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*Review*

# Plant-Derived Extracellular Vesicles for Cosmetic and Regenerative Applications: Current Evidence, Research Trends, and Future Perspectives

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## Abstract

Plant-derived extracellular vesicles (PDEVs), also referred to as plant exosomes or exosome-like nanovesicles, have emerged as promising natural bioactive nanoparticles for cosmetic and regenerative applications. Owing to their biocompatibility, intrinsic bioactive cargo, and ability to interact with mammalian cells, PDEVs are increasingly investigated as agents for skin rejuvenation, wound healing, photoprotection, pigmentation control, and skin barrier enhancement. However, the available evidence remains fragmented across different plant sources and experimental models. This review aimed to summarize and critically evaluate the current evidence regarding the cosmetic and regenerative properties of PDEVs. Experimental studies investigating the effects of PDEVs on skin cells, reconstructed skin models, animals, or human subjects were systematically identified and analyzed. The available evidence consistently demonstrated that PDEVs promote skin regeneration and tissue repair. The most frequently reported effects included enhanced keratinocyte and fibroblast proliferation and migration, accelerated wound closure, increased collagen synthesis, reduced oxidative stress, activation of antioxidant defense pathways, and suppression of inflammatory responses. Additional studies reported improvements in skin barrier function, hydration, photoprotection, pigmentation control, and cellular senescence. Collectively, the available studies demonstrate consistent regenerative, antioxidant, anti-inflammatory, and skin-protective effects of PDEVs. Overall, PDEVs represent multifunctional bioactive nanomaterials with substantial potential for cosmetic applications. While clinical translation remains limited by regulatory and standardization challenges, cosmetic use appears to offer a more immediate route toward commercialization. Further standardization, mechanistic studies, and clinical investigations are required to support the broader implementation of PDEV-based technologies.

**Keywords:** plant-derived extracellular vesicles; regenerative medicine; wound healing; cosmeceuticals; drug delivery

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## 1. Introduction

Plant-derived extracellular vesicles (PDEVs), also referred to as plant exosomes or exosome-like nanovesicles, have recently emerged as a promising class of natural bioactive nanoparticles with potential applications in biotechnology, medicine, and cosmetic science [1,2]. These membrane-enclosed nanosized structures are secreted by plant cells and participate in intercellular communication through the transport of proteins, lipids,

metabolites, messenger RNAs, and small regulatory RNAs [3]. Similar to mammalian extracellular vesicles, PDEVs are increasingly recognized as important mediators of biological signaling and molecular transport.

In recent years, growing attention has been directed toward the interaction of PDEVs with mammalian cells. Experimental evidence indicates that plant-derived vesicles can be internalized by various human cell types and modulate multiple biological processes associated with tissue regeneration, oxidative stress responses, inflammation, and cellular homeostasis [4,5]. These findings have stimulated interest in their potential use as naturally derived bioactive agents for skin care, regenerative medicine, and dermatological applications.

Compared with mammalian extracellular vesicles, PDEVs offer several practical advantages. They can be isolated from edible plants, medicinal herbs, agricultural by-products, algae, and plant cell cultures, providing potentially scalable and sustainable production platforms [6]. Furthermore, PDEVs generally exhibit low toxicity, low immunogenicity, and high biocompatibility [7,8]. Their lipid bilayer membrane protects encapsulated biomolecules from degradation and may facilitate transport across biological barriers, making them attractive candidates for both therapeutic and cosmetic applications.

An additional feature that distinguishes PDEVs from conventional botanical ingredients is their dual functionality. Besides carrying endogenous bioactive compounds that may directly influence cellular responses, PDEVs can also serve as natural nanocarriers for the delivery of therapeutic molecules, nucleic acids, antioxidants, peptides, and plant secondary metabolites [9–11]. Recent studies further suggest that the biological properties of PDEVs may be enhanced through bioengineering approaches. In addition to passive loading strategies, molecular modification of donor plants could facilitate the generation of PDEