Section: Dermatology

Systematic Review

EFFICACY AND SAFETY OF ORAL TRANEXAMIC ACID IN MELASMA: A SYSTEMATIC REVIEW OF OBSERVATIONAL STUDIES

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ABSTRACT

Background: Melasma is a chronic, relapsing facial hyperpigmentary disorder that disproportionately affects women and individuals with darker skin phototypes, with substantial psychosocial impact. Oral tranexamic acid (TXA), an antifibrinolytic agent, is increasingly used off-label for melasma. Existing syntheses have largely pooled randomized and non-randomized designs or have restricted analysis to randomized controlled trials (RCTs), leaving the real-world observational evidence base for oral TXA under-characterized. **Objective:** To systematically review observational studies (prospective and retrospective cohorts and case series) evaluating the efficacy and safety of oral TXA, alone or as an adjuvant, for melasma. **Materials and Methods:** PubMed/MEDLINE, Embase, Scopus, and Cochrane CENTRAL were searched from inception to July 2026, supplemented by reference-list and grey-literature screening, following PRISMA 2020 methodology. Eligible studies reported original observational data on oral TXA in patients with melasma with extractable pre-/post-treatment outcomes; RCTs and non-oral-route-only studies were excluded. Two reviewers independently performed selection, extraction, and risk-of-bias assessment (adapted NIH Quality Assessment Tool for before-after studies). Substantial heterogeneity in outcome reporting precluded meta-analysis; findings were synthesized narratively. **Results:** Eight observational studies published between 2012 and 2026 met eligibility criteria, including single- and multi-centre cohorts, retrospective reviews, and one large multicentre propensity-score-matched electronic health record (EHR) cohort. Oral TXA regimens ranged from 250 mg twice daily to 1000 mg per day for 8 weeks to over 2 years. Across four studies reporting a percentage-improvement metric, values ranged from 64.8% to 89.7%; these figures reflect two different outcome constructs (categorical good-to-excellent/improved response rates in two studies vs. continuous percentage reduction in MASI/mMASI score in two others) and are not directly comparable or pooled. Adverse events were predominantly mild and self-limited (gastrointestinal upset, hypomenorrhoea/oligomenorrhoea); thromboembolic events were rare, reported in one large retrospective cohort (1/561, in a patient with underlying thrombophilia) and not detected as significantly increased in the largest propensity-matched real-world safety cohort identified. **Conclusion:** Observational, real-world data are consistent with oral TXA being a generally well-tolerated treatment for melasma, with improvement in severity reported across all included studies; however, because this evidence base consists exclusively of observational, largely uncontrolled designs, these findings cannot establish efficacy and should be regarded as hypothesis-generating rather than confirmatory. They complement, but do not substitute for, RCT evidence. Standardisation of dosing regimens, outcome measures, and long-term thromboembolic safety surveillance is warranted.

INTRODUCTION

Melasma is a common, chronic, and frequently relapsing disorder of facial hyperpigmentation that disproportionately affects women of reproductive age and individuals with darker Fitzpatrick skin phototypes.[1,2,3] Its pathogenesis is multifactorial, involving ultraviolet-induced melanogenesis, hormonal influences, and a prominent dermal vascular/angiogenic component, and it is associated with meaningful reductions in quality of life and self-esteem.[1,2] Conventional first-line therapies topical depigmenting agents, chemical peels, and laser or light-based devices are frequently limited by partial response, irritant or post-inflammatory sequelae, and high relapse rates, driving interest in systemic adjuncts.[1,2]

