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Exosomes in Skin Rejuvenation: Systematic Review of Anti-Aging Effects and Clinical Applications

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ABSTRACT

Introduction: Exosomes, tiny extracellular vesicles (EVs) from different cell types, are gaining attention in dermatology due to their unique properties. They enhance cell communication, transport bioactive substances, and influence immune responses, making them valuable for skin regeneration, wound healing, and addressing skin conditions.

Objectives: This systematic review explored current evidence regarding the efficacy, safety, and mechanisms of exosomes in skin rejuvenation.

Methodology: The search strategy included several databases: PubMed, Google Scholar, MEDLINE, Wiley, Web of Science, and EBSCO. The search for PubMed, MEDLINE, Wiley, Web of Science, and EBSCO used keywords: (Exosomes) AND (Skin Rejuvenation OR Skin Aging OR Skin Wrinkles), with MEDLINE limited to title-only searches. Google Scholar utilized broader terms: (Exosomes) OR (Extracellular Vesicles) OR (Exosomes Secreted by Human Circulating Fibrocytes) AND (Skin Rejuvenation OR Skin Wrinkles OR Skin Aging OR Skin Elasticity).

Results: Of the 1032 papers extracted through the database search, 21 articles were considered suitable for the systematic review. The reviewed studies consistently demonstrated that EVs and exosome-based therapies significantly improve skin elasticity, reduce wrinkle depth, enhance hydration, and modulate pigmentation. These effects were supported by molecular evidence showing increased collagen and elastin synthesis, reduced oxidative stress, and suppression of matrix metalloproteinases. Treatments derived from adipose stem cells, platelets, plants, and milk exhibited favorable safety profiles with minimal adverse events and high patient satisfaction.

Conclusion: In conclusion, extracellular vesicles and exosome therapies represent a promising, minimally invasive approach for skin rejuvenation and anti-aging. However, further standardized clinical trials with larger cohorts and longer follow-up are needed to confirm efficacy, optimize protocols, and ensure long-term safety. Integrating EV-based treatments into personalized skincare regimens could revolutionize dermatological anti-aging strategies.

Introduction

Exosomes are small extracellular vesicles (EVs), typically around 100 nm in diameter, that are released by cells and carry various molecular components from their originating cells, such as RNA, DNA, proteins, lipids, amino acids, and metabolites [1]. All cell types produce EVs, which can be found in all body fluids, with exosomes being a specific type originating from endosomes. Their composition indicates that they play a significant role in facilitating cell communication [2].

Research has shown that exosomes facilitate communication and transfer between cells in the skin, contributing to the balance and upkeep of tissue health. This process reveals a significant connection with the underlying mechanisms of persistent inflammatory skin disorders [3,4]. Moreover, extracellular vesicles produced by mesenchymal stem cells (MSC-EVs), highlighted for their involvement in wound healing, contribute beneficial properties such as promoting blood vessel formation, reducing inflammation, and preventing fibrosis. This has led to the recent application of stem cell-derived exosomes in conditioned media for skin rejuvenation treatments [5]. Various extracellular vesicles derived from stem cells (SC-EVs) have also been identified as contributing to anti-aging effects [6]. Research shows that exosomes obtained from mesenchymal stem cells sourced from human umbilical cord blood (UCB-MSCs) can enhance the migration of cells and stimulate collagen production in human dermal fibroblasts (HDFs), thereby addressing key markers of skin aging such as loss of elasticity and dermal thinning [7].

The effectiveness of exosomes in clinical applications hinges on the standardization of their isolation techniques. Currently, ultracentrifugation is acknowledged as the benchmark method for this purpose. However, alternative techniques have emerged, including ultrafiltration, immunoaffinity methods, and precipitation. The challenge with these approaches lies in achieving a selective isolation of exosomes without contaminating the sample with other extracellular matrix components. To obtain samples of pure exosomes, it is often necessary to combine various methods, which can raise costs, and necessitates more advanced technical skills [8]. After isolating the exosomes, it is important to analyze them to characterize their purity and concentration due to variability in final yield. Electron microscopy is useful for examining morphology and visualizing the structures associated with the exosome membrane. Dynamic light scattering and nanoparticle tracking assess size distribution and concentration. Additionally, immunological techniques like flow cytometry and western blotting utilize specific markers to identify exosomes, which typically express tetraspanins (CD9, CD63, CD81) and heat shock proteins (HSP70, HSP90) [9,10]. Mass spectrometry is utilized to identify and quantify the molecular constituents of exosomes, including proteins, nucleic acids, and lipids. Furthermore, quantitative reverse transcription polymerase chain reaction (qRT-PCR) is employed to confirm and quantify the RNA present within the exosomes [11–13].

Exosomes have recently gained attention as a potential method for nucleic acid-based therapies. Their natural compatibility with the body, capability of traversing biological barriers, and minimal immunogenic response make them particularly appealing. Since exosomes are produced by cells within the human body, they are thought to elicit fewer inflammatory reactions [14]. Additionally, when compared to regenerative cell therapies, where live cells such as stem cells are utilized to mend or replace damaged tissues, exosomes offer various benefits, including enhanced stability, lower toxicity levels, better compatibility with bodily systems, and diminished chances of immune rejection and tumor formation due to the absence of living cells in their application [15].

Exosomes are natural mediators of cell communication and tissue repair, showing significant potential for skin rejuvenation and anti-aging. They enhance collagen synthesis, reduce wrinkles, improve elasticity, diminish pigmentation,

and promote regeneration, making them better suited than cell-based therapies due to their lower risk of immunogenicity [16]. These outcomes align closely with clinical endpoints evaluated in current studies, including wrinkle depth, hydration, pigmentation modulation, and patient satisfaction. However, clinical applications are limited by inconsistent isolation methods, variability in exosome quality, and a lack of standardized protocols.

Objectives

This systematic review explored current evidence regarding the efficacy, safety, and mechanisms of exosomes in skin rejuvenation and anti-aging, situating findings within the broader context of aesthetic and regenerative dermatology. It also evaluated how different isolation techniques affect therapeutic outcomes and identified research gaps to guide future studies and clinical standardization.

Methods

This systematic review, registered with PROSPERO under the identifier CRD420250655603, was conducted following the PRISMA framework guidelines for systematic reviews and meta-analyses [Figure 1].

Literature Search Strategy

The search strategy involved several databases, including PubMed, Google Scholar, MEDLINE, Wiley, Web of Science, and EBSCO. For PubMed, MEDLINE, Wiley, Web of Science, and EBSCO. The search used simplified keywords: (Exosomes) AND (Skin Rejuvenation OR Skin Aging OR Skin Wrinkles). MEDLINE specifically limited the results to title-only searches. In contrast, Google Scholar utilized broader terms such as: (Exosomes) OR (Extracellular Vesicles) OR (Exovesicles) OR (Exosomal Membrane Proteins) OR (Mesenchymal Stem Cell-Derived Exosomes) OR (Exosomes Secreted by Human Circulating Fibrocytes) OR (Plant-Derived Exosome-Like Nanoparticles) OR (Exosomes of Adipose Stem Cells) AND (Skin Rejuvenation OR Skin Wrinkles OR Skin Aging OR Skin Elasticity). The search covered publications from January 2018 through March 2025, capturing both preclinical and clinical studies within this timeframe [2].

