerous studies. However research needs to incorporate holistic patient-centered endpoints because MASI remains sole and subjective outcome measure deserves broader integration in upcoming scientific investigations. The use of oral TXA belongs as part of an holistic treatment strategy instead of functioning as a standalone therapeutic agent. TXA should find its best success rate through combination treatments with topical solutions alongside medical procedures combined with personalized lifestyle changes for different patient groups. Future research needs to establish standardized treatment protocols along with extended observation times and thorough safety monitoring in combination with psychosocial assessment after treatment.

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