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EXO

EXOSOME SERUM

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WHAT IS AN EXOSOME?

Exosomes are a type of extracellular vesicles (EVs) that play a crucial role in how cells interact with each other. These tiny entities are enclosed by a membrane and range in size from 30 to 150 nm. Exosomes are released from nearly all types of cells and are found in the body. However, exosomes can also be derived from plant cells which may include fruits, vegetables, or other plants. Plant-derived exosomes (pExosomes) can carry a wide range of bioactive compounds, including proteins, lipids, and vitamins. Exosomes are unique because they carry the traits and functions of their parent cells and can transport bioactive chemicals from donor cells to recipient cells. In the context of skin health and dermatology, exosomes have garnered significant attention due to their role in cell communication and their potential in regenerative medicine and cosmetic applications.

Promoting Wound Healing

Exosomes have been extensively studied in the context of wound healing, particularly in the case of burn wounds. During an injury, cells release exosomes that aid in the healing process. These immune cells help clean the wound and reduce the risk of infection. Exosomes also contain pro-inflammatory proteins that stimulate the release of cytokines and chemokines. These substances initiate the recruitment of immune cells to the wound site and activate wound healing. Additionally, exosomes contain growth factors that stimulate the growth of fibroblasts, helping to close the wound. Exosomes also support cell-to-cell communication by containing microRNA (miRNAs) that regulate gene expression in the cells around the wound. This promotes the formation of new blood vessels, increasing blood flow to the wound site. The increased blood flow delivers oxygen and nutrients to the wound, further accelerating the healing process. Exosomes can reduce inflammation and increase the production of extracellular matrix and growth factors, resulting in improved skin quality and healing. This is favourable as exosomes facilitate accelerated and efficient wound healing by promoting the natural repair processes needed to restore the skin after an injury.

Dermal effects: ↑recovery of important cellular functions, ↑ migration, ↑proliferation, ↑differentiation, ↓inflammation, ↑ angiogenesis, ↑re-epithelialization, ↑collagen, ↑ immunoregulation, ↑wound closure, ↓healing time, ↑ aesthetic healing

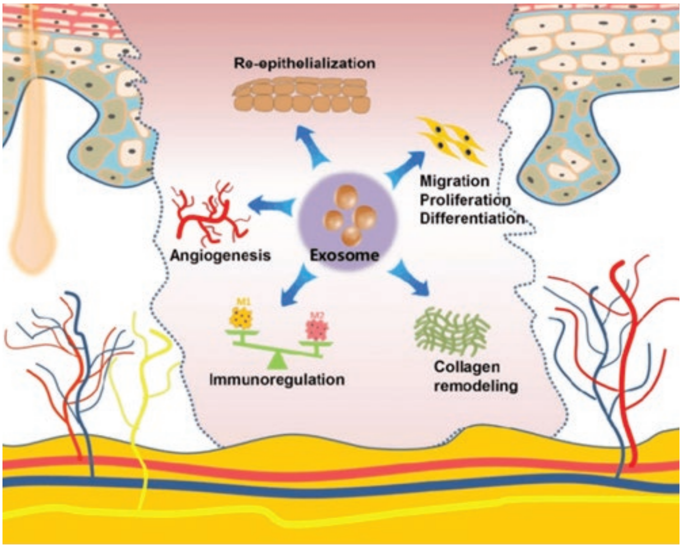

Figure 2. Role and regulatory mechanism of exosomes on the skin and wound healing. Exosomes exert their repair capacity in skin injury by promoting skin cell migration, proliferation and differentiation, enhancing re-epithelization, stimulating angiogenesis, remodelling collagen, and regulating the immune function (Xing *et al.*, 2020).

