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Review Article

Low-dose oral tranexamic acid for melasma: a narrative review and practical thromboembolic risk assessment framework

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ABSTRACT

Oral tranexamic acid has become an important off-label option for melasma, but persistent concern about thromboembolism limits its use in routine dermatologic practice. This narrative review summarizes current evidence on the efficacy and thromboembolic safety of low-dose oral tranexamic acid and translates the findings into a practical pretreatment risk assessment framework. Peer-reviewed randomized trials, comparative studies, observational cohorts, systematic reviews, and meta-analyses identified through PubMed/MEDLINE, Embase, and reference screening up to March 2026 were reviewed qualitatively. The clinical literature consistently shows improvement in melasma severity, most often with 250 mg twice daily for 8 to 12 weeks. The placebo-controlled trial by Del Rosario et al reported a 49% reduction in modified melasma area and severity index after 3 months, compared with 18% under placebo. Melasma-specific safety evidence is reassuring in carefully selected patients. The most relevant propensity score-matched cohort found no significant increase in venous thromboembolism through 365 days, and pooled randomized-trial data reported no thromboembolic events. However, broader database analyses have produced conflicting signals, and a small residual risk cannot be excluded. Adverse effects are usually mild and include menstrual changes, gastrointestinal symptoms, and headache. Low-dose oral tranexamic acid should not be used casually but may have a favorable benefit-risk profile only after structured screening and avoidance of major thrombotic risk factors.

Keywords: Tranexamic acid, Melasma, Thromboembolism, Venous thromboembolism, Hyperpigmentation, Off-label use

INTRODUCTION

Melasma is a chronic, relapsing disorder of acquired hyperpigmentation that mainly affects sun-exposed facial skin. It is particularly frequent in women of reproductive age and in individuals with Fitzpatrick skin types III to VI, and it is associated with substantial psychosocial distress and impaired quality of life.[1-3]

Current pathogenetic concepts define melasma as a multifactorial photoaging-associated disorder rather than a purely epidermal pigmentary condition. Ultraviolet radiation, visible light, hormonal influences, genetic susceptibility, melanocyte hyperreactivity, basement membrane disruption, dermal inflammation, and vascular signaling all contribute to the clinical phenotype.[1-4] This complexity explains why melasma is difficult to treat and why relapse is common even after initially successful clearing.

Strict photoprotection and topical depigmenting therapy remain the foundation of treatment. Hydroquinone, triple-combination creams, azelaic acid, kojic acid, retinoids, chemical peels, and selected energy-based procedures may improve pigmentation, but long-term control is often limited by recurrence, irritation, access, cost, and the risk of post-inflammatory hyperpigmentation, especially in darker phototypes.[3,5]

Tranexamic acid is a synthetic lysine analogue developed as an antifibrinolytic drug.[6] In dermatology, it has emerged as a systemic, topical, and intradermal option for melasma after mechanistic and clinical observations linked inhibition of the plasmin pathway to reduced melanogenesis and vascular activity.[7-12] The most widely used oral regimen for melasma is 250 mg twice daily, a dose far below that used for acute hemostatic indications.[6,13,14]

Despite increasing clinical use, oral tranexamic acid remains controversial because its core pharmacologic effect is antifibrinolysis. The central practical question is therefore not only whether it improves melasma, but whether low-dose treatment can be prescribed safely in patients who have been screened for thrombotic risk. This review summarizes the clinical efficacy evidence, critically evaluates the thromboembolic safety literature, and proposes a practical screening framework for routine dermatologic use.

METHODS

This article was prepared as a structured narrative review. PubMed/MEDLINE and Embase were searched from database inception through March 2026 using combinations of the terms tranexamic acid, melasma, oral tranexamic acid, thrombosis, thromboembolism, venous thromboembolism, safety, and adverse events. Reference lists of key reviews, randomized trials, and observational studies were screened manually for additional relevant publications.

A targeted post-search update was performed during proof correction on 20 July 2026 to identify major safety or long-term effectiveness studies published after the prespecified March 2026 search closure. Such studies are explicitly identified as post-search evidence and were not incorporated into the original structured search yield.

