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Cross-Kingdom Cargo Blending: A Dual-Vesicle Approach to Brightening and Repair in Melasma and Photoaging

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ABSTRACT

Background:Skin conditions such as melasma and photoaging involve pigment dysregulation, oxidative stress, and reduced dermal matrix integrity. Extracellular vesicles (EVs) derived from human mesenchymal stem cells (hEVs) show promise for dermal repair via pro-collagen and regenerative cargo, while plant-derived exosome-like nanoparticles (pEVs) provide antioxidant/anti-pigmentation signals. **Objective:**To propose a novel "Cross-Kingdom Cargo Blending" strategy wherein filtration-based enrichment concentrates exosomal RNA/protein cargo from both sources, enabling modular formulation of an essence for brightening and repair. **Methods/Concept:**We outline filtration protocols for size- and charge-based isolation, rationalize cargo roles (hEVs: pro-collagen/wound-healing; pEVs: anti-UV/pigment regulation), and present an application pathway for a modular essence aimed at melasma/photoaged skin. **Significance:**This dual-vesicle strategy bridges human repair biology and botanical protective biology, offering an innovative platform aligned with advanced EV analytics and cosmetic personalization.
Keywords:extracellular vesicles; stem-cell EVs; plant-derived vesicles; pigmentation; photoaging; modular essence; cargo blending.

1. Introduction

Melasma and photoaging share underlying biological features: ultraviolet (UV)-induced reactive oxygen species (ROS), melanogenesis up-regulation, and dermal matrix degradation (collagen/elastin) leading to uneven tone and texture. Traditional actives (vitamin C, niacinamide, retinoids) address these partly but lack biologically integrated repair. Extracellular vesicles, nanosized lipid-bound particles secreted by cells, carry proteins, lipids and RNAs that modulate cell behaviour. Human MSC-derived EVs (hEVs) have shown efficacy for dermal repair—promoting fibroblast migration, collagen deposition, angiogenesis and reducing inflammation. ([turn0search12]) Plants secrete exosome-like nanoparticles (pEVs)

which recent studies show can carry antioxidant/anti-UV/anti-melanogenesis signalling, penetrate the skin barrier, and deliver pigment-regulating cargos with minimal immunogenicity. ([turn0search11])
Here we propose a cross-kingdom blending: isolate and concentrate cargo-rich vesicles from hEVs and pEVs, then combine into a modular essence for targeted brightening and repair. The novelty lies in blending human repair-oriented vesicles with plant protective vesicles, delivered via an essence format tailored to melasma/photoaging.

2. Scientific Rationale

2.1 hEV Cargo for Dermal Repair

hEVs carry microRNAs (e.g., miR-19b, miR-192-5p) and proteins that modulate TGF-β/Smad and ECM pathways, promoting collagen restoration, reducing fibrosis and improving wound healing outcomes. ([turn0search12], [turn0search14])

2.2 pEV Cargo for Pigment Regulation & UV Protection

pEVs from sources such as Codium fragileor Panax ginsengshow anti-melanogenic activity in skin models, reduce UV-induced oxidative stress (ROS/NLRP3/IL-18), suppress AP-1/MAPK signalling and lower melanin formation. ([turn0search9], [turn0search11])

2.3 Cargo Blending Approach: Complementarity

By blending hEVs (repair focus) with pEVs (protection/brightening focus), we hypothesize synergistic outcomes: (i) reduce melanin formation and oxidative stress (via pEVs) and (ii) regenerate dermal matrix and improve tone/texture (via hEVs). Filtration-based quantification ensures reproducible inputs.

3. Methods (Proposed Workflow)

3.1 Isolation & Concentration

Pre-clear hMSC-CM and botanical juice (e.g., green tea/ginseng) by 0.45 μm → 0.22 μm filtration.

Use tangential-flow ultrafiltration (TFF) to concentrate e.g., 100–300 kDa cut-off membranes.

Follow with size-exclusion or charge-based chromatography to isolate 50–150 nm vesicles, remove protein/lipoprotein contaminants in line with MISEV2023 standards.

3.2 Cargo Enrichment & Quantification

Quantify particles via Nanoparticle Tracking Analysis (NTA): mode size, concentration.

Assess cargo load: protein content (BCA), RNA content (RiboGreen) and optionally specific microRNA assays (hEVs) or pigment-regulating miRNAs (pEVs). ([turn0search18])

Create blend ratios by particle count and cargo normalization (e.g., 70% hEVs + 30% pEVs, ensuring same total particles).

3.3 Essence Formulation

※Vehicle: serum base (aqueous/glycol mix) with pH ~6.0, low surfactant stress on vesicles; include light-protective packaging.

※Three ratios tested:

- Repair-dominant(70% hEV : 30% pEV)

- Balanced(50:50)

- Bright/Protection-dominant(30% hEV : 70% pEV)

3.4 In-vitro & Preclinical Evaluation

Pigmentation model: UV-exposed keratinocyte/melanocyte co-culture; melanin content, TYR/TRP1 expression.

Dermal repair model: fibroblast migration/scratch; collagen I/III expression; 3D skin equivalent with UV+age insult.

Compare each ratio vs single-source controls for melanin suppression + matrix repair metrics.

3.5 Safety & Documentation

Ensure endotoxin-free (for hEVs) and pesticide-free (for pEVs) via standard assays.

Document particle:protein/RNA index, size distribution, cargo miRNA/protein panel.

Human cell-origin materials must comply with applicable cosmetic/regulatory guidelines.

4. Potential Outcomes & Interpretation

※Brightening/depigmentation: pEV-rich blends expected to reduce melanin content, TYR/TRP1 expression, and oxidative stress markers (e.g., HO-1, 8-OHdG) via pigment-regulating cargo. ([turn0search9])

※Repair/matrix improvement: hEV-dominant blends expected to increase fibroblast migration, collagen deposition and reduce matrix-metalloproteinase activity. ([turn0search0])

※Hybrid benefit: Balanced blends may offer both visible brightening (tone-evening) and improved texture (dermal density) for photoaged skin.

※Demonstrated cargo quantification + blend reproducibility ensures label-ready claims and batch-to-batch consistency.

5. Discussion

This cross-kingdom cargo blending addresses unmet needs in melasma/photoaging: cocktails that both protect pigment regulationand repair dermal structure. By isolating and quantifying the key cargo from each vector (hEVs and pEVs), the formulation offers transparency and mechanistic grounding often absent in cosmetic claims. Challenges include: sourcing scalable pEVs with reproducible cargo, ensuring stability of blended vesicles in formulation, and regulatory classification of human-derived EVs in cosmetic products. Future work should include stability studies, dose-response clinical trials and investigation of specific microRNA/protein cargos responsible for brightening vs repair.

6. Conclusion

Cross-kingdom cargo blending of human stem-cell EVs and plant-derived vesicles offers a compelling new paradigm for brightening and repair essences targeting melasma and photoaging. The strategy combines rigorous filtration-based quantification, modular ratio formulation (repair- vs bright-dominant) and an evidence-based mechanism. With appropriate QC, safety controls and clinical validation, this approach has strong potential to advance personalized, high-performance skincare.

Supportive References

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