Inclusion and Exclusion Criteria

Inclusion Criteria

Original research articles involving human participants, animal models, or relevant in vitro cell cultures; investigating the effects of extracellular vesicles (EVs), exosomes, or stem cell-conditioned media; reporting quantitative or qualitative

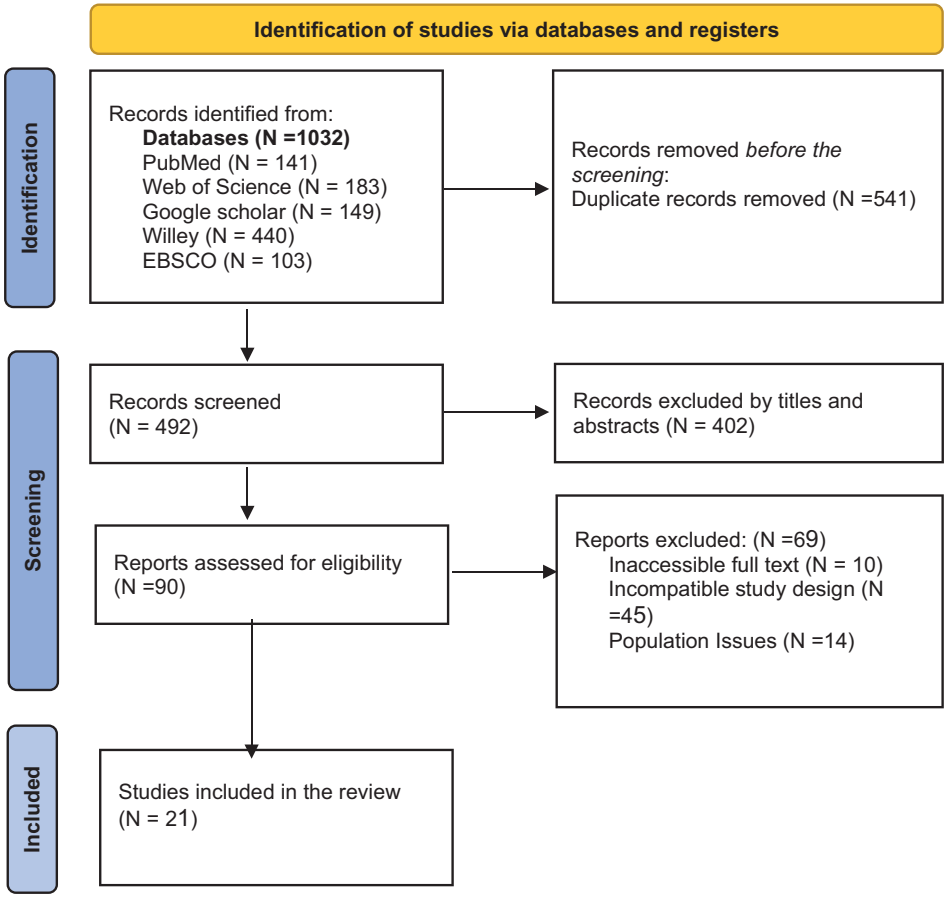

Figure 1. PRISMA flow diagram for selecting studies in the systematic review.

outcomes relevant to skin aging or rejuvenation, including skin elasticity, wrinkle reduction, hydration, pigmentation, molecular markers of aging, or safety profiles; published in peer-reviewed journals in English.

Exclusion Criteria

Non-primary literature such as review articles, editorials, or conference abstracts; studies focused on non-skin tissues or disease models unrelated to skin aging; studies lacking sufficient methodological detail to assess quality; absence of relevant outcome data; duplicate publications or overlapping datasets.

Note on Language Restriction

The search was limited to English-language publications due to constraints in translation and quality assessment. We acknowledge that this may have introduced a potential language bias, meaning relevant studies published in other languages may have been omitted [3,4].

Selection of Articles and Data Extraction

Two independent authors reviewed and screened the full text of eligible studies based on predefined criteria. The data were manually extracted into an Excel spreadsheet. Data extraction was performed using a standardized form to collect key information from each study, including study design, sample size, EV source and preparation method, treatment protocols, outcome measures (e.g., skin elasticity, wrinkle reduction, hydration), molecular findings, safety data, and patient-reported outcomes. Discrepancies between reviewers were resolved through discussion or consultation with a third reviewer to ensure accuracy and consistency.

Quality Assessment

The Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to evaluate methodological quality across six domains: selection bias (randomization/allocation), performance bias (blinding of participants/personnel), detection bias (blinding of outcome assessors), attrition bias (missing data handling), reporting bias (selective outcome reporting), and other biases (e.g., conflicts of interest). Each domain was rated as low, high, or unclear, with the overall risk reflecting the highest bias level identified [5]. The SYRCLE Risk of Bias tool was applied to systematically assess the rigor of animal experiments, focusing on factors such as selection bias, baseline characteristics, performance bias, detection bias, attrition bias, reporting bias, and other methodological elements [6]. In vitro studies face similar methodological challenges, particularly concerning design integrity, and researchers have adapted this tool for use in cell-based investigations [7].

Moreover, the methodological quality of nonrandomized studies (retrospective, prospective, cohort, and case-control) was assessed using the Methodological Index for Non-Randomized Studies (MINORS) tool [8]. Each study was assigned a unique identifier and categorized by design. Twelve criteria were evaluated on a scale from 0 to 2, where 0 indicated not reported, 1 represented inadequate reporting, and 2 denoted adequate reporting. Criteria 1–8 applied to all studies, while items 9–12 were specific to comparative studies. Total scores ranged from 0 to 16 for non-comparative studies and from 0 to 24 for comparative designs, with higher scores indicating better methodological quality.

The Methodological Quality of Case Series and Case Reports tool was also applied to assess four domains: selection (criteria for participant inclusion), ascertainment (accuracy in outcome measurement), causality (plausibility of cause-effect relationships), and reporting (completeness of methodological details) [38]. Higher total scores indicated stronger methodological clarity. Although there is no universally established cutoff to categorize risk levels as "low," "moderate," or "high," individual item scores and overall performance were critically analyzed to assess study reliability [9].

Results

A total of 1032 papers were extracted from five databases (PubMed, Web of Science, Google Scholar, Wiley, and EBSCO). After screening and eligibility assessment, 21 studies were considered suitable for inclusion in the systematic review (Figure 1).

Table 1 summarizes studies published between 2019 and 2025 which evaluated exosome-based interventions for skin rejuvenation, anti-aging, and repair. These included preclinical in vitro and in vivo animal models, clinical trials, and retrospective evaluations, conducted across multiple countries including China, South Korea, the USA, Italy, Vietnam, and Indonesia.