Anti-inflammatory Properties

Exosomes play a crucial role in reducing inflammation and are beneficial for treating various inflammatory skin conditions. Atopic dermatitis (AD), i.e., eczema, is an example of an inflammatory skin condition with general treatment options that can lead to skin thinning and eczema flare-ups upon stopping treatment. Eczema prevalence in adults increased from 7.9% in 1997 to 12.6% in 2018. Interestingly, exosomes released from keratinocytes contain anti-inflammatory mediators such as transforming growth factor beta (TGF-β), which can suppress the activation of T cells and reduce inflammation. Exosomes released from mast cells can also contain regulatory cytokines such as Interleukin (IL)-10 and TGF-β, which can suppress the activation of T cells and reduce inflammation. Indicating exosomes can reduce inflammation and promote skin barrier restoration by increasing ceramide and dihydroceramide production.

Interestingly, pExosomes secreted by cells involved in inflammation have superior inflammatory affinity and targeting capabilities. This facilitates improved delivery to inflammatory cells via the interaction of surface antibody receptors on the cell surface which can lead to enhanced anti-inflammatory effects.

Dermal effects: ↓inflammation, ↓ redness, ↓ swelling, ↓ pain, ↓ itching, ↑ dermal barrier function, ↑ ceramide, ↑ dihydroceramide

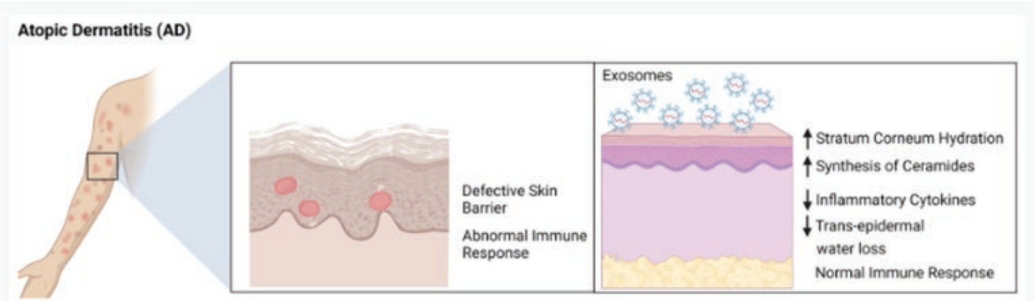

Figure 3. Role of exosomes in ameliorating atopic dermatitis (AD) (Thakur *et al.*, 2023).

Stimulating Collagen Production

Exosomes can benefit skin care as these vesicles can contain proteins, lipids, and other molecules that promote healing, hydration, and skin protection. These included components can boost collagen production, reduce inflammation, and shield the skin from environmental stressors. Additionally, exosomes can enhance the effectiveness of other active ingredients like hyaluronic acid, peptides, and antioxidants. This is confirmed by a study illustrating how Adipose stem cell derived-condition media (ASC-CM) and Bone marrow stem cell-derived (BMSC)-exosomes can decrease reactive oxygen species (ROS) and tumour necrosis factor-alpha (TNF-α) while increasing TGF-β, resulting in higher matrix metalloproteinase-1 (MMP-1) and pro-collagen type I. This leads to increased collagen synthesis, improved elasticity, and reduced wrinkle formation, making it an effective anti-ageing therapy. Exosomes can also help reduce wrinkles and fine lines by stimulating collagen production and repairing skin blemishes such as sun damage and acne scars. The proteins and lipids in exosomes can hydrate the skin, thus improving its texture. Additionally, exosomal ingredients like cytokines, nucleic acids, proteins, and other bioactive compounds can protect the skin from environmental stressors and reduce the appearance of dark spots and other discolouration. Overall, pExosomes offer promising therapeutic and anti-ageing benefits by improving skin tone, dermal elasticity, and aesthetic appearance.

