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The Role of Mesenchymal Stem Cell-Derived Exosomes in Skin Regeneration in Photoaging: A Systematic Literature Review

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Keywords:
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Abstract

Photoaging is a form of skin aging caused by chronic exposure to ultraviolet (UV) radiation, which induces oxidative stress, inflammation, and collagen degradation. Mesenchymal stem cell-derived exosomes (MSC-Exos) have demonstrated potential to support skin regeneration through their bioactive cargo, which influences cellular proliferation, collagen synthesis, antioxidant responses, and inflammatory regulation. This systematic literature review aimed to analyze the role of MSC-Exos in skin regeneration associated with photoaging. The reviewed literature indicates that MSC-Exos can enhance fibroblast activity, promote extracellular matrix repair, reduce matrix metalloproteinase expression, and regulate molecular pathways involved in skin regeneration. In vitro and in vivo studies have shown relatively consistent evidence supporting the anti-photoaging and regenerative effects of MSC-Exos. However, variations in mesenchymal stem cell sources, exosome isolation and characterization methods, dosages, administration routes, and experimental models have limited direct comparability among studies. Although preclinical findings are promising, further clinical research using standardized protocols is required to establish the safety, efficacy, and translational potential of MSC-Exos for photoaging treatment.

INTRODUCTION

Photoaging is an extrinsic skin aging process primarily caused by chronic exposure to ultraviolet (UV) radiation. This condition is characterized by wrinkle formation, pigmentation changes, reduced elasticity, and alterations in dermal structure resulting from collagen and elastin degradation (Zeng et al., 2026). UV exposure increases the production of reactive oxygen species (ROS) and activates the MAPK/AP-1 signaling pathway, which subsequently promotes the expression of matrix metalloproteinases (MMPs) (Gao et al., 2018; Kwon et al., 2019). Increased MMP activity accelerates collagen degradation, while UV radiation also reduces type I procollagen synthesis, thereby exacerbating extracellular matrix (ECM) damage in the skin (Gao et al., 2021).

Mesenchymal stem cell-derived exosomes (MSC-Exos) have emerged as a potential cell-free regenerative therapy approach because they contain various bioactive molecules, including proteins, lipids, messenger RNAs (mRNAs), and microRNAs. These components regulate cellular proliferation, migration, inflammation, oxidative stress responses, and skin tissue regeneration processes (Liu et al., 2021). Several studies have demonstrated that MSC-Exos can reduce ROS production and MMP expression, enhance collagen synthesis, and protect fibroblasts and keratinocytes against UV-induced damage. These effects are

associated with the regulation of several molecular pathways, including Nrf2, MAPK/AP-1, and TGF-β/Smad signaling pathways (Gao et al., 2021; Zhang et al., 2024).

Despite their promising potential, research on MSC-Exos for photoaging remains predominantly based on in vitro and in vivo models, while clinical evidence in humans remains limited (Gao et al., 2018; Lu et al., 2016; Rolo et al., 2023; Xu et al., 2022). Differences in MSC sources, exosome isolation and characterization methods, dosages, administration approaches, and evaluated outcomes have resulted in variability among study findings (Estupiñan et al., 2025).

The novelty of this systematic review lies in its comprehensive and rigorous evaluation of the role of MSC-Exos specifically in photoaging, rather than skin regeneration in general. Unlike previous reviews, this study applies a systematic search strategy across multiple databases following PRISMA 2020 guidelines, critically evaluates the methodological quality of included studies using validated assessment tools (SYRCLE Risk of Bias Tool and JBI Critical Appraisal Tools), and synthesizes evidence across multiple outcome domains, including cellular proliferation, collagen synthesis, MMP expression, oxidative stress, inflammation, apoptosis, and cellular senescence. Furthermore, this review evaluates evidence regarding molecular mechanisms and bioactive cargo involved in MSC-Exos activity, identifies limitations related to standardization, dosage, and safety, and provides evidence-based recommendations for future research and clinical translation (Chi et al., 2026; Mahrooghi et al., 2026; Wang et al., 2026; Wen et al., 2025). By integrating these aspects, this review provides a comprehensive reference for researchers, clinicians, and stakeholders investigating the therapeutic potential of MSC-Exos for photoaging.

