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REVIEW ARTICLE

A comprehensive review of platelet-rich plasma for the treatment of dermatologic disorders

Jessica N. Pixley, Madison K. Cook, Rohan Singh, Jorge Larrondo and Amy J. McMichael

Wake Forest Department of Dermatology, Medical Center Boulevard, Winston-Salem, NC, USA

ABSTRACT

Platelet-rich plasma (PRP) offers anti-inflammatory and regenerative properties through angiogenesis, cell differentiation, and proliferation. Although studied in many dermatologic conditions, its efficacy is not well-understood. Our objective is to review the use and effectiveness of PRP for dermatologic conditions. A literature search was performed through PubMed and yielded 54 articles published between January 2000 and November 2021; articles written in English were reviewed. Intradermal injections were associated with increased hair density in androgenic alopecia. Successful treatment of inflammatory nail diseases with PRP has been reported. Improvement in psoriasis was described, but only two studies were available. PRP was associated with higher patient self-assessment scores of photoaging and fine lines. Treatment with PRP in melasma has been associated with improved subjective satisfaction, but not with objective measures of disease improvement. PRP can serve as a safe and potentially effective adjunct for hair loss, vitiligo, nonhealing wounds, photoaging, and acne scars. An important barrier to interpreting PRP research is lack of standardization of PRP preparation protocols, inconsistent clinical endpoints, and frequent combination treatments. However, PRP is relatively noninvasive, has a well-established safety profile, and patient satisfaction is often high as patients perceive great benefit from treatment with PRP.

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KEYWORDS
Platelet-rich plasma; dermatology; hair loss

I. Introduction

Platelet-rich plasma (PRP) is an autologous preparation rich in platelets, fibrinogen, fibrin, chemokines, and leukocytes; it is an emerging treatment for a variety of dermatologic conditions (1). The general steps of preparation include venipuncture, collection of 10 to 60 ml of whole blood, and addition of an anticoagulant such as acid citrate dextrose or sodium citrate, which prevents platelet activation, degranulation, and premature secretion of effector molecules. The initial centrifugation of the whole blood separates the red blood cells (RBCs) from the plasma, and subsequent centrifugation separates the PRP, containing copious platelets and leukocytes, from the acellular, platelet-poor plasma (2). Depending on the desired components and specific protocol, varying amounts of the platelet-rich buffy coat layer are collected with trace residual RBCs. The PRP pellet is next treated with calcium chloride or thrombin to trigger platelet activation and fibrin polymerization (3). The final preparation is rich in platelets, usually concentrated around 1 million/mL, and between 2 to 8 times greater than in whole blood.

The general term 'platelet-rich plasma' can be subcategorized based on leukocyte and fibrin content into 4 subtypes of PRP, although the primary subtype that is described in dermatology studies is pure PRP (P-PRP) (2). Leukocyte-platelet-rich PRP (L-PRP) is characterized by a leukocyte concentration higher than in whole blood. L-PRP has been extensively studied in maxillofacial surgery, periodontics, and orthopedic conditions, but has not been studied in dermatologic diseases. Leukocyte-poor PRP or pure PRP (P-PRP) is an extension from classic platelet transfusions and was first produced using plasmapheresis with a cell separator attached to the patient (2). P-PRP was first reported for maxillofacial surgery, and is also used in esthetic dermatology, and various orthopedic conditions. Pure platelet-rich fibrin (P-PRF) is a concentrate of platelets in a fibrin matrix and is used in oral and maxillofacial surgery and rotator cuff injuries. Leukocyte and platelet-rich fibrin (L-PRF) contains a fibrin matrix that is remodeled over time with continuous activation of platelets, and is used in periodontic procedures, rotator cuff tears, and wound healing (2).

In addition to platelets, fibrin, and leukocytes, PRP also possesses the components of alpha granules, which include: platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), epithelial growth factor, transforming growth factor beta (TGF-β), insulin-like growth factor (IGF), serotonin, dopamine, histamine, adenosine, and calcium. Growth factors offer a variety of functions, including promotion of mitogenesis and differentiation of stem cells, fibroblasts, keratinocytes, and endothelial cells. They induce cell proliferation, chemotaxis, and angiogenesis, thus promoting cell differentiation, proliferation, and regeneration.

PRP has been extensively studied and implemented in the fields of oral and maxillofacial surgery in addition to orthopedics (4,5). More recently, the regenerative potential of PRP has been directed towards a range of cosmetic, surgical, and chronic conditions. This review will focus on the applications of PRP

CONTACT Jessica N. Pixley pixleyjn@vcu.edu Department of Dermatology, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC 27157, USA

in medical dermatology, cosmetic dermatology, and wound healing.

2. Methods

A literature search of clinical trials, review articles, and meta-analyses was performed through PubMed using the following key words: *platelet-rich plasma, PRP, platelet gel*, and *platelet fibrin*. A total of 54 articles published between January 2000 and November 2021 that were written in English were reviewed and included based on the relevance to the objectives of the paper.

3. Results

3.1. Androgenetic alopecia

Androgenetic alopecia is the most common form of hair loss in both men and women, affecting about half of the population (6). It is a hereditary condition characterized by hair follicle sensitivity to dihydrotestosterone (DHT), where circulating testosterone is converted by 5α-reductase to DHT. This causes shortening of the anagen phase of hair growth, which manifests as a decrease in hair diameter, conversion of terminal hairs to vellus hairs, and thinning in the frontal and vertex scalp of men or generalized thinning in women (6). Finasteride, a 5α-reductase inhibitor, and minoxidil, which directly stimulates the hair follicles, are the only 2 drugs that are currently Food and Drug Administration (FDA)-approved to treat androgenetic alopecia. Additional therapies including spironolactone, an aldosterone receptor antagonist, and cyproterone acetate, are used off label to achieve anti-androgen effects. Additional interventions for androgenic alopecia may include microneedling and low-level laser therapy. Although finasteride and minoxidil are effective for some patients (7), treatment is often required for indefinite periods of time and efficacy is largely dependent on patient adherence. Adverse effects may be a potential deterrent: finasteride use in pregnancy is associated with potential fetal genital malformation (8,9). Topical minoxidil may cause local scalp irritation, while low-dose oral minoxidil is associated with hypertrichosis and cardiovascular adverse events in a dose-dependent manner (10). Due to the potential side effects and varying efficacy of the available treatment options, there is interest in emerging therapies such as PRP to treat androgenic alopecia.