Tranexamic acid (TXA), a synthetic lysine analogue that competitively inhibits the conversion of plasminogen to plasmin, was originally developed as a haemostatic agent and is approved for menorrhagia and peri-procedural bleeding prophylaxis. In melasma, TXA is thought to act by reducing plasmin-mediated release of free arachidonic acid and α-melanocyte-stimulating hormone from keratinocytes, and by dampening the vascular and inflammatory components of melasma pathogenesis.[1,2,3] TXA has been studied via oral, topical, and intradermal (microinjection) routes, and existing systematic reviews and meta-analyses have generally pooled evidence across routes and study designs,[4,5] or, more recently, have restricted quantitative synthesis to randomized controlled trials (RCTs).[6] Network meta-analyses have further compared administration routes,[7] and dosing regimens.[8] Most recently, a 2026 systematic review and meta-analysis published in this journal restricted its quantitative synthesis to RCTs and found that TXA combined with hydroquinone, rather than TXA alone, produced the most consistent benefit versus placebo,[9] reflecting the current emphasis of quantitative evidence synthesis on randomized, placebo-controlled designs such as the benchmark trial of Del Rosario et al,[10] in which 250 mg oral TXA twice daily produced a 49% reduction in modified MASI (mMASI) at 3 months versus 18% with placebo. In routine clinical practice, however, oral TXA is prescribed across a considerably broader range of doses, durations, and patient populations than represented in placebo-controlled RCTs, which are typically small, short in follow-up, and conducted in selected populations. Observational cohorts, prospective case series, retrospective chart reviews, and, increasingly, large administrative or electronic health record (EHR) cohorts provide complementary real-world data on effectiveness and, critically, on long-term safety, particularly regarding the theoretical risk of venous thromboembolism (VTE) associated with antifibrinolytic therapy. To our knowledge, no prior systematic review has specifically isolated and synthesized observational-study evidence for oral TXA in melasma. We therefore conducted a systematic review restricted to observational designs to characterize the real-world efficacy and safety profile of oral TXA in the treatment of melasma.

MATERIALS AND METHODS

Protocol and registration

This review was conducted and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement.

Eligibility Criteria

Eligibility was defined using a PICOS framework:

Population: patients of any age or sex with a clinical diagnosis of melasma.

Intervention: oral tranexamic acid, at any dose or duration, as monotherapy or as an adjuvant to topical or procedural therapy.

Comparator: none required; pre-/post-treatment (within-patient) comparison or a concurrent non-randomized comparison group were both acceptable.

Outcomes: change in Melasma Area and Severity Index (MASI) or modified MASI (mMASI), clinician- or patient-rated global improvement, and/or adverse events including thromboembolic and other safety outcomes.

Study design: prospective cohort studies, retrospective cohort/chart-review studies, and case series (≥10 patients) were eligible. Randomized controlled trials (e.g., placebo-controlled or dose-randomized designs such as that of Karn et al,[11], in vitro/animal studies, case reports with fewer than 10 patients, narrative reviews, conference abstracts without extractable data, and studies evaluating only non-oral (topical or intradermal) TXA were excluded.

Information sources and search strategy

PubMed/MEDLINE, Embase, Scopus, and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from database inception to July 2026, supplemented by manual screening of reference lists of relevant reviews and meta-analyses and a search of grey literature and conference proceedings. Search terms combined controlled vocabulary and free-text terms for "tranexamic acid," "melasma"/"chloasma," and "oral"/"systemic," combined with Boolean operators (e.g., ("tranexamic acid" OR "antifibrinolytic agents") AND ("melasma" OR "chloasma") AND ("oral" OR "systemic" OR "tablet")). No date restriction was applied. The search yielded a total of 357 records: PubMed/MEDLINE (n=95), Embase (n=140), Scopus (n=100), and Cochrane CENTRAL (n=22).

Study selection

Titles and abstracts were screened independently by two reviewers against the eligibility criteria; full texts of potentially eligible records were then independently assessed by the same reviewers. Disagreements were resolved by discussion or, where necessary, adjudication by a third reviewer. The

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study selection process is summarised in the PRISMA flow diagram (Figure 1).

Data extraction

A standardised, piloted extraction form was used to capture: first author and year, country, study design, sample size, TXA dose/regimen/duration, comparator (if any), concurrent therapies, outcome measures and effect estimates, adverse events (including thromboembolic events), and follow-up duration. Extracted data are summarised in Table 1.