Dermal effects: ↑ collagen, ↓ inflammation, ↑ protection from environmental stressors, ↑ effectiveness of other ingredients, ↑ skin elasticity, ↓ wrinkles, ↓ fine lines, ↑ scar appearance, ↓ pigmentation, ↑ skin tone, ↑ aesthetic appearance

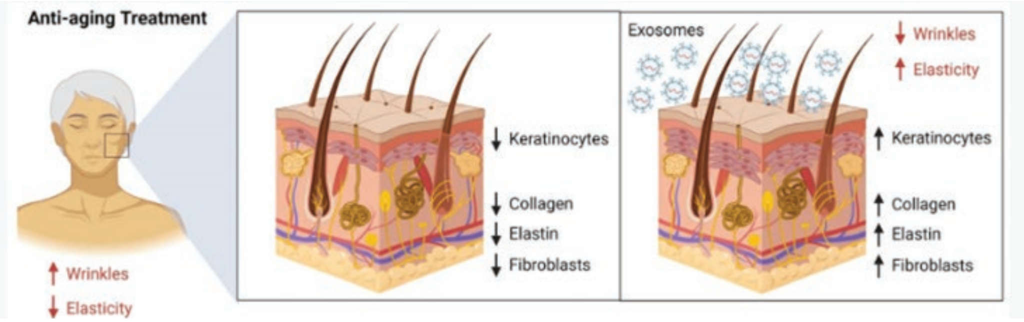

Figure 4. Role of exosomes for anti-ageing treatment (Thakur *et al.*, 2023).

Enhancing Skin Regeneration

Facial rejuvenation includes a wide variety of treatments, from laser resurfacing to chemical peels. Amid facial rejuvenation, a new technique is gaining attention: exosome facial rejuvenation. This innovative procedure uses stem cells and the body's natural healing powers to produce long-lasting, natural-looking results. The process begins with a fat biopsy from the patient, which is then processed to extract the stem cells and exosomes. The stem cells and their exosomes are then injected into the facial skin, which is shown to stimulate the body's natural healing process. The exosome facial rejuvenation process can help to reduce wrinkles, dark circles, and age spots. The process also helps to improve skin tone and elasticity by increasing collagen production. In addition, exosomes have demonstrated their aesthetic skin regeneration capacity by employing exosomes in skin flap reconstruction. Exosome use in skin flap reconstruction involves direct injection into the skin flap to promote angiogenesis and wound healing. Studies have demonstrated that injecting exosomes derived from adipose mesenchymal stem cells (MSCs) into a skin flap can significantly improve the survival rate of the flap and reduce scarring. Therefore, the ability of exosomes to stimulate the production of collagen and elastin, both crucial for skin regeneration, makes exosomes an attractive option for reconstructive surgery.

Dermal effects: ↑ regeneration of skin cells, ↑ skin rejuvenation, ↑ natural healing, ↑ long-lasting effects, ↑ natural-looking results, ↓ wrinkles, ↓ pigmentation, ↑ collagen, ↑ elastin, ↑ skin elasticity, ↑ skin tone, ↓ scarring, ↑ aesthetic appearance

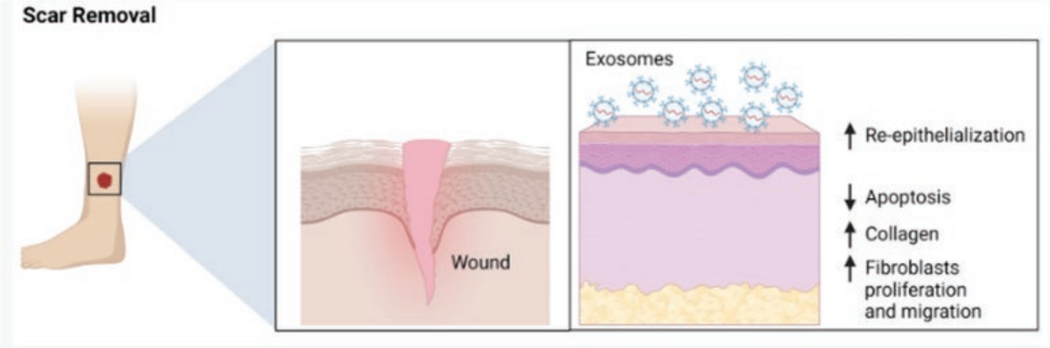

Figure 5. Role of exosomes in the treatment of scars (Thakur *et al.*, 2023).