PRP is used in the management of various hair loss disorders, including androgenetic alopecia. Although not fully understood, PRP is believed to have a therapeutic effect on hair loss through alpha granule activation and release of VEGF, IGF, and PDGF, which bind to receptors on stem cells in the bulge area of the hair follicle and activate the MAPK/ERK pathway. This results in follicular proliferation, differentiation, and a prolonged anagen phase of the hair cycle (8,11,12).

A total of three meta-analyses and two randomized clinical trials that focused on the use of PRP for androgenic alopecia were identified (Table 1). In the first meta-analysis, there was an increase in hair density in the PRP group but not in cross-sectional thickness, while the second found an increase in hair density (6,12). The third meta-analysis initially found an increase in hair density and cross-sectional thickness, but these were not statistically significant in the pooled results (13). One RCT found improvement in vellus hair density and diameter with combination PRP and minoxidil (14). The second RCT found a smaller decrease in hair density in PRP-treated patients compared to the control group after four weeks post treatment (15).

3.2. Alopecia areata

Alopecia areata (AA) is a common form of nonscarring hair loss, with an estimated prevalence ranging from 0.2% to 1.7% in the United States (16). The underlying pathogenesis of AA involves autoimmune-mediated lymphocytic attack of the anagen bulb and premature cessation of the anagen growth phase. Prognosis varies greatly, and risk factors for worse outcomes include young age of onset, family history of AA, and co-occurrence with other autoimmune disorders (17). There are currently no FDA-approved medications for AA, but topical, intralesional, and oral corticosteroids; topical and oral minoxidil; and topical and oral Janus kinase (JAK) inhibitors have been utilized for treatment with positive outcomes (18). PRP has been implicated as a new emerging therapy for AA with clinical trials supporting its efficacy in disease management, although preparation protocols vary among providers and no comparison studies are available. In addition to the growth factors released, other mechanisms that support the use of PRP for AA include its activation of anti-apoptotic factors (Bcl-2, Akt), which cause prolonged survival of the dermal papilla cells and prolongation of the anagen phase of hair growth. PRP also promotes immunologic suppression through the increased activation of TGF-β, an immune modulator cytokine that is thought to be involved in disease pathogenesis (19).

A total of 3 RCTs on PRP use in patients with AA were evaluated (Table 1). The first study found improved SALT scores compared to placebo in the PRP group, the second study found similar improvements between the control and PRP treatment groups after 3 different treatments with no significant difference from physicians' or patients' assessments, and the final study had greatest improvement in the intralesional corticosteroid group followed by the PRP group.

3.3. Cicatricial alopecia

Cicatricial alopecia comprises a group of disorders in which peribulbar lymphocytic inflammation leads to destruction of the hair follicle and replacement by fibrous tissue that prevents hair regrowth (20). One multicenter study found the scarring alopecias together comprise approximately 26.8% of total alopecias, of which the most common was frontal fibrosing alopecia (FFA) with a prevalence of 40.1% of cicatricial alopecias (21,22). Treatment of scarring alopecia is challenging, with treatments utilized including oral finasteride, dutasteride, topical, intralesional, and systemic steroids, minoxidil, topical tacrolimus, and oral hydroxychloroquine. Several subtypes including central centrifugal cicatricial alopecia (CCCA), lichen planopilaris (LPP), and FFA have been successfully treated with PRP, although current literature is limited to a few case reports. Of the four case reports available, 2 described a subjective improvement in hair density, 1 described improved perifollicular erythema and scaling, and the last described complete regression of scalp erythema and scaling (Table 1).

3.4. Chronic vitiligo

Vitiligo is an acquired, idiopathic autoimmune disorder characterized by melanocyte destruction leading to depigmented or