Risk of bias assessment

Given the predominance of single-arm designs, risk of bias for the seven single-arm/pre-post studies.[12-18] was assessed using an adaptation of the United States National Institutes of Health (NIH) Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group, evaluating clarity of eligibility criteria, blinding/objectivity of outcome assessment, adequacy of follow-up, and consideration of confounding. Because the propensity-score-matched EHR cohort of Hernandez et al,[19] compares TXA-exposed patients with a matched non-exposed control cohort, a no-control-group instrument does not adequately capture its design; this study was instead assessed using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, applying comparable domains (eligibility criteria, exposure/outcome measurement, follow-up, and confounding control). The healthy-control comparison in Demirbas et al,[18] was used only for baseline inflammatory-marker analysis and not for the MASI efficacy outcome, so the before-after instrument remained appropriate for that study's efficacy assessment. Each study received an overall qualitative rating of Good, Fair, or Poor (Table 2).

Data synthesis

Because of substantial heterogeneity in TXA regimens, outcome measures (categorical responder rates versus continuous MASI/mMASI reduction), follow-up duration, and concurrent co-interventions, a quantitative meta-analysis was not considered appropriate or statistically meaningful for this observational-study subset. Findings were therefore synthesised narratively and, where a directly comparable percentage improvement metric was reported, displayed graphically. [Figure 2]

RESULTS

Study selection

The search and selection process is summarised in Figure 1. After removal of duplicates and screening of titles/abstracts and full texts, eight observational studies met all eligibility criteria and were included in the qualitative synthesis.[12,13,14,15,16,17,18,19] Seven of the eight studies contributed extractable efficacy (MASI/mMASI or global-improvement) data; all eight contributed safety data.

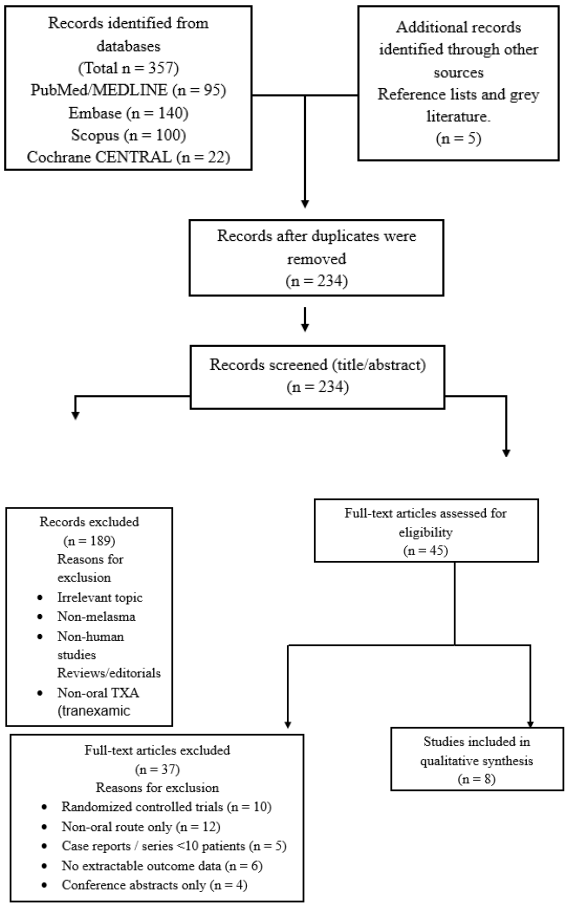


Figure 1: PRISMA 2020 flow diagram of study identification, screening, and inclusion. Records identified from databases

PubMed/MEDLINE (n=95), Embase (n=140), Scopus (n=100), Cochrane CENTRAL (n=22); additional records from other sources (n=5); records after duplicates removed (n=234); records screened (n=234); records excluded at title/abstract (n=189); full-text articles assessed (n=45); full-text articles excluded with reasons (n=37); studies included in qualitative synthesis (n=8).