The studies explored the therapeutic potential of exosomes derived from diverse sources such as human adipose-derived stem cells (ASCs), platelet extracts, placental mesenchymal stem cells, bovine milk, fungi, and plant extracts. Two recent animal studies on plant-derived exosomes were also identified (Adel et al., 2025a; Adel et al., 2025b), which demonstrated accelerated wound healing and modulation of inflammatory cell counts, supporting their role in tissue repair and potential anti-aging applications [13–15].

Exosome isolation methods most commonly included ultracentrifugation, density gradient centrifugation, filtration, and proprietary purification approaches. Delivery methods varied from topical applications, often enhanced with microneedling or adjunct therapies, to subcutaneous or intradermal injections. Treatment protocols ranged from single in vitro applications to multi-week topical regimens in clinical settings [16,17].

Table 1. Study characteristics for exosome-based interventions for skin aging and related conditions.

First author, year	Study design	No. of samples / Type	Mean (SD) age (years)	Sex (M/F, N)	Skin type / Targeted condition	Source of exosomes	Exosome preparation method & Delivery	Dosage & Concentration
Nguyen et al., 2024 [13]	Prospective, placebo-controlled clinical trial (Vietnam)	3	30–40	NR	Aging, photoaging	ASCs	Tangential flow filtration + sucrose cushion ultracentrifugation; Topical	1 µg ASC-sEVs (~1.21×10^9 particles), 2 µg NR, 1 µg NAD+, 1 µg Res in 0.1 mL saline; once daily × 8 weeks
Svolacchia et al., 2024 [14]	Retrospective clinical evaluation (Italy)	72	Mean 48 (34–68)	72F	Aging, wrinkles, hyperpigmentation, photoaging	Adipose-derived MSCs	Microfiltration (20/40 µm) + ultrafiltration (0.20 µm) with Skin-B®; Injection	3 mL (~450 million CD81+ vesicles); single session; FU at 15 & 30 days
Wyles et al., 2024a [15]	Prospective, single-arm, evaluator-blinded (USA)	56	54 (11)	4M/48F	Fitzpatrick I–VI; aging, wrinkles, pigmentation, loss of luminosity	HPE	Leukocyte-depleted, pooled apheresed platelets; Topical (twice daily)	12 weeks, twice daily
Wyles et al., 2024b [16]	Prospective, single-center, longitudinal (USA)	20	54 (11)	2M/18F	Fitzpatrick I–II (19), III–VI (1); aging, senescence	HPE	Platelet extract (method NR); Topical (twice daily)	12 weeks, twice daily
Chernoff et al., 2023 [17]	Non-randomized controlled trial (USA)	40	34–72	5M/35F	Aging (wrinkles, pores, pigmentation, oiliness)	Placental MSC-derived (Kimera Labs)	Purified in saline (cGMP); Topical infusion + ultrasound/LED; some + CaHA	1.0 cc = 1 million exosomes; single session; FU at 15 & 30 days; additional CaHA, NO serum, exfoliation, LED
Park et al., 2023a [18]	12-week RCT, split-face (South Korea)	28	54 (7.8), range 43–66	8M/20F	Fitzpatrick III (43%), IV (57%); aging (wrinkles, elasticity, hydration, pigmentation)	ASCEs	Lyophilized vials (SRLV-5, ExoCoBio); reconstituted; Topical + microneedling (1 mm)	2 mL = 5×10^9 particles/ session; 3 sessions (q3wks); FU 6 weeks
Park et al., 2023b [19]	Case series (South Korea)	5	25–43	5F	Wound healing, scar reduction (surgical, burns, keloids)	Pharyngeal-derived exosomes (EXOP, Exodew)	Lyophilized, reconstituted; Topical ± microneedling	½–⅓ vial/session; 3–5 sessions; interval 1–3 days
Proffer et al., 2022 [20]	Prospective, single-arm trial (USA)	5	54 (11), range 10–80	8M/48F	Fitzpatrick I–IV; facial photodamage, wrinkles, erythema, pigmentation	HPE	Allogeneic, leukocyte-reduced platelet extract (proprietary); Topical	Twice daily × 6 weeks + skincare regimen

Table 1 continues

First author, year	Study design	No. of samples / Type	Mean (SD) age (years)	Sex (M/F, N)	Skin type / Targeted condition	Source of exosomes	Exosome preparation method & Delivery	Dosage & Concentration
Jo et al., 2022 [21]	Clinical pilot (placebo-controlled) + in vitro (Korea)	16 volunteers	40–50	16F	Aging (wrinkles, elasticity, hydration, pigmentation)	LpEVs (skin of young women)	Ultracentrifugation; Topical with 5% mannitol	In vitro: 0.625–10% LpEVs (24h); Clinical: 5% mannitol + LpEVs; BID × 4 weeks
Lu et al., 2024[22]	In vitro + non-randomized clinical trial (China)	31 humans + animals	26–45	31F	Anti-aging (moisturization, wrinkle reduction)	Bovine milk-derived exosomes	Density gradient centrifugation; Topical	60 μg/mL MK-Exo; BID × 28 days
Han et al., 2022 [23]	In vitro + in vivo (China)	40 humans + 24 mice	Humans: 20–35	Mice: F	UV-induced aging (wrinkles, pigmentation, collagen loss)	FELNVs (Phellinus linteus)	Isolated FELNVs; Human: 2% PL cream; Animal: topical pre-UV	Humans: 2% PL × 28 days; Mice: 3×/wk × 4 weeks; In vitro: 10–100 μg/mL
Li et al., 2024a [24]	Preclinical, in vitro + in vivo (China, Taiwan, Malaysia)	39 nude mice	8 weeks	24M/15F	Senescence, skin aging	HADSCs	Ultracentrifugation; Subcutaneous injection	10×, 20×, 40× HADSC-CM; injections at days 10 & 20
Wang et al.., 2019 [25]	In vitro + in vivo mouse study (China)	6 BALB/c mice	NR	NR	Skin rejuvenation, photoaging	UCMSCs	Ultrasonication + centrifugation/filtration (eEVs); ultracentrifugation (nsEVs); Intradermal injection	In vitro: 200 μg/mL × 3 days; In vivo: 200 μg EVs/200 μL PBS, single
Sanada et al., 2022 [26]	In vitro + immunohistochemistry (Japan)	Triplicate assays + 16 human tissues	<40 (young), >60 (old)	11M/5F	Aging (↓ collagen synthesis in fibroblasts)	DSPCs (SF8428 line), compared with HDF & ASCs	Ultracentrifugation (100,000×g, 70 min), 0.2 μm filter; Culture medium addition	Dose-dependent; 50 μg/mL most effective; 24h incubation
Li et al., 2024b [27]	In vitro (China)	Human dermal fibroblasts	NR	NR	Aging (oxidative stress)	Cow's milk (MK-Exo)	Sucrose density gradient centrifugation + ultracentrifugation; In vitro	Single 24h treatment, dose-dependent
Cho et al., 2022 [28]	In vitro transcriptomics (South Korea)	NR	NR	NR	Aging, regeneration, moisturization	Plant-derived (ginseng, green tea, cica, purslane)	High-pressure processing, ultracentrifugation, ATPS; In vitro	2% extracts or 1×10^8/mL plant exosomes; 6h treatment