Eligible publications included randomized controlled trials, comparative clinical studies, retrospective cohorts and case series, systematic reviews, and meta-analyses addressing the efficacy or safety of tranexamic acid in melasma. For thromboembolic contextualization, high-quality epidemiologic data from non-dermatologic oral tranexamic acid use were included when directly relevant to biological plausibility or risk interpretation. Animal studies, non-peer-reviewed abstracts without full publication, and studies restricted to acute high-dose hemostatic use without relevance to chronic dermatologic prescribing were not used as core evidence.

The evidence was synthesized qualitatively, with emphasis on study design, sample size, comparator selection, treatment duration, event ascertainment, and applicability to routine melasma care. Because of heterogeneity in route of administration, adjunctive treatments, duration, outcome measures, and risk selection, no de novo meta-analysis was performed. Approximate Oxford Centre for Evidence-Based Medicine levels of evidence were assigned descriptively in the evidence tables to help readers distinguish randomized, matched-cohort, systematic-review, and uncontrolled evidence; these ratings are not a substitute for formal GRADE certainty assessment.

PHARMACOLOGICAL RATIONALE

Hemostatic mechanism

Tranexamic acid competitively inhibits plasminogen activation by reversibly binding to lysine-binding sites on plasminogen. This reduces conversion of plasminogen to plasmin and suppresses fibrinolysis.[6,13,14] In trauma, surgery, obstetrics, and other bleeding-related contexts, this mechanism stabilizes fibrin clots and reduces bleeding-related morbidity.

The same mechanism accounts for the persistent concern about thrombosis. Reduced fibrinolysis could theoretically favor persistence or propagation of a pathologic thrombus after coagulation has already been activated. This concern is biologically plausible, but its clinical expression depends on baseline thrombotic risk, indication, dose, treatment duration, and patient selection.

Cutaneous anti-melanogenic and anti-angiogenic effects

In melasma, tranexamic acid is believed to act through plasmin-dependent pathways that are distinct from its acute hemostatic indication. Ultraviolet exposure increases keratinocyte plasminogen activator activity, which can amplify downstream mediators involved in melanogenesis, inflammation, and dermal vascular remodeling. Experimental and translational studies suggest that tranexamic acid may reduce arachidonic acid and prostaglandin signaling, attenuate alpha-melanocyte-stimulating hormone-related melanocyte activation, and decrease release of angiogenic mediators such as vascular endothelial growth factor and basic fibroblast growth factor.[7-12]

These mechanisms are consistent with modern models of melasma that include not only epidermal pigment overproduction but also basement membrane damage, vascular change, mast-cell activation, and dermal inflammation.[1-4] However, pharmacokinetic data at dermatologic low-dose regimens remain limited. It is therefore reasonable to present tranexamic acid as mechanistically plausible and clinically supported, but not to overstate exact systemic or cutaneous concentration thresholds.

Clinical efficacy of oral tranexamic acid

The controlled clinical literature consistently supports oral tranexamic acid as an effective treatment for melasma. Improvement is usually reported within 8 to 12 weeks, and most studies use or approximate the regimen of 250 mg

twice daily.[15-21] Selected clinical trials and comparative studies are summarized in Table 1.

The placebo-controlled trial by Del Rosario et al remains the most clinically informative randomized trial of oral treatment. Forty-four patients with moderate-to-severe melasma were randomized, and 39 completed the protocol. After 3 months, modified melasma area and severity index decreased by 49% in the oral tranexamic acid group compared with 18% in the placebo group.[15] The treatment effect attenuated after discontinuation but remained numerically greater than placebo, supporting a true treatment effect while also illustrating the relapsing nature of melasma.

Comparative studies show that oral therapy is not the only effective route. In a randomized comparison by Batra et al, oral tranexamic acid and transepidermal delivery using a dermaroller both improved melasma area and severity index scores, with similar final improvement.[16] A 2025 randomized trial comparing oral and topical tranexamic acid also found significant improvement in both arms without a statistically significant between-group difference.[17] These findings suggest that route selection should be individualized according to severity, systemic risk profile, patient preference, access to procedures, and tolerance for repeated visits.

