Platelet Rich Plasma as a Potential Treatment for Melasma: A Review

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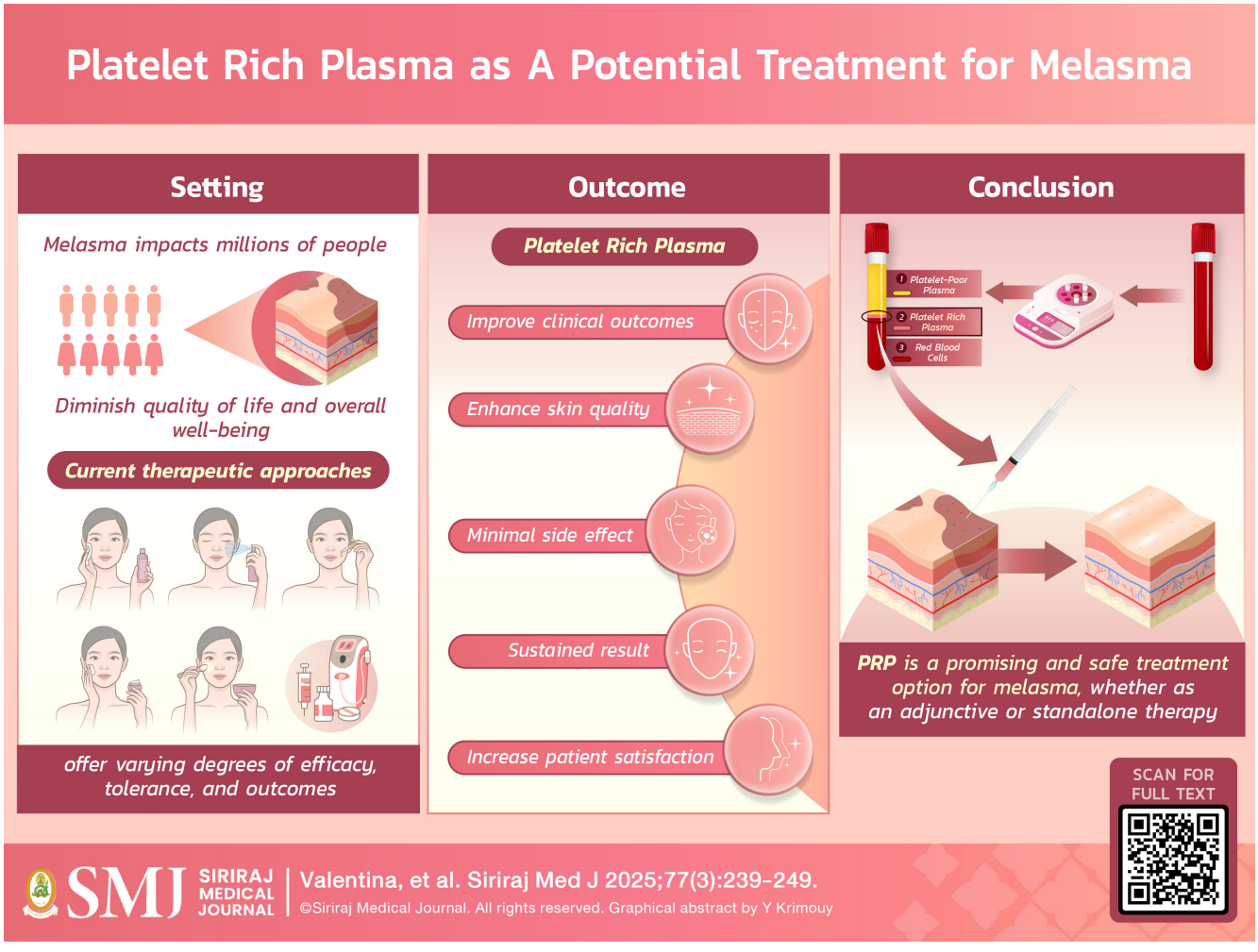

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Received 31 October 2024 Revised 4 December 2024 Accepted 5 December 2024
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https://doi.org/10.33192/smj.v77i3.271926

ABSTRACT

Melasma impacts millions of individuals globally. It is characterized by hyperpigmented macules that predominantly affect the centrofacial region. Although not medically dangerous, melasma can significantly diminish quality of life and overall well-being. Current therapeutic approaches offer varying degrees of efficacy, tolerance, and outcomes, underscoring the need for further research to identify treatments that are both effective and safe. Platelet-rich plasma (PRP), an autologous plasma enriched with a high concentration of platelets, has gained attention in the medical field for its regenerative properties and favorable benefit-risk profile. In dermatology and aesthetic medicine, PRP has demonstrated efficacy in applications such as wound healing, skin rejuvenation, alopecia, acne scarring, and, more recently, pigmentation disorders. This review explores the potential of PRP as a treatment modality for melasma, suggesting that PRP, whether used as an adjunctive or standalone therapy, may significantly enhance treatment outcomes. Nevertheless, despite promising evidence supporting its use, further research is required to establish robust biomolecular mechanisms and evaluate the long-term safety and efficacy of PRP in managing melasma.