Table 1. Evaluation of PRP in androgenic alopecia, alopecia areata, and cicatricial alopecia.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Mao et al. (6)	Androgenic alopecia	Studies conducted until January 2019	Meta-analysis of 11 articles	262; 179 males, 83 females	• Subcutaneous PRP injection • Control: normal saline injection	• Hair density (hairs/cm^2) • Hair cross-sectional area (hairs/cm^2)	Increased hair density in PRP over control groups: mean difference (MD)=49.78; Heterogeneity (I^2)= 63%, 95% CI 36.25–63.30, $p > .00001$ from 4 articles. No statistically significant increase in hair cross section in all 4 articles.
Gupta et al. (12)	Androgenic alopecia	N/A	Meta-analysis of 10 articles	165 men	• Subcutaneous PRP injection • Control: normal saline injection	• Hair density (hairs/cm^2)	Increased hair density in PRP over control group: 0.58 (95% confidence interval [CI]: 0.35–0.80) and 0.51 (95% CI:0.23–0.80, $p < .0004$), in baseline and placebo, respectively.
Giordano et al. (13)	Androgenic alopecia	N/A	Meta-analysis of six studies	177	• PRP injection alone • PRP + PDRN injections • PRP + Dalteparin + protamine microparticle • Control: interfollicular placental extract (dalteparin + protamine microparticles)	• Hair density (hairs/cm^2) • Hair thickness (cross section hairs/10 $^{-4}$ mm^2)	Increased hair density in PRP group (MD = 17.90, 95%CI 5.84–29.95, p=.004) Increased hair cross-sectional thickness (MD 0.22, 95%CI 0.07–0.38, $p = .005$) The pooled results did not show statistically significant differences in percentage increase in hair number (MD 24.12%, 95%CI 12.76–60.99, $p = .20$) and hair thickness (MD 32.63%, 95%–I 16.23–81.48, $p = .19$) among patients treated with PRP.
Pakhomova et al. (14)	Androgenic alopecia	N/A	RCT	69 men	• PRP injections monotherapy • 5% minoxidil solution • Combination with PRP + 5% minoxidil	• Hair density (hairs/cm^2) • Average hair diameter (μm) • Proportion of vellus hair (%)	The highest increase in hair density occurred in the combination group at 32% ($p = .00004$), with 16% in the minoxidil group ($p = .00073$), and 12% in the PRP group ($p = .000067$). The greatest increase in average hair diameter was 26% in the combination group ($p = .00004$), followed by 12% in the PRP group ($p = .001947$), and 2% in the minoxidil group ($p = .338$). For vellus hair there was a 17% increase in the PRP group ($p = .002225$), followed by a 2% increase in the minoxidil group($p = .7647$), and a 30% decrease in the combination group ($p = .00082$).
Gressenberger et al. (15)	Androgenic alopecia	N/A	RCT	30 men	• Intracutaneous PRP injections • Control: intracutaneous physiological saline	• Hair density (hairs/cm^2) • Average hair diameter (μm)	The PRP group had a lesser decrease in hair density (6.5 hairs/ cm^2) at 4 weeks post treatment compared to placebo (9 hairs/cm^2, $p = .817$). Hair diameter measured in micrometers increased by 1.7 in the PRP treated group compared to 1.1 in the placebo group after treatment ($p = .523$).
Gupta et al. (23)	Alopecia areata	New Delhi, India	Randomized, split-head study	27	• PRP injections • Control: normal saline injections	• Severity of Alopecia Tool (SALT) score, percentage reduction in cytokines	SALT score was reduced by 9.05% in the PRP group compared to 4.99% in the placebo group ($p = .049$). There was decreased expression of the inflammatory cytokines IFN-λ in the PRP-treated scalp ($p = .001$) and IL-17 ($p = .009$), and an increase in the expression of FOXP3, an immune modulating cytokine ($p = .011$).

(*continued*)

Table 1. Continued.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Ragab et al. (24)	Alopecia areata	N/A	Randomized clinical trial	60	• Intradermal PRP injections • Fractional CO_2 laser + topical PRP • Microneedling followed by topical PRP	• SALT score	Patients in all 3 groups improved after treatment, with intradermal PRP injections and fractional CO_2 Topical PRP had greater (80%) reduction in SALT score compared to microneedling with topical PRP (70%); no intergroup difference by physicians ($p = .268$) or patients ($p = .147$).
Hedge et al. (25)	Alopecia areata	New Delhi, India	Randomized split-scalp study	50	• PRP injections • Control: triamcinolone acetonide injections	• SALT score	There were similar improvements in PRP- and steroid-treated groups with 44% of each showing near complete regrowth compared to placebo (20%). There was a decreased SALT in all compared to baseline ($p = .001$ for each) with greatest absolute hair growth with intralesional corticosteroids followed by PRP, followed by placebo.
Ozcan et al. (26)	FFA	N/A	Letter to the editor	1 female	• PRP injections	• Clinical and trichoscopical perifollicular erythema and scaling	All outcomes improved after 1 month of PRP injections.
Dina et al. (20)	CCCA	USA	Letter to the editor	1 female	• PRP injections	• Subjective evaluation of hair density	Greater than 50% improvement in hair density of scalp vertex.
Dina et al. (20)	LPP	USA	Letter to the editor	1 female	• PRP injections	• Subjective evaluation of hair density	Normal hair density with only minimal perifollicular erythema and scaling.
Bolanca et al. (27)	LPP	N/A	Case report	1 female	• PRP injections	• Trichoscopy, subjective symptoms	Complete regression of itching and hair shading, no perifollicular erythema or scaling.

Table 2. Evaluation of PRP in vitiligo.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Khattab et al. (28)	Nonsegmental and symmetrical vitiligo	Egypt, May 2018–May 2019	Prospective comparative study	52	• Intradermal PRP injection + excimer laser • Control: Excimer laser only	• % repigmentation	The combination group had higher repigmentation compared with excimer laser alone, with excellent (75–100%) response in 34.6% of patients compared to 0% in the placebo group, and good (50–75%) response in 50% compared to 34.6% in placebo. ($p = 000$).
Afify et al. (29)	Nonsegmental vitiligo with ≥6 patches	Ain Shams University Hospital, December 2018–November 2019	Randomized clinical trial	20	• Fractional CO_2 laser, intradermal PRP injection • Combined fractional CO_2 with PRP • Combined fractional CO_2 with NB-UVB • Combined fractional CO_2 with PRP and NB-UVB • Control: no treatment	• Surface area as determined by computer-assisted grid (VACAG)	Vitiligo patches in all treatment groups had improved surface area of disease: 1.5% reduction in CO_2 laser group, 0.4% in PRP group, 0.2% in CO_2 laser with PRP group, 0.4% in CO_2 laser with NB-UVB group, and 0.5% reduction in CO_2 laser with PRP and NB-UVB group. No difference between the different regimens ($p = .122$).
Kadry et al. (30)	Stable nonsegmental vitiligo	1 facility in Cairo, June 2014–June 2016	Prospective, randomized, intrapatient, comparative controlled study	30	• PRP intradermal injections alone • Combined PRP and fractional CO_2 • CO_2 laser alone • Control: no treatment	• computer-assisted grid (VACAG), mean improvement score by physician (MISP), visual analog scale (VAS), and histopathological evaluation.	The combination CO_2 laser and PRP, and PRP alone, had the highest improvement; surface area measured by VACAG was 57.01 in the PRP alone group, 54.22 in the CO_2 and PRP combined group, 38.08 in the CO_2 laser alone group, and 13.79 in the control group. MISP and VAS were highest in the CO_2 and PRP group, and the PRP monotherapy group, with a MISP of 3.20 and 2.97, and VAS of 6.87 and 6.67 in the CO_2 and PRP combination and PRP monotherapy groups, respectively ($p < .001$).
Abdelghani et al. (31)	Stable nonsegmental vitiligo	Cairo, Egypt, January 2016–January 2017	prospective, randomized comparative trial	80	• Laser alone • PRP intradermal injections alone • Combined laser and PRP • Combined laser and NB-UVB.	• VAS • 5 point scale for repigmentation: (grade 1: 1-5%, grade 2: 6–25%, grade 3: 26–50%, grade 4: 51-75%, and grade 5: 76-100%)	Treatment with combination laser and PRP had highest mean percent repigmentation (63.40), followed by 39.70 in laser and NB-UVB, 31.65 in laser alone, and 27.25 in PRP alone. The mean VAS score was highest in combination laser and PRP (61.60), followed by 40.73 in combination laser and NB-UVB, 31.70 in laser alone, and 27.98 in PRP alone ($p = .000$).
Deng et al. (32)	Localized stable vitiligo	2 Beijing Hospitals	Randomized, prospective, case-control study	60	• Combined intradermal PRP injections + 308-nm excimer laser • PRP injections alone • Laser alone	• Vitiligo disease activity (VIDA) score	The laser plus PRP group had an increase in repigmentation with a total effective rate of 80% compared to 25% in the PRP alone group and 35% in the laser alone group ($p < .05$ for both), but no significant difference between the PRP and laser groups.

