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Dual-Source Filtration for Purity & Safety: A Research Framework for Medical-Grade Cosmeceutical Serums

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ABSTRACT

Extracellular vesicles (EVs) from human stem-cell cultures and plant sources show promise for dermal regeneration and antioxidant defense, but translation requires rigorous purification and safety controls.

Objective:To outline and justify a dual-source workflow that isolates nanosized vesicles (50–150 nm) from human mesenchymal stem-cell conditioned media (hMSC-CM) and botanical extracts using ultrafiltration (UF)followed by size-exclusion chromatography (SEC), combined under sterile, endotoxin-free(human EVs) and pesticide-free(plant EVs) specifications. Methods/Significance:The platform aligns with MISEV2023 guidance on EV production, separation, characterization, and reporting, and leverages recent advances demonstrating SEC's advantages for EV purity and reproducibility. Outcomes (anticipated):Hybrid human–plant vesicle serums for post-procedure recovery and photoaging support, backed by preclinical potency assays and dermatologist-relevant endpoints.

1. Introduction

EVs are nanoscale, lipid-bilayer vesicles that carry microRNAs, proteins, and lipids with roles in tissue repair and immune modulation. hMSC-EVs accelerate wound closure, enhance collagen remodeling, and reduce inflammation in skin models and early clinical translation, positioning them as cell-free candidates for regenerative dermatology. Plant-derived exosome-like nanoparticles (PELNs) provide biocompatible carriers rich in antioxidant/anti-inflammatory phytochemicals and can aid skin delivery. Standardized isolation and safety testing are essential to avoid protein/lipoprotein co-isolation, residual endotoxin, or agricultural contaminants. BioMed Central +3 PubMed Central +3 PubMed +3

Hypothesis.A dual-source, orthogonal purification(UF→SEC) can yield high-purity hMSC-EVs and PELNs that are analytically defined, reproducible, and safe for medical-grade cosmeceuticalapplications. This design follows MISEV2023 recommendations emphasizing transparent reporting of production, separation, and functional assays. ISeV Journals +1

2. Rationale and Prior Evidence

2.1 Human hMSC-EVs for skin regeneration

Systematic and narrative reviews show hMSC-EVs promote angiogenesis, fibroblast proliferation, and remodeling with favorable safety compared to cell therapy; recent meta-analyses and umbrella reviews extend efficacy signals across wound repair contexts. PubMed Central +2 Wiley Online Library +2

2.2 Plant-derived vesicles (PELNs) as protective nanocarriers

Recent updates describe PELNs from citrus, ginger, grape, and green tea as stable, non-toxic vesicles that carry intrinsic antioxidants, enhance barrier function, and may facilitate cutaneous delivery of co-actives. MDPI +1

2.3 Why UF→SEC?

SEC increasingly replaces precipitation/ultracentrifugation for applications demanding higher EV purity and functional reproducibility, offering superior removal of protein contaminants and lipoproteins across biofluids. ScienceDirect +2 Frontiers +2

3. Methods (Proposed Workflow)

3.1 Source materials

Human:Serum-free hMSC-CM (mycoplasma-negative cell banks, early passages; chemically defined media).

Plant:Food-grade or pharmacopeial botanicals (e.g., Camellia sinensis, Citrusspp., Zingiber officinale), washed and cold-pressed/juiced under HACCP.

3.2 Purification sequence

1. Pre-clear:0.45 µm → 0.22 µm filtration of CM/plant juice to remove cells/debris.

2. Tangential-flow UF:100–300 kDa membranes to concentrate vesicles and remove <10 nm solutes.

3. SEC:Calibrated porous media to collect 50–150 nm EV fractions, minimizing co-isolated proteins/lipoproteins.

4. Sterile formulation:Isotonic buffer (pH 6.0–7.0), oxygen-barrier packaging; 2–8 °C storage (stability per ICH). Method reporting will follow MISEV2023checklists (inputs, yields, fraction IDs). ISeV Journals +1

3.3 Characterization & release

- Identity/size:NTA/TRPS (mode 50–150 nm), cryo-TEM; human EV markers (CD9/CD63/CD81) and negative controls; plant vesicle markers per PELN literature.

- Purity:Particle:protein ratio; ApoB/lipoprotein depletion indices; RNA content.

- Potency (in vitro):Fibroblast scratch closure, keratinocyte migration, VEGF/IL-10 modulation, UV-ROS suppression in 3D skin models.

- Safety:

✔Endotoxin:LAL (chromogenic) with low endotoxin recovery (LER)controls and TLR4-blocking in bioassays, acknowledging masking risks documented for LPS in formulated matrices. ScienceDirect +2 PubMed +2

✔Pesticides (plant):Targeted LC–MS/MS panel vs. MRLs; require non-detect (nd) for release.