Systematic reviews and meta-analyses reinforce the efficacy signal. A network meta-analysis comparing oral, topical, and intradermal tranexamic acid found improvement across administration routes and suggested advantages for oral therapy in several pooled comparisons.[18] A dose-focused network meta-analysis suggested that 750 mg daily for 12 weeks may be statistically optimal, while 250 mg twice daily remains a clinically common and pragmatic regimen.[19] Earlier and recent meta-analyses also support efficacy while emphasizing heterogeneity and limited follow-up.[20,21]

The patient populations in these studies are clinically important because melasma biology, visible-light responsiveness, and post-inflammatory hyperpigmentation risk vary with skin type. Reporting of Fitzpatrick skin type and ethnicity is inconsistent across the oral-tranexamic-acid literature. The 2025 oral-versus-topical trial explicitly enrolled women with Fitzpatrick skin types III and IV, whereas some earlier studies are more readily characterized by geographic or ethnic context than by standardized phototype reporting.[15-17] This limits unqualified extrapolation to Fitzpatrick skin types V to VI and to older patients with different comorbidity and thrombotic-risk patterns.

THROMBOEMBOLIC SAFETY

Why concern persists

Concern about thrombosis follows directly from the antifibrinolytic mechanism of tranexamic acid.[6,13,14] However, theoretical risk alone is insufficient for clinical decision-making.

The relevant clinical question is whether low-dose oral tranexamic acid, used for melasma in screened patients, produces an observable increase in thromboembolic events.

The largest external signal comes from a nationwide Danish historical prospective cohort of approximately 2.0 million women aged 15 to 49 years, in which oral tranexamic acid prescriptions were mainly used for heavy menstrual bleeding.[22] The adjusted incidence rate ratio for venous thromboembolism was 4.0, whereas arterial thrombosis was not significantly increased. Importantly, the absolute risk remained low, with a number needed to harm of 78,549 women per 5-day treatment course.[22] This study is relevant for biological plausibility, but it is not directly equivalent to chronic dermatologic low-dose prescribing after risk screening.

Melasma-specific observational evidence

The most informative melasma-specific safety study is the multicenter propensity score-matched electronic health record cohort by Hernandez et al.[23] The study used TriNetX data from 108 U.S. health care organizations and compared adult melasma patients exposed to oral tranexamic acid after diagnosis with matched unexposed controls. Patients with major thrombotic or confounding risk contexts, including coagulation disorders, systemic estrogen exposure, recent surgery, malignancy, prior thromboembolism, and pregnancy, were excluded. This design approximates the risk-screened prescribing approach advocated in dermatology practice.

Propensity score matching yielded 682 well-balanced pairs. For the venous thromboembolism analysis, the reported analyzable denominators were 628 oral-TXA-exposed patients and 634 controls; these endpoint-specific denominators explain the unequal numbers and are not a transcription error. Venous thromboembolism risk did not differ significantly at 120 days, 180 days, or 365 days. No arterial thromboembolic events were reported in the exposed cohort during follow-up, and no significant differences were observed for proxy outcomes such as diagnostic evaluation for thrombosis or initiation of anticoagulant or thrombolytic therapy.[23]

Earlier clinical series are directionally consistent. Lee et al retrospectively analyzed 561 melasma patients treated with oral tranexamic acid for a median of 4 months. One deep vein thrombosis occurred, and the patient was subsequently found to have protein S deficiency, an important unrecognized predisposing condition.[24] Lam et al reported 26 women treated for more than 6 months, with a mean duration of 17.4 months and treatment up to 28 months, without thromboembolic events.[25] These studies are uncontrolled and cannot exclude rare-event risk, but

they are clinically reassuring when interpreted alongside the larger matched cohort.

Systematic review evidence

Pooled safety data also do not show a clear thromboembolic signal in randomized oral-tranexamic-acid prescribing. Kuceki et al reviewed oral tranexamic acid studies across indications and identified 51 randomized controlled trials including 2,597 participants and 23 observational studies including 67,018 participants treated with oral tranexamic acid below 4 g daily.[26] No thromboembolic events were reported in the randomized-trial population, whereas 27 events were observed in observational studies.[26] The contrast is expected: randomized trials are smaller, shorter, and more selected, whereas observational studies capture more heterogeneous baseline risk.

Dermatology-focused reviews similarly describe oral tranexamic acid as generally well tolerated when used after appropriate screening.[27,28] The available evidence therefore supports a nuanced interpretation. Low-dose oral tranexamic acid is not proven to be risk-free, but current data do not demonstrate a clinically meaningful excess thromboembolic risk in appropriately selected melasma patients. Key safety evidence is summarized in Table 2.