Study characteristics

Included studies were published between 2012 and 2026 and originated from China,[12] Singapore,[13,14] India,[15] the United States,[16,19] Canada,[17] and Turkey.[18] Designs comprised prospective single-arm case series, retrospective chart-review cohorts, one retrospective survey, and one large propensity-score-matched EHR safety cohort. Oral TXA regimens ranged from 250 mg twice daily (the most common regimen) up to 500 mg twice daily (1000 mg/day) in the highest-dose study identified, with treatment durations ranging from 8 weeks to more than 2 years of continuous or intermittent use.[16,17] Full study characteristics are presented in Table 1.

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Table 1: Characteristics included observational studies

Study (year)	Design	N	Oral TXA regimen	Duration	Efficacy outcome measure	Key finding
Wu et al. (2012)	Prospective, single-arm case series	74	250 mg twice daily	6 months (F/U >6 mo)	Physician + patient global grading	Good-to-excellent response in 64.8%; recurrence 9.5%
Lee et al. (2016)	Retrospective cohort (tertiary centre)	561	250 mg twice daily (median)	Median 4 months	Clinical improvement (physician-rated)	89.7% improved; relapse rate 27.2%
Tan et al. (2017)	Retrospective case series (adjuvant)	25	250 mg twice daily + topical therapy	Mean 3.7 months	MASI (blinded photographic review)	MASI fell from 8.8±4.2 to 2.7±1.6 (69% reduction, p<0.01)
Nagaraju et al. (2018)	Prospective single-arm cohort	30	500 mg twice daily	Not stated (with biopsy F/U)	mMASI, MELASQOL, histology/IHC	Significant clinical improvement correlating with reduced epidermal pigmentation and Melan-A staining
Simpson et al. (2022)	Retrospective survey	42	650 mg half-tablet (325 mg) twice daily	Mean 12.7 months	Patient-reported improvement	73.8% reported at least "a little" improvement; side effects in 16.7%, all reversible
Lam et al. (2024)	Retrospective case series (long-term safety)	26	250 mg twice daily	7–28 months (mean 17.4)	Melasma Severity Scale	Sustained effect; well tolerated; no thromboembolic events beyond 6 months
Demirbas et al. (2025)	Retrospective cohort (+ 80 healthy controls)	80	500 mg per day	3 months	MASI, inflammatory markers	MASI fell from median 12.9 to 4.5 (65.1% reduction, p<0.001)
Hernandez et al. (2026)	Propensity-score-matched EHR cohort	682 matched pairs (1,364 total)	650 mg (TriNetX-coded exposure; frequency not specified	Retrospective, variable	Thromboembolic incidence	Oral TXA use for melasma not associated with increased thromboembolism vs matched controls

Risk of bias across studies

Among the seven studies assessed with the before-after tool, most were rated "Fair", primarily reflecting the inherent absence of a control group and, in several retrospective cohorts, unblinded outcome assessment.[13,15,17] One study incorporating blinded photographic review was rated "Good".[14] The propensity-score-matched EHR cohort, assessed separately using the NIH cohort-study instrument appropriate to its matched-control design, was also rated "Good", reflecting its use of statistical matching to address confounding.[19] A summary is presented in Table 2.

Table 2: Risk-of-bias assessment included observational studies

Study	Outcome assessors blinded / objective measure	Adequate follow-up (≥80%)	Confounders considered	Overall rating*
Wu et al. (2012)	Partial (2 physicians + patient)	Yes	No	Fair
Lee et al. (2016)	No (unblinded retrospective chart review)	Not fully reported	Partial (family history examined)	Fair
Tan et al. (2017)	Yes (3 independent blinded reviewers)	Yes	No	Good
Nagaraju et al. (2018)	Partial (histology adds objectivity)	Not fully reported	No	Fair
Simpson et al. (2022)	No (patient-reported survey)	Yes (by design)	Partial (Fitzpatrick type recorded)	Fair
Lam et al. (2024)	No (retrospective chart review)	Yes (by design)	Partial (comorbidities recorded)	Fair
Demirbas et al. (2025)	Partial (lab-based outcomes objective)	Yes	Partial (matched controls)	Fair-Good
Hernandez et al. (2026)	Yes (objective EHR-coded outcomes)	Yes (database-derived)	Yes (propensity-score matched)	Good

*Wu et al. through Demirbas et al,[12-18] rated using an adaptation of the NIH Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group; Hernandez et al,[19] which used a propensity-matched external comparison group, rated using the NIH Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies applied to comparable domains.