Keywords: Melasma; melasma treatment; platelet-rich plasma (PRP) (Siriraj Med J 2025; 77: 239-249)

INTRODUCTION

Melasma is a formidable cosmetic issue and ranks among the three most prevalent skin issues in medical aesthetic practice, alongside acne and wrinkles. While melasma is not a dangerous condition, it can considerably affect an individual's physical appearance, resulting in emotional and psychosocial distress associated with embarrassment, frustration, low self-esteem, and interpersonal interactions, ultimately diminishing quality of life.[1–7] Melasma is characterized by irregular brown macules symmetrically distributed on sun-exposed areas of the body, particularly on the face. It is a common reason for seeking dermatological care, primarily affecting women (especially during the menacme). Managing melasma is notably challenging in dermatology, as many treatment approaches frequently yield variable outcomes that fall short of patient expectations.[8] Melasma treatments vary in efficacy and often present issues such as irritation, post-inflammatory hyperpigmentation, and rebound hyperpigmentation[9], highlighting the need for adjunctive or novel alternative therapies.

Platelet-rich plasma (PRP) is a procedure that uses centrifuged blood with a high concentration of platelets in a small plasma volume.[2,10] PRP is a regenerative treatment that remains under investigation. This therapy has garnered significant attention in the medical field due to its favorable benefit-risk profile. The application of PRP has shown promising results for individuals unresponsive to conventional therapies. Numerous skin conditions progress over time and necessitate extended treatment; however, managing these conditions can be challenging due to significant adverse effects, suboptimal therapeutic responses, and high recurrence rates. PRP may serve as a promising treatment option for such complex skin disorders.

As a novel therapeutic approach, PRP has demonstrated potential in treating various skin and cosmetic conditions, including alopecia, wound healing, skin rejuvenation, and acne scarring.[11] Recent studies have indicated positive outcomes for PRP therapy in managing skin hyperpigmentation, especially in individuals with melasma. However, the understanding of PRP's therapeutic efficacy in melasma treatment remains limited. This review aims to examine the efficacy and mechanism of PRP as an alternative and adjunctive therapy for treating melasma.

Melasma

Melasma is a prevalent chronic skin hyperpigmentation that impacts a significant proportion of the global population.[11–13] Melasma presents as brownish macules with uneven borders, symmetrically located on sun-exposed areas of the body, predominantly on the centrofacial areas of the forehead, cheeks, nose, philtrum, and chin.[1–3,6,9,11,12,14–19] Melasma predominantly occurs in women with dark hair, brown eyes, and dark skin. Its prevalence reaches 75% in pregnant women and typically manifests throughout their reproductive years.[20] A population-based study in 2010 reported pigmentation issues as a leading cause of skin treatment requests, affecting 23.6% of men and 29.9% of women.[1] In Southeast Asia, 40% of women seek dermatological care for melasma, with a female-to-male ratio of 9:1 and onset occurring between the ages of 20 and 30. Individuals at a higher risk include those of reproductive age, pregnant individuals, and those with Fitzpatrick skin types III-IV.[6,15,17]

The pathogenesis of melasma is intricate, multifaceted, and not completely elucidated. Melasma results from dysregulation in melanogenesis, with contributing factors such as sun exposure, hormonal fluctuations during pregnancy, use of oral contraceptives and other steroids, hormone replacement therapy, photosensitizing cosmetics and medications, antiseizure therapy, and genetic predisposition.[1,3,4,6,9,11,12,14,16,17,20–22] Melasma is also associated with vascular factors, inflammation, and skin barrier dysfunction.[19] Histopathological studies have shown increased dermal vascularity, basement membrane disruption, higher melanocyte count, increased melanosome, solar elastosis, mild inflammatory cell infiltration, and greater melanin deposition in the dermis and/or epidermis of melasma-affected skin.[3,9,20] Sun exposure is the primary catalyst for melasma, as it stimulates melanogenic activity, upregulating melanin synthesis and its transfer to keratinocytes, leading to increased eumelanin deposition in the epidermis.[1,15,23]

Melasma is diagnosed clinically. Wood's lamp examination can ascertain the distribution of melanin pigment in the dermis or epidermis to assess the type of melasma (epidermal, dermal, or mixed).[20] Dermoscopic evaluation can assess the intensity of melanin pigmentation and the regularity of pigment network, which may suggest the location and density of melanin pigment deposition. It can also be utilized to evaluate the severity of melasma.[1,20] The Melasma Area and Severity Index (MASI) and modified MASI (mMASI) score are standard scales for evaluating the extent and severity of facial melasma.[1] In contrast, the Melasma Quality of Life scale (MELASQOL) assesses the impact of melasma on patients' quality of life.[7]

