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Melasma Management: A Review of Current Treatment Options

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Abstract

Melasma is a common pigmentary disorder characterized by dark patches on the face, neck, and sternum, most frequently affecting women of reproductive age. Beyond its cosmetic impact, melasma can significantly affect self-esteem and quality of life. Its development involves multiple factors, including genetic predisposition, hormonal influences, ultraviolet radiation, and skin barrier dysfunction. Diagnosis relies on clinical examination, supported by dermoscopy, Wood's lamp examination, histopathology, and advanced imaging, which also help differentiate it from other pigmentary disorders. Management has evolved considerably, with topical agents and chemical peels remaining first-line options, either alone or in combination. Advances in laser and light-based therapies have expanded treatment choices, while newer modalities such as platelet-rich plasma and microneedling offer less invasive yet effective alternatives. Combination approaches often provide superior outcomes. This review summarizes current knowledge on pathogenesis, diagnostic tools, and therapeutic strategies, aiming to guide clinicians toward effective, individualized, and sustainable management of melasma.

Keywords: Chemical peels, Classification, Laser, Melasma, Systemic therapy, Topical treatments

Introduction

Melasma is an acquired hyperpigmentation disorder of sun-exposed skin, most common in women of childbearing age with genetic susceptibility.[1] It typically presents symmetrically in centrofacial, malar, or mandibular patterns, though extra-facial forms on the neck, arms, and sternum also occur.[2] Predominantly facial involvement links melasma to anxiety, depression, and reduced quality of life. Studies from Nepal, Saudi Arabia, and Brazil highlight its high prevalence, making it a leading reason for dermatology visits, with many cases idiopathic.[1] Diagnosis is clinical and can be aided by dermoscopy, Wood's lamp, and advanced noninvasive imaging. Hormonal, thyroid, liver, and cortisol assessments may also support evaluation based on clinical history.[3]

Methods

A literature search was conducted using PubMed, Google Scholar, and Directory of Open Access Journals to identify studies on melasma and its management. Keywords included 'melasma', 'hyperpigmentation' and 'chloasma', combined with terms for treatments 'laser', 'IPL', 'picosecond laser', 'chemical peel', 'microneedling', 'hydroquinone', 'retinoid', 'tranexamic acid'. Boolean operators and quotation marks were applied to optimize search results, and studies published between 2015 and 2025 August were considered. Reference lists of included articles were also screened to identify additional relevant studies. Inclusion criteria comprised articles published in English, human studies (including randomized controlled trials, observational studies, case series, meta-analysis, and narrative or systematic reviews), and publications reporting clinical outcomes of therapeutic interventions for melasma. Exclusion criteria included animal or in vitro studies, conference abstracts, editorials, commentaries without original data, and non-English publications. This review categorized evidence levels based on the

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studies included in our analysis. We acknowledge that higher-level evidence may exist for some interventions but was beyond the scope of this narrative review.

Pathogenesis: The pathogenesis of melasma is complex, and recent studies have greatly expanded our understanding of it. It was once thought to involve only melanocytes, but it is now known to include interactions between keratinocytes and melanocytes, excessive melanin and melanosome accumulation in the epidermis and dermis, increased mast cells and blood vessels, damage to the basement membrane, changes in the extracellular matrix, and photoaging (solar elastosis).[4] Key risk factors for melasma include genetic predisposition, UV and visible light exposure, skin phototype, hormonal influences (pregnancy, contraceptives, hormone therapy), cosmetics, photosensitizing medications, anticonvulsants, and zinc deficiency. Pregnancy-related endocrine, vascular, immune, and metabolic changes further increase susceptibility, with progesterone playing a major role. Extra-facial melasma is more common in women using contraceptives, hormone therapy, or during pregnancy. Its chronic, relapsing course and multifactorial pathogenesis make management challenging.[5,6]

Classification: Melasma lesions are typically classified into three types based on their location: Centrofacial type, which is the most common; Malar (cheek type), and Mandibular type.[7] Extra-facial melasma has been recently described.[2] Wood's lamp examination and histopathological analyses classify melasma into three subtypes: epidermal type, dermal type and mixed type. The overall classification is summarized in Figure 1.