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Efficacy outcomes

Across the four studies reporting a directly extractable percentage-improvement metric, values ranged from 64.8% to 89.7% (Figure 2). These four percentages are not derived from a single common metric: the 64.8% and 89.7% figures represent the proportion of patients achieving a categorical "good-to-excellent" or "improved" response, whereas the 69% and 65.1% figures represent the mean percentage reduction in continuous MASI/mMASI scores. Because these are conceptually distinct constructs, the range should not be read as a single, pooled magnitude of effect. In a Chinese prospective case series of 74 patients treated with 250 mg twice daily for 6 months, 64.8% achieved a good-to-excellent physician- and patient-rated response.[12] In the largest retrospective cohort (561 patients treated in a Singapore tertiary centre), 89.7% of patients showed clinical improvement, typically apparent within 2 months of initiation.[13] In a smaller Singapore cohort of 25 patients with melasma refractory to topical therapy, oral TXA used adjunctively over a mean of 3.7 months reduced mean MASI scores from 8.8±4.2 to 2.7±1.6, a 69% reduction ($p<0.01$).[14] Most recently, a Turkish retrospective cohort of 80 patients treated with 500 mg daily for 3 months showed a reduction in median total MASI score from 12.9 to 4.5 (65.1% reduction, $p<0.001$), accompanied by favourable changes in systemic inflammatory markers.[18] Two further studies reported significant improvement without a single comparable percentage metric: an Indian cohort of 30 patients with refractory melasma treated with 500 mg twice daily showed significant clinical improvement that correlated with reduced epidermal pigmentation and Melan-A immunostaining on paired skin biopsies,[15] and a retrospective survey of 42 patients with Fitzpatrick skin types III-VI who took half of a 650 mg TXA tablet (325 mg) twice daily found that 73.8% of patients reported at least "a little" improvement in their melasma, with the degree of improvement appearing to correlate with treatment duration.[16] A Canadian retrospective case series specifically evaluating treatment beyond 6 months (up to 28 months) found that clinical improvement was maintained with continued therapy.[17]

Of these, only the two continuous-metric studies are directly comparable to the RCT evidence: the 69% and 65.1% reductions in MASI/mMASI score,[14,18] are numerically higher than the 49% mMASI reduction reported in the principal placebo-controlled RCT,[10] most plausibly reflecting the absence of blinding and placebo comparison, unblinded outcome assessment, and non-specific benefit from concurrent sun protection inherent to observational designs, rather than necessarily superior efficacy. The categorical "good-to-excellent"/improved response rates of 64.8% and 89.7%,[12,13] are a proportion-of-patients metric rather than a percentage score reduction, so they are not on the same scale as the RCT's 49% mMASI reduction and should not be numerically compared to it.

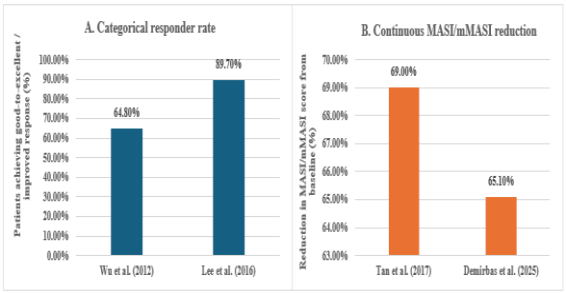


Figure 2: Improvement in melasma severity from baseline across included observational studies, presented as two separate panels by outcome construct

Note: A (categorical responder rate) and B (continuous MASI/mMASI reduction) are plotted on separate axes because they represent conceptually distinct outcome constructs; values are single-study outcomes and are not pooled, meta-analyzed, or directly comparable across panels.

