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Efficacy of Exosome-Based Therapies for Skin Rejuvenation and Inflammatory Diseases: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - NA.

Review Stage at time of this submission - Risk of bias assessment.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202620066

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 February 2026 and was last updated on 21 February 2026.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis evaluates the clinical efficacy and safety of exosome-based therapies in dermatology using the PICOS framework:

Population (P): Adult human subjects with chronic inflammatory dermatoses (atopic dermatitis, psoriasis, sensitive skin) or undergoing aesthetic skin rejuvenation (photoaging, atrophic acne scars)

Intervention (I): Topically applied, sonophoresis-assisted, or intradermally injected exosomes or extracellular vesicles from any cellular source (adipose-derived MSCs, umbilical cord MSCs, platelets, or autologous blood)

Comparison (C): Placebo, vehicle control, active comparator (e.g., platelet-rich plasma, normal saline), or pre-treatment baseline

Outcomes (O): Primary: clinical improvement rate and standardized clinical severity scores (ECCA, mPASI, IGA). Secondary: objective biophysical parameters (TEWL, skin hydration, elasticity, erythema indices) and safety profiles

Study design (S): Randomized controlled trials, controlled clinical trials, prospective single-arm trials, and early-phase safety studies in human subjects.

Rationale Chronic inflammatory dermatoses and aesthetic skin conditions share a common pathophysiology of impaired skin barrier integrity and dysregulated immune responses. Conventional treatments—including topical corticosteroids, calcineurin inhibitors, systemic biologics, and energy-based devices—frequently provide incomplete relief with notable adverse effects including skin atrophy, immunosuppression, and prolonged post-procedural downtime.

Exosomes (30–200 nm extracellular vesicles) have emerged as a compelling cell-free therapeutic

paradigm. Derived primarily from mesenchymal stem cells, they carry pleiotropic bioactive cargo—including microRNAs, growth factors, and functional proteins—that collectively orchestrates immunomodulation, barrier restoration via ceramide and filaggrin synthesis, and dermal collagen remodeling, without the translational risks of whole-cell therapies.

Although individual clinical trials and narrative reviews have highlighted the potential of exosome-based interventions, no prior quantitative systematic review and meta-analysis has evaluated their clinical efficacy across a spectrum of dermatological conditions or objectively quantified barrier-restoring capabilities through validated biophysical metrics. This evidence gap impedes the establishment of standardized clinical protocols. The present SRMA provides the first aggregated quantitative evidence base to guide clinical practice and future research in exosome-based dermatology.

Condition being studied This review focuses on two pathophysiologically related dermatological condition categories unified by impaired skin barrier function and chronic cutaneous inflammation:

Chronic Inflammatory Dermatoses: Including atopic dermatitis (AD), psoriasis vulgaris, and sensitive skin syndrome. AD is a chronic relapsing inflammatory disease affecting 15–20% of children and 1–3% of adults globally, characterized by Th2-skewed immune dysregulation, deficiency of barrier proteins (filaggrin and ceramides), elevated IgE, and intense pruritus. Psoriasis affects approximately 2–3% of the global population, featuring keratinocyte hyperproliferation and Th17/IL-23-axis–driven inflammation. Sensitive skin syndrome involves cutaneous hyperreactivity, barrier impairment, and neurovascular dysregulation.

Aesthetic Skin Conditions: Including facial photoaging, skin laxity, and atrophic acne scarring, characterized by loss of dermal collagen and elastin, pigmentation irregularities, and compromised epidermal barrier function resulting from UV exposure, intrinsic aging, or post-inflammatory remodeling.

Both categories share underlying pathophysiological mechanisms of barrier dysfunction and aberrant inflammatory signaling, constituting the primary therapeutic targets of the exosome-based interventions evaluated in this review.

METHODS

Search strategy A systematic literature search will be conducted across three major electronic databases from inception to February 15, 2026:
PubMed / MEDLINE
Embase
Cochrane Central Register of Controlled Trials (CENTRAL)
Search string:
("exosomes" OR "extracellular vesicles" OR "mesenchymal stem cell secretome" OR "MSC-derived exosomes") AND ("skin rejuvenation" OR "skin aging" OR "photoaging" OR "acne scar" OR "psoriasis" OR "atopic dermatitis" OR "eczema" OR "erythema" OR "sensitive skin" OR "skin barrier" OR "transepidermal water loss")
Additional searches will include ClinicalTrials.gov and WHO ICTRP for unpublished or ongoing trials, and manual screening of reference lists from included studies and relevant reviews.
No language restriction will be applied during database searching. Full-text eligibility assessment will be limited to English-language articles. Two independent reviewers will perform title/abstract and full-text screening using a standardized form, with disagreements resolved by consensus or a third reviewer.