Other adverse effects and tolerability

At melasma doses, adverse effects are usually non-thrombotic, mild, and reversible. The most commonly described events are menstrual irregularities, especially hypomenorrhea or oligomenorrhea, gastrointestinal symptoms such as nausea or epigastric discomfort, and occasional headache.[15-18,24-28] These effects generally do not require hospitalization and often resolve after dose reduction or discontinuation.

Rare hypersensitivity reactions, palpitations, and nonspecific complaints have been described, but causal attribution is difficult in small uncontrolled series.[24-28] No convincing signal of ocular toxicity has been reported at standard dermatologic doses, although acquired defective color vision remains a labeled contraindication and should be respected in routine prescribing.[6,27,28]

PRACTICAL RISK ASSESSMENT BEFORE PRESCRIBING

Safe use of oral tranexamic acid depends more on patient selection than on indiscriminate laboratory testing. The literature supports a structured history-based assessment focused on prior thrombosis, inherited or acquired thrombophilia, estrogen exposure, active malignancy, renal impairment, pregnancy, planned surgery, and immobilization.[22-28] A practical pretreatment checklist is provided in Table 3.

Oral tranexamic acid should generally be avoided in patients with previous venous thromboembolism, pulmonary embolism, ischemic stroke, myocardial infarction, known thrombophilia, active malignancy, clinically relevant renal impairment, acquired defective color vision, hypersensitivity to tranexamic acid, or subarachnoid hemorrhage.[6,22,27,28] The threshold for avoidance should also be low in patients with a first-degree relative who had venous thromboembolism before age 50 years, recurrent or unprovoked thrombosis in the family, multiple concurrent venous thromboembolism risk factors, prolonged immobilization, or planned major surgery.

Concurrent estrogen exposure deserves particular caution. Even though direct melasma-specific trial evidence is limited, combined estrogen-progestin contraception and estrogen replacement therapy are prothrombotic contexts in which an additional antifibrinolytic drug is difficult to justify for an elective dermatologic indication.[22,27,28]

In routine practice, oral tranexamic acid should be avoided during systemic estrogen exposure. If systemic treatment is strongly desired, a non-estrogen contraceptive strategy, such as a progestin-only or non-hormonal method, should be discussed before reconsidering oral tranexamic acid, with appropriate medical risk assessment.

Informed consent is essential because oral tranexamic acid use for melasma is off-label. Counseling should include the expected therapeutic timeframe, the need for strict photoprotection and topical maintenance therapy, the possibility of relapse after discontinuation, common adverse effects, warning symptoms of thrombosis, and the need to stop treatment and seek medical advice if new thrombotic risk factors arise.

DISCUSSION

The present review supports low-dose oral tranexamic acid as an effective adjunctive treatment for melasma and suggests that thromboembolic risk is low in patients who are carefully screened before treatment. The efficacy signal is consistent across randomized, comparative, and pooled analyses, while the safety signal is reassuring rather than alarming. In practical terms, reluctance to use oral tranexamic acid solely because it is an antifibrinolytic is no longer well aligned with the most relevant melasma-specific evidence.

However, reassurance should not be converted into overconfidence. The absence of a thromboembolic signal in selected datasets is not proof of zero risk. Most trials are small, many are short, and the populations enrolled in melasma studies are often younger and healthier than the broader dermatology population. Rare adverse events are difficult to quantify precisely, and the confidence intervals around thromboembolic outcomes remain wide.[15-23,26]

The Hernandez cohort is particularly important because it addresses the question most relevant to clinical practice:

whether oral tranexamic acid prescribed for melasma after exclusion of major risk factors is associated with thromboembolic outcomes.[23] Its negative result is the best current direct reassurance.

Nevertheless, the retrospective design, reliance on coded electronic health record outcomes, and possibility of residual confounding justify continued caution.

A broader TriNetX analysis by Hopson and Lipner reported an increased thromboembolic signal among oral tranexamic acid users. Because the study population and exposure context were not restricted to low-dose treatment in carefully screened patients with melasma, direct applicability to dermatologic prescribing is limited. Nevertheless, the finding precludes claims of zero risk and reinforces the need for disciplined patient selection.[29]

Table 1: Selected randomized and comparative studies of oral tranexamic acid in melasma.

Study (year)	Design and population context	Intervention/ comparator	Duration/ endpoint	Approxi-mate LoE	Main efficacy finding
Del Rosario et al (2018)[15]	Double-blind placebo-controlled RCT; 44 patients with moderate-to-severe melasma; Single-center U.S. randomized trial; predominantly Hispanic study population.	Oral tranexamic acid 250 mg twice daily versus placebo; both arms used sunscreen.	3 months treatment plus 3 months follow-up; mMASI endpoint.	Oxford 1b	mMASI decreased by 49% with oral tranexamic acid versus 18% with placebo at 3 months; no serious adverse events reported.
Batra et al (2022)[16]	Randomized comparative hospital-based study; 40 patients from a North Indian tertiary-center setting; Fitzpatrick distribution not clearly reported in the article text.	Oral tranexamic acid 250 mg twice daily versus transepidermal tranexamic acid delivered with dermaroller.	12 weeks treatment; follow-up to 24 weeks; MASI endpoint.	Oxford 2b	Both groups showed marked MASI improvement; final reduction was similar between groups; relapse occurred in 1 oral-TXA patient at 24 weeks.
Heydari et al (2025)[17]	Single-center randomized trial; 50 women with melasma; Fitzpatrick skin types III-IV.	Oral tranexamic acid 250 mg twice daily versus topical tranexamic acid 5% cream twice daily.	12 weeks; MASI endpoint.	Oxford 2b	Both arms improved significantly; oral MASI reduction was numerically greater but the between-group difference was not statistically significant.

Table 2: Key evidence informing thromboembolic safety of oral tranexamic acid.

Study (year)	Design/population	Clinical context	Approxi-mate LoE	Main thromboembolic finding	Key limitation
Meaidi et al (2021)[22]	Nationwide historical prospective cohort of approximately 2.0 million women aged 15-49 years.	Short-course oral tranexamic acid, mainly for heavy menstrual bleeding.	Oxford 2b; indirect for melasma	Adjusted incidence rate ratio for venous thromboembolism was 4.0; arterial thrombosis was not significantly increased; absolute risk remained low.	Different indication, dosing pattern, and risk context than screened dermatologic use.
Hernandez et al (2026)[23]	Multicenter propensity score-matched TriNetX EHR cohort; 682 matched pairs; VTE-specific analyzable denominators 628 exposed and 634 controls.	Melasma patients exposed to oral tranexamic acid after diagnosis; major thrombotic risk contexts excluded.	Oxford 2b	No significant increase in venous thromboembolism at 120, 180, or 365 days; no arterial events in exposed patients during follow-up.	Retrospective coded data; residual confounding and rare-event imprecision remain possible.
Lee et al (2016)[24]	Retrospective melasma cohort; 561 patients.	Median oral-TXA treatment duration 4 months.	Oxford 4	One deep vein thrombosis was reported; the affected patient was later found to have protein S deficiency.	Uncontrolled retrospective design and limited rare-event inference.
Lam et al (2024)[25]	Retrospective case series; 26 women.	Treatment beyond 6 months; mean 17.4 months; range up to 28 months.	Oxford 4	No thromboembolic events reported.	Small sample and no control group.
Kuceki et al (2025)[26]	Systematic review; 51 randomized trials and 23 observational studies.	Oral tranexamic acid below 4 g daily across indications.	Oxford 1a; indirect for melasma	No thromboembolic events in 2,597 randomized participants; 27 events in 67,018 observational participants.	Marked heterogeneity in indication, dose, and follow-up; not melasma-specific.

Continued.

Study (year)	Design/population	Clinical context	Approxi-mate LoE	Main thromboembolic finding	Key limitation
Hopson et al (2026)[29]	Retrospective TriNetX cohort across oral-TXA users.	Broader oral-TXA exposure; not restricted to melasma or risk-screened low-dose dermatologic use.	Approxima te Oxford 2b; indirect for melasma.	Reported an increased thromboembolic signal.	Non-melasma population/exposure heterogeneity, coded retrospective data, and residual confounding limit direct applicability.
Sun et al (2026)[30]	Single-center retrospective cohort; 244 Asian women (122 oral, 122 topical).	Oral TXA 500 mg/day versus topical TXA; follow-up to 24 months.	Approxima te Oxford 2b.	No thromboembolic events recorded; any adverse event 41.0% oral versus 22.1% topical.	Published after search closure; only 48 oral and 51 topical patients had observed 24-month MASI; underpowered for rare thrombotic events and subject to residual confounding.