First author, year	Study design	No. of samples / Type	Mean (SD) age (years)	Sex (M/F, N)	Skin type / Targeted condition	Source of exosomes	Exosome preparation method & Delivery	Dosage & Concentration
Guo et al., 2022 [29]	In vitro (China)	6 (3 ADSCs, 3 HDFs)	ADSCs: 25±5; HDFs: >60	6F	Aging (senescence, ECM synthesis)	ADSCs	Ultracentrifugation (110,000×g)	20 µg/mL ADSC-Exos; single treatment, measured 0–72h
Vu et al., 2022 [30]	In vitro (Vietnam)	Triplicate assays	NR	NR	Aging, ECM integrity	UCMSCs ± TGF-β priming	Differential centrifugation; In vitro	10 µg/mL; single treatment
Oh et al., 2018 [31]	In vitro (South Korea)	NR	NR	NR	Aging (photoaging, senescence)	Human iPSCs	ExoQuick-TC™ precipitation; In vitro	3×10^8–315×10^8 particles/mL; 24–48h
Adel et al., 2025a [32]	Preclinical, in vivo (rat wound model)	40 rats	NR	NR	Wound healing, skin repair	Plant-derived exosomes	Ultracentrifugation from plant extracts; Intradermal injection	Dose-dependent, single & repeated
Rasti et al., 2025b [33]	Preclinical, in vivo (rat inflammation model)	36 rats	NR	NR	Wound healing, inflammation	Plant-derived exosomes	Ultracentrifugation & purification; Local injection	Repeated injections; inflammatory outcomes measured

Abbreviations: ADSCs: adipose-derived stem cells, ASCs: adipose stem cells, CM: conditioned medium, EVs: extracellular vesicles, FELNVs: fungi exosome-like nanovesicles, F: female, HADSCs: human adipose-derived stem cells, HDF: human dermal fibroblasts, HPE: human platelet extract, iPSCs: induced pluripotent stem cells, LpEVs: Lactobacillus plantarum extracellular vesicles, M: male, NA: not applicable, NR: not reported, SD: standard deviation.

Of the 21 included studies, 14 (61%) investigated exosomes as monotherapy, while nine (39%) combined them with adjunctive modalities such as microneedling, vitamin C, nitric oxide serum, hydrogels, or calcium hydroxylapatite (CaHA). This distribution provides insight into the independent effects of exosomes and their potential for synergy in combination therapies [18].

Table 2 presents an overview of clinical and experimental studies investigating extracellular vesicles (EVs), exosomes, and stem cell-derived products in relation to skin aging parameters such as elasticity, wrinkle reduction, hydration, and collagen synthesis [10]. Both preclinical and clinical findings highlight the substantial benefits of these therapies for skin rejuvenation [13]. Consistent improvements were reported in skin elasticity, wrinkle reduction, hydration, and extracellular matrix remodeling, with supporting molecular evidence showing enhanced collagen and elastin synthesis alongside reduced oxidative stress markers [24]. For instance, adipose-derived stem cell conditioned medium (HADSCs-CM) restored collagen levels after UVA-induced damage [24], while human platelet extract (HPE) reduced senescent cells and inflammatory markers, thereby facilitating ECM repair [16]. In addition, plant- and milk-derived exosomes demonstrated antioxidant and moisturizing effects, contributing to skin barrier protection and improved hydration [22].

Mechanistically, EV- and exosome-based treatments act by:

- modulating oxidative stress and inflammation [9]
- suppressing matrix metalloproteinases (MMPs) [28]
- promoting fibroblast proliferation and migration [26]
- activating collagen synthesis and ECM gene expression pathways [30]

Moreover, production and isolation methods such as ultrafiltration, ultracentrifugation, density gradient centrifugation, and lyophilization were shown to affect both the purity and therapeutic potential of exosomes [1]. Importantly, specific exosomal cargoes, including microRNAs, growth factors, and ECM-related proteins, were implicated in driving anti-aging effects [2].

Overall, the findings from Table 2 demonstrate that EV- and exosome-based therapies represent promising, minimally invasive, biologically active approaches for skin rejuvenation and anti-aging [11]. Future research should focus on optimizing dosage, refining delivery methods, ensuring long-term safety, and validating efficacy across diverse exosome sources [10]. Due to their level of detail, the full versions of Table 1 (study characteristics) and Table 2 (clinical and experimental outcomes) are provided in the Supplementary Materials. Concise summaries are included here to highlight the most clinically relevant findings.

Table 3 displays the quality assessment of one RCT study using the ROB 2 quality assessment tool [35]; this RCT showed a low risk of bias.

Bias and Quality Assessment

The methodological evaluation of the included studies was conducted using SYRCLE's Risk of Bias (RoB) tool for preclinical studies [36], MINORS for non-randomized clinical studies [37], and Methodological Quality Tool of case reports and case series [38], as summarized in Tables 4 and 5.

Preclinical Studies (SYRCLE Assessment)

Table 4 presents the quality assessment of animal and in vitro studies. Most studies demonstrated low concerns for baseline characteristics and attrition, indicating that the cell populations or animal subjects were generally homogeneous and data loss was minimal [24]. However, several studies lacked detailed reporting on random allocation, allocation concealment, and blinding procedures for treatment administration and outcome assessment [1]. These shortcomings suggest that while the studies generally maintained rigorous experimental conditions, certain aspects of the study design require greater transparency to strengthen reproducibility. Overall, animal studies typically achieved low-to-moderate methodological clarity, whereas in vitro studies showed moderate robustness, with room for improved reporting of experimental controls and randomization procedures [24].

Nonrandomized Clinical Studies (MINORS Assessment)

The MINORS (Methodological Index for Non-Randomized Studies) evaluation (Table 5) indicated that most of the non-randomized studies clearly defined their aims, employed consecutive patient inclusion, and applied appropriate endpoints aligned with study objectives [13]. Prospective data collection and follow-up periods were generally well conducted, and attrition was minimal [14]. Nevertheless, prospective calculation of study size was consistently absent, and comparative studies often faced challenges related to establishing adequate control groups, ensuring baseline equivalence, and confirming group comparability [18]. These limitations affected their overall methodological rigor. Non-comparative studies scored in the lower-to-mid-range, reflecting minor but important opportunities for improving study design, while comparative studies achieved moderate robustness, demonstrating adequate but improvable methodological clarity and statistical analysis [13,18].

Case Series Study (The Methodological Quality of Case Series and Case Reports tool)

The Methodological Quality of Case Series and Case Reports tool of case series (Table 6) showed that the case series

Table 2. Summary of clinical and experimental outcomes of extracellular vesicle and exosome-based therapies for skin aging and rejuvenation.