Participant or population Adult human subjects (aged ≥18 years) presenting with one of the following conditions: (1) chronic inflammatory dermatoses, including atopic dermatitis, psoriasis vulgaris, or sensitive skin syndrome; (2) aesthetic skin conditions, including facial photoaging, skin laxity, or atrophic acne scarring. Studies enrolling pediatric populations, subjects with active systemic infections, malignancy, or immunosuppressive therapy will be excluded.

Intervention Exosomes or extracellular vesicles (EVs) derived from any cellular source, including adipose-derived mesenchymal stem cells (ADMSCs), Wharton's jelly/umbilical cord MSCs, platelets, or autologous blood. Delivery routes include topical application (creams/ointments), device-assisted transdermal delivery (fractional CO2 laser, radiofrequency microneedling, sonophoresis), or intradermal injection.

Comparator Eligible comparators include: (1) placebo or vehicle control (e.g., normal saline, hyaluronic acid sponge without active EV content); (2) active comparator (e.g., platelet-rich plasma, standard topical therapy); (3) pre-treatment baseline measurement in single-arm studies. Studies with no outcome measurement at baseline or follow-up will be excluded.

Study designs to be included The following study designs will be included: randomized controlled trials (RCTs), including split-face and split-body designs; non-randomized controlled clinical trials; prospective single-arm clinical trials with pre- and post-treatment outcome measurements; and early-phase (Phase 1/2) safety and dose-escalation trials. Retrospective studies, case reports, animal studies, in vitro studies, conference abstracts without full-text data, and review articles will be excluded.

Eligibility criteria Inclusion criteria:
Human clinical studies published in peer-reviewed journals
Intervention involves topical, transdermal, or intradermal exosome/EV application
At least one quantifiable outcome reported (clinical score, biophysical parameter, or safety data)
Full-text available
Exclusion criteria:
Non-human or in vitro studies
Plant-derived or non-MSC synthetic nanovesicle studies without EV characterization
Studies not reporting extractable outcome data
Duplicate publications of the same study cohort
Studies where exosomes are combined with systemic biologics as the primary comparator intervention.

Information sources Electronic databases: PubMed/MEDLINE, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL), searched from inception to February 15, 2026. Trial registries: ClinicalTrials.gov and WHO International Clinical Trials Registry Platform (ICTRP) for ongoing or unpublished trials. Grey literature: manual screening of reference lists of all included studies and relevant narrative reviews. No direct author contact is planned unless critical outcome data are missing from published reports.

Main outcome(s)
Primary outcomes:
Clinical improvement rate (dichotomous): proportion of patients achieving predefined clinical success (e.g., IGA responder rate, GAIS improvement); reported as Risk Ratio (RR) with 95% CI
Continuous clinical severity score reduction (continuous): change in standardized scores including ECCA, mPASI, IGA, or equivalent; reported as Standardized Mean Difference (SMD) with 95% CI
Outcome assessment timepoints: end-of-treatment and final follow-up (whichever is latest reported).

Additional outcome(s)
Secondary outcomes:
Skin elasticity: change in Cutometer R2/R5/R0 values; reported as SMD with 95% CI
Transepidermal water loss (TEWL): change measured by Tewameter; reported as mean difference (MD) or percentage change
Stratum corneum hydration: change measured by Corneometer; reported as MD or percentage change
Erythema index: change in erythema spectrophotometry or a* value; reported as MD
Safety and tolerability: incidence of adverse events (AEs) and serious adverse events (SAEs); reported narratively.

Data management Literature screening and data management will be conducted using Rayyan systematic review software for duplicate removal and title/abstract screening. A standardized data extraction form (Microsoft Excel) will be used to collect the following variables: first author, publication year, country, study design, sample size, patient diagnosis, exosome source and delivery method, follow-up duration, outcome measures with baseline and post-treatment values, and adverse event data. Two reviewers will independently extract data; discrepancies will be resolved through discussion or adjudication by a third reviewer. Extracted data will be stored in a password-protected institutional server.

Quality assessment / Risk of bias analysis Methodological quality will be assessed using the Cochrane Risk of Bias tool version 2 (RoB 2.0) for randomized controlled trials, evaluating five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selection of reported results.

For non-randomized and single-arm studies, the Newcastle-Ottawa Scale (NOS) adapted for prospective cohort studies will be applied, assessing selection, comparability, and outcome domains.