The management of melasma poses challenges for clinicians and patients. Supportive treatment often begins with avoiding sun exposure or applying sunscreen to mitigate disease progression.[14,23] However, effective treatment necessitates active intervention. Numerous melanogenesis inhibitors have been developed, although many raise significant toxicity concerns and common skin adverse effects, including erythema, dry skin, irritation, desquamation, and hypopigmentation.[8,15,24] Available treatment options for melasma include topical depigmenting agents, such as hydroquinone, kojic acid, glycolic acid, azelaic acid, retinoids, corticosteroids, arbutin, and niacinamide; oral therapies such as tranexamic acid, melatonin, cysteamine, and glutathione; chemical peels; and laser and light therapies.[8,9,11,14,15,25] Current therapeutic approaches exhibit varying degrees of efficacy, leading to inconsistent and predominantly poor outcomes, varying side effects, and a significant recurrence rate post-therapy cessation.[8,11,13,22,23,26]

Platelet-Rich Plasma (PRP)

PRP is a biological product characterized by a small volume of autologous plasma with a platelet concentration three to seven times higher than that of whole blood[2,16], achieved through centrifugation and platelet suspension.[9,11,14,27] Typically, blood comprises approximately 94% red blood cells (RBCs), 6% platelets, and 1% white blood cells. PRP preparation alters the ratio of RBCs to platelets, resulting in a composition of 95% platelets and 5% RBCs.[28] The optimal platelet concentration for effective PRP therapy in skin treatments is 1-1.5 million platelets/μL.[10]

Platelets are small cellular fragments derived from megakaryocytes and contain two types of storage granules: alpha granules and dense granules.[10] Alpha granules are crucial for PRP therapy due to their high concentration of growth factors, including vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), transforming growth factor-β (TGF-β), epidermal growth factor (EGF), insulin-like growth factor-1 (IGF-1), and fibroblast growth factor (FGF)[10,15] which are instrumental in mediating various mechanisms such as cell differentiation, proliferation, and regeneration. Meanwhile, dense granules contain ADP, ATP, calcium, serotonin, and glutamate, which contribute significantly to the therapeutic benefits of this treatment.[10] Within 10 minutes following PRP injection, 70% of the growth factors in alpha granules are secreted, with at least 95% released within one hour. For up to seven days, platelets continue producing and releasing supplementary growth factors.[10,29]

The clinical applications of PRP have expanded across multiple medical fields. PRP is frequently used in plastic surgery, particularly for treating chronic wounds, ulcers, and burns.[30] PRP has emerged as a promising therapeutic method in aesthetic and dermatological medicine in recent years, demonstrating effective outcomes in wound healing, alopecia with or without scarring, skin rejuvenation, acne scars, and pigmentation disorders.[3,10,15,16,27,28,30] Research indicates that PRP enhances skin quality and increases collagen and elastic fiber production, as it stimulates the proliferation of human dermal fibroblasts and boosts type I collagen synthesis.[28] The ability to stimulate collagen synthesis, reduce recovery time, and yield lasting results renders PRP a compelling therapeutic alternative in cosmetic dermatology.[31]

PRP therapy exhibits an enhanced safety profile due to its autologous nature.[10,14] Adverse effects of PRP are infrequent and minor, including localized pain, infection, skin discoloration, allergic reactions, and thrombus formation.[25] Absolute contraindications include severe thrombocytopenia, platelet dysfunction, unstable

hemodynamics, sepsis, and localized infection at the injection site. Relative contraindications include NSAID administration within 48 hours preceding treatment, glucocorticoid injections within two weeks prior, recent illness or fever, cancer, anemia with hemoglobin below 10 g/dL, moderate thrombocytopenia, and tobacco use.[10]

Currently, there is no global consensus or standardized protocol for optimal PRP preparation.[16,32] PRP preparation typically commences with the collection of 10 to 60 cc of venous blood, which is subsequently transferred into a tube containing dextrose citrate acid or sodium citrate to inhibit platelet activation, degranulation, and premature release of effector molecules. A first centrifugation separates the RBCs from the plasma, after which the yellow-colored plasma supernatant is extracted and subjected to a second centrifugation to isolate plasma rich in platelets and leukocytes from platelet-poor plasma. Following centrifugation, two-thirds of the supernatant plasma is discarded, and the remaining plasma containing a platelet pellet is classified as PRP. The final product typically has a platelet concentration of approximately 1 million/mL, two to eight times higher than whole blood.[15,27,29,32]

PRP as a treatment option for melasma

PRP is an innovative treatment approach for melasma, with numerous case reports and studies have demonstrated its efficacy. Research indicates that PRP, whether used in combination with other treatments or as an independent therapy, is associated with notable clinical improvement in patients with melasma, leading to high patient satisfaction.[15] Patients undergoing PRP treatment achieve a more balanced complexion and improved skin quality, including reduced wrinkles, enhanced elasticity, and increased moisture.[9] Moreover, compared to other melasma therapies, PRP treatment results in fewer adverse effects and reduced pigmentation rebound.[3,16,21,33]