The primary objective of this systematic literature review was to analyze the role of mesenchymal stem cell-derived exosomes in skin regeneration associated with photoaging, with particular emphasis on their effects on oxidative stress, inflammation, collagen synthesis, extracellular matrix degradation, and related molecular mechanisms. Specifically, this review aimed to: (1) identify and characterize published studies investigating MSC-Exos or MSC-derived extracellular vesicles in photoaging models; (2) synthesize evidence regarding the effects of MSC-Exos on key outcomes, including fibroblast and keratinocyte proliferation and migration, collagen and ECM synthesis, MMP expression, oxidative stress, inflammation, apoptosis, and cellular senescence; (3) evaluate the methodological quality and risk of bias of included studies; (4) identify molecular pathways and bioactive cargo associated with observed effects; (5) compare findings across different MSC sources, including adipose tissue-derived, umbilical cord-derived, and bone marrow-derived MSCs; (6) assess the translational potential and safety considerations of MSC-Exos for clinical applications; and (7) provide evidence-based recommendations for future research directions.

This systematic literature review aimed to analyze the role of mesenchymal stem cell-derived exosomes in skin regeneration associated with photoaging, particularly their effects on oxidative stress, inflammation, collagen synthesis, extracellular matrix degradation, and underlying molecular mechanisms.

METHOD

Research Identification

This study was a systematic literature review that examined the role of mesenchymal stem cell-derived exosomes (MSC-Exos) in skin regeneration associated with photoaging. The methodology was structured based on study identification, selection, and quality assessment stages. The literature search was conducted using international databases, including PubMed, ScienceDirect, and Scopus, with Google Scholar used as an additional source.

The literature search was performed using a combination of keywords: ("mesenchymal stem cell" OR "mesenchymal stromal cell" OR MSC) AND (exosome OR "extracellular vesicle" OR "small extracellular vesicle") AND (photoaging OR "skin photoaging" OR photodamage OR "UV-induced skin damage" OR UVA OR UVB) AND ("skin regeneration" OR collagen OR fibroblast OR keratinocyte). These keywords were selected to identify studies investigating MSC-derived exosomes or extracellular vesicles in skin repair associated with ultraviolet-induced damage.

All identified articles were collected, and duplicate records were removed. The remaining articles were screened based on titles and abstracts to determine their relevance to the research focus. Eligible articles then underwent full-text assessment before being included in the final synthesis.

Research Selection

The researcher applied inclusion criteria in the form of *original research* articles in English or Indonesian, *in vitro*, *in vivo*, and clinical research, and using exosomes or *extracellular vesicles* derived from *mesenchymal stem cells*. The study must use *a photoaging*, *photodamage*, or skin damage model due to UVA or UVB exposure and report at least one output related to skin regeneration, such as proliferation or migration of fibroblasts and keratinocytes, collagen synthesis, *matrix expression of metalloproteinases* (MMP), oxidative stress, inflammation, apoptosis, cell senesen, or changes in skin structure. Articles published 2021-2026 are considered in the selection process.

Research articles are excluded if they are in the form *of reviews*, *systematic reviews*, *meta-analysis*, editorials, comments, letters, case reports, or *conference* abstracts. Studies are also excluded if they only discuss MSC without evaluating exosomes or *extracellular vesicles* separately, use *conditioned medium* or *secretome* without vesicle isolation, use vesicles derived from non-MSC cells, or discuss skin regeneration and wound healing unrelated to *photoaging* or exposure to ultraviolet radiation.

All article titles and abstracts are assessed based on the inclusion and exclusion criteria that have been set. Articles that meet the criteria at the initial stage are then continued to the *full text review stage*. The final selection is carried out to determine articles that are in accordance with the research objectives and can be included in the *systematic literature review*. This stage follows the research selection pattern for sample articles that screen the title-abstract and then continue with a full-text assessment.

Research Quality Assessment

The methodological quality of the articles was assessed based on the design of each study. In *vivo* studies in animals were assessed using the SYRCLE Risk of Bias Tool, while *in vitro studies* were assessed based on methodological components that included clarity of

cell models, control groups, UVA or UVB exposure procedures, MSC sources, exosome isolation and characterization methods, intervention doses, experimental replication, output measurement methods, and statistical analysis. The quality of exosome or *extracellular vesicles* characterization was also considered based on the suitability of the vesicle identification and characterization methods.

If clinical research is found in humans, the quality of the research is assessed using instruments that are in accordance with the study design, such as *JBI Critical Appraisal Tools* or relevant *risk of bias* instruments . Assessments are carried out systematically on all articles that pass the selection stage to ensure that the submitted research has adequate methodological quality and is relevant to the focus of the research. Articles with severe methodological weaknesses are carefully considered in the synthesis and interpretation of the results.

Data Analysis

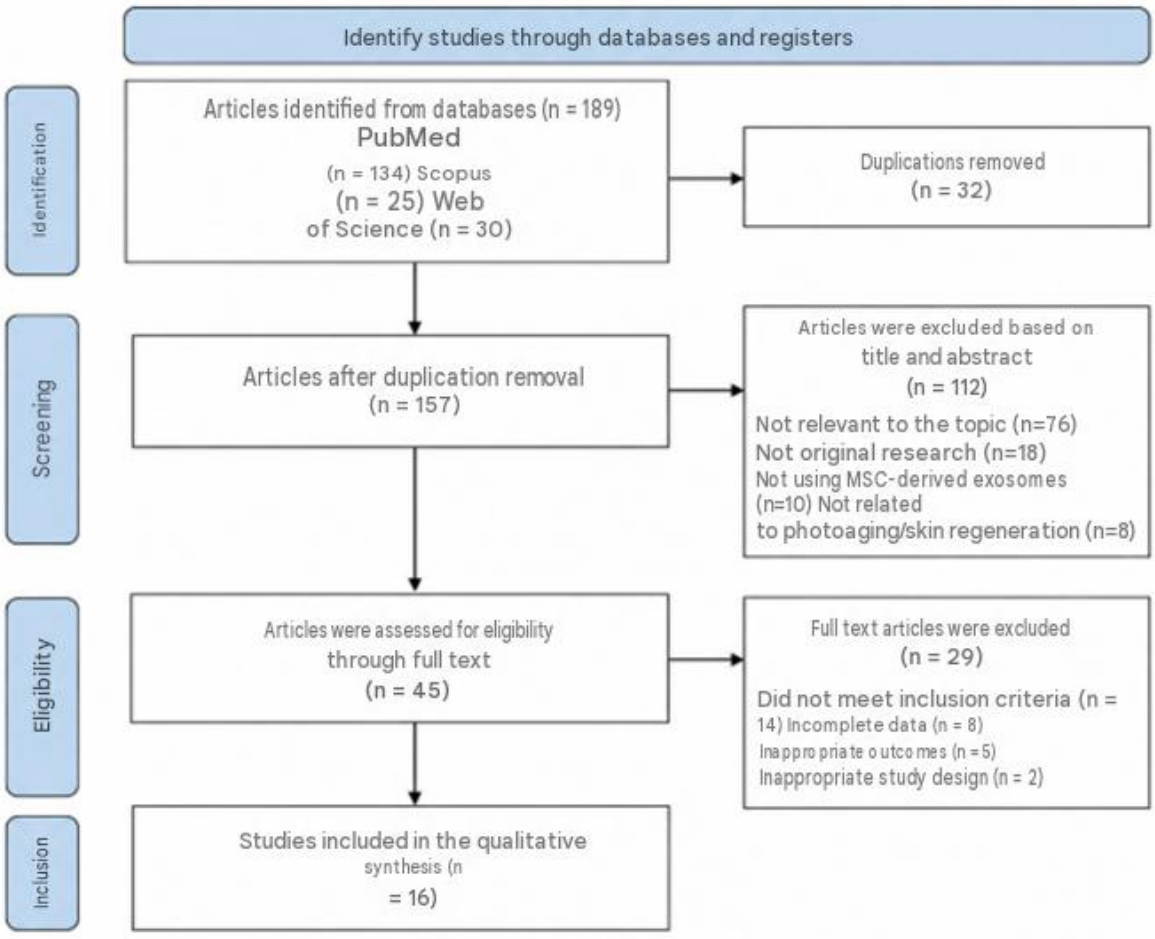


Figure 1. PRISMA Flowchart for Article Selection

A literature search through three databases yielded a total of 189 articles, consisting of 134 articles from PubMed, 25 articles from Scopus, and 30 articles from the Web of Science. All articles were then entered into a literature management application for identification and removal of duplicate articles. After the deduplication process, the remaining articles were proceeded to the screening stage based on titles and abstracts.

