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Narrative Review

Regenerative biologics for aging skin: A narrative review comparing exosomes, mesenchymal stem cell secretome, and platelet-rich plasma

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ABSTRACT

Skin aging reflects a gradual decline in extracellular matrix integrity, cellular senescence, and chronic inflammation. Regenerative biologics such as exosomes, mesenchymal stem cell (MSC) secretome, and platelet-rich plasma (PRP) offer biologically driven approaches aimed at restoring dermal homeostasis. Exosomes and MSC secretome demonstrate antioxidant, immunomodulatory, and collagen-stimulatory effects in multiple preclinical models. Early human data reports improvements in texture, fine lines, erythema, and procedural recovery, especially when used with microneedling or laser resurfacing. PRP remains the most clinically validated therapy, supported by randomized trials demonstrating enhanced periorbital rejuvenation, dermal remodeling, and global photoaging improvement. While exosomes and secretome show strong biological promise, current limitations include product heterogeneity, regulatory constraints, and limited long-term data. PRP offers the most favorable balance of evidence, safety, and accessibility. Further comparative studies are needed to clarify optimal clinical use.

Key words: Skin aging, Photoaging, Exosomes, Extracellular vesicles, Mesenchymal stem cell secretome, Platelet-rich plasma, Regenerative dermatology

INTRODUCTION

Skin aging is driven by intrinsic factors—such as mitochondrial decline, collagen fragmentation, and telomere attrition—and extrinsic insults, such as UV radiation and pollution. These changes trigger fibroblast senescence, extracellular matrix (ECM) degradation, and chronic inflammation [1-3]. Clinically, this manifests as wrinkles, laxity, dyschromia, and impaired barrier recovery.

A shift toward regenerative dermatology has introduced biologic therapies targeting cellular communication and tissue restoration rather than solely corrective interventions. Exosomes, MSC secretome, and PRP represent three leading biologic platforms with converging but distinct mechanisms.

Exosomes are nanoscale vesicles rich in proteins, lipids, and microRNAs that regulate cellular signaling [2,4,5]. MSC secretome contains soluble trophic factors and extracellular vesicles with strong reparative and immunomodulatory effects [6-9]. PRP offers an autologous source of platelet-derived growth factors integral to wound healing [10-12]. This review compares these modalities with emphasis on mechanisms, evidence, and translational considerations.

MATERIALS AND METHODS

This work is a narrative review based on a structured search of PubMed, Scopus, Web of Science, and Google Scholar for articles published between 2015 and 2025. The keywords included *exosomes*, *mesenchymal stem cell*

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secretome, *conditioned medium*, *platelet-rich plasma*, *skin aging*, and *rejuvenation*. Only peer-reviewed, English-language studies relevant to biologic mechanisms, clinical applications, and safety were included. Non-scientific sources and unreviewed commercial materials were excluded. Due to the heterogeneity of study designs, findings were synthesized qualitatively without meta-analysis.

Ethics Statement

This article is a narrative review and does not involve human subjects, patient data, or clinical interventions. Therefore, ethical approval and informed consent were not required.

RESULTS

Exosomes in Skin Rejuvenation

Biological rationale

Exosomes derived from MSCs, dermal fibroblasts, and platelets deliver bioactive molecules capable of stimulating fibroblast proliferation, enhancing collagen I/III synthesis, reducing MMP expression, and attenuating oxidative stress [1-5]. Their microRNA cargo (such as miR-21, miR-29, and miR-146a) modulates pathways central to skin aging [2,3].

Clinical evidence

Clinical use remains emergent but promising. Prospective studies and split-face trials show improvements in fine wrinkles, skin smoothness, erythema, and accelerated healing when exosomes are applied after microneedling, Q-switched toning, or fractional laser resurfacing [4-7]. Most evidence highlights exosomes' synergistic role alongside controlled dermal injury.

Limitations

Challenges include heterogeneity in sources (MSC, fibroblast, platelet), differences in isolation techniques, batch variability, and undefined potency metrics [5-7]. Regulatory classification as biologics limits routine injectable use. Long-term safety data is not yet available.

Mesenchymal Stem Cell Secretome/Conditioned Medium

Biological rationale

MSC secretome includes cytokines (e.g., VEGF, HGF), matrix-modulating proteins, antioxidants, and extracellular vesicles produced during MSC culture [6-9]. Secretome promotes fibroblast proliferation, collagen/elastin synthesis, angiogenesis, and reduced oxidative stress. Umbilical cord MSC secretome demonstrates notable wound-healing and anti-inflammatory potential [7].