hypopigmented macules and patches. The disease can be psychologically distressing to patients and may significantly impair quality of life (QOL). The prevalence of vitiligo is between 0.4 and 4% worldwide (3). Pathogenesis has been hypothesized to involve aberrations in immune regulation, melanogenesis, and metabolic function, and treatment has been attempted with a range of topical, systemic, and procedural therapies that include topical and systemic corticosteroids, calcineurin inhibitors, fractional CO_2 lasers, narrow-band ultraviolet B (NB-UVB) phototherapy, and surgical transplantation of autologous melanocytes. However, these treatment options offer limited response, particularly in difficult-to-treat acral zones, require prolonged treatment duration, and may convey a risk of long-term (ultraviolet) UV light exposure. PRP promotes melanocyte regeneration, anti-inflammatory pathways, and enhancement of intracellular adhesions, and therefore offers potential treatment benefit for patients with vitiligo.

No meta-analyses were available; four RCTs and an additional comparable study are presented below (Table 2). There is wide variability in both outcome measures and therapies used, making outcomes difficult to compare among these studies. The 5 vitiligo studies reviewed each used PRP in combination with different laser therapies, which included excimer laser, fractional CO_2 laser, and NB-UVB. In 3 of these studies, the combination of PRP with laser therapies had the highest improved outcomes, while 2 of these studies had no difference or a nonsignificant increase. Only 2 studies included intradermal PRP injections alone: in 1 of these studies, combination PRP with fractional CO_2 laser and PRP intradermal injections alone both had improved endpoints compared with CO_2 laser alone or no treatment groups, although the combination group had the highest improvement. In another study, the highest improvement in percentage repigmentation occurred in combination PRP and laser therapy, while PRP alone had the lowest improvement, but in this study, the type of laser used was not reported. In another study, there was no significant difference between the PRP and laser groups. Overall, PRP injection in combination with laser therapy appears to have some benefit compared to control, but frequently this benefit was insignificant.

3.5. Melasma

Melasma is a chronic disorder of recurrent hyperpigmentation characterized by hyperfunctional melanocytes and increased melanin deposition in the epidermis and dermis. The characteristic yellow-brown patches of hypermelanosis typically present in a symmetric centrofacial, malar, or mandibular pattern involving the sun-exposed skin (33,34) Although the etiology is not well understood, pathogenesis has been attributed to an interplay between hormonal levels, UV light, inflammation, and free radical formation, all of which affect keratinocytes and fibroblasts and therefore melanogenesis (34). Melasma has been reported with varying prevalence, at 8.8% in the Hispanic female Texas population, and as high as 40% in southeast Asian females presenting to dermatology clinic (35). There is a female-to-male ratio of 9:1. Particularly, individuals of reproductive age, pregnant, or Fitzpatrick skin types III-V are at increased risk. Onset is usually between ages 20–30 (34,36). Treatment options include topical therapies: hydroquinone, azelaic acid, tretinoin, corticosteroids; systemic therapies: glutathione and tranexamic acid; and procedures: topical bleaching, pulsed light or laser treatments. These therapies often offer variable results with frequent cutaneous side effects (33).

PRP has been proposed as a potential treatment for melasma based on the wound healing and angiogenic effects of the constituent growth factors PDGF, TGF-β1, and TGF-β2. Inhibition of tyrosinase by TGF-β1 may also play a therapeutic role. Tyrosinase is the rate-limiting enzyme in melanogenesis and may be inhibited through an effect on transcription factors such as microphthalmia-associated transcription factor (MITF) and via delayed activation of extracellular signal-related kinase activation.

There are limited studies on PRP use in the treatment of melasma, and only 1 meta-analysis, a nonrandomized controlled clinical trial, and a prospective study were available for this review. Although all studies used the Melasma Area and Severity Index (MASI), the therapies used ranged from intradermal PRP injections, tranexamic acid, laser, microneedling, and growth factor concentrate injections. The strongest available evidence favors subjective patient and physician satisfaction over improvement in objective measurements like the Melasma Area and Severity Index (MASI) (Table 3).

3.6. Inflammatory nail disorders

Inflammatory nail disorders are a group of conditions that may be isolated to the nail or concomitant with systemic disease. These disorders include lichen planus, lichen striatus, and idiopathic trachyonychia. Treatment of nail lichen planus has been attempted with topical tacrolimus, intralesional or systemic steroids, azathioprine, and etretinate, although efficacy is variable (39). Nail lichen striatus and idiopathic trachyonychia are both conditions that may spontaneously resolve. Persistent lichen striatus has been treated with intralesional triamcinolone, while persistent trachyonychia may be treated with topical or intramatricial corticosteroids, tazarotene gel, or topical 5-fluorouracil cream (40,41).