Safety outcomes

Adverse events across the included studies were predominantly mild, transient, and self-limited. Gastrointestinal discomfort (5.4%) and hypomenorrhoea (8.1%) were the most frequently reported adverse events in the earliest cohort, with a melasma recurrence rate of 9.5% after treatment discontinuation.[12] In the largest cohort, adverse events occurred in 7.1% of patients (mostly gastrointestinal or menstrual), and one patient developed deep vein thrombosis requiring prompt discontinuation; this patient was subsequently found to have familial protein S deficiency.[13] In the retrospective survey, 7 out of 42 patients (16.7%) experienced side effects, including pulsatile headache, abdominal discomfort, malaise and nausea, menstrual changes, rhinorrhoea, and lower extremity numbness.[16] All side effects were completely resolved upon discontinuation of TXA, and no long-term side effects were identified. In the Canadian long-term cohort, two patients developed gastrointestinal upset (one discontinuing treatment), with no thromboembolic events observed even with treatment durations extending to 28 months.[17] Most notably, in the largest identified real-world safety dataset, a multicentre, propensity-score-matched electronic health record cohort, oral TXA use for melasma was not associated with a statistically significant increase in thromboembolic events compared with matched non-users,[19] consistent with reassuring findings from a large Danish national cohort study of oral TXA and thrombosis risk in women prescribed the drug for non-melasma indications.[20]

DISCUSSION

This systematic review synthesizes, for the first time to our knowledge, observational-study evidence specifically for oral tranexamic acid in melasma, distinct from prior syntheses that pooled randomized

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and non-randomized designs,[4,5] or restricted analysis to RCTs alone.[6,9] Across eight observational studies spanning more than a decade and diverse geographic and clinical settings, oral TXA was consistently associated with improvement in melasma severity, as reported by the original investigators, with a generally favorable and predictable safety profile dominated by mild, self-limited gastrointestinal and menstrual adverse effects.

Where a construct-matched comparison is possible, the magnitude of improvement reported in the observational cohorts using a continuous MASI/mMASI reduction metric (69% and 65.1%) is numerically higher than, but should not be read as superior to, that reported in the principal placebo-controlled RCT (49% mMASI reduction versus 18% with placebo).[10] This numerical difference most plausibly reflects the absence of blinding and placebo comparison, unblinded outcome assessment, and non-specific benefit from concurrent sun protection inherent to observational designs, rather than a true efficacy advantage of oral TXA in real-world use over trial conditions; the categorical "good-to-excellent"/improved response rates reported elsewhere in this evidence base (64.8% and 89.7%) reflect a different, proportion-of-responders construct and are not directly comparable to either figure. This pattern is broadly consistent with that noted in earlier pooled meta-analyses, in which tranexamic-acid-only observational studies showed larger standardized effect sizes than the incremental benefit seen when TXA was added to routine treatment in controlled comparisons,[4] a difference generally attributed to the methodological limitations of uncontrolled designs rather than to differential drug efficacy. This gap likely reflects several sources of bias intrinsic to single-arm, open-label observational designs: the absence of a placebo arm to account for regression to the mean, natural fluctuation of melasma with season and sun exposure, and non-specific benefit from concurrent sun-protection counselling; unblinded outcome assessment in several cohorts.[13,15,17] and heterogeneous, sometimes subjective, outcome definitions (categorical "good-to-excellent" grading versus continuous MASI change). These findings should therefore be interpreted as evidence of real-world effectiveness and tolerability under routine clinical conditions, complementing not replacing the internal validity of RCT evidence such as that recently synthesised in this journal, where TXA combined with hydroquinone, rather than TXA monotherapy, showed the most robust benefit against placebo.[9] Optimal dosing remains incompletely resolved. Observational evidence suggests that doses as low as 325 mg twice daily may be effective in some patients,[16] while other studies have used 250 mg twice daily or 500 mg daily with comparable results.[12,13,14,15,18] This is broadly consistent with network meta-analytic modelling suggesting that 250 mg three times daily (750 mg/day) for 12 weeks may be optimal, with 250 mg twice daily a reasonable option to support adherence.[8] Most observational cohorts in this review used regimens within this range, supporting convergence between real-world prescribing patterns and modelled optimal dosing.