In 2014, Cayrili et al.[30] reported the advantageous application of PRP as an alternative treatment for melasma, with over 80% reduction in epidermal hyperpigmentation in a patient with centrofacial melasma following three biweekly PRP sessions, with the initial objective of skin rejuvenation. Furthermore, no melasma recurrence was observed up to six months post-treatment. Yew et al.[12] found that intralesional PRP as an adjunctive therapy reduced pigmentation in two cases of melasma unresponsive to conventional treatments. Administered over two sessions at four-week intervals, alongside monthly Q-switched Nd:YAG 1064 nm laser treatments and daily topical alpha arbutin, PRP was associated with a reduction in mMASI scores. Garg et al.[35] documented improvement in a case of recalcitrant melasma unresponsive to multiple treatments, including topical depigmentation agents (e.g., topical steroids, tretinoin, hydroquinone, kojic acid, and arbutin), oral tranexamic acid, and chemical peels. Six intradermal PRP sessions achieved clinical improvement and a lowered MASI score, with no recurrence over a three-month follow-up. Recent reports by Wulandari et al.[18] and Shahraki et al.[31] further indicated positive responses in melasma patients treated with microneedling-PRP characterized by brighter skin and significant reductions in brown patches. In other words, PRP can reduce pigmentation and revitalize the skin, enhancing the patient's overall appearance.

Sirithanabadeekul et al.[9] conducted a randomized, split-face, placebo-controlled trial using PRP as an alternative treatment for melasma. Four sessions of intradermal PRP with two-weeks interval significantly improved melasma within six weeks, as evidenced by significantly lower mMASI score, decreased melanin levels, increased patient satisfaction, and reduced wrinkles. These findings are consistent with those of Tuknayat et al.[21] and Rout et al.[6], who observed significant melasma improvements following three intradermal PRP sessions at four-week intervals, with minimal side effects and no recurrence over a three-month follow-up. Rout et al.[6] reported a 77% reduction in mMASI in mild melasma, a 52% reduction in moderate melasma, and a 50% reduction in severe melasma. The improvement of pigmentation depended on skin type, gender, and the type and pattern of melasma. In addition, patients experienced significant improvement in skin quality and reduced wrinkles.[21] Similarly, González-Ojeda et al.[3] reported that three intradermal PRP sessions at 15-day intervals resulted in a significant reduction in the intensity and extent of hyperpigmentation, as assessed by the MASI score, along with improvements in patients' self-perception and quality of life as measured by MELASQOL.

Hofny et al.[11] documented the prospective therapeutic efficacy of PRP as an alternative treatment for melasma, employing two different techniques: microneedling with a dermapen and intradermal microinjection with microneedles. Both techniques resulted in notable improvements in melasma patients, as evidenced by a significant decrease in MASI and mMASI scores following three PRP sessions at four-week intervals. The findings are consistent with a randomized clinical trial by Boparai et al.[26], which demonstrated improvements in melasma following three microneedling sessions with PRP administered every three weeks. No significant adverse effects or recurrence were observed up to 18 weeks post-treatment. A study

TABLE 1. Studies on the use of PRP for melasma treatment.

Study design	Study group and Methods	PRP preparation	Outcomes	Side effects
Tuknayat et al. (2021)[21] An open-labeled prospective therapeutic trial involving 40 patients with melasma.	Intradermal PRP (0.1 ml/cm²) Treatment was conducted over 3 sessions at a month interval.	10 ml of venous blood. 1st centrifugation: 1,600 rpm for 10 minutes. 2nd centrifugation: 4,000 rpm for 10 minutes.	There was a significant reduction in mMASI score at the end of the study (from 13.7 to 6.258, with mean reduction of 54.5%). >90% of patients were satisfied with the treatment results.	There were no serious side effects except xerosis (35%) and pruritus (25%). No recurrence was observed in patients during the 3-month follow-up period.
González-Ojeda et al. (2022)[3] A self-controlled clinical trial on 20 female patients with melasma.	Intradermal PRP Treatment was performed over 3 sessions with 15-day intervals.	Venous blood was collected into a tube containing 3.8% sodium citrate. Centrifugation: 2,500 rpm for 11 minutes. Activation by adding 0.1 units of 10% calcium chloride (CaCl2) for every 1ml of PRP.	There was a significant regression of hyperpigmentation in intensity and extension based on MASI score (from 15.5 ± 8.4 to 9.5 ± 7.2, p=0.001). There was a significant improvement in self-perception and quality of life, as indicated by MELASQOL score (from 42 ± 14.8 to 16.6 ± 7.2, p=0.008).	No local or regional complications were reported.
Sirithanabadeekul et al. (2020)[9] A randomized split-face, single-blinded prospective trial on 10 female patients with bilateral mixed-type melasma.	• PRP side: intradermal PRP (0,1ml/cm²) • Other side (control): intradermal normal saline Treatment consisted of 4 sessions, administered every 2 weeks.	13.5ml venous blood and 1.5ml citrate dextrose A were mixed. Centrifugation: 3,200 rpm for 4 minutes.	Intradermal PRP demonstrated a significant improvement in both mMASI score (p=0.042) and melanin levels (p=0.038) at week 6. There was 28.9% improvement on PRP side, while control side showed 9% improvement. Melanin index values showed no statistically significant difference between the two sides, although a trend toward reduced pigmentation was observed on the PRP side.	Mild side effects, including bruising, were observed, all of which resolved spontaneously within a few days.
Boparai et al. (2020)[26] A randomized clinical trial involving 30 patients with facial melasma.	Microneedling with dermaroller + topical PRP Treatment was performed over 3 sessions at 3-week intervals.	Venous blood was collected into a tube containing sodium citrate. 1st centrifugation: 1,500 rpm for 10 minutes. 2nd centrifugation: 4,000 rpm for 10 minutes. Activation by adding 0.1ml CaCl2 to 1ml PRP.	There was a significant decrease in MASI score (from 12.73 to 6.09, p<0.05) at week 18. Reduction in MASI score was noted starting from week 3. A total of 10%, 30%, and 60% of patients showed improvement of <25%, 25-<50%, and 50-<75%, respectively.	No serious side effects except transient mild erythema in 80% of patients after procedure. No recurrence of melasma was observed during the follow-up period, which extended up to 18 weeks.