PRP has been proposed as a treatment for inflammatory nail disorders based on its anti-inflammatory properties and constituent growth factors. Literature evaluating treatment of these disorders with PRP is limited to an intra-individual comparable study and 2 case reports. Of these studies, a case report each of nail lichen striatus and idiopathic trachyonychia reported resolution of pretreatment nail changes after intramatricial PRP, and the comparable trial found greater improvement in combination PRP and triamcinolone than in triamcinolone alone (Table 4).

3.7. Psoriasis

Psoriasis is a chronic papulosquamous condition characterized by scaly, erythematous plaques predominately involving the extensor surfaces (44). Psoriasis affects up to 3% of the population worldwide and has a negative impact on patients' overall QOL, including professional, social, and psychological functioning (44). Treatment options include topical corticosteroids, topical vitamin D analogs, off-label use of topical calcineurin inhibitors, phototherapy, and systemic therapy with TNF-α, IL-17, and IL-23 blockers, methotrexate, and topical and systemic retinoids (44). Although treatment options for psoriasis have expanded greatly over the last 15 years, there are significant side effects and contraindications, and treatment dissatisfaction remains high, with 50% of patientswith moderate psoriasis and

Table 3. Evaluation of PRP in melasma.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Mumtaz et al. (37)	Melasma	Rahim Yar Khan, 10/ 1/ 2019–4/30/ 2020	Nonrandomized, controlled clinical trial	64	• Intradermal PRP injections • Tranexamic acid	• MASI score	The PRP group had improved MASI at weeks 4, 12, and 24 compared to control ($p = .01$,.0001, and.02, respectively).
Zhao et al. (33)	Melasma	N/A	Meta-analysis of 10 studies	395	• Intradermal PRP • PRP + tranexamic acid • PRP + laser • microneedling	• MASI score	Of the 9 studies reporting MASI score, the efficacy of PRP alone had a standardized mean reduction in MASI of 1.18 ($p = .02$), but after sensitivity analysis and subsequent removal of 1 study this was not significant. ($p = .492$). The most efficacious treatment based on subjective patient and physician satisfaction was combination PRP and microneedling. ($p < .05$ for all).
Sthalekar et al. (38)	Melasma	N/A	Prospective study	30	• Growth factor concentrate (GFC) injections	• Modified MASI (mMASI) categorized into 'mild' (0–8), 'moderate' (8–16), and 'severe' (16–24)	Number of patients with severe melasma decreased from 23.1% at the beginning of the study to 7.7% at conclusion. The number of patients with moderate melasma decreased from 23.1% to 19.2%, while the number of patients with mild disease increased from 53.8% to 73.1%. ($p < .05$ for all) (32).

Table 4. Evaluation of PRP in inflammatory nail disorders.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Rehman et al. (42)	Lichen planus-associated nail dystrophy	N/A	Intra-individual comparable study	26	• Combination intramatricial PRP injection and triamcinolone • Intramatricial triamcinolone alone	• Clinical response: good (>50% improvement), moderate (25–50%), poor (<25%)	Fingernails treated with combination therapy had a good response in 50% of nails, moderate response in 34.6%, and poor response in 15%, compared to the triamcinolone monotherapy group which had good response in 11.5%, moderate in 38.4%, and poor in 50% of nails ($p = 0.001$). In toenails, treatment with combination therapy had a good response in 48% of nails, moderate response in 16%, and poor response in 36%, compared to the triamcinolone monotherapy group which had good response in 12%, moderate in 24%, and poor in 64% of nails ($p = .004$).
Kaur et al. (43)	Nail lichen striatus	New Delhi	Case report	1 male	• Intramatricial PRP injection	• Clinical exam, onychoscopy	Resolution of pretreatment nail changes
Kaur et al. (43)	Idiopathic trachyonychia	New Delhi	Case report	1 female	• Intramatricial PRP injection	• Clinical exam	Resolution of pretreatment nail changes

40% of patients with severe psoriasis dissatisfied with their current treatments (45).

The pathogenesis of psoriasis involves an inflammatory cascade that is not fully understood but is believed to be mediated by NF-κβ, which serves as a link between immune cells and epithelial keratinocytes and leads to the dysregulated epidermal hyperplasia present in psoriasis (46). The mechanism for which PRP is proposed as a potential treatment for psoriasis is through inhibition of NF-κβ by the growth factors released from platelets (46). The evidence of PRP for plaque psoriasis is minimal and weak, with no RCTs, and the available studies have either no control, or compare combination PRP injections with methotrexate to standard care with methotrexate monotherapy. Nevertheless, data from 2 prospective clinical studies suggest some benefit from PRP (Table 5).

3.8. Wound healing

Systemic conditions such as diabetes mellitus frequently predispose to nonhealing wounds. The prevalence of such chronic illnesses is estimated at 422 million worldwide. Diabetic foot ulcers have a worldwide prevalence of 6.3% and a prevalence in North America of 13.0% (48). Among patients with diabetes, 6% are estimated to develop diabetic foot ulcers, and 85% of all amputations are preceded by an ulcer. Chronic vein abnormalities that predispose individuals to venous ulcers are estimated to be present in up to 50% of individuals (49,50). PRP has been utilized for nonhealing wounds such as diabetic foot ulcers and vascular venous ulcers due to its coagulating, antimicrobial, and regenerative properties (50).

There is currently vast literature assessing the efficacy of PRP in wound healing and includes dozens of RCTs and over 20 meta-analyses. We reviewed PRP for the use of coccygeal pressure ulcers, leprosy ulcers, ulcers of the lower leg, and skin ulcers generally, most of which had improved surface area of the ulcer when treated with PRP (Table 6).