Differential diagnoses: Differential diagnoses for melasma include ephelides, lentigines, post-inflammatory hyperpigmentation, phototoxic dermatitis, and drug-induced pigmentation, as well as rarer conditions like lichen planus pigmentosus, discoid lupus erythematosus, pigmented contact dermatitis, and ochronosis. These disorders often resemble melasma due to their brownish pigmentation and distribution on sun-exposed areas. Diagnosis relies on a detailed clinical history and examination, with biopsy considered in uncertain cases. Tools such as Wood's lamp (UV 320–400 nm) can help assess pigment depth. Dermoscopy, a noninvasive method, aids in visualizing melanin distribution and vascular changes. Histopathology may confirm melasma by showing rete ridge flattening, solar elastosis, and mild inflammatory infiltrates. Electron microscopy can further assess melanosome density and melanin content in affected versus normal skin.[6]

Advances in the treatment of melasma: Recent research on melasma treatment modalities emphasizes advancements in both topical and systemic therapies, laser technologies, and combination approaches. Melasma remains a challenging skin condition due to its complex pathogenesis, recurrence, and individual variability. The highlights of the latest findings in its treatment include:

1 Topical Agents

1.1 Tyrosinase Inhibitors: Tyrosinase inhibitors such as hydroquinone, thiamidol, kojic acid, arbutin, n-butylresorcinol, and azelaic acid reduce hyperpigmentation by blocking melanin synthesis.

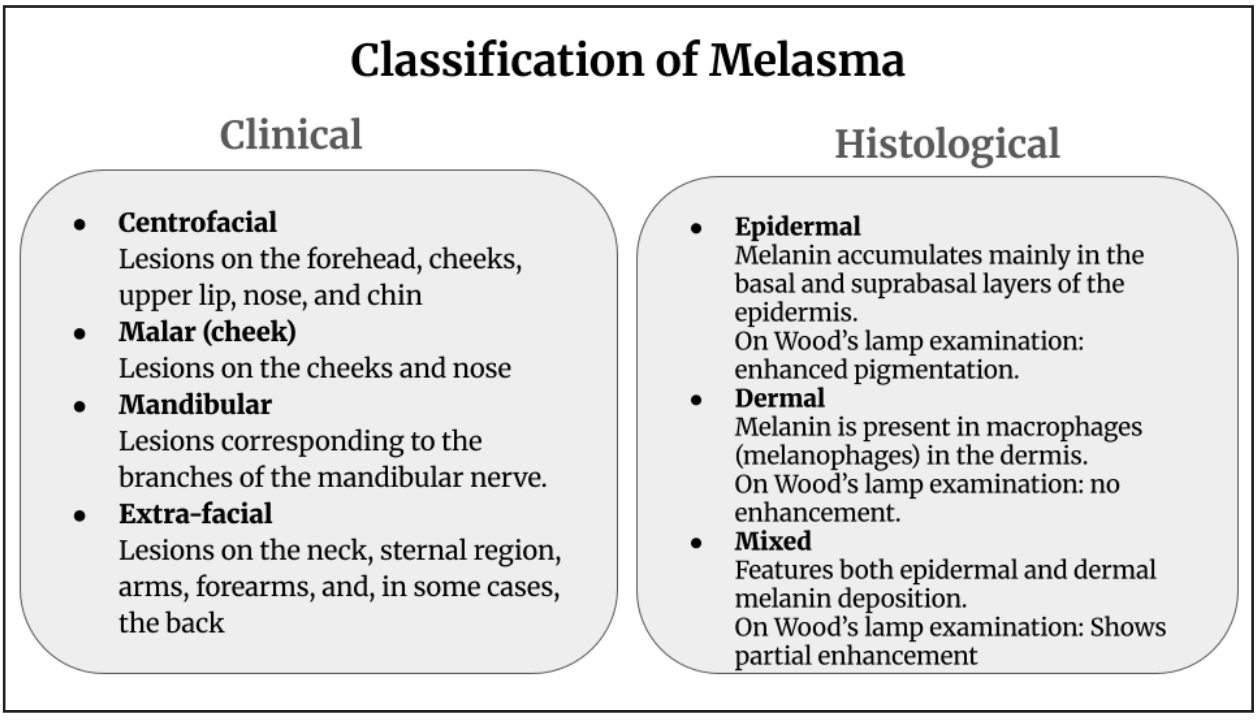

Figure 1: Clinical and histological classification of melasma.