Clinical Evidence

Early clinical studies show improvements in hydration, elasticity, radiance, and superficial wrinkles following topical, microneedling-assisted, or intradermal secretome application [6,8]. Secretome enhances re-epithelialization and reduces erythema post-laser resurfacing [7,9].

Limitations

As an allogeneic biologic, secretome varies by donor characteristics and culture conditions. Regulatory classification as an advanced biologic increases oversight [13]. Evidence remains promising but less mature than that for PRP.

Platelet-Rich Plasma (PRP)

Biological rationale

PRP contains concentrated platelets that release PDGF, TGF-β, VEGF, EGF, and IGF-1 upon activation—promoting fibroblast proliferation, angiogenesis, ECM synthesis, and tissue repair [10-12]. Its autologous nature ensures minimal immunogenicity.

Clinical evidence

PRP is the most extensively studied regenerative biologic. Randomized trials and histologic studies show improvements in fine wrinkles, periorbital pigmentation, dermal thickness, and overall photoaging [11,12,14,15]. Combination treatments—microneedling + PRP or fractional laser + PRP—yield consistently superior outcomes [11,14].

Limitations

Variability exists between preparation systems, platelet concentrations, leukocyte content, and injection techniques. Nevertheless, PRP remains a clinically reliable and safe modality.

Comparative Synthesis

Strength of evidence

PRP exhibits the strongest clinical evidence and longest track record [10-12,14-16]. Exosomes show robust mechanistic rationale with emerging clinical

support [1-5]. Secretome presents excellent preclinical data with early but limited human studies [6-9].

Safety

PRP has a well-established safety profile [10-12,14]. Exosomes and secretome appear safe but require better-defined manufacturing standards and long-term data [5,13].

Regulatory considerations

PRP is widely permitted as a minimally manipulated autologous biologic. Exosomes and secretome face stricter biologic regulations [5,13].

To support comparative interpretation, two summary tables were constructed. Table 1 outlines the biological characteristics, mechanisms, evidence strength, and limitations of PRP, MSC secretome, and exosomes. The table clearly demonstrates that PRP currently has the strongest clinical and histologic evidence, whereas secretome offers broad reparative signaling, and exosomes provide advanced molecular precision but remain the least standardized. Table 2 synthesizes practical recommendations for clinical integration across various procedural contexts, including microneedling, fractional resurfacing, and recovery optimization.

DISCUSSION

Regenerative biologics represent a pivotal evolution in dermatologic anti-aging interventions, emphasizing cellular communication and intrinsic repair mechanisms rather than externally imposed structural correction. Although exosomes, MSC secretome, and PRP share overlapping pathways—collagen induction, fibroblast activation, angiogenesis, and inflammatory modulation—their biological precision, clinical maturity, and translational readiness differ significantly.

Exosomes: Mechanistic Sophistication, Early-Stage Translation

Exosomes embody the most advanced biological design, functioning as naturally targeted delivery systems for microRNAs, proteins, and lipids. Their ability to modulate oxidative stress pathways, downregulate MMPs, suppress NF-κB, and enhance type I collagen synthesis positions them as elegant molecular regulators of skin aging [1-4]. However, clinical application remains at an early phase, with current evidence largely limited to small studies and adjunctive procedural use [4,5]. Major translational barriers include variability in manufacturing, the absence of standardized potency assays, and stringent regulatory oversight. Without GMP-certified exosomal platforms and long-term safety data, their role remains primarily experimental.

MSC Secretome: Broad, Physiologic Repair Signaling

Secretome contains a diverse array of soluble factors and extracellular vesicles that more closely mimic the native paracrine activity of MSCs. This breadth of signaling—spanning angiogenesis, antioxidant pathways, ECM remodeling, and immunomodulation—offers a physiologic and multi-modal regenerative approach [6-9]. Early clinical results show meaningful

Table 1: Comparative summary of PRP, MSC secretome, and exosomes in skin rejuvenation

Parameter	PRP	MSC secretome	Exosomes
Biological source	Autologous platelets	Allogeneic MSC-derived factors	MSC/fibroblast/platelet EVs
Key mechanisms	Growth factor–mediated fibroblast activation	Broad reparative signaling & immunomodulation	miRNA-driven targeted molecular regulation
Evidence strength	Strong (multiple RCTs)	Moderate (early clinical data)	Emerging (small early trials)
Clinical benefits	Texture, fine lines, periorbital aging	Hydration, elasticity, recovery	Redness reduction, post-procedure healing
Limitations	Preparation variability	Donor variability	Lack of standardization & regulatory constraints
Safety	Excellent	Generally safe; allogeneic	Appears safe; long-term data limited
Best use	Microneedling combination	Adjunct to resurfacing	Post-laser healing+procedural booster