Articles that met the inclusion criteria were then assessed through a full text review before being determined as articles included in the final synthesis.

RESULTS AND DISCUSSION

Research Characteristics

Table 1. Research characteristics of MSC-derived exosomes/EVs in photoaging

Researcher	Country of design	MSC Source	EV/Exos Isolation	Photoaging model	Dosage/route	Key molecular and histological/clinical findings
Choi et al. (2019)	South Korea; *in vitro*	Adipose/HASC	*Tangential flow filtration*; TEM, NTA, WB	HDF + UVB 50 mJ/cm²	1×10^8 particle/mL	↑ proliferation/migration; ↑ collagen I–V, elastin, TIMP1, TGF-β1; ↓ MMP-1/2/3/9
Zhang et al. (2020)	China; *in vivo* + skin penetration	hUCMSC	Ultracentrifugation	Photoaged rat skin; pig skin for penetration	Topical + *sponge spicules*; non-specific dosage	Exosome penetration ↑ 5.87 times; ↓ *microwrinkles* and histological abnormalities; ↑ ECM components
Xu et al. (2020)	China; *in vitro/in vivo*	ADSC	Non-specific	Fibroblasts and mice + UVB	100–200 μg/mL; 150–300 μg subcutaneous/week × 8 weeks	↓ wrinkles, ROS, macrophage infiltration, senesens; ↑ epidermal proliferation, SOD1/CAT
Gao et al. (2021)	China; *in vitro*	ADSC	Non-specific	HDF + UVB	Non-specific	↓ ROS, DNA damage, MMP-1; ↑ procollagen I via Nrf2, MAPK/AP-1 and TGF-β/Smad
Liu et al. (2021)	China; *in vitro*	UCMSC, 3D culture	Non-specific	HaCaT + UVB 60 mJ/cm²	Non-specific	↑ proliferation/migration and collagen I; ↓ apoptosis, senesens and MMP-1
Wu et al. (2021)	China; *in vitro/in vivo*	hUCMSC	Non-specific; TEM/NTA/WB	HaCaT and mice with acute UV photodamage	600 μg *in vitro*; 1 mg subcutaneous *in vivo*	↓ ROS, inflammation, DNA damage and apoptosis; 14-3-3ζ → ↑ SIRT1, antioxidant and autophagy responses
Yan et al. (2023)	China; *in vitro*	BMSC	Non-specific; HSP70/CD9	HDF + UVB	Tiered concentration; non-specific	miR-29b-3p → ↓ MMP including MMP-2, oxidative stress/apoptosis; ↑ migration and collagen I

Researcher	Country of design	MSC Source	EV/Exos Isolation	Photoaging model	Dosage/route	Key molecular and histological/clinical findings
Gao et al. (2023)	China; *in vitro/in vivo*	ADSC, miR-1246 *overexpression*	Non-specific	HSF + UVB; Kunming rats	Non-specific	↓ MMP-1/MAPK-AP1 and NF-κB; ↑ TGF-β/Smad/procollagen I; ↓ wrinkle and thickening of the epidermis
Yan et al. (2023)	China; *in vitro*	BMSC	Non-specific	HDF + UVB	Tiered dosage; non-specific	↓ ROS, LDH, TNF-α, IL-6, IL-1β, MMP-1/3; ↑ SOD and collagen I; MAPK/AP-1 inhibition
Sun et al. (2024)	China; *in vitro/in vivo*	hUCMSC-sEV	Non-specific; TEM/NTA/WB	Fibroblasts + UVA; photoaging mice	Intradermal/*microneedle*; non-specific dosage	↓ oxidative stress, MMP-1, DNA damage and collagen degradation; PZP-related effects
Zhang et al. (2024)	China; *in vitro/in vivo*	AMSC and HUMSC	Filtration + concentration + ultracentrifugation	HaCaT, HDF, T-Skin + UVB; mice	200 ng/μL *in vitro*; 200 μg/subcutaneous rat	↓ ROS, inflammation, DNA damage, senesens and MMP; ↑ migration/ECM/hydration; TIMP1 → Notch1 inhibition
Huynh et al. (2025)	Vietnam; *in vitro/in vivo*	ADSC hypoxia	Ultracentrifugation; TEM/CD9/CD63/CD81	HDF and photoaging mice	50 or 100 μg/mL, topical 2×/week × 6 weeks	↓ SA-β-gal, p16/p21, MMP-1/2/3, wrinkles/thickness; ↑ proliferation, hydration, elasticity and density of collagen
Cui et al. (2025)	China; *in vitro/in vivo*	Hair-follicle MSC	Non-specific	HDF + UVB; *photoaging mice*	10–20 μg/mL; 20 μg *in vivo*	↑ proliferation/migration, collagen I/III, TGF-β1/p-Smad2/3; ↓ MMP-1/senesens; miR-125b-5p/TGF-β1/Smad
Estupiñan et al. (2025)	AS; clinical *split-face*, investigator-blinded	ASC	Commercial products; two-stage filtration	15 *mild–moderate* photoaging patients	Topical after RFMN, 3 sessions	Improvement of wrinkles, dyschromia, erythema, texture; ↑ collagen I/GAG; no significant difference from PRP