Hydroquinone 4% remains a first-line therapy[6], effective alone or in triple combination with tretinoin and corticosteroids.[8] Thiamidol 0.2% is the most potent human tyrosinase inhibitor to date, showing strong clinical effectiveness.[6] Cream containing alpha-arbutin 5% and kojic acid 2% was effective in treating melasma, showing a lower recurrence rate and fewer adverse events compared with standard triple combination therapy (TCC).[9] Hydroquinone use is restricted in many countries due to risks such as depigmentation, ochronosis, and carcinogenicity.[10] Hydroquinone remains the gold standard for hyperpigmentary disorders, but is limited by concerns regarding ochronosis, irritant reactions, and regulatory restrictions. These limitations highlight the need for safer alternatives where kojic acid and its derivatives show promise due to their tyrosinase inhibition, anti-inflammatory, and antioxidant properties, though challenges with stability and skin irritation remain.

1.2 Topical retinoids: Retinoids, derived from vitamin A, include metabolites such as retinaldehyde (retinal) and retinoic acid, collectively referred to as retinol derivatives. Tretinoin (all-trans-retinoic acid) is a potent topical retinoid that inhibits matrix metalloproteinases (MMPs) via AP-1 suppression. Used in acne at 0.01–0.4% in gels or creams, tretinoin and other retinoids (adapalene, tazarotene, isotretinoin, retinol) regulate cell differentiation, proliferation, and apoptosis, inhibit tyrosinase and melanin synthesis, reduce oxidative stress, limit melanosome transfer, and speed melanin degradation.[6,9] Retinoids hold considerable potential in cosmeceutical applications; however, further studies are required to establish their efficacy at the concentrations commonly present in over-the-counter formulations.

1.3 Tranexamic acid: Tranexamic acid (TA) is gaining prominence as a versatile agent for treating melasma. Topical TA at 5% concentration has been well tolerated in clinical studies.[4] TA showed comparable efficacy with modified Kligman formula in a 2024 study. TA could be used as a primary or maintenance therapy, with additional benefit of avoiding the perilesional halo as seen with Kligman use.[11] A 2025 network meta-analysis found that injectable TA combined with 4% hydroquinone achieved the greatest MASI (Melasma Area and Severity Index) reduction in comparison to other interventions.[12] TA (50 mg/mL) applied post-microneedling produced the greatest reduction in melasma severity and highest patient satisfaction, outperforming both microneedling with metformin (15% solution) and topical Kligman's regimen. These findings support microneedling-assisted TA delivery as a more effective therapeutic option for melasma.[13]
TA shows anti-pigmentary, anti-inflammatory, and anti-vascular effects, with better efficacy and tolerability than metformin or the modified Kligman regimen. Current evidence is limited by small samples, short follow-up, lack of blinding, and variability in formulations and pharmacokinetics.

1.4 Metformin: Recent studies highlight the potential of topical metformin as a promising treatment for melasma. A 2024 RCT by Hussain et al. compared 30% metformin cream with 4% hydroquinone in 62 patients. Evaluations up to 16 weeks showed that topical 30% metformin was more effective and safer than 4% hydroquinone for epidermal melasma.[14] In a 2025 RCT of 50 women with melasma, 40% topical metformin was compared with TCC for 2 months. Metformin showed greater early MASI reduction at 2 weeks, while outcomes were comparable by 8 weeks, supporting topical metformin as a safe alternative to TCC.[15] A once-weekly 30% topical metformin peel-off mask demonstrated efficacy comparable to previously reported daily formulations, suggesting a convenient and well-tolerated alternative regimen.[16] Topical metformin offers a safe, effective, and practical alternative for managing melasma, with efficacy comparable to established therapies with no reported systemic or cutaneous side effects. However, further RCTs with larger sample sizes are needed to confirm its efficacy, optimal percentage, and duration of treatment.

1.5 Antioxidants: Antioxidants such as cysteamine, silymarin, glutathione, and polypodium leucotomos extract (PLE) have shown promise in melasma, with some achieving efficacy comparable to hydroquinone and others enhancing results when combined with topical or physical therapies.[17] Glutathione has been shown to accelerate efficacy as a whitening agent when combined with micro needling.[18] Lycopene, vitamin C, E, and ferulic acid also appear useful as adjuvants, while zinc sulfate and melatonin show limited benefit.[17]
Evidence supports a significant role for antioxidants in melasma treatment, some antioxidants match the efficacy of conventional therapies, while others enhance outcomes when combined with treatments or procedures such as lasers. Further research is needed to clarify their mechanisms, long-term efficacy, and optimal use in larger patient populations.

2 Physical

2.1 Chemical Peeling: Chemical peeling has been effective used alone or in combination with other therapies. Commonly studied superficial peeling agents include salicylic acid, lactic acid, glycolic acid, and TCA. Among these, the latter two agents have the most evidence for effectiveness.[19]

2.1.1 Salicylic acid: A 2024 multicentric, randomized, double-blind, placebo-controlled trial 30% salicylic acid showed significant improvement in mMASI scores. The combination of 30% salicylic acid and 10% niacinamide was found to be effective and safe for treating chloasma,[20] suggesting its potential as a promising therapy for melasma.

2.1.2 Glycolic acid: Glycolic acid, a small molecule derived from sugarcane, is a widely used alpha-hydroxy acid peel. Its skin-penetrating ability makes it a preferred exfoliating agent. Research highlights its keratolytic properties and ability to stimulate the germinal layer and fibroblasts, contributing to its therapeutic effects. In melasma, 70% glycolic acid peels are as effective as TA mesotherapy, though TA better prevents recurrence, while glycolic acid offers higher patient compliance due to its topical use.[21] A systematic review involving 1,075 subjects reported glycolic acid peels as the safest and most effective chemical peel for reducing MASI scores in melasma.[22]

GA is a safe and effective option that shows good patient compliance. Given the chronic nature of melasma, larger randomized multicenter trials with longer follow-ups are needed to confirm these findings.

2.1.3 Trichloroacetic acid: TCA peels are widely used in dermatology to address various skin conditions, including melasma, acne, and xanthelasma palpebrarum. A split-face, randomized trial involving Hispanic women assessed the addition of superficial TCA peels to a regimen of hydroquinone and tretinoin found that combining TCA peels with topical treatments significantly reduced melasma severity without notable adverse effects.[23] Future studies should use multi-center designs with larger sample sizes to enhance generalizability and minimize bias.

2.2 Platelet-Rich Plasma: Platelet-rich plasma (PRP) inhibits melanin synthesis by delaying extracellular signal-regulated kinase activation. Intradermal PRP over three sessions produced greater MASI score reduction than TA.[24] PRP offers a minimally invasive alternative or adjunct therapy, though further research is needed to optimize protocols and assess long-term safety and efficacy.

2.3 Microneedling: Microneedling, stimulates collagen by creating controlled micro-injuries while preserving the epidermis and enhancing drug absorption. Combining microneedling with triple cream improves MASI scores faster than triple cream alone.[25] Dissolvable microneedles (DMNs) offer advanced delivery, showing antioxidant effects, reduced melanin in vitro, and clinical efficacy against chloasma and age spots.[26] Although the technique is generally low-risk, erythema, irritation, mild edema, and pain is observed. Despite the scarcity of large, well-controlled studies, studies have shown significant improvement in various dermatologic conditions. Future studies should optimize protocols, depth, and suitability for diverse skin types.

3. Systemic Treatments:

3.1 Tranexamic Acid: TA reduces melanogenesis by inhibiting the plasminogen/plasmin system and UV-induced pigmentation. Significant melasma improvement is seen when combining oral TA with topical hydroquinone[27] Oral TA was well-tolerated for melasma for up to 28 months with no thromboembolic events.[28] A network meta-analysis suggested the optimal dose as 750 mg/day for 12 weeks. While thrombotic risk limits use, recent evidence indicates TA can be safely extended beyond six months in patients without thromboembolic history, with monitoring.[29]

TA markedly reduced melasma severity. Among the treatment routes, oral TA produced the greatest reduction in MASI scores, followed by injectable and then topical forms. Oral administration often causing gastrointestinal symptoms like gastritis, nausea, and heartburn.[30]

Future large-scale studies with more diverse populations are needed to validate these findings and establish the optimal dose, frequency, duration, and long-term safety profile.

3.2 Polypodium Leucotomos Extract: PLE is a natural fern-derived antioxidant that has gained attention as a potential addition to melasma treatments. Its photoprotective properties may help minimize UV-induced pigmentation, making it a promising option.[8] However, the evidence on PLE's benefit in melasma is mixed; larger, well-designed trials are needed to confirm its effectiveness and establish optimal dosing.