Targeted Delivery of Therapeutic Agents

pExosomes show great promise as nanocarriers for various treatments due to their unique ability to cross biological barriers and migrate into tissue areas without a blood supply. However, their insufficient targeting ability sometimes restricts their clinical applications, necessitating advanced strategies for improved efficacy. To enhance tissue-specific targeting ability, studies have suggested conjugating exosomes with selected peptides through surface functionalization to enable the targeting of specific skin conditions. In terms of cosmeceutical exosome employment, it can be possible to intrinsically localize a targeted cell or tissue to selectively address a specific skin concern like pigmentation or improve aesthetic healing of scars. This is beneficial since targeted delivery of therapeutic agents can deliver therapeutic agents directly to target cells, increasing the efficacy of treatments and reducing side effects.

Dermal effects: ↑tissue-specific targeting, ↓ pigmentation, ↑ scar appearance, ↑ treatment efficacy, ↓ side effects, ↑ aesthetic appearance

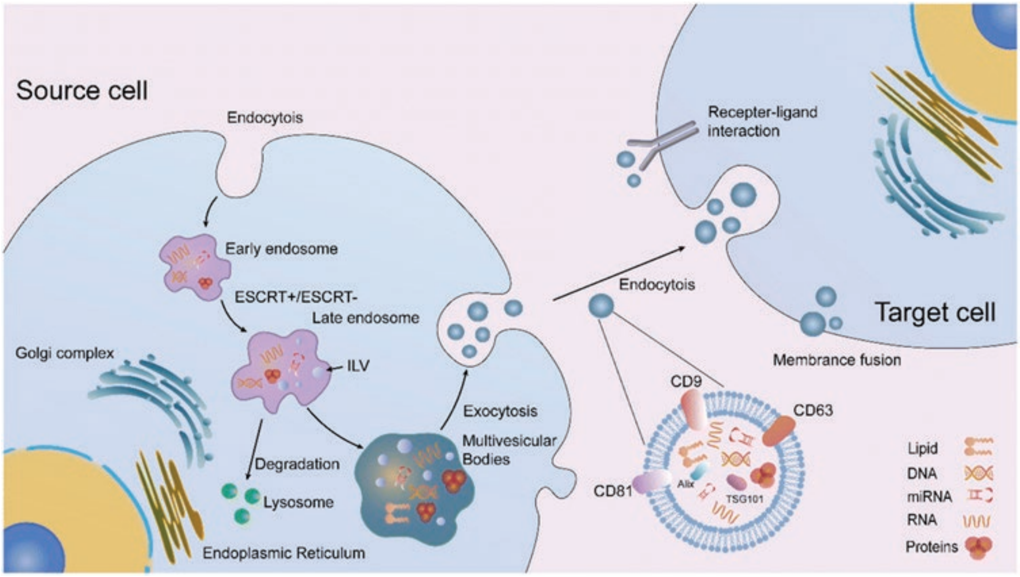

Figure 6. Illustration of the principles behind exosome-based targeted therapeutic agent delivery (Zhang *et al*., 2023).

Immunomodulatory Effects

Findings strongly implicate exosomes as a crucial component in modulating the immune system during a variety of different physiological perturbations. Therefore, the potential importance of exosomes and the significant roles they exercise in cellular communication is imperative for future skin care approaches. Research revealed that exosomes can contain immunomodulatory molecules such as miRNAs, that are shown to regulate the expression of genes involved in immune responses. For example, it was discovered that exosomes released from mast cells contain miRNAs that stimulate the downregulation of pro-inflammatory cytokines expressions such as IL-4 and IL-13 which have demonstrated potential to reduce inflammation in AD patients. Immune system modulation facilitated by Exosomes can lead to reduced inflammation and improve overall skin health.