TABLE 1. Studies on the use of PRP for melasma treatment. (Continue)

Study design	Study group and Methods	PRP preparation	Outcomes	Side effects
Hofny et al. (2019)[11] A randomized clinical trial on 23 adults Egyptian melasma patients with Fitzpatrick skin types III-IV.	• Right side of the face: micro-needling with dermapen + topical PRP • Left side of face: intradermal PRP Treatment was conducted over 3 sessions at 4-week intervals	10 mL of venous blood was collected into a tube containing ethylenediamine-tetraacetic acid (EDTA). 1st centrifugation: 160 g for 10 minutes. 2nd centrifugation: 400 g for 10 minutes. Activation by adding 1 ml of 3% CaCl2 to 1.5 ml of PRP.	There was a significant decrease in MASI (from 11.86 ± 5.25 to 6.96 ± 4.82, with 34.8% significant to excellent improvement) and mMASI scores (from 5.71 ± 2.56 to 2.90 ± 2.05, with 47.8% significant to excellent improvement) on both sides of the face following treatment (p<0.000). However, no significant difference was found when comparing the two sides.	Most patients experienced greater pain on the left side than on the right side of the face. All patients reported less downtime (in swelling, redness, and soreness) on the left side of the face compared to the right side following the procedure.
Panda et al. (2022)[13] A randomized prospective comparative study with 60 participants diagnosed with melasma.	• Group A: micro-needling with dermaroller only • Group B: Micro-needling with dermaroller + topical PRP Treatment was performed over 3 sessions at a month interval.	5 ml of venous blood was collected into a tube containing anticoagulant. 1st centrifugation: 1,500 rpm for 10 minutes. 2nd centrifugation: 3,000 rpm for 20 minutes.	There was a significant reduction in MASI scores in both groups (Group A from 10.2 ± 6.2 to 7.6 ± 5.4, with 62.5% moderate improvement, p=0.001 vs Group B from 10.6 ± 5.9 to 4.9 ± 3.5, with 37% moderate improvement, 59.2% significant improvement, 3.7% excellent improvement, p=0.0001). Microneedling + PRP had a superior effect due to higher MASI score reduction and better patient satisfaction than microneedling alone.	The side effects were transient and generally well tolerated, including mild pain during the procedure, along with mild erythema and localized edema, which resolved within 48-72 hours. Notably, Group B reported a shorter recovery time in terms of redness and swelling.
Gharib et al. (2021)[33] A single-center clinical trial involving 26 patients with melasma.	• Group 1: micro-needling + topical PRP • Group 2: micro-needling + topical tranexamic acid (TXA) 4mg/ml Both treatments were conducted over 4 sessions.	10 ml of venous blood was collected into a tube containing acid citrate dextrose. 1st centrifugation: 1,500 rpm for 10 minutes. 2nd centrifugation: 3,700 rpm for 10 minutes. Activation by adding calcium gluconate to PRP in a 1:9 ratio.	There was a statistically significant difference between the two groups (p<0.017). Microneedling + PRP gave better results in MASI score (from 6.48 ± 3.37 to 3.17 ± 2.05, with 50% improvement) than microneedling + TXA (from 9.06 ± 2.95 to 5.23 ± 3.51, with 42% improvement).	• PRP group: pain (100%), erythema (46.15%), post-inflammatory hyperpigmentation (PIH, 7.69%) • TXA group: pain (84.62%), erythema (53.46%), PIH (15.38%) There were no significant differences between the two groups regarding side effects.
Mumtaz et al. (2021)[23] Non-randomized controlled trial on 64 patients with melasma.	• Group A: intradermal PRP 1ml • Group B: intradermal TXA 4mg/ml Both treatments were administered over 3 sessions at 4-week intervals.	15-20 ml of venous blood was collected into a tube containing sodium citrate. 1st centrifugation: 1,500 rpm for 10 minutes. 2nd centrifugation: 4,000 rpm for 10 minutes. Activation by adding 0.1 ml CaCl2 to 1 ml PRP.	Intradermal PRP showed significantly better results than intradermal TXA at 4 weeks (p=0.01), 12 weeks (p=0.0001), and 24 weeks (MASI score decreased from 29.84 ± 5.14 to 8.72 ± 3.40 in PRP group vs 29.56 ± 4.39 to 14.97 ± 4.33 in TXA group, p=0.02).	No specific side effects of the treatment were reported.