3.3 Glutathione: Oral glutathione (250–500 mg) significantly reduced melanin index across several trials, and combined topical–oral therapy outperformed monotherapy.[31] Oral glutathione plus modified Kligman's regimen has been effective in reducing melasma, though slightly less so than oral TA.[32]

IV glutathione showed limited evidence. Overall, both topical and oral forms provide moderate, unsustainable benefits with variable safety and cost profiles. Larger trials are needed to clarify optimal dosing, long-term safety, and comparative efficacy against established treatments.

4. Light and Laser Treatments

4.1 Ablative Fractionated Resurfacing Lasers: CO_2 (10,600 nm) and Er:YAG (2940 nm) lasers ablate tissue by targeting water, with fractionated ablation enhancing drug delivery, removing melanin, promoting neocollagenesis, and reducing melanocyte–keratinocyte interactions. In a study of 40 Egyptian women, a single low-power fractional CO_2 session plus Jessner's peel showed similar mMASI improvement and safety compared to Jessner's peel alone but recurrence of melasma was observed indicating that melasma requires continuous management.[33] Fractional CO2 laser was effective in reducing erythema of inflammatory facial acne in adolescent men[34] This therapy may benefit melasma although optimized combination protocols are needed.

4.2 Picosecond lasers: Picosecond lasers target melanin with ultra-short pulses, minimizing thermal

Table 1:- Overview of the treatment methods of melasma along with key considerations and findings

Treatment / Intervention	Study Type	Key Findings / Outcomes	Outcome Measure	CEBM Level	References
Topical hydroquinone	Review articles, network meta-analysis of RCTs	Gold standard but limited by risks like ochronosis.	Qualitative, MASI, mMASI, or hemi-MASI.	1	Goel A et al.[5], Philipp-Dormston W et al.[6], Liu Y et al.[8], Shivaram K et al[10]
Topical retinoids (tretinoin, adapalene, tazarotene)	Review article	Shows potential, but efficacy varies with formulation concentration.	Qualitative	5	Philipp-Dormston W et al.[6], Goel A et al.[9]
Tranexamic acid (topical/injectable)	Narrative review, RCTs, network meta-analyses	Reduces melasma severity; microneedling-assisted delivery shows higher MASI reduction.	Qualitative,MASI, mMASI, PGA	1	Piętowska Z et al.[4], Susmitha M et al.[11], Nukaly H et al.[12], Al Mohammady A et al.[3]
Kojic acid, arbutin	RCT, review article	Moderate pigment reduction; stability and irritation challenges.	Melanin Index (MI), mMASI, PGA	2	Tantanasrigul P et al.[9], Philipp-Dormston W et al.[6]
Topical metformin	RCTs, split-face studies	Safe and effective, early MASI reduction comparable to triple cream.	MASI, hemi-MASI	2	Hussain A et al.[14], Manager K et al.[15] , El-Komy M et al.[16]
Thiamidol 0.2%	Review article	Shows strong clinical effectiveness.	Qualitative	5	Philipp-Dormston W et al.[6]
Oral tranexamic acid	RCTs, systematic review, retrospective case series, meta-analysis	Most effective systemic option; GI side effects common.	Melasma severity scale(MSS), mMASI, MASI, MI, and hemi-MASI scores.	1	Shihab N et al. [27], Lam K et al.[28], Wang W et al.[29], Calacattawi R et al.[30]
Glutathione (oral)	Systematic review, RCT	Reduces melanin index and pigmentation; moderate benefit.	MI, mMASI scores	1–2	Sarkar R et al.[31], Rao N [32]
Antioxidants (glutathione, cysteamine)	Systematic reviews, split-face studies	Enhance pigmentation reduction when combined with other treatments.	MASI,mMASI, hemi-MASI	1–3	Sarkar R et al.[31] Mohamed M et al. [18]
Polypodium leucotomos extract	Network meta-analysis	Photoprotective benefits; evidence remains mixed.	mMASI	1	Liu Y et al. [8]
Chemical peels	RCTs, split-face studies, systematic review	Improve MASI; glycolic acid effective; TCA enhances results; recurrence possible.	Narrowband reflectance spectrophotometry (NRS), mMASI, and Global Melasma Severity Assessment (GMSA).	1–2	Xiong Y et al.[20], Khan N et al.[21], Sarkar R et al. [22] ,Lorenzo-Ríos D et al.[23]
Microneedling	Book, network meta-analysis	Improves MASI; combination therapy shows faster improvement.	MASI and mMASI	1–2	Litchman G et al.[25] Wang W et al.[26]
Platelet-rich plasma (PRP)	Split-face comparative study	Reduces MASI more than topical TA in some studies.	mMASI	3	Abd Elraouf IG et al.[24]
Intense pulsed light (IPL)	Meta-analysis	Safe, noninvasive pigment reduction with high satisfaction; recurrence possible.	MASI	1	Yi J et al.[43]
Ablative fractional resurfacing	RCT, review	Improves pigmentation and allows better drug delivery; recurrence common.	mMASI	2–3	Gad El-Karim M et al.[34], Elmorsy E et al. [33]
Picosecond lasers	Split-face RCT, retrospective study, narrative review	Enhanced outcomes with topical agents; 730 nm may be superior for dermal melasma.	mMASI, patient satisfaction), objective findings, and software analysis improvements,MASI	2–3	Feng J et al.[35], Liu X et al.[36], Takaya K et al.[37]
Q-switched lasers	Review, observational, cohort study	Reduce pigmentation effectively; combining with topical agents improves outcomes.	Pigmentation Area and Severity Score (PSI), MI, and erythema index (EI) , MASI (mMASI), digital photography, skin microscopy, colorimetry, physician ratings, and patient satisfaction scores	3–4	Liu Z[42]