Dermal effects: ↑ immune system modulation, ↑ gene expression regulation, ↓ pro-inflammatory cytokines, ↓ inflammation, ↑ skin health

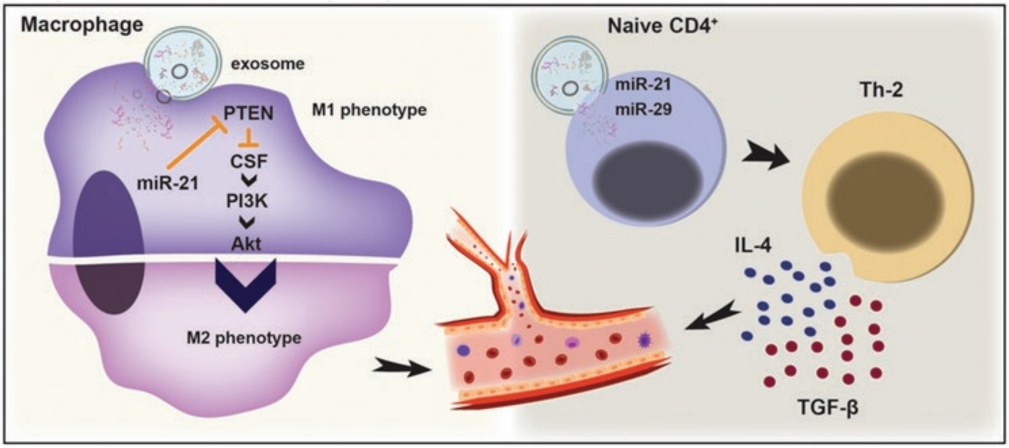

Figure 7. Immunomodulatory effects of exosomes during regulation of the inflammatory response (Moeinabadi-Bidgoli *et al.*, 2023).

Safety and Biocompatibility

The efficiency and safety of exosomes require a methodical examination to determine their individuality and purity. The International Society for Extracellular Vesicles (ISEV) released Minimal Information for Studies of Extracellular Vesicles (MISEV) guidelines in 2014 and 2018 to standardize EVs isolation and characterization procedures, addressing the essential characteristics to consider in EVs-based studies to ensure safety when developing and employing exosomes. Apart from the safety ensured by the released guidelines, pExosome carriers are considered safe due to being superiorly biocompatible, enabling easier uptake of ingredients by cells and avoiding drug resistance. Additionally, pExosome carriers can enhance ingredient stability and half-life if optimally formulated which further contributes to the safety and efficacy of exosome-based products. This low-risk safety profile of pExosomes can be attributed to the natural derivation of exosomes providing safe options for various therapeutic and cosmetic applications.

Dermal effects: ↓risk of dermal irritation, ↑skin compatibility,↑biodegradability,↑ingredient effectiveness

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Potential in Personalized Medicine

Personalized or precision medicine is based on using patient-specific information like genetic background or environmental and lifestyle factors to make decisions about the best course of treatment. Many biological patient-specific factors can be traced to blood or tissue biomarkers and many of those biomarkers can be found on/in EVs. Thus, EVs can be used to diagnose disease and ideally, if biomarkers can be identified early, for preventative medicine. Patient-specific biomarkers and early biomarkers using EVs allow tailored decisions from an aesthetic point of view to potentially allow the development of individualized skincare regimens able to address the skincare needs of different individuals.

Dermal effects: ↑tailored skincare, ↑skin health, ↓ reduced side-effects, ↑preventative action