First author, year	Skin elasticity improvement & patient satisfaction	Wrinkle reduction	Skin hydration	Collagen/elastin increase	Pigmentation changes	Adverse events	Conclusion	Therapy type
Nguyen et al., 2024 [13]	104% increase (API-100)	NR	+19% hydration (GPSkin Barrier)	NR	↓ melanin (API-100), inconsistent with Antera 3D	NR	ASC-sEVs improved skin texture, hydration, elasticity, pore reduction	Monotherapy
Svolacchia et al., 2024 [14]	High satisfaction (Berardesca Scale)	Significant ($p<0.0001$)	Improved hydration ($p<0.0001$)	ECM upregulation (RNA-seq)	NR	None	Ultrafiltration-extracted vesicles safe & effective for wrinkles, inflammation	Monotherapy
Wyles et al., 2024a [15]	NR	94.6% noted wrinkle improvement	87.3% improvement in aging	↑ collagen thickness, ↑ elastin	↓ pigmentation (36%)	Dry skin (16.3%)	Platelet-derived EVs improved skin texture, tone, pigmentation	Monotherapy
Wyles et al., 2024b [16]	Reduced p16^INK4a, ↓ telomere damage	NR	NR	↑ ECM-related genes	NR	NR	Topical HPE reduced senescence signaling, ↑ ECM remodeling	Monotherapy
Chernoff et al., 2023 [17]	High patient satisfaction	Quantificare imaging: improved	NR	NR	↓ unwanted pigment	None	MSC exosomes + adjunct infusion/NO serum improved angiogenesis, wrinkles	Combination
Park et al., 2023a [18]	↑11.3% elasticity	Wrinkle reduction (Ra, Rt, Rz)	+6.5% hydration	↑ collagen, elastic fibers	↓ melanin index (–9.9%)	Mild transient erythema, petechiae	Microneedling + HACS enhanced rejuvenation	Combination
Park et al., 2023b [19]	Wound healing/ scar reduction	NR	NR	NR	NR	NR	Case reports: exosomes expedited wound healing, scar reduction	Monotherapy
Proffer et al., 2022 [20]	↑ Skin Health Score	Wrinkles ↓ (VISIA-CR, PRIMOS)	9/56 dry skin	↑ skin health, collagen	↓ brown spots, ↑ luminosity	Dryness 16.1%	Topical platelet exosomes safe, effective for photodamage	Monotherapy
Jo et al., 2022 [21]	↑27% elasticity (Cutometer)	↓15.9% wrinkle index (Antera 3D)	↑21% hydration	↑ Type I procollagen, ↑ HAS2 (in vitro)	↓ pigmentation (image analysis)	NR	LpEVs boosted ECM genes, reduced wrinkles, improved pigmentation	Monotherapy
Lu et al., 2024 [22]	↑7% elasticity	Wrinkle area ↓9.6%	+5.6% hydration	Restored Col I/III post-UV	NR	NR	MK-Exo moisturized, ↓ wrinkles, ↑ ECM markers	Monotherapy

Table 2 continues

First author, year	Skin elasticity improvement & patient satisfaction	Wrinkle reduction	Skin hydration	Collagen/elastin increase	Pigmentation changes	Adverse events	Conclusion	Therapy type
Han et al., 2022 [23]	↑ collagen density	Wrinkle % improved ($p<0.05$)	NR	↑ COL1A2 expression	↓ brown/UV spots	NR	Fungal exosome-like vesicles demonstrated cross-species anti-aging via miRNAs	Monotherapy
Li et al., 2024a [24]	↓ dermal thickness, ↑ collagen	NA	NR	↑ collagen restoration post-UVA	NR	NR	HADSC-CM reduced dermal aging, ↑ collagen & VEGF	Monotherapy
Wang et al.., 2019 [25]	NR	NR	NR	↑ collagen, ↓ MMP-1/MMP-3	NR	NR	UCMSC EVs enhanced wound healing, ↓ UVB damage	Monotherapy
Sanada et al., 2022 [26]	NR	NR	NR	↑ COL1A1 & procollagen I	NA	NA	DSPC exosomes ↑ collagen via Akt/ANP32B pathway	Monotherapy
Li et al., 2024b [27]	NR	NR	NR	Oxidative stress ↓ (↑ SOD, ↓ MDA)	NR	NR	Exosome-loaded gel reduced oxidative stress in HDFs	Combination
Cho et al., 2022 [28]	NR	↓ MMP12/13 expression	↑ hydration inferred	↑ LOX, ↑ ECM gene expression	NR	NR	Plant exosomes modulated transcriptome, stabilized collagen	Monotherapy
Guo et al., 2022 [29]	↑ type I collagen (~6000 pg/mL vs 4000)	NR	NR	↑ ECM proteins	NR	NR	ADSC exosomes reduced senescence, enhanced collagen	Monotherapy
Vu et al., 2022 [30]	NA	NA	NA	↑ collagen, ↑ elastin	NA	NA	UCMSC EVs ↑ ECM components, fibroblast migration	Monotherapy
Oh et al., 2018 [31]	NR	NA	NR	↑ collagen I, ↓ MMPs	NR	NR	iPSC-Exo restored ECM in photoaged fibroblasts	Monotherapy
Adel et al., 2025a [32]	NR	NR	NR	↑ wound closure rates, ↑ collagen deposition	NR	NR	Plant-based exosome injections accelerated skin wound healing	Monotherapy
Adel et al., 2025b [33]	NR	NR	NR	NR	↓ inflammatory cell infiltration	NR	Plant exosomes modulated immune cell counts, supported tissue repair	Monotherapy
Ellistasari et al., 2022 [34]	NR	NR	NR	↑ collagen (Exo-HUVEC dose-dependent)	NR	NR	Exo-HUVEC improved photo-aging fibroblast recovery	Monotherapy

Table 3. ROB quality assessment of the RCT study.

Study ID	Selection Bias	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias	Overall RoB
Park et al., 2023a[18]	Unclear	Low	Unclear	Low	Low	Low	Low

is strong in selection, ascertainment, and reporting, adequately presenting patient experiences and documenting key exposures and outcomes [38]. However, the causality evaluation is weaker, lacking evidence of challenge/re-challenge phenomena or dose-response effects, which limits causal inference.

In summary, the overall assessment highlights that the included preclinical, nonrandomized clinical, and case series studies demonstrated adequate methodological rigor and reliable reporting of outcomes. Key areas for improvement include enhanced reporting of randomization and allocation methods in preclinical studies, prospective sample size justification in clinical studies, and strengthened causality evaluation in case series. This comprehensive appraisal ensures that conclusions drawn from these studies are grounded in a clear understanding of their methodological strengths and limitations.