*Evidence levels were assigned according to the Oxford Centre for Evidence-Based Medicine (2011) criteria

damage while fragmenting pigment Studies show effective melasma clearance, with fewer side effects than nanosecond Nd:YAG lasers.[35] Combining picosecond lasers with topical agents like TA enhances outcomes.[36] The 730-nm picosecond laser, demonstrated potentially greater efficacy for acquired dermal melanocytosis than the conventional 1064-nm laser, without increasing complications.[37] Overall, they offer precise, safe, and effective treatment, adaptable to melasma type and skin characteristics.

4.3 Q-switched lasers: Q-switched (QS) lasers deliver ultra-short, high-intensity pulses at wavelengths like ruby (694 nm), alexandrite (755 nm), and Nd:YAG (532 or 1064 nm) that selectively target melanin. The 1064 nm QS Nd\:YAG is widely used for melasma, often alongside other treatments. Side effects like guttate hypopigmentation, melasma rebound, and post-inflammatory pigmentation, especially with high fluences are observed.[38] Fractional 694 nm QS ruby lasers are effective and safe for darker skin. In a study of 26 Chinese patients, combining the laser with sonophoresis and vitamin C reduced mean MASI scores from 15.51 ± 3.00 to 10.02 ± 4.39 after three months, with minimal side effects.[39] Low-fluence QS-laser treatment has gained popularity for its effectiveness and lower recurrence risk.[38] The four-step Fotona laser protocol is particularly effective, addressing pigmentation, vascular components, and skin texture, especially in Latin patients.[40]

Long-pulse QSNd:YAG Lasers demonstrated superior efficacy compared to Picosecond Alexandrite Laser in treating melasma, particularly in patients with Fitzpatrick skin types III–IV.[41] A 2025 study revealed oral TA plus 1064 nm QS laser appears the most widely used and effective treatment as compared to other methods.[42]

Combining QS devices with topical lightening agents improves response rates and shortens treatment time. Treatment outcomes depend on factors like laser wavelength and spot size, and duration. Low-fluence QS Nd\YAG shows good initial results but needs frequent sessions, has a high recurrence rate, and often requires more treatments than other laser options.

4.4 Intense Pulsed Light (IPL): Intense pulsed light (IPL) is a safe, non-invasive, and effective treatment for melasma, offering rapid pigmentation reduction and high patient satisfaction. Studies show IPL-based therapies lower MASI scores and provide visible improvements with minimal downtime.[43] While generally well tolerated, recurrence can occur, making maintenance or combination treatments beneficial for sustained results. Future research with larger, multicenter cohorts, longer follow-up periods, and standardized protocols could provide more robust and generalizable evidence.

Conclusion

Melasma is a complex disorder requiring a multifaceted approach. While traditional treatments like hydroquinone and chemical peels remain foundational, therapies like TA, topical metformin, PRP, microneedling, and laser/light-based technologies (QS and picosecond lasers) offer promising, targeted options. Table 1 lists the various methods used in the treatment of melasma. Despite advances, recurrence and variable responses persist, highlighting the need for personalized, combination-based treatment plans. Future research should optimize therapies, clarify molecular mechanisms, and explore safer agents to provide more effective, long-term management and improve patient quality of life.

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