Somewhat related to wound healing is use of PRP in reconstructive techniques such as fat grafting. Autologous fat grafting is a technique commonly used in soft tissue reconstruction and augmentation during plastic and reconstructive surgery of the face, breast, and buttocks due to its bioavailability and convenience of administration. Although the results are satisfactory in the short-term, these benefits often do not persist into the long term, primarily because autologous fat grafts have a high absorption rate (20–80%) (51).

PRP-assisted lipotransfer has been proposed as a technique to increase the viability of the grafted fat and aid in cosmesis after breast tumorectomy. After review of literature, several meta-analyses and controlled studies of fat grafting and breast reconstruction were identified. Only 1 had statistically significant results, finding an increase in microvessel density after PRP (Table 6).

3.9. PRP in cosmetic dermatology

PRP is widely used in cosmetic dermatology for skin rejuvenation and treatment of photoaging and acne scars. The proposed underlying therapeutic mechanism of PRP in cosmetic dermatology involves remodeling of the extracellular matrix via increased expression of matrix metalloproteinases, proliferation of fibroblasts, and collagen synthesis (60).

Table 5. Evaluation of PRP in psoriasis.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Chakravdhanula et al. (46)	Plaque psoriasis	Single center	Prospective pilot study	21	• Combination PRP injection and methotrexate (MTX), or MTX monotherapy	• Psoriasis Area Severity Index (PASI) score	Combination group had reduced erythema, induration, and desquamation, with 62.5% achieving PASI75, and 12.5% achieving PASI90, whereas no patient treated with MTX monotherapy achieved PASI50 although they did improve 35–40% from baseline.
Kauhl et al. (47)	Plaque psoriasis	N/A	Prospective uncontrolled trial	30	• Subdermal PRP injections	• Average lesion size (cm^2)	Average lesion decreased from 8.2 cm^2 to 0.3 cm^2 and 80% of patients achieved complete clearance of skin lesions (PASI100) with the remaining 20% of patients achieving at least PASI70 ($p < .00001$).

Table 6. Evaluation of PRP in wound healing.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Ucar et al. (52)	Stage II coccygeal pressure ulcers	Patients were enrolled January 10–December 31, 2018	RCT	60	• PRP gel and gas dressing • Control: serum physiologic dressing	• Pressure Ulcer Scale for Healing (PUSH) scale	PRP group was found to have decreased ulcer area (2.83 cm^2), exudate amount (score of 0.93) and tissue type (score of 1.2), compared to the control group (5.00, 1.93, 1.97, respectively). ($p = .001$ for all measurements).
Saha et al. (53)	Trophic ulcers in leprosy	Single center, August 2016–May 2018	Observer-blind RCT	118	• Intra-and peri-lesional PRP injections • Control: platelet-poor plasma gel	• Surface area of ulcers (cm^2)	The surface area of the ulcers decreased by 91.10% in the PRP injection group compared to 79.77% the control group. ($p<.001$).
Semenic et al. (54)	Chronic lower leg ulcers	Slovenia	Randomized double-blind trial	60	• PRP gel • Control: hydrogel	• Surface area of ulcers (cm^2)	Wound area in the PRP gel group decreased to 35.1% of the initial area compared to 89.95% in the control group ($p = .001$) with a similar decrease in wound circumferences (54.62% in experimental group, compared to 91.28% in control group; $p = 0.001$).
Paposio et al. (55)	Chronic skin ulcers	N/A	RCT	40	• PRP injections • Control: standard wound care	• Closure rate (cm^2/day)	Control and experimental groups had similar healing rates; however, the experimental group had a higher wound closure rate at .2287 cm^2/day compared to the control group which had a rate of 089 cm^2/day ($p = .0257$)
Sasaki et al. (56)	Autologous fat grafting	February 2015–May 2018	Preliminary, case controlled, clinical trial	10	• Equivalent volumes of combined fat: PRP injections • Control: equivalent volumes of fat: normal saline	• Complex VISIA Investigational Facial Skin Analysis and Facial Vectra XT 3D Volumetric Analysis Imaging • Cortex Facial Skin Analysis	Outcomes were assessed at 3, 6, and 12 months, with a higher but statistically nonsignificant increase in mean volume assessment of the fat/PRP sites from baseline (3 D Vectra Analysis).
Mandour et al. (57)	PRP fat grafting in repair of medium-size tympanic membrane perforation	Tanta University, Egypt, December 2016–December 2017	Prospective randomized controlled study	50	• Myringoplasty with fat graft enriched with PRP • Myringoplasty with cartilage perichondrium graft	• Rates of successful closure at 3-month follow-up • Mean overall improvement in pure tone average and air-bone gap	PRP group had 92% graft take rate at 1 month and 88% at 3 months, compared to 96% at 1 month and 92% at 3 months for control. Mean overall improvement in pure tone average was 18.08 dB in PRP group and 18.24 dB in control. Air bone gap was 14.12 dB in PRP group and 15.64 dB in control ($p > .05$).
Nolan et al. (58)	Autologous fat grafting in diabetic foot ulcers	Single center	3-armed RCT	18	• Fat grafting • Fat grafting with PRP • Control: routine podiatry care	• Biopsies obtained at weeks 0, 1, and 4 with quantitative histology/ immunohistochemistry (H&E, CD31, and Ki67)	Fat grafting group with PRP had increased mean microvessel density at 1 week to 1645 microvessels/mm^2 ($p = .035$).
Chen et al. (51)	Autologous fat grafting	January 2010–January 2020	Meta-analysis of 36 studies	1697 patients	• Control: Fat grafting with cell-assisted lipotransfer (CAL) • PRP-assisted lipotransfer	• Rate of fat survival	CAL- and PRP-assisted lipotransfer improved the fat survival rate 48–71% for CAL and 40–70% for PRP ($p = .0001$ for both), but the difference in fat survival rate between CAL and PRP (71% and 70%) was not significant ($p = .7175$).
Anzarut et al. (59)	Postoperative wound drainage in patients undergoing bilateral reduction mammaplasty	Patients from offices of 11 plastic surgeons recruited between July and December 2004	Blinded, randomized, controlled trial	111	• Topical autologous platelet gel applied to 1 breast after hemostasis achieved • Control: standard treatment in contralateral breast	• Total drainage, mL • NRS (numerical rating scale) average pain score	Total drainage was 70.6 in treatment breasts and 72.2 in control ($p = .672$) Average pain score was 3.3 in treatment breasts and 3.5 in control ($p = .163$).