TABLE 1. Studies on the use of PRP for melasma treatment. (Continue)

Study design	Study group and Methods	PRP preparation	Outcomes	Side effects
Abd Elraouf et al. (2023)[14] A randomized split-face prospective comparative study on 40 facial melasma patients with Fitzpatrick skin types III-IV.	• Right side of the face: Intradermal TXA 4 mg/ml was injected at a dose of 0.05 ml per injection point with a distance of 1cm per point. • Left side of the face: intradermal PRP 1 ml per session Both treatments were performed over 3 sessions at 4-week intervals.	10 ml of venous blood was collected into a 3.2% sodium citrate tube. 1st centrifugation: 3,000 rpm for 7 minutes. 2nd centrifugation: 4,000 rpm for 5 minutes. Activation by adding 0.1 ml CaCl2 to 0.9 ml PRP.	There was a significant decrease in mMASI score of both groups (p<0.001), but the percentage decrease on the PRP side was higher than on the TXA side (53.66 ± 11.27% vs 45.67 ± 8.10%).	• TXA side: pain (62.5%), erythema (55%) • PRP side: pain (7.5%), erythema (32.5%) There was no statistically significant difference between the two groups regarding side effects.
Gamea et al. (2022)[22] A randomized comparative study involving 40 female patients with melasma.	• Group A: Topical TXA 5% in liposome-based cream applied twice daily for 12 weeks • Group B: Topical TXA 5% combined with 4 sessions of intradermal PRP every 3 weeks	10-15 ml of venous blood was collected into a tube containing sodium citrate. 1st centrifugation: 2,000 rpm for 3 minutes. 2nd centrifugation: 5,000 rpm for 5 minutes. Activation by adding 0.1ml CaCl2 to 1ml of PRP.	Both groups exhibited significant improvement in mMASI scores (p<0.001); however, the treatment response was significantly greater in Group B than Group A (35% good to excellent response vs 20% good to excellent response, p=0.024). Patient satisfaction was notably higher in Group B compared to Group A, with the difference reaching statistical significance (p=0.029).	• Group A: rebound pigmentation (10%) • Group B: rebound pigmentation (5%), moderate pain during PRP injection (60%), transient erythema <24 hours after injection (50%)
Tawanwongsri et al. (2024)[5] A randomized prospective investigator-blinded controlled trial on 26 patients with mixed-type melasma.	• Group A: intradermal PRP (0.1 ml/cm^2) conducted over 3 sessions with 4 weeks interval • Group B: intradermal PRP + oral TXA 500 mg/day for 12 weeks	16ml of venous blood was collected into a tube containing acid citrate dextrose and gel. Centrifugation: 3,200 rpm for 10 minutes.	There was a significant decrease in mMASI score in both groups (group A from 4.3 to 3.6 vs group B from 6.4 to 3.6), but the median change was significantly higher in group B than in group A (2.90 vs 0.90, p=0.006).	15.4% of patients experienced transient erythema and swelling, which resolved within 4 hours, along with mild pain during injection. In Group B, 1 patient experienced transient mild gastrointestinal discomfort during the 1st week of oral TXA administration, with no subsequent symptoms reported.

TABLE 1. Studies on the use of PRP for melasma treatment. (Continue)

Study design	Study group and Methods	PRP preparation	Outcomes	Side effects
Rout et al. (2023)[17] A randomized comparative split-face prospective study on 20 female patients with Fitzpatrick skin types IV-V who had mixed-resistant melasma and bilateral facial involvement.	• Facial Side A: Intradermal PRP (0.1 ml/cm²) every 2 weeks for 7 sessions • Facial Side B: 1064 nm Q-switched Nd-YAG laser administered weekly for 12 weeks	No details on the PRP preparation procedure were provided.	Hemi mMASI score on PRP side decreased from 7.52 to 3.05, while on laser side decreased from 7.67 to 5.43. PRP administration showed significant improvement in pigmentation within 12 weeks of treatment.	Some patients experienced mild redness and burning post-procedure which resolved within a few days. PRP side has lower incidence compared to laser side. PRP side has lower relapse rate of melasma after 3 months compared to the laser side.
Adel et al. (2021)[34] A randomized prospective split-face study involving 20 Egyptian female patients with refractory melasma.	• Right side of the face: intradermal PRP + intense pulsed light (IPL) • Left side of face: intradermal PRP only Treatment was performed over 4 sessions at 2-week intervals.	8 ml of venous blood was drawn and centrifuged. 1.5 ml of PRP was injected intradermally into the melasma area using the papule method.	There was a significant decrease in MASI score after treatment ($p<0.05$), but there was no statistically significant difference between the two groups ($p>0.05$).	The side effects were minimal, temporary, and well tolerated.

by Panda et al.[13] yielded comparable results, concluding that microneedling followed by topical application of PRP effectively treated melasma, leading to decreased MASI scores, higher patient satisfaction, and sustained MASI score reductions three months post-treatment.