Discussion

EVs have demonstrated significant potential in the field of regenerative medicine, especially within dermatology and aesthetic applications [10]. However, transitioning from laboratory research to practical clinical implementation faces several substantial challenges. Key issues include the difficulties of large-scale production, variations between different batches, regulatory obstacles, and the urgent need for consistent therapeutic formulations [1]. Unlike conventional synthetic drug carriers, EVs originate from biological sources, which can result in variability in their composition, effectiveness, and stability [3,5]. It is essential to tackle these issues to ensure their safe and efficient use in clinical practice. Therefore, our review explored the current evidence regarding the efficacy, safety, and mechanisms of exosomes in skin rejuvenation [9]. Importantly, the evidence also highlights their role in addressing hallmark features of skin aging such as loss of collagen, reduction in elasticity, wrinkle formation, and pigmentation changes, demonstrating that exosome therapies are not only rejuvenating but also strongly anti-aging in their clinical outcomes [10]. The evidence from the diverse studies underscores the therapeutic potential of EVs, exosomes, and stem cell-derived products for skin rejuvenation and anti-aging applications [11]. These studies encompass a variety of EV sources, including human adipose-derived stem cells (HADSCs), adipose stem cells (ASCs), human platelet extracts (HPEs), plant-derived exosomes, milk-derived exosomes, and fibroblast-derived EVs, and utilize different preparation methods such as ultrafiltration, ultracentrifugation, and freeze-drying [7,13,21,22].

Skin Elasticity and Wrinkle Reduction

Improvements in skin elasticity were consistently reported. Li et al. demonstrated that HADSCs-conditioned medium restored collagen levels reduced by UVA exposure in a dose-dependent manner, indicating enhanced elasticity at the molecular level [24]. Nguyen et al. reported a striking 104% increase in skin elasticity using ASC-derived small EVs, alongside significant wrinkle reduction and hydration improvements [13]. Similarly, Jo et al. found that Lactobacillus plantarum-derived EVs (LpEVs) increased elasticity by 27% and reduced wrinkles by 16% after four weeks of topical application [21]. Topical application of human platelet extract (HPE) containing platelet EVs also showed promising results. Wyles et al. observed that 38% of subjects exhibited at least a 5% improvement in wrinkle area, with increased collagen thickness and elastin content confirmed by histology [15]. Park et al. combined human adipose stem cell-conditioned medium (HACS) with microneedling to achieve an 11.3% increase in skin elasticity and a 13% reduction in wrinkle depth, demonstrating the potential for synergistic treatment approaches [18].

Overall, across the included studies, 61% investigated exosome therapies as monotherapy and 39% as combination treatments (e.g., with microneedling, vitamin C, hydrogels, or CaHA). This breakdown underscores that while exosomes alone exert measurable anti-aging benefits such as wrinkle reduction and collagen restoration, adjunctive approaches may enhance or accelerate these effects, a distinction important for clinical translation and future trial design [10].

Similarly, a study demonstrated that EVs can enhance anti-aging effects, reduce pigmentation issues, and facilitate scar-free wound healing [9]. Their efficacy can be further improved alongside methods like microneedling and hydrogels [12]. Additionally, while mammalian EVs show promising biological activities for cosmetic uses, plant-derived EVs have also proven effective for similar cosmeceutical applications [21,28]. Moreover, another review highlights the potential of exosomes as a valuable resource in aesthetic medicine and dermatology. The authors presented numerous therapeutic options for skin rejuvenation, hair loss treatment, healing acne

Table 4. Quality assessment of included animal and in vitro studies.

Study ID	Study Type	Selection Bias	Baseline Characteristics	Allocation Concealment	Performance	Detection	Attrition	Reporting	Other	Overall Methodological Clarity
Li et al., 2024a [24]	Animal	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Li et al., 2024a [24]	In vitro	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Li et al., 2024b [27]	In vitro	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Moderate
Lu et al., 2024 [22]	Animal	Unclear	Unclear	Unclear	Low	Low	Low	Low	Low	Low
Lu et al., 2024 [22]	In vitro	Unclear	Unclear	Unclear	Low	Unclear	Low	Low	Unclear	Moderate
Cho et al., 2022 [28]	In vitro	Unclear	Low	High	High	Unclear	Low	Unclear	Unclear	High
Han et al., 2022 [23]	Animal	Low	Low	High	Unclear	High	Low	Unclear	Low	High
Han et al., 2022 [23]	In vitro	Unclear	Low	Unclear	Unclear	Unclear	Low	Unclear	Low	Moderate
Ellistasari et al., 2022 [34]	In vitro	Unclear	Low	High	High	Unclear	Low	Unclear	Unclear	High
Guo et al., 2022 [29]	In vitro	Unclear	Low	High	High	Unclear	Low	Unclear	Unclear	High
Jo et al., 2022 [21]	In vitro	Unclear	Low	High	High	Unclear	Low	Unclear	Unclear	High
Sanada et al., 2022 [26]	In vitro	Unclear	Low	High	High	Unclear	Low	Unclear	Unclear	High
Vu et al., 2022 [30]	In vitro	Unclear	Low	High	High	Unclear	Low	Unclear	Unclear	High
Wang et al., 2019 [25]	Animal	Unclear	Low	High	High	Unclear	Low	Low	Low	High
Wang et al., 2019 [25]	In vitro	Low	Low	High	High	Unclear	Low	Unclear	Unclear	High
Oh et al., 2018 [31]	In vitro	Unclear	Low	High	High	Unclear	Low	Low	Low	High

Table 5. MINORS Quality Assessment of Nonrandomized Clinical Studies.

Study ID	Clearly Stated Aim	Consecutive Patients	Prospective Data Collection	Appropriate Endpoints	Unbiased Assessment	Follow-Up Period	Loss <5%	Sample Size Calculation	Adequate Control (Comparative)	Contemporary Groups (Comparative)	Baseline Equivalence	Adequate Statistical Analyses	Total Score
Proffer et al., 2022 [20]	2	1	2	2	1	1	2	0	-	-	-	-	11/16
Nguyen et al., 2024 [13]	2	1	2	2	1	2	2	0	-	-	-	-	12/16
Chernoff et al., 2023 [17]	2	1	2	2	1	2	2	0	0	2	1	1	16/24
Svolacchia et al., 2024 [14]	2	1	2	2	1	2	2	0	-	-	-	-	12/16
Wyles et al., 2024a [15]	2	1	2	2	2	2	2	0	-	-	-	-	13/16
Wyles et al., 2024b [16]	2	1	2	2	1	2	2	0	-	-	-	-	12/16
Lu et al., 2024 [22]	2	0	2	2	0	2	2	0	2	2	2	1	15/24
Han et al., 2022 [23]	2	0	2	2	1	1	2	0	2	2	0	1	14/24
Jo et al., 2022 [21]	2	1	2	2	1	1	0	0	2	2	1	2	16/24
Sanada et al., 2022 [26]	2	1	0	2	1	2	2	0	2	2	1	1	17/24

Table 6. Methodological Quality Tool of case reports and case series [38].

Items	Selection	Ascertainment		Causality		Reporting		
Study ID	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Park et al., 2023b [19]	Yes	Yes	Yes	Yes	No	No	Yes	Yes

Selection: [question 1]. Do the patient(s) represent the whole experience of the investigator (center), or is the selection method unclear to the extent that other patients with similar presentations may not have been reported? Ascertainment: [question 2]. Was the exposure adequately ascertained? [question 3]. Was the outcome adequately ascertained? Causality: [question 4]. Were other alternative causes that may explain the observation ruled out? [question 5]. Was there a challenge/re-challenge phenomenon? [question 6]. Was there a dose-response effect? [question 7]. Was the follow-up long enough for outcomes to occur? Reporting: [question 8] Are the cases described with sufficient details to allow other investigators to replicate the research or enable practitioners to make inferences about their practice?

scars, and managing wounds [12]. Current studies suggest that exosomes can influence essential biological processes, including the formation of blood vessels, the growth of fibroblasts, and the production of collagen, positioning them as a compelling alternative to more invasive treatment approaches [10].