Our literature review identified 7 meta-analyses focused on acne scars, and 21 RCTs on acne, facial rejuvenation, and photoaging. Most studies investigated PRP as an adjunct therapy to other cosmetic treatments, and although there are some findings favoring PRP, these studies are heterogenous and difficult to compare (Table 7).

3.10. Newer applications and current research on PRP

In addition to the broad array of medical conditions for which PRP has been implicated, several additional medical conditions are currently being evaluated for potential benefit from PRP, including pilonidal sinus disease, wound healing after cesarean section, and periorbital hyperpigmentation (65–67).

An additional focus of active research is elucidating the heterogeneity that is frequently present in studies of PRP treatment. A study of 39 PRP samples from patients undergoing treatment for alopecia evaluated effect of PRP preparation technique on growth factor expression. The growth factors TGFβ1, PDGF, EGF, VEGF, and FGF 2 were quantified but differences in expression were not found to be related to PRP preparation technique (68). It is likely that further research will focus on elucidating possible genetic or environmental factors that may underlie growth factor differences and therefore variability in clinical response to PRP therapy.

4. Discussion

PRP is an autologous therapy prepared from venous blood that has promising results as a surgical adjuvant or regenerative medicine preparation in an array of orthopedic, periodontic, rheumatologic, and dermatologic diseases, and specifically for such chronic dermatologic conditions such as alopecia, melasma, and vitiligo. The therapeutic mechanism of action of PRP occurs via the components that include PDGF, VEGF, TGF-β1, TGF-β2, IGF, fibroblasts, fibrin, and leukocytes. PRP is frequently employed for its immune modulation or suppressive properties, which may be beneficial in conditions such as alopecia areata and vitiligo, in which inflammation has a large role in disease pathogenesis. PRP offers anti-inflammatory, angiogenic, and regenerative properties that may be useful against a broad assortment of conditions including vitiligo, melasma, wound healing, photoaging and acne scars (22). As a surgical adjuvant or wound healing aide, PRP preparations amplify the process of fibrin plug formation. In melasma, TGF-β1 has an inhibitory effect on tyrosinase, the rate-limiting enzyme in melanogenesis, which is in addition to the wound healing and angiogenic effects of the other growth factors. The anti-inflammatory effect in psoriasis is proposed to be through platelet growth factor inhibition of NF-κβ. In androgenic alopecia, activation of MAPK/ERK pathway results in follicular proliferation and differentiation. It is frequently a combination of these mechanisms through which PRP works. One study of erectile function in mice found that PRP may offer neuroprotective benefits as well as its identified anti-inflammatory and regenerative properties (69). In many treated conditions, it is difficult to distinguish between mechanism of anti-inflammatory or anabolic effects of PRP.

There are multiple limitations to the evaluation of PRP studies which limit the conclusions of this review. Although P-PRP is the primary formulation used in dermatology, preparation protocols are not standardized between institutions and frequently are not reported in the literature. In addition, among studies for many dermatologic conditions, the endpoints vary widely limiting the ability to compare studies. Case reports of PRP for cicatricial alopecias reported clinical improvement in terms of subjective improvements in hair density or improvement in perifollicular erythema and scaling. Studies of PRP in vitiligo used a widely varying range of endpoints: the 5 studies reviewed in this paper used a range of endpoints including: percent repigmentation, surface area as determined by computer-assisted grid (VACAG), mean improvement score by physician (MISP), visual analog scale (VAS), and vitiligo disease activity (VIDA) score. In psoriasis, 1 study used PASI while the other study used average lesion size as the clinical endpoints. Clinical endpoints in cosmetic conditions are similarly varied, and include photoaging scores, global esthetic improvement scale, optical coherence tomography, and mean optical density.

Even when studies used the same clinical endpoints, such as the 3 RCTs of alopecia areata that used the SALT scores, there is not consistent benefit from PRP. Only 1 RCT had improvement in the PRP group compared to placebo, with the other 2 RCTs noted similar improvements between the control and PRP treatment groups or greatest improvement in the intralesional corticosteroid group. Similarly, although all the studies we reviewed of androgenic alopecia used hair density and cross-sectional thickness as clinical endpoints, the literature varied widely with some studies showing an increase in both of these endpoints while other studies had no difference or a nonsignificant increase between the treatment and control groups. The inconsistent findings across the androgenic alopecia literature make a case for standardizing the PRP preparation protocol and administration design. In 1 meta-analysis, increased hair density at 6 months was correlated with increased number of sessions, decreased interval between sessions, younger patients, female patients, and whole-head (vs split-scalp) administration (70).

An additional issue with evaluating PRP studies is that frequently PRP is administered in combination with other treatment modalities, rendering these studies extremely difficult to compare. The 5 vitiligo studies reviewed used PRP in combination with different laser therapies, which included excimer laser, CO_2 laser, and NB-UVB. In some of these studies, PRP in combination with laser therapies had improved clinical outcomes, but in other studies there was no difference or a nonsignificant increase in clinical outcomes. There is a similar issue with PRP in melasma studies, with PRP frequently used in combination with tranexamic acid, laser, and microneedling, while for psoriasis, 1 study used PRP in combination with methotrexate vs methotrexate monotherapy, and the second study used intralesional PRP injections in an uncontrolled study. Future research on PRP will be best served by standardization of PRP preparation protocols, study design including treatment groups, and clinical endpoints measured.