Nada et al.[36] conducted a case-control study comparing two melasma treatment approaches: topical hydroquinone (HQ) 2% administered for nine weeks and intradermal PRP administered in four sessions at three-week intervals. At week 13, the PRP group exhibited a mean MASI score reduction of 54.79%, whereas the HQ group demonstrated a reduction of 24.52%. This indicated that PRP may serve as a more alternative to standard melasma therapies. A split-face study by Rout et al.[17] compared the efficacy of intradermal PRP administered biweekly over seven sessions with weekly 1064 nm Nd:YAG Qs laser treatment for 12 weeks in patients with mixed resistant melasma. The results showed significant pigmentation improvement and a lower relapse rate on the PRP-treated side three months post-treatment compared to the Nd-YAG Qs laser side. These findings suggested PRP may serve as a primary and maintenance therapy for mixed-resistant melasma.

Recent studies indicate that PRP significantly outperforms tranexamic acid (TXA) in treating melasma, particularly in the long-term.[4,14,23,33,37] This indicates PRP's potential to surpass conventional therapies. According to Mumtaz et al.[23], PRP demonstrated statistically significant outcomes by week 12. In split-face studies[4,14], TXA 4 mg/ml was administered intradermally on the right side of the face, while PRP was injected intradermally on the left side. After 12 weeks, a statistically significant reduction in mMASI scores was observed on both sides, but the percentage reduction was greater on the PRP side than the TXA side without notable side effects. Research comparing the benefits of microneedling combined with PRP and microneedling combined with TXA[33] indicated that melasma patients receiving microneedling-PRP had superior improvement compared to those treated with microneedling-TXA. Consequently, without contraindications to PRP administration, PRP may be a practical option for treating melasma.

Bikash et al.[38] and Tekam et al.[39] evaluated the efficacy of PRP combined with HQ comparing it to the gold standard of HQ alone. It was concluded that the combination of microinjection/microneedling PRP with topical HQ 4% enhanced melasma treatment efficacy. Gamea et al.[22] evaluated the effectiveness of topical TXA 5% versus its combination with intradermal PRP administered every three weeks for 12 weeks. Both groups exhibited a notable decrease in mMASI scores following therapy, leading to a recommendation of PRP as a safe adjunctive therapy to enhance the effectiveness of TXA in treating melasma. Tawanwongsri et al.[5] evaluated the efficacy and safety of combined PRP and oral TXA against standalone PRP, finding that after 12 weeks, the improvement in mMASI scores was more significant in the group receiving three intradermal PRP sessions at four-week intervals alongside oral TXA at a dosage of 500mg/day for 12 weeks. No significant adverse effects were observed, except for mild and tolerable gastrointestinal symptoms. Zhang et al.[40] confirmed that combining intradermal PRP and oral TXA can enhance therapy efficacy and reduce the risk of melasma recurrence for up to six months post-treatment. Adel et al.[34] investigated the effectiveness of PRP injection alone administered over four sessions at two-week intervals and its combination with intense pulsed light (IPL) in patients with refractory melasma. A notable reduction in melasma scores was observed after six weeks of PRP treatment, although no statistically significant difference was identified between the two groups concerning mMASI scores and patient satisfaction.

Mechanisms of PRP action on melasma

PRP has shown notable potential as a treatment for melasma. However, the exact mechanism responsible for its therapeutic effects remains inadequately comprehended and is only tentatively hypothesized.[6] The therapeutic efficacy of PRP relies on the premise that the degranulation of alpha granules following platelet activation results in the release of multiple growth factors, including EGF, TGF-β, and PDGF. These factors bind to specific receptors on various cells, initiating signal transduction pathways that lead to gene expression and the release of proteins involved in melanogenesis and tissue repair.[2,11,16,21] Two primary processes underlying the effects of PRP on melasma include suppressing melanin synthesis facilitated by TGF-β1 and EGF and enhancing skin volume facilitated by PDGF.[10,11,13,14]

Transcriptional examination of skin samples from melasma patients revealed the upregulation of numerous genes associated with melanin formation, including microphthalmia-associated transcription factor (MITF), tyrosinase, and tyrosinase related protein (TYRP).[16] A randomized clinical trial by Hofny et al.[2] reported a significant reduction in TGF-β protein expression in the skin lesions of melasma patients compared to healthy skin, potentially attributable to UV exposure, which is linked to the suppression or cessation of TGF-β production at transcriptional and translational levels. Conversely, PRP treatment can elevate TGF-β protein expression to levels nearly equivalent to those of healthy skin, correlating with significant clinical improvement. These findings indicate that alterations in TGF-β protein expression in the skin lesions of melasma patients corroborate its involvement in the pathogenesis of the disorder and possess therapeutic implications.