Risk of bias assessments will be performed independently by two reviewers, with disagreements resolved by consensus. Results will be summarized in a risk of bias summary plot generated using RevMan 5.4. Overall certainty of evidence for primary outcomes will be evaluated using the GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework.

Strategy of data synthesis For controlled trials providing quantitative outcome data, a random-effects meta-analysis (DerSimonian-Laird method) will be conducted to account for anticipated clinical heterogeneity arising from variation in exosome sources, delivery methods, and study populations. Dichotomous outcomes will be expressed as Risk Ratio (RR) with 95% CI; continuous outcomes will be expressed as Standardized Mean Difference (SMD) or Mean Difference (MD) with 95% CI, depending on whether outcomes are measured on comparable or differing scales.
Statistical heterogeneity will be quantified using the I^2 statistic and Cochrane Q test. I^2 values of 25%, 50%, and 75% will be considered indicative of low, moderate, and high heterogeneity, respectively. For single-arm studies where direct comparison is not feasible, a structured narrative synthesis will be conducted following SWiM (Synthesis Without Meta-analysis) reporting guidelines. All analyses will be performed using RevMan 5.4.

Subgroup analysis Pre-specified subgroup analyses will be conducted for primary outcomes to explore potential sources of clinical heterogeneity:
Exosome source: ADMSCs vs. umbilical cord MSCs vs. platelet-derived vs. autologous blood-derived
Delivery method: topical application vs. device-assisted delivery vs. intradermal injection
Disease category: inflammatory dermatoses vs. aesthetic/aging indications
Follow-up duration: short-term (≤4 weeks) vs. medium-term (5–12 weeks) vs. long-term (>12 weeks)
Subgroup analyses will only be performed if a minimum of two studies are available per subgroup. Results will be interpreted cautiously given the limited number of eligible controlled trials.

Sensitivity analysis Sensitivity analyses will be performed to assess the robustness of primary meta-analysis findings:
Risk of bias exclusion: re-running analyses after excluding studies rated as high overall risk of bias per RoB 2.0 or NOS assessment
Study design restriction: limiting analyses exclusively to randomized controlled trials (RCTs), excluding non-randomized controlled trials
Statistical model: comparing results from random-effects vs. fixed-effects models to evaluate the influence of the pooling method
Leave-one-out analysis: sequentially removing one study at a time to identify any single study with disproportionate influence on the pooled estimate
Significant changes in pooled estimates following sensitivity analyses will be transparently reported and discussed as limitations of the evidence base.

Language restriction No language restriction will be applied during database searching. Full-text screening will be limited to English-language articles.

Country(ies) involved Taiwan (primary institution). Collaborative affiliations may include international co-authors pending manuscript finalization.

Other relevant information Funding: This study received no external funding. All analyses were conducted independently without commercial sponsorship from exosome manufacturers or distributors.
Conflicts of interest: The authors declare no conflicts of interest relevant to the subject matter of this review.
Protocol deviations: Should any deviations from this registered protocol become necessary during the review process (e.g., modifications to eligibility criteria or outcome prioritization), these will be transparently documented and justified in the final published manuscript.
PRISMA compliance: The final manuscript will be reported in full accordance with the PRISMA 2020 statement and the PRISMA 2020 for Abstracts checklist.
Future research context: The findings of this clinical meta-analysis will inform a subsequent preclinical investigation examining the effects of human umbilical cord-derived MSC exosomes in a murine model of atopic dermatitis, as well as a planned animal-model–focused meta-analysis evaluating exosome interventions across preclinical dermatology studies.

Keywords Exosomes; Extracellular vesicles; Systematic review; Meta-analysis; Atopic dermatitis; Psoriasis; Skin barrier; Skin rejuvenation; Dermatology.

Dissemination plans The results of this systematic review and meta-analysis will be submitted for publication in a peer-reviewed international dermatology or regenerative medicine journal (target journals include Journal of the European Academy of Dermatology and Venereology, Dermatologic Therapy, or Journal of Cosmetic Dermatology). Findings will additionally be presented at relevant international conferences in dermatology and regenerative medicine. The

registered protocol on INPLASY will be publicly accessible upon approval to ensure research transparency and to minimize duplication of systematic review efforts in this rapidly evolving field.

Contributions of each author

Author 1 - CHIA-TA WU - Conceived the study, designed the protocol, performed data extraction, conducted statistical analysis, drafted and revised the manuscript, and approved the final version.
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