Although the efficacy of PRP has frequently been inconclusive, investigation and treatments are rarely limited by adverse effects, with severe adverse effects even more rare. Adverse effects, when present, vary based on mechanism of PRP application, but frequently include injection site pain or erythema, although intra-tendinous or intracapsular injection in orthopedic conditions has been associated with bruising (25). When present, symptoms associated with PRP injections quickly resolved and did not persist. An intra-articular PRP study found that 75% of patients in the PRP group experienced a mild synovitis at one week that resolved spontaneously (71). A RCT of intradermal PRP for rejuvenation of photoaged skin reported local

Table 7. Evaluation of PRP in repair of acne scars, chronic photoaging, and facial rejuvenation.

Study	Condition assessed	Study country: setting: time period	Study design	Number of patients	Therapies	Outcome measures	Outcomes
Long et al. (61)	Atrophic acne scars	N/A	Meta-analysis of 8 studies	311 patients	• Topical PRP + microneedling • Intradermal PRP injections + microneedling	• Goodman and Baron qualitative scores	Improvement was greater in combination therapy than in microneedling alone (MD −16.48, $p<.001$), with results favoring intradermal PRP over topical PRP.
Abuaf et al. (60)	Dermal collagen proliferation, facial rejuvenation	Single center in Turkey, September 2013–December 2013	Prospective, open-label, nonrandomized controlled clinical study	20	• Intradermal PRP injection • Control: intradermal saline	• Mean optical density (MOD)	Skin regions treated with PRP had a higher mean optical density (MOD) of collagen (1019) compared to pretreatment (539) and saline injection (787) ($p < .001$ for PRP side). Patients receiving intradermal PRP treatment had an improvement of 89.05%, compared to a 46.01% improvement in patients in the control group. Improvement ratio from PRP to control was 1.93:1 ($p < .001$ for both).
Gawdat et al. (62)	Glogau photoaging types II and III	N/A	Randomized, split-face study	20	• Intradermal PRP injections • Control: intradermal mesotherapy, a readymade growth factor solution	• Global Esthetic Improvement Scale (GAIS) • Optical coherence tomography (OCT).	No difference between treatment groups according to GAIS at 1 month ($p>.05$). Evaluation by OCT had an increase in both epidermal and dermal thickness after mesotherapy (182–222.55 μm and 220.75–282.85, respectively) and PRP (173.35–222.60, and 226.10-286.70, respectively) ($p<.05$ for all). No significant difference between the 2 treatments was found from OCT ($p > .05$).
Alam et al. (63)	Glogau class II or greater photoaging	Single center, Illinois, August 21, 2012–February 16, 2016	Randomized, masked, split-face clinical trial	27	• Intradermal PRP injections • Control: intradermal normal saline injections	• Photoaging scores	No significant difference between PRP and normal saline in fine lines, mottled pigmentation, skin roughness, or skin sallowness. However, participant self-assessment scores were higher for the PRP-treated side compared with the normal saline side in texture (2.0 vs 1.21 $p = 0.02$) and wrinkles (1.74 vs 1.21 $p = 0.03$) 6 months after injections.
Faghihi et al. (64)	Atrophic facial acne scars	N/A	Split-face, randomized clinical trial	16	• Combination CO_2 laser plus intradermal PRP injections • Control: CO_2 laser plus intradermal normal saline	• Objective dermatologic evaluation on a quartile grading scale	At 1 month, 0% in either group had 'excellent' response, 12.5% and 6.3% had 'good,' 56.3% and 43.7% had 'fair', and 31.2% and 50% had 'poor' improvement in the combination group and FCL monotherapy group, respectively. At 6 months, 0% in either group had 'excellent' response, 31.2% and 31.2% had 'good,' 56.3% and 37.5% had 'fair,' and 12.5 and 50.312 had 'poor' in the combination group and FCL monotherapy group, respectively. No significant improvement was found via objective dermatologic evaluation at either time point ($p = .15$, 0.23).

redness in 18 of 19 patients, swelling in 16, bruising in 14, and pruritus, skin scaling, and skin dryness each in 1 participant. There were no adverse effects at 12 months (63).

The therapeutic application of PRP has been most extensively studied in orthopedics and dentistry (72–75); however, there have been scientific investigations on the extent to which PRP's clinical impact is brought about by factors believed to be directly involved the agent's mechanism of action. For instance, Rodrigues et al. conducted a RCT (PRP vs. saline) where improvement in hair count and density was not correlated with platelet count, nor level of growth factors (76). Therefore, the constituents of administered PRP in the future many vary from that of the current protocols. Similar publications that have quantified specific growth factor composition and platelet concentrations have demonstrated lack of significance of measured constituent quantities. This finding is likely due to inter-individual variations, the short-term effect of platelets only active over a 7-day period, and growth factors being consumed locally or dissolved in the blood after a few days. It seems more likely that stem cell composition and composition of leukocyte formulation—which are diverse and varied in their function, will be more impactful on the efficacy of a PRP preparation.

Despite the appeal of PRP's relative noninvasiveness, well-established safety profile, and scientific mechanism of action, PRP is not an FDA-approved treatment. It is therefore offered to patients as a possibly promising treatment that is expensive and not covered by insurance. The cost of a single PRP injection can be up to $750, and a single treatment course can range between $500 and $2500. It is therefore important that patients be counseled that PRP is not equally well-studied among dermatologic conditions, and for many conditions is still considered an experimental treatment.

The use of PRP in clinical medicine has expanded into many different medical fields. Many studies, as covered in this review, describe its potential utility in the management of a variety of diseases and conditions. While PRP may be considered a potentially efficacious and safe alternative for difficult-to-treat dermatologic conditions like alopecia, the cost, variable results, and inaccessibility limit its use. For case-by-case situations with patients who are able to afford it and have failed previous treatments for their conditions, PRP may serve a greater role in disease management. As the breadth of uses of PRP expands, so to do future directions and avenues of study.

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ORCID

Jessica N. Pixley http://orcid.org/0000-0001-9049-1808
Rohan Singh http://orcid.org/0000-0001-6532-1639

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This manuscript is not associated with a data set.

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