Hydration and Pigmentation Effects

Hydration improvements were notable in several studies. Nguyen et al. reported a 19% increase in skin moisture following ASC-sEV treatment, while Jo et al. documented a 21% hydration increase with LpEVs [13,21]. Pigmentation improvements were evident as well. Nguyen et al. observed decreased melanin content with ASC-sEVs, and Jo et al. reported a 16% reduction in pigmentation with LpEVs [13,21]. Wyles et al. also noted a 36% reduction in pigmentation following topical antioxidant and platelet EV treatment, indicating potential benefits for photoaged or hyperpigmented skin [15]. Bedina Zavec recently reviewed the various roles of EVs in skin rejuvenation, particularly their ability to modulate pigmentation and improve moisture retention [9]. Our findings support these observations and provide new quantitative data on hydration and pigmentation reduction, enhancing the evidence base for clinical applications [13,21].

Safety and Patient Satisfaction

All studies in our review reported favorable safety profiles. Mild, transient adverse events such as erythema, edema, or dryness were noted, but these resolved without intervention. No serious adverse events were reported, indicating good tolerability [13,15,18]. Patient satisfaction was high, reflecting perceived improvements in skin texture, elasticity, and overall appearance [13,21]. Similarly, recent reviews emphasized that safety is paramount, and the positive tolerability profiles noted in the studies support the clinical feasibility of EV-based treatments for skin aging [9,12]. Studies indicated that EV-based treatments for skin rejuvenation were safe, with only mild, temporary side effects like erythema, edema, or dryness, which resolved quickly [13,15]. No serious adverse event was reported, resulting in high patient satisfaction regarding skin texture and appearance [13,21]. Future research should involve larger, randomized trials to confirm long-term safety and efficacy [10,11]. Standardizing EV isolation and characterization per MISEV guidelines will improve reproducibility [1], and more mechanistic studies are needed to clarify how EVs promote skin rejuvenation [4].

Molecular and Cellular Mechanisms

Mechanistic insights from these studies reveal that EVs modulate oxidative stress, extracellular matrix (ECM) remodeling, and cellular senescence. Li et al. and Nguyen et al. reported decreased reactive oxygen species (ROS) and malondialdehyde (MDA) levels, alongside increased superoxide dismutase (SOD) activity, suggesting enhanced antioxidant defense. These studies observed suppression of matrix metalloproteinases (MMP1 and MMP3), key enzymes involved in collagen degradation, contributing to the preservation and restoration of dermal collagen [24,13].

Several recent reviews provide comprehensive insights into the molecular mechanisms underlying skin aging and potential therapeutic approaches [9,10,12]. López-Otín et al. outlined the key hallmarks of aging, including genomic instability, telomere attrition, epigenetic alterations, and loss of proteostasis, while discussing emerging relevant treatment strategies [10]. Krutmann et al. focused on dermal aging, highlighting fibroblast dysfunction and extracellular matrix degradation, and evaluating existing and novel anti-aging interventions [9]. Zhang et al. emphasized the role of natural compounds in counteracting oxidative stress and inflammation, underscoring their therapeutic potential [12].

Fibroblast proliferation and migration were stimulated by EV treatments, as seen in Wyles et al. and Park et al., supporting dermal regeneration [15,18]. Molecular analyses revealed upregulation of collagen types I and III (COL1A1, COL3A1), elastin, and other ECM-related genes, confirming enhanced matrix synthesis [24,26]. Jo et al. identified miRNAs and proteins within EV cargo that likely mediate these effects via Akt and TGF-β signaling pathways [21]. Human platelet extract (HPE) treatments reduced senescent cell burden and inflammatory markers, promoting ECM remodeling and rejuvenation [15,16]. Plant-derived EVs provided antioxidant and moisturizing benefits, with milk exosomes

also enhancing barrier proteins [22]. These mechanisms are visually summarized in Figure 2: Mechanisms of Action of Exosomes in Skin Rejuvenation.

Sources and Preparation Methods

The source of EVs influences their bioactivity. Adipose-derived stem cell EVs [24,13,18] consistently showed strong regenerative effects. Platelet EVs contributed to collagen and elastin synthesis and reduced inflammation [15,16]. Plant-derived EVs offered complementary antioxidant and moisturizing effects, expanding therapeutic options [21]. Preparation methods such as ultrafiltration, ultracentrifugation, and freeze-drying impact EV stability and potency [13, 24, 21]. Standardizing these protocols is critical to reproducibility and clinical translation [1].

Recent evaluations have underscored the importance of rigorous isolation and characterization techniques [1,7]. Johnson et al. demonstrated the highest compliance with MISEV2023 by applying a multi-step isolation (LEAP) approach that utilized both positive markers (CD63, CD9) and negative markers (calnexin), along with detailed functional EV characterization. In contrast, Kwon et al. achieved only partial compliance with MISEV2018 since they used a single-step isolation method (ExoSCRT™) and omitted negative marker analyses (e.g., calnexin and cytochrome C) [1]. Similarly, Svolacchia et al. relied solely on ultrafiltration, which does not align with the MISEV2023 preference for multi-step methods [14]. These observations highlight that the EV source and isolation strategy play a critical role in determining EV purity and functional reproducibility [1,7].

In summary, a thorough analysis of these studies shows that extracellular vesicles and exosome-based therapies derived from various sources can improve skin elasticity, reduce wrinkles, enhance hydration, and modulate pigmentation