Description: *ADSC/ASC/AMSC = adipose-derived mesenchymal/stromal cells; UCMSC/hUCMSC/HUMSC = umbilical cord mesenchymal stromal cells; BMSC = bone marrow mesenchymal stromal cells; HDF = human dermal fibroblast; ECM = extracellular matrix; RFMN = radiofrequency microneedling. The term "exosome" is retained as per the*

original author's terminology, although MISEV2023 advocate the use of the term EV when the origin of endosomal biogenesis has not been specifically proven (Welsh et al., 2024).

Synthesis Based on Outcomes

Table 2. Synthesis Based on Outcomes

Domain outcome	Supporting studies	Consistency	Synthesis
Proliferation/migration	≥8/14	Consistent	EV/Exos restores proliferation, viability or migration of fibroblasts/keratinocytes after UV
Collagen/ECM synthesis	≥13/14	Consistent, quantitatively heterogeneous	↑ collagen I/III, procollagen I, elastin/ECM; improvement of collagen density and histology
MMP/TIMP	≥11/14	Very consistent	↓ MMP-1 is most consistent; also MMP-2/3/9; ↑ TIMP1 in some studies
ROS/antioxidants	≥7/14	Consistent	↓ ROS/oxidative damage; ↑ SOD/CAT or antioxidant response
Inflammation/cytokines	≥5/14	Consistent	↓ TNF-α, IL-6, IL-1β and inflammatory infiltration
Apoptosis/senesens	≥8/14	Consistent	↓ apoptosis, SA-β-gal, p16/p21/p53 and *cell-cycle arrest*
Nrf2	2 Direct study	Consistent, limited evidence	Activation of Nrf2 related to ROS and MMP-1 degradation
MAPK/AP-1	3 Mechanistic studies	Consistent	Inhibition of p38/JNK/ERK–c-Jun/c-Fos related to ↓ MMP
TGF-β/Smad	3 Mechanistic studies	Consistent	Activation of the pathway related to ↑ procollagen/collagen
NF-κB	≥1 hands-on study	Limited evidence	miR-1246 prevents IκB-α degradation and NF-κB activation
Notch	1 study	Preliminary evidence	TIMP1 in EVs inhibits Notch1/Hes1 and marker senesens

The most powerful and recurring finding is the restoration of the balance between collagen synthesis and ECM degradation. HASC-EVs increase some types of collagen, elastin and TIMP1 while lowering MMP-1/2/3/9, while subsequent ADSC, BMSC and UCMSC studies consistently confirm a decrease in MMP-1 accompanied by recovery of type I collagen (Choi et al., 2019; Gao et al., 2021; Yan et al., 2023; Zhang et al., 2024).

Quality concerns mainly stem from the dominance of preclinical studies, relatively small animal sample sizes, different UV protocols, the use of protein mass-based doses versus particle counts, and non-uniform characterization of EVs. Based on MISEV2023, TEM or the presence of CD9/CD63/CD81 alone is not sufficient to conclude a preparation is exclusively an "exosome"; the source, separation techniques, characterization, non-vesicular contaminants, and the association of biological effects with EVs need to be reported transparently (Welsh et al., 2024).