Safety, and particularly thromboembolic risk, is the central clinical concern limiting broader adoption of oral TXA for a cosmetically motivated indication. Reassuringly, across a cumulative observational experience of many hundreds of patients and, in the largest identified cohort, a propensity-matched real-world database of substantially greater scale,[19] venous thromboembolism was rare and, where observed, occurred in the context of an underlying thrombophilia.[13] This pattern is consistent with a large Danish national cohort study, which found that overall thrombosis risk associated with oral TXA use in women was low, albeit not zero, and dependent on baseline risk factors.[20] These data collectively support pre-treatment screening for personal or family history of thromboembolic disease and known thrombophilia, consistent with existing consensus guidance,[2,3] rather than supporting a blanket contraindication.

Strengths and limitations

This review's principal strength is its deliberate focus on observational designs, which more closely approximate real-world prescribing conditions, patient diversity, and long-term follow-up than short, selectively enrolled RCTs, and which incorporate the largest published safety dataset (a propensity-matched EHR cohort) yet synthesised in the melasma literature. Several limitations warrant emphasis. First, the heterogeneity of outcome measures and regimens precluded meta-analysis, limiting quantitative precision. Second, most included studies lacked a concurrent control group and independent, blinded outcome assessment, introducing risk of performance and detection bias, as formally reflected in the risk-of-bias ratings. [Table 2] Third, several cohorts were small and single-centre, limiting generalisability, and retrospective designs are inherently susceptible to selection and recall bias and incomplete adverse-event capture. Fourth, publication bias favouring positive findings cannot be excluded. Finally, this review was restricted to English-language publications; however, the methodology strictly follows PRISMA 2020 guidelines.

Implications for practice and future research

Taken together with existing RCT evidence, this review supports oral TXA as a reasonable therapeutic option for appropriately selected patients with melasma, particularly those with refractory or recurrent disease, after individualized assessment of thromboembolic risk. Future research priorities include prospective, adequately powered multicentre observational registries with a standardized core outcome set (e.g., consistent use of mMASI plus a validated quality-of-life instrument), extended pharmacovigilance for rare thromboembolic events, and head-to-head comparative-effectiveness studies

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of dosing regimens identified as plausibly optimal by network meta-analysis.[8]

CONCLUSION

This systematic review of eight observational studies found that oral tranexamic acid was consistently associated with improvement in melasma severity and a generally favorable safety profile under real-world conditions. However, because all included studies were observational and largely lacked concurrent controls, blinding, and a common outcome metric, these findings demonstrate association rather than efficacy and cannot exclude bias from regression to the mean, natural disease fluctuation, or unblinded assessment; they should be regarded as hypothesis-generating and complementary to, rather than a substitute for, randomized controlled trial evidence. Thromboembolic events appear rare and were, in the largest available datasets, not significantly associated with oral TXA use for this indication, though individualized risk assessment remains prudent. Standardization of dosing regimens and outcome reporting would strengthen future evidence synthesis in this area.

Conflicts of Interest

The authors declare no conflicts of interest.

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Data Availability Statement

The data extraction tables generated for this review are available from the corresponding author upon reasonable request.

Ethics Approval

Not applicable; this is a secondary analysis of previously published, de-identified data and did not require ethics committee approval.