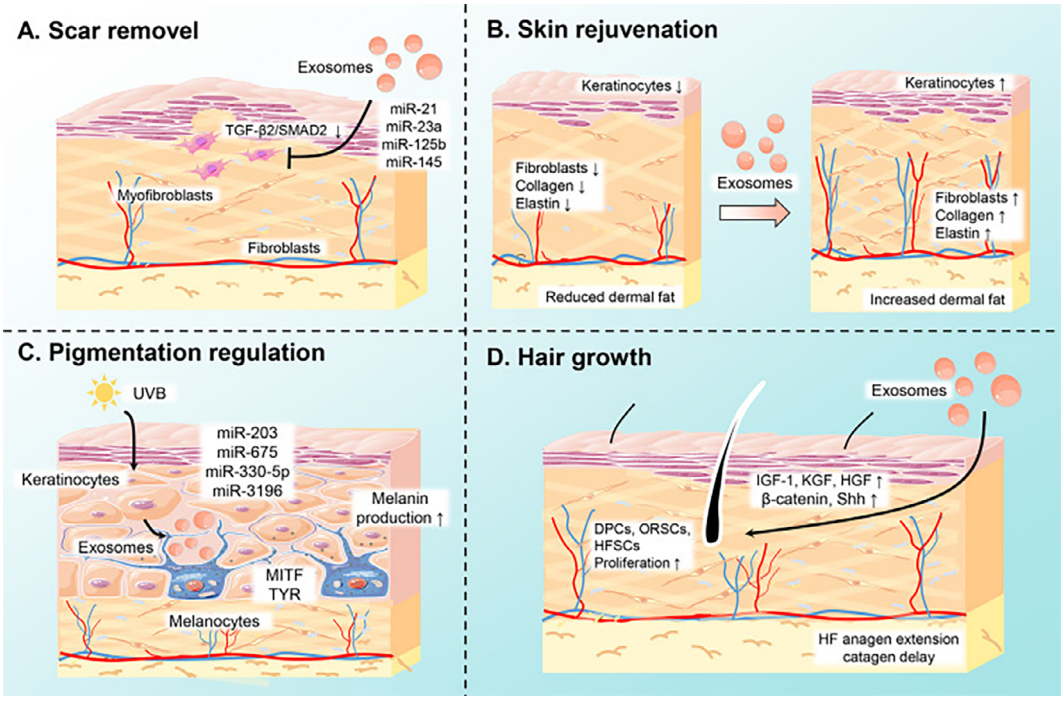

Figure 2. The mechanisms of exosomes in cutaneous medical aesthetics. (A) Exosomes from umbilical cord-derived MSCs, enriched in miR-21, miR-23a, miR-125b, and miR-145, targeted the TGF-β2/SMAD2 pathway to inhibit the differentiation of fibroblasts to myofibroblasts, resulting in reduced excessive fibrosis and scar formation. (B) Exosomes could improve keratinocytes and fibroblasts function, enhance collagen and elastin synthesis, and increase dermal fat, thus promoting the regenerative and restorative capacity for skin anti-aging. (C) After exposure to the UVB, the keratinocyte-derived exosomes modulated their miRNA content to increase melanocyte pigmentation via miR-3196 and MITF-dependent signaling pathways or miR-203 and MITF-independent signaling pathway. The miR-330–5p overexpressing in keratinocyte-derived exosomes decreased the melanin production and TYR expression in melanocytes. And the miR-675 from keratinocyte exosomes involved in H19 lncRNA downregulation-stimulated melanogenesis, by inhibiting MITF expression. (D) The dermal papilla cells-derived exosomes promoted the viability of DPCs, ORSCs, and HFSCs, increased the expression of IGF-1, KGF, HGF, β-catenin, and Shh, and also accelerated the onset of HF anagen, postponed catagen, longer hair shafts in the skin of mice. Hair Follicle Stem Cells, HFSCs; Dermal Papilla Cells, DPCs; Hair Follicle, HF; Outer Root Sheath Cells, ORSCs; Transforming Growth Factor Beta, TGF-β; Keratinocyte Growth Factor, KGF; Insulin-Like Growth Factor, IGF; Hepatocyte Growth Factor, HGF; Sonic Hedgehog, Shh; Ultraviolet B, UVB; Melanocyte Inducing Transcription Factor, MITF; Tyrosinase, TYR [39].

[10,13,15,21,24]. By directly targeting fundamental hallmarks of aging such as collagen loss, diminished elasticity, wrinkle formation, and pigmentation, exosome therapies provide compelling anti-aging outcomes in addition to general rejuvenation [10]. These treatments are considered safe and well tolerated, with high patient satisfaction reported [13,15,18]. Future research should focus on standardizing methods for isolating and characterizing extracellular vesicles, optimizing dosing and delivery routes, and conducting larger randomized controlled trials to confirm their efficacy and long-term safety [1,10,11]. Additionally, combining extracellular vesicle therapies with other techniques, such as microneedling, may improve clinical outcomes [18].

Limitations

This review is limited by the small sample size of some studies and because it relied on in vitro and animal models, which restrict the generalizability of the results to diverse human populations [21]. Furthermore, the lack of standardized EV characterization and quantification protocols hinders reproducibility and clinical translation [1,7]. Additionally, most studies had relatively short follow-up periods, which limits insights into these treatments' durability and long-term safety [13]. To address these shortcomings, future research should focus on conducting large, multicenter randomized controlled trials with standardized regimens, uniform outcome measures, and long-term follow-up [10].

Conclusion

This systematic review indicates that therapies using EVs and exosomes show promise for skin rejuvenation, offering benefits such as improved elasticity, reduced wrinkles, enhanced hydration, and better pigmentation while maintaining safety. Beyond general rejuvenation, these therapies explicitly target anti-aging endpoints, including wrinkle reduction, improved elasticity, collagen restoration, and pigmentation control, making them highly relevant to aesthetic and regenerative dermatology. These treatments utilize EV cargo to combat oxidative stress and reduce cellular aging. Notably, approximately 61% of the included studies evaluated exosomes as monotherapy, while 39% combined them with adjunctive modalities, highlighting both the independent anti-aging efficacy of exosomes and their potential to achieve synergistic outcomes when paired with complementary techniques. Future studies should standardize EV isolation and dosing processes, conduct large-scale randomized trials for long-term safety and clinical benefits, and explore combining EV therapies with techniques like microneedling. Proper scrutiny is crucial as these biologics could transform anti-aging treatments.

Abbreviations: ADSC-Exos: Adipose-Derived Stem Cell Exosomes; ASC: Adipose-derived Stem Cells; CaHA: Calcium Hydroxylapatite; COL1A1: Type I Collagen Alpha 1 Chain; COL3A1: Type III Collagen Alpha 1 Chain; DSPCs: Dermal Stem/Progenitor Cells; ECM: Extracellular Matrix; EVs: Extracellular Vesicles; FELNVs: Fungi Exosome-like Nanovesicles; FGF: Fibroblast Growth Factor; GAIS: Global Aesthetic Improvement Scale; HACS: Human Adipose Cell Secretome; HADSCs: Human Adipose-derived Stem Cells; HPE: Human Platelet Extract; iPSCs-Exo: Induced Pluripotent Stem Cell-Derived Exosomes; LpEVs: Lactobacillus plantarum-derived Extracellular Vesicles; MDA: Malondialdehyde; MINORS: Methodological Index for Non-Randomized Studies; MK-Exo: Milk-derived Exosomes; MMPs: Matrix Metalloproteinases; MSC-EVs: Mesenchymal Stem Cell-derived Extracellular Vesicles; PRIMOS: Phase-shifting Rapid In vivo Measurement Of Skin; qRT-PCR: Quantitative Reverse Transcription Polymerase Chain Reaction; ROS: Reactive Oxygen Species; SASP: Senescence-Associated Secretory Phenotype; sEVs: Small Extracellular Vesicles; SOD: Superoxide Dismutase; SYRCLE: Systematic Review Centre for Laboratory Animal Experimentation; TGF-β: Transforming Growth Factor Beta; UCMSCs: Umbilical Cord Mesenchymal Stem Cells; VEGF: Vascular Endothelial Growth Factor.

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