Biological Plausibility and MSC Source Comparison

The effects of MSC-EVs on *photoaging* have strong biological plausibility because photoaging is the result of oxidative, inflammatory, senesens, and imbalance between matrix synthesis and degradation. MSC-EVs carry regulatory proteins and RNA that can enter fibroblasts and keratinocytes so that some of these processes are modulated simultaneously. In ADSC-EVs, inhibition of MAPK/AP-1 reduces MMP-1, while activation of TGF-β/Smad increases type I procollagen; activation of Nrf2 in parallel reduces oxidative load (Gao et al., 2021). This suggests that the effects of MSC-EVs are not just antioxidant, but also involve matrix *remodeling* and improvement of cell homeostasis.

Certain EV cargoes provide stronger causal evidence. BMSC-Exos carries miR-29b-3p that targets MMP-2, miR-1246-enriched ADSC-Exos inhibits MAPK/AP-1 while increasing TGF-β/Smad, hUCMSC-Exos carries 14-3-3ζ that activates SIRT1, while AMSC/HUMSC-EVs carry TIMP1 that suppresses Notch1 and senesens markers (Yan et al., 2023; Gao et al., 2023; Wu et al., 2021; Zhang et al., 2024). The findings of PZP in hUCMSC-sEV and miR-125b-5p/TGF-β1/Smad in HFMSC-Exos further support the concept that regenerative effects are determined by cargo composition, not simply the presence of vesicles (Sun et al., 2024; Cui et al., 2025).

Among MSC sources, adipose-derived MSCs have the most extensive evidence base, ranging from *in vitro*, animal, to human studies. ADSC-EVs repeatedly improve the migration of fibroblasts, ROS, MMP, collagen, wrinkles and skin parameters, but the large number of studies does not mean ADSC has been shown to be superior to other sources (Choi et al., 2019; Xu et al., 2020; Gao et al., 2021; Huynh et al., 2025).

Umbilical cord MSCs also show a broad spectrum of activity against keratinocytes and fibroblasts through antioxidant protection, antiapoptosis, anti-senesens and *ECM remodeling* (Liu et al., 2021; Wu et al., 2021; Sun et al., 2024). Comparative studies by Zhang et al. even show that AMSC-EV and HUMSC-EV are equally effective in improving wrinkles, hydration, inflammation and ECM through TIMP1/Notch1, so there is currently no solid basis to claim a single source is superior (Zhang et al., 2024).

Evidence of bone marrow MSCs is more limited and comes mainly from *in vitro* HDF models. Two studies showed a decrease in ROS, TNF-α, IL-6, IL-1β and MMP as well as an increase in collagen/migration via miR-29b-3p and MAPK/AP-1, but there has been no *in vivo* or clinically comparable validation of ADSC/UCMSC in this body of evidence (Yan et al., 2023).

Standardization, Clinical Translation, and Safety

Isolation methods are an important source of heterogeneity. Choi et al. used *tangential flow filtration*, Zhang et al. used filtration or concentration followed by ultracentrifugation, while other studies used ultracentrifugation or procedures that were not fully reported in the publication summary (Choi et al., 2019; Zhang et al., 2024). These differences can affect *yield*, purity, protein/lipoprotein contamination, and cargo composition so that the two preparations that are both called "exosomes" are not necessarily equivalent biological products. MISEV2023 therefore advocate EV terminology, reporting of cell sources and culture conditions, separation procedures, physical and molecular characterization, and adequate functional control (Welsh et al., 2024).

The dose heterogeneity was also very large. Xu et al. administered 150–300 μg subcutaneously per week for eight weeks, Wu et al. used 1 mg subcutaneously in the acute photodamage model, Zhang et al. used 200 μg per rat, while Huynh et al. used a topical preparation of 50–100 μg/mL twice weekly (Xu et al., 2020; Wu et al., 2021; Zhang et al., 2024; Huynh et al., 2025). The unit differences between total proteins, concentrations, and particle counts make *dose-response* between studies indirectly comparable.