REFERENCES

1. Bala HR, Lee S, Wong C, Pandya AG, Rodrigues M. Oral tranexamic acid for the treatment of melasma: a review. Dermatol Surg. 2018;44(6):814-825. doi:10.1097/DSS.0000000000001518.
2. Perper M, Eber AE, Fayne R, et al. Tranexamic acid in the treatment of melasma: a review of the literature. Am J Clin Dermatol. 2017;18(3):373-381. doi:10.1007/s40257-017-0263-3.
3. Taraz M, Niknam S, Ehsani AH. Tranexamic acid in treatment of melasma: a comprehensive review of clinical studies. Dermatol Ther. 2017;30(3):e12465. doi:10.1111/dth.12465.
4. Kim HJ, Moon SH, Cho SH, Lee JD, Kim HS. Efficacy and safety of tranexamic acid in melasma: a meta-analysis and systematic review. Acta Derm Venereol. 2017;97(7):776-781. doi:10.2340/00015555-2668.
5. Zhang L, Tan WQ, Fang QQ, et al. Tranexamic acid for adults with melasma: a systematic review and meta-analysis. Biomed Res Int. 2018;2018:1683414. doi:10.1155/2018/1683414.
6. Calacattawi R, Alshahrani M, Aleid M, 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(1):2361106. doi:10.1080/09546634.2024.2361106.
7. 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;23:1150-1164. doi:10.1111/jocd.16104.
8. 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;89:189-194. doi:10.25259/IJDVL_530_2021.
9. Scabine Pessotti N, Civile VT, Brandao TA, Steiner D. The use of tranexamic acid to treat melasma: a systematic review and meta-analysis. Dermatol Ther. 2026;2026(1):6691762. doi:10.1155/dth/6691762.
10. Del Rosario E, Florez-Pollack S, Zapata L Jr, Hernandez K, Tovar-Garza A, Rodrigues M, Hynan LS, Pandya AG. Randomized, placebo-controlled, double-blind study of oral tranexamic acid in the treatment of moderate-to-severe melasma. J Am Acad Dermatol. 2018;78(2):363-369. doi:10.1016/j.jaad.2017.09.053.
11. Karn D, Kc S, Amatya A, Razouria EA, Timalsina M. Oral tranexamic acid for the treatment of melasma. Kathmandu Univ Med J (KUMJ). 2012;10(40):40-43. PMID:23575051.
12. Wu S, Shi H, Wu H, Yan S, Guo J, Sun Y, et al. Treatment of melasma with oral administration of tranexamic acid. Aesthetic Plast Surg. 2012;36(4):964-970. doi:10.1007/s00266-012-9899-9.
13. Lee HC, Thng TGS, Goh CL. Oral tranexamic acid (TA) in the treatment of melasma: a retrospective analysis. J Am Acad Dermatol. 2016;75(2):385-392. doi:10.1016/j.jaad.2016.03.001.
14. Tan AWM, Sen P, Chua SH, Goh BK. Oral tranexamic acid lightens refractory melasma. Australas J Dermatol. 2017;58(3):e105-e108. doi:10.1111/ajd.12474.
15. Nagaraju D, Bhattacharjee R, Vinay K, Saikia UN, Parsad D, Kumaran MS. Efficacy of oral tranexamic acid in refractory melasma: a clinico-immuno-histopathological study. Dermatol Ther. 2018;31(5):e12704. doi:10.1111/dth.12704.
16. Simpson J, Peng L, Ting W. Evaluation of oral tranexamic acid as a novel treatment for melasma with a high benefit–risk ratio. J Cosmet Dermatol. 2022;21(11):6393-6399. doi:10.1111/jocd.15305.
17. Lam K, Mansour D, Sutton AM. Oral tranexamic acid treatment beyond 6 months for melasma patients: a retrospective case series. JAAD Int. 2024;15:195-196. doi:10.1016/j.jdin.2024.03.006.
18. Demirbas A, Ulutas Demirbas G, Diremsizoglu E, Esen M. Dual benefits of oral tranexamic acid: reducing melasma severity and inflammation. J Cosmet Dermatol. 2025;24(5):e70257. doi:10.1111/jocd.70257.
19. 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;24:64-66. doi:10.1016/j.jdin.2025.09.005.
20. Meaidi A, Mørch LS, Torp-Pedersen C, Lidegaard Ø. Oral tranexamic acid and thrombosis risk in women. EClinicalMedicine. 2021;35:100882. doi:10.1016/j.eclinm.2021.100882.

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