Table 3: Practical pretreatment checklist for oral tranexamic acid in melasma.

Screening step	Practical definition or trigger	Suggested action if abnormal
Detailed personal thrombotic history	Prior deep vein thrombosis, pulmonary embolism, cerebral venous thrombosis, ischemic stroke, myocardial infarction, known thrombophilia, or prior unexplained anticoagulation.	Do not prescribe routinely; select an alternative melasma strategy or obtain specialist risk assessment if the indication is compelling.
Family history focused on early or recurrent thrombosis	First-degree relative with venous thromboembolism before age 50 years, recurrent/unprovoked thrombosis, or known inherited thrombophilia.	Avoid routine oral tranexamic acid; consider hematology review if systemic therapy is still being considered.
Medication and estrogen-exposure review	Combined oral contraceptive pill, estrogen patch/ring, estrogen replacement therapy, anticoagulants, antiplatelet therapy, or other relevant interacting treatment.	Avoid oral tranexamic acid during systemic estrogen exposure. Discuss non-estrogen contraception, such as progestin-only or non-hormonal methods, before reconsidering therapy.
Pregnancy, breastfeeding, or planned conception	Current pregnancy, lactation, or active attempt to conceive.	Avoid elective oral tranexamic acid for melasma; use photoprotection and topical/procedural alternatives as appropriate.
Renal function	Serum creatinine/eGFR abnormality or known clinically significant renal impairment.	Avoid or dose-adjust only with appropriate medical oversight because tranexamic acid is renally cleared.
Temporary high-risk states	Major surgery, prolonged immobilization, acute serious illness, active malignancy, or long-haul travel combined with other VTE risk factors.	Postpone, interrupt, or avoid treatment during high-risk intervals.
Ocular and drug-specific contraindications	Acquired defective color vision, hypersensitivity to tranexamic acid, or subarachnoid hemorrhage history.	Do not prescribe oral tranexamic acid.
Informed consent and monitoring plan	Off-label use, expected 8-12 week assessment, relapse risk, common adverse effects, warning symptoms of thrombosis, and stop rules.	Document consent before initiation; stop therapy and seek medical review for suspected thrombotic symptoms or new major risk factors.

A clinically defensible approach is therefore neither avoidance of oral tranexamic acid in all patients nor casual prescribing. Patients with major thrombotic risk should be offered topical, procedural, or combination alternatives. Patients without major risk factors can be considered for

low-dose oral therapy as part of a broader melasma plan that includes photoprotection, topical maintenance, periodic reassessment, and discontinuation when the benefit no longer justifies ongoing exposure.

The practical treatment endpoint also requires clarification. Most studies use change in MASI or modified MASI at 8 to 12 weeks as the primary efficacy endpoint, not complete pigment clearance. In routine care, treatment success should therefore be defined as a meaningful reduction in severity and improved patient-relevant control after approximately 12 weeks, combined with acceptable tolerability and absence of new risk factors. If there is minimal or no response at 12 weeks, oral tranexamic acid should be discontinued rather than continued indefinitely.

For responders, the literature does not establish an evidence-based tapering regimen or a validated intermittent oral maintenance strategy. Because melasma is chronically relapsing and the Del Rosario trial showed attenuation of effect after discontinuation, patients should be counseled that relapse is possible.[15] A cautious practical approach is to limit oral therapy to the shortest useful course, commonly 3 to 6 months in published practice patterns, and then transition to strict ongoing photoprotection, visible-light protection with tinted sunscreen where appropriate, and topical maintenance therapy. Extended treatment beyond 6 months has been reported without thromboembolic events in small series, but the evidence is insufficient to justify routine indefinite oral maintenance.[25,26]