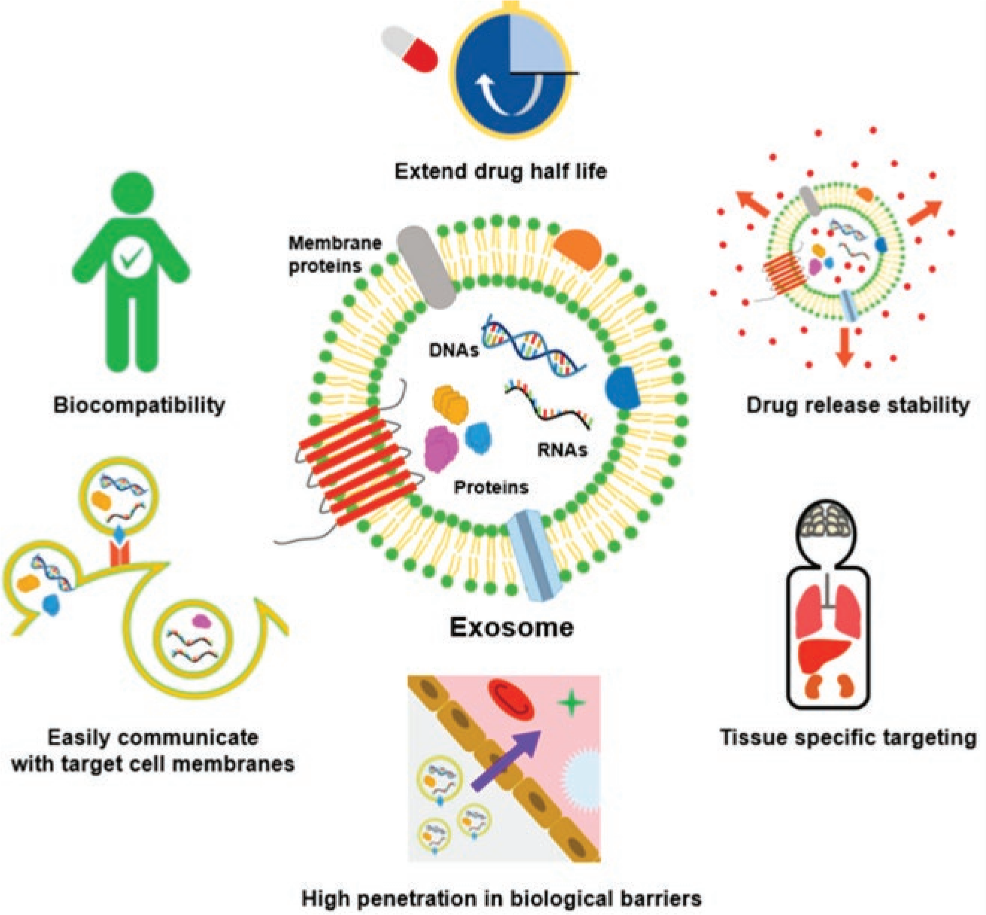

Figure 8. Explaining the advantages of high biocompatibility and tissue-specific targeting for personalized medicine as exhibited by exosomes (Kim *et al.*, 2021).

EXOSOMES, THE FUTURE OF AESTHETIC SKINCARE

In conclusion, exosomes demonstrate significant potential regarding wound healing, anti-inflammatory capacity, stimulating collagen production, enhancing skin regeneration, allowing targeted delivery of therapeutic agents, rendering immunomodulatory effects and can be considered a future leader in personalized medication. Considering the potential benefits of exosomes for the skin and their application in dermatology, BioMedical Emporium eagerly anticipates that through the development of scientific-based, target-design treatment formulations, that aesthetic- and skincare therapies will be transformed.

ABBREVIATIONS

AD:	atopic dermatitis
ASC-CM:	adipose stem cell derived-condition media
BMSC:	bone marrow stem cell-derived
EVs:	extracellular vesicles
IL:	interleukin
ISEV:	International Society for Extracellular Vesicles
miRNA:	microRNA
MISEV:	Minimal Information for Studies of Extracellular Vesicles
MMP:	matrix metalloproteinase
MSCs:	mesenchymal stem cells
PRP:	platelet-rich plasma
pExosomes:	plant-derived exosomes
RNA:	ribonucleic acid
ROS:	reactive oxygen species
TGF-β:	transforming growth factor beta
TNF-α:	tumour necrosis factor-alpha

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