Table 2: Clinical integration and practical recommendations

Clinical scenario	Most suitable biologic	Rationale
Collagen induction/dermal remodeling	PRP	Reliable growth-factor–driven fibroblast activation; strongest evidence
Post-laser recovery (ablative/non-ablative)	Secretome or exosomes	Superior anti-inflammatory, healing acceleration, barrier recovery
Patients needing rapid downtime reduction	Exosomes	Best redness reduction and post-procedure comfort
Patients preferring autologous therapy	PRP	Excellent safety and regulatory simplicity
Enhancing hydration and elasticity	Secretome	Broad trophic signaling and ECM support
Maximal synergistic rejuvenation	PRP+Secretome/Exosomes	Complementary mechanisms (stimulation+modulation)

improvements in elasticity, hydration, and recovery post-resurfacing. Secretome has advantages over exosomes in manufacturing scalability and biological robustness, yet it remains limited by donor variability, regulatory complexities, and non-standardized assays.

PRP: Clinically Established and Translationally Mature

PRP remains the benchmark among regenerative biologics. Its mechanisms—rooted in platelet-derived growth factor release—are highly aligned with phases of wound healing and dermal repair [10-12]. Randomized controlled trials consistently demonstrate improvements in fine lines, periorbital changes, and overall texture [10-12,14,15], while histologic evidence confirms enhanced collagen density and dermal architecture. Unlike exosomes and secretome, PRP benefits from strong regulatory acceptance, minimal immunogenicity, affordability, and widespread accessibility. Its limitations, centered on preparation variability, are comparatively minor and manageable.

Current evidence establishes a clear functional hierarchy among regenerative biologics for aging skin. PRP remains the most reliable and clinically validated modality, supported by controlled trials, histologic data, and predictable safety. MSC secretome represents an intermediate option with broad reparative signaling and promising early clinical results, yet still limited by variability and the need for stronger standardization. Exosomes, while mechanistically the most advanced, remain the least standardized and least supported by high-quality clinical data, placing them at the earliest stage of translational readiness.

In practice, the most consistent outcomes arise from procedure-integrated applications rather than standalone biologics. PRP combined with microneedling reliably enhances collagen induction. Secretome or exosomes applied after laser resurfacing accelerate recovery and improve dermal remodeling. Increasingly, clinicians use multi-modal, tailored combinations to achieve synergistic benefits aligned with individual patient needs and aging profiles.

The comparative tables reinforce the therapeutic hierarchy observed in current literature. As illustrated in **Table 1**, PRP remains the most evidence-supported biologic, driven by reproducible growth-factor stimulation and strong safety. Secretome occupies an intermediate position with wide-ranging reparative signals, while exosomes—although mechanistically sophisticated—are constrained by standardization and regulatory gaps. **Table 2** highlights that optimal outcomes arise from procedure-integrated approaches. PRP reliably enhances collagen induction with microneedling, whereas secretome and exosomes are superior as post-resurfacing modulators, accelerating healing and improving overall rejuvenation. These tables emphasize that biologics should be selected based on therapeutic precision, patient needs, and procedural context.

Remaining Gaps and Future Directions

Despite promising developments, regenerative biologics cannot advance without resolving several critical gaps. The field urgently requires standardized potency assays, direct comparative trials, and robust long-term safety data, particularly for allogeneic products. Clear dose–response parameters and protocol standardization are also needed to minimize clinical variability. Future studies must incorporate biomarker-based, imaging, and histologic endpoints to objectively quantify outcomes. Only through these scientific refinements can regenerative therapies transition from emerging innovations to reliable, evidence-driven dermatologic interventions. Advancements in GMP manufacturing, machine-learning–assisted phenotyping, and personalized biologic formulations may further refine regenerative dermatology.

CONCLUSION

Exosomes, MSC secretome, and PRP each offer unique regenerative advantages for aging skin. At present, PRP remains the most validated option for routine clinical use. Exosomes and secretome demonstrate compelling biological potential and are likely to become central tools in dermatologic rejuvenation as manufacturing quality and evidence advance.

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