After closure of the prespecified search, Sun et al. reported a 24-month retrospective cohort of 244 Asian women (122 oral, 122 topical). Oral tranexamic acid was associated with a modestly greater adjusted MASI improvement at 24 months (oral-topical difference in change in MASI, -1.54; 95% CI, -2.33 to -0.75), similar relapse rates (29.5% versus 25.4%), and more adverse events (41.0% versus 22.1%); no thromboembolic events were recorded. However, only 48 oral and 51 topical patients had observed 24-month MASI, and the study was not powered to exclude rare thrombotic events.[30]

Limitations

This review has limitations. It is a narrative synthesis rather than a systematic review with de novo quantitative pooling. The included studies are heterogeneous with respect to route of administration, dose, adjunctive therapies, outcome measures, population phototype reporting, and follow-up. Many randomized trials are underpowered for rare thromboembolic events, and long-term prospective safety data beyond 6 to 12 months remain limited. A considerable proportion of efficacy data derives from selected populations, which may limit generalizability to Fitzpatrick skin types V to VI, older patients, patients with comorbidities, and populations with different baseline thrombotic risk. Finally, direct pharmacokinetic data for dermatologic low-dose regimens remain sparse, so mechanistic interpretations should remain cautious.

CONCLUSION

Low-dose oral tranexamic acid, most commonly 250 mg twice daily, is a clinically meaningful off-label adjunctive option for melasma. Across randomized and observational evidence, it consistently improves melasma severity and is generally well tolerated. Current melasma-specific data are reassuring and do not demonstrate a clinically meaningful increase in thromboembolic events in carefully selected patients; however, broader database analyses have produced conflicting signals, and a small residual risk cannot be excluded. Oral tranexamic acid should nevertheless be prescribed within a structured safety framework. Pretreatment screening should exclude prior thrombosis, known thrombophilia, systemic estrogen exposure, active malignancy, relevant renal impairment, and temporary high-risk states. Treatment should be accompanied by explicit off-label counseling, strict photoprotection, topical maintenance therapy, and periodic reassessment. Future research should prioritize prospective long-term safety studies, diverse patient populations with explicit Fitzpatrick-type reporting, and comparative trials against modern combination regimens.

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REFERENCES

1. Passeron T, Picardo M. Melasma, a photoaging disorder. Pigment Cell Melanoma Res. 2018;31:461-5.
2. Passeron T. Melasma pathogenesis and influencing factors: an overview of the latest research. J Eur Acad Dermatol Venereol. 2013;27:5-6.
3. Ogbechie-Godec OA, Elbuluk N. Melasma: an up-to-date comprehensive review. Dermatol Ther (Heidelb). 2017;7:305-18.
4. Yamaguchi Y, Hearing VJ. Physiological factors that regulate skin pigmentation. Biofactors. 2009;35:193-9.
5. Levin MK, Ng E, Bae YS, Brauer JA, Geronemus RG. Treatment of pigmentary disorders in patients with skin of color with a novel 755 nm picosecond, Q-switched ruby, and Q-switched Nd:YAG nanosecond lasers: a retrospective photographic review. Lasers Surg Med. 2016;48:181-7.
6. Tengborn L, Blombäck M, Berntorp E. Tranexamic acid: an old drug still going strong and making a revival. Thromb Res. 2015;135:231-42.
7. Maeda K, Tomita Y. Mechanism of the inhibitory effect of tranexamic acid on melanogenesis in cultured human melanocytes in the presence of keratinocyte-conditioned medium. J Health Sci. 2007;53:389-96.