✔Bioburden/sterility:Per cosmetic-device context; mycoplasma-free certification for hMSC production.

✔Irritation/sensitization:HRIPT and in vitro cytokine panels.

4. Safety-by-Design and Quality System

- Endotoxin-free (human EVs):Controlled upstream culture, endotoxin-screened raw materials, validated cleaning; spike-and-recovery/LER investigations to prevent false negatives; JoVE protocols provide practical controls for endotoxin avoidance and evaluation. PubMed +1

- Pesticide-free (plant EVs):Certified supply chains; pre-harvest/COA verification; SEC helps reduce low-MW contaminants; LC–MS confirmation on final bulk. MDPI

- Documentation:Batch records include NTA counts, mode size, purity indices, endotoxin (EU/mL), pesticide panel, sterility/bioburden, and potency readouts—MISEV-aligneddata package for each lot. PubMed Central

5. Experimental Plan

5.1 Preclinical

※In vitro:

- Human dermal fibroblasts: scratch closure (%/24–48 h), COL1A1/COL3A1 qPCR, pro-collagen ELISA.

- Keratinocytes: migration, IL-1α/IL-8 after UV-A; antioxidant endpoints in ROS probes.

- 3D skin equivalents: TEER recovery, histology (H&E, Masson), OCT microvasculature.

※In vivo (non-clinical):

- Murine tape-stripping & UV-photodamage: TEWL, erythema, histologic collagen ratios.

- Safety: local tolerance; HRIPT (human) for finalized serum.

Justification: Cutaneous benefit signals for hMSC-EVs and plant vesicles are well documented across wound and photodamage models, enabling power calculations for effect sizes (e.g., wound closure and dermal density). PubMed Central

5.2 Early clinical (cosmetic endpoints)

Randomized, split-face adjunct after fractional laser (n≈30): downtime (erythema/edema days), profilometry (Ra/Rz), ultrasound dermal density, blinded photo-scoring, and non-invasive cytokine tape-strips. This mirrors EV-based cutaneous studies and adheres to cosmetic-claim boundaries. ScienceDirect

6. Application Concept: Medical-Grade Cosmeceutical Serum

※Target use:Post-procedure recovery and photoaging support.
※Formulation:Aqueous serum (pH 6.0–7.0) with HA/panthenol; EV integrity preserved (no surfactants that disrupt vesicle membranes).
※Dose guidance:Start at 1–5 × 10^9 particles/mL (per NTA) adjusted by in-vitro EC50; apply in clinic (3–4 sessions, 2–4 weeks apart) + home-use for 4–8 weeks; finalize after Phase 0/feasibility data. (SEC-based workflows report robust particle recovery with improved purity, supporting dose precision.) Frontiers

7. Regulatory & Ethics

※Nomenclature & reporting:Use “extracellular vesicles (EVs)” per MISEV2023; avoid definitive “exosome” biogenesis claims unless demonstrated. ISeV Journals

※Claims & path:Cosmetic (non-therapeutic) language for over-the-counter serums; consider device/drug routes if therapeutic claims are

pursued (requires RCTs and regional regulatory submissions).

※Human-cell sourcing:IRB/ethics approvals, donor consent, traceability, mycoplasma-free certification.

※Plant sourcing:HACCP/GACP principles; sustainability documentation.

8. Discussion

Innovation.The dual-source UF→SEC strategy provides orthogonal purification that increases vesicle purity and removes confounders (free proteins, lipoproteins), directly addressing reproducibility concerns raised in EV research and enabling credible cosmetic translation. PubMed Central

Mechanistic complementarity.hMSC-EVs provide pro-regenerative signals (angiogenesis, matrix remodeling), while PELNs contribute antioxidant/anti-inflammatory support and may enhance delivery of co-actives—yielding a broader, more resilient efficacy profile. PubMed Central +1

Risk controls.Endotoxin masking (LER) can produce false "clean" results; validated LAL with LER challenges and orthogonal bioassays (e.g., TLR4 blockade) are mandatory. Agricultural inputs demand pesticide screening with LC–MS; release requires non-detect. ScienceDirect +1

Limitations.EV heterogeneity persists despite SEC; standardized reporting and potency assays are needed. Plant vesicle composition varies by species and harvest; strict specification and COAs mitigate variability. Long-term stability and scale-up economics require further study. ISeV Journals

9. Conclusion

A dual-source filtrationplatform—UF concentration followed by SEC purification—can generate high-purity, safety-verifiedhuman and plant EV preparations suited for medical-grade cosmeceutical serums. By adhering to MISEV2023standards, implementing endotoxin-freeand pesticide-freerelease criteria, and validating function with skin-relevant bioassays and early clinical endpoints, this approach offers a credible path from bench to clinic-adjacent skincare.

Key references

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