The TGF-β family regulates various cellular activities in the skin, including cell proliferation, differentiation, and melanogenesis.[2,12] TGF-β is a critical growth factor for melasma treatment as it modulates melanocyte pigment synthesis.[6,17] Prior research has demonstrated that TGF-β1 can limit melanin production by directly suppressing the expression of paired-box homeotic gene 3 (PAX3), which encodes a transcription factor crucial for melanocyte proliferation and/or survival, and by downregulating MITF, which is crucial for the transcriptional regulation of tyrosinase, TYRP1, and TYRP2.[2,5,10,21,25] Conversely, another study revealed that TGF-β1 can reduce melanogenesis through delayed extracellular signal-regulated kinase (ERK) activation.[5] TGF-β1 strongly inhibits the MITF promoter's transcriptional activity, thus decreasing MITF expression and consequently inhibiting tyrosinase gene transcription.[2,10,15,17,30] The formation of eumelanin and reduction of pigmentation can be diminished by lowering the expression of tyrosinase and other enzymes involved in melanin biosynthesis.

Prior research has demonstrated that melasma is a melanocytic disorder and a photoaging skin disease. Ultraviolet exposure elevates the levels of MMP-2 and MMP-9, leading to the degradation of collagen types IV and VI in the skin and resulting in basement membrane damage, thereby facilitating the infiltration of melanocytes and melanin into the dermis.[16] Consequently, conventional therapy targeting melanosome or melanocyte activity may prove inadequate for treating this condition. On the other hand, PRP induces a pigmentary lightening effect by promoting basement membrane repair facilitated by laminin, collagen IV, and tenascin, which are stimulated by TGF-β1 produced upon PRP activation, thereby inhibiting the migration of melanocytes and melanin into the dermis.[5,10,11,13,16,22]

EGF is widely used in cosmetic formulations for skin

lightening, wound healing, and reducing post-inflammatory hyperpigmentation from lasers or UV exposure.[25] EGF can influence the activity of pro-inflammatory mediators released by damaged keratinocytes, such as prostaglandin-E2 (PGE2), which stimulates melanogenic activity in the skin by regulating melanocyte dendrite formation, proliferation, and tyrosinase expression. EGF can limit melanogenesis by suppressing PGE2 expression and activating the ERK pathway, thereby reducing tyrosinase enzyme activity and ultimately decreasing melanin synthesis.[5,10,21,23] The improvement in pigmentation following PRP treatment is also attributed to increased skin volume induced by PDGF stimulation. PDGF plays a critical role in angiogenesis, collagen production, and the formation of extracellular matrix component, particularly hyaluronic acid, which enhances skin tone and volume, leading to a radiant complexion.[5,10,11,16,21,25,30]

The synergy of bioactive compounds present in PRP improves pigmentation in patients with melasma. PRP possesses bacteriostatic, anti-inflammatory, and reparative properties that rectify the aberrant hyperpigmentation metabolism associated with melasma.[40] Growth factors, fibrin, and leukocytes present in PRP can modulate and restore the overall architecture of the skin layer, enhance skin barrier function, re-establish microcirculation, reduce hyperpigmentation, and stimulate collagen synthesis and epidermal regeneration to enhance skin quality and texture. They can also minimize the risk of re-pigmentation in the area.[6,17,31,40] Thus, the therapeutic efficacy of PRP is thought to be associated with the restoration of aberrant pigment metabolism and numerous reparative actions that address compromised skin-barrier integrity, inflammation, and vascular alterations contributing to the etiology of melasma.

CONCLUSION

Platelet-rich plasma (PRP) is emerging as a promising and safe treatment option for melasma, potentially serving as either an adjunctive or alternative therapy. When used as a first-line treatment, PRP has shown the ability to significantly improve clinical outcomes and enhance skin quality, with minimal adverse effects and sustained results. Combining PRP with other melasma therapies may further reduce hyperpigmentation and increase patient satisfaction. However, individual responses to PRP can vary, and multiple sessions may be required to achieve optimal results. PRP's mechanism of action is believed to involve the growth factors in alpha granules, which may suppress melanin production while promoting skin volume. Nevertheless, further research is needed to fully understand the efficacy of PRP in treating melasma. Specifically, biomolecular studies and clinical trials are essential to determine optimal treatment protocols and assess the long-term safety and efficacy of PRP therapy.

Data Availability Statement

The data supporting the findings of this review are available within the article.

DECLARATION

Grants and Funding Information

No grants and funding were received for this review article.

Conflict of Interest

The authors have declared that there are no conflicts of interest.

Registration Number of Clinical Trial

None

Author Contributions

Conceptualized the study and wrote the main manuscript text, S.V.; Reviewed, revised, and approved the final manuscript, D.A.A.S.L. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

None

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