8. Maeda K. Mechanism of action of topical tranexamic acid in the treatment of melasma and sun-induced skin hyperpigmentation. Cosmetics. 2022;9:108.
9. Forbat E, Al-Niaimi F, Ali FR. The emerging importance of tranexamic acid in dermatology. Clin Exp Dermatol. 2020;45:445-9.
10. Taraz M, Niknam S, Ehsani AH. Tranexamic acid in treatment of melasma: a comprehensive review of clinical studies. Dermatol Ther. 2017;30:e12465.
11. Kim SJ, Park JY, Shibata T, Fujiwara R, Kang HY. Efficacy and possible mechanisms of topical tranexamic acid in melasma. Clin Exp Dermatol. 2016;41:480-5.
12. Tse TW, Hui E. Tranexamic acid: an important adjuvant in the treatment of melasma. J Cosmet Dermatol. 2013;12:57-66.
13. Roberts I, Perel P, Prieto-Merino D, Shakur H, Coats T, Hunt BJ, et al. Effect of tranexamic acid on mortality in patients with traumatic bleeding: prespecified analysis of data from randomised controlled trial. BMJ. 2012;345:e5839.
14. Perel P, Ker K, Morales Uribe CH, Roberts I. Tranexamic acid for reducing mortality in emergency and urgent surgery. Cochrane Database Syst Rev. 2013;(1):CD010245.
15. Del Rosario E, Florez-Pollack S, Zapata L Jr, Hernandez K, Tovar-Garza A, Rodrigues M, et al. Randomized, placebo-controlled, double-blind study of oral tranexamic acid in the treatment of moderate-to-severe melasma. J Am Acad Dermatol. 2018;78:363-9.
16. Batra J, Brar BK, Kumar S, Arora H. Tranexamic acid in melasma: comparative evaluation of therapeutic efficacy of oral tranexamic acid versus its transepidermal administration. J Cutan Aesthet Surg. 2022;15:394-9.
17. Heydari B, Habibzadeh Meibodi GA, Ebrahimzadeh Ardakani M, Ramezani V, Heidari F. Randomized clinical trial on the efficacy of oral tranexamic acid versus topical tranexamic acid in treatment of melasma. J Cosmet Dermatol. 2025;24:e70428.
18. Liang R, Luo H, Pan W, Yang S, Peng X, Kuang B, et al. Comparative efficacy and safety of tranexamic acid for melasma by different administration methods: a systematic review and network meta-analysis. J Cosmet Dermatol. 2024;23:1150-64.
19. Wang WJ, Wu TY, Tu YK, Kuo KL, Tsai CY, Chie WC. The optimal dose of oral tranexamic acid in melasma: a network meta-analysis. Indian J Dermatol Venereol Leprol. 2023;89:189-94.
20. Zhang L, Tan WQ, Fang QQ, Zhao WY, Zhao QM, Gao J, et al. Tranexamic acid for adults with melasma: a systematic review and meta-analysis. Biomed Res Int. 2018;2018:1683414.
21. Calacattawi R, Alshahrani M, Aleid M, Aleid F, Basamih K, Alsugair G, et al. Tranexamic acid as a therapeutic option for melasma management: meta-analysis and systematic review of randomized controlled trials. J Dermatolog Treat. 2024;35:2361106.
22. Meaidi A, Mørch LS, Torp-Pedersen C, Lidegaard Ø. Oral tranexamic acid and thrombosis risk in women. EClinicalMedicine. 2021;35:100882.
23. Hernandez T, Penny K, Culotta N. Oral tranexamic acid use for melasma is not associated with thromboembolism: findings from a multicenter propensity score-matched electronic health record cohort. JAAD Int. 2026;24:64-6.
24. Lee HC, Thng TG, Goh CL. Oral tranexamic acid in the treatment of melasma: a retrospective analysis. J Am Acad Dermatol. 2016;75:385-92.
25. Lam K, Mansour D, Sutton A. Oral tranexamic acid treatment beyond 6 months for melasma patients - a retrospective case series. JAAD Int. 2024;15:195-6.
26. Kuceki G, Mendez D, Garza-Dueñas GG, Kruithoff C, Fonseca LO, Lal K. No thromboembolic events observed in randomized controlled trials of oral tranexamic acid: a systematic review and descriptive synthesis. J Am Acad Dermatol. 2025;93:1086-8.
27. Kim KM, Lim HW. The uses of tranexamic acid in dermatology: a review. Int J Dermatol. 2023;62:589-98.
28. Konisky H, Balazic E, Jaller JA, Khanna U, Kobets K. Tranexamic acid in melasma: a focused review on drug administration routes. J Cosmet Dermatol. 2023;22:1197-206.
29. Hopson ARL, Lipner SR. Increased risk of thromboembolic events with oral tranexamic acid in a large retrospective cohort using TriNetX. J Am Acad Dermatol. 2026;94(4):1283-5.
30. Sun Z, Fan Z, Xiang G. Long-term comparative effectiveness and safety of oral versus topical tranexamic acid for melasma: a 24-month single-center retrospective cohort study (2020-2024). Dermatol Ther. 2026;2026:9928647.

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