The route of administration also determines translation. Subcutaneous injections provide direct access to the dermis but are more invasive, while topical EV penetration through intact skin is limited. The use *of sponge spicules* increased the penetration of hUCMSC-Exos by about 5.87 times in experimental models, whereas Estupiñan et al.'s clinical trial used RFMN to create microchannels prior to topical administration (Zhang et al., 2020; Estupiñan et al., 2025). Consequently, such clinical outcomes cannot be attributed entirely to exosomes, as RFMN itself stimulates neocollagegenesis and both sides of the face get the procedure (Estupiñan et al., 2025).

The translational gap is still large. Of the 14 main studies synthesized, only one was a direct clinical study on facial *photoaging*, with 15 participants, a *non-randomized split-face* design , and no statistical analysis for clinical assessment due to small sample sizes. Although both sides showed increased wrinkles, dychromia, erythema, texture, collagen I and glycosaminoglycans and no serious *adverse events were found* , the results were more appropriately considered preliminary clinical evidence, rather than definitive evidence of effectiveness (Estupiñan et al., 2025).

The safety aspect has also not been inferred from the small study. The FDA states that exosome products used to treat human conditions are within the regulatory scope of drugs or biological products and require pre-marketing assessment; the FDA has also warned that there are no FDA-approved exosome products in its safety notice (FDA, 2019). By 2025, the FDA sent a *warning letter* against the marketing of products claimed to be "human umbilical cord mesenchymal stem cell-derived exosomes" because they are marketed as new drugs and biological products that have not yet been approved (FDA, 2025). It emphasizes the need for donor control, sterility, purity, *batch-to-batch consistency*, contaminant potential, stability, and *potency assay* prior to clinical application.

The next research priorities are product standardization based on MISEV2023; dose quantification with the number of particles as well as proteins; direct comparative studies between ADSCs, UCMSCs, and BMSC-EVs; mechanistic studies with *loss-of-function* to prove active cargo; *dose-finding* and local pharmacokinetics; and multicenter RCTs with vehicle control groups or RFMNs only. Clinical outcomes should combine validated *photoaging* scales with objective measurements of elasticity, hydration, transepidermal water loss, wrinkle profilometry, histological collagen, MMP/TIMP, and long-term safety monitoring (Welsh et al., 2024; Estupiñan et al., 2025).

Limitations

The interpretation of this review is limited by the dominance *of in vitro* and animal studies, the heterogeneity of MSC sources, UVA/UVB models, EV separation techniques, dose units, routes of administration, and outcomes assessed. Some studies use engineered or conditioned exosomes, e.g. *miR-1246-overexpressing exosomes* or ADSCs under hypoxia conditions, so the results cannot be directly generalized to natural MSC-Exos (Gao et al.,

2023; Huynh et al., 2025). In addition, the terminology of "exosomes" in older studies did not necessarily meet the standards of nomenclature and characterization of MISEV2023, while current clinical evidence is still too small and confounded by companion therapies to allow for strong meta-analysis or causal conclusions (Welsh et al., 2024; Estupiñan et al., 2025). Overall, the current evidence is strong at both the biological and preclinical levels but still low to the early stage at the clinical translational level, so MSC-derived EVs are more appropriately positioned as promising experimental regenerative therapies rather than standard therapies for *photoaging*.

CONCLUSION

Mesenchymal stem cell-derived exosomes (MSC-Exos) demonstrate promising potential for skin regeneration in photoaging. Based on the reviewed studies, MSC-Exos can enhance the proliferation and migration of fibroblasts and keratinocytes, promote collagen synthesis and extracellular matrix (ECM) production, and reduce the generation of reactive oxygen species (ROS), inflammatory responses, apoptosis, cellular senescence, and matrix metalloproteinase (MMP) expression. These effects are mediated through various molecular pathways, including Nrf2, MAPK/AP-1, TGF-β/Smad, SIRT1, and TIMP1/Notch1 signaling pathways, as well as through bioactive cargo such as microRNAs and specific proteins.

In vitro and in vivo evidence has shown relatively consistent findings supporting the anti-photoaging and regenerative effects of MSC-Exos. However, variations in MSC sources, exosome isolation and characterization methods, dosages, administration routes, and experimental models have resulted in limited comparability among studies. Human clinical evidence remains limited; therefore, larger-scale clinical studies with standardized methodologies are required to further establish the efficacy, safety, optimal dosage, and translational potential of MSC-Exos as a regenerative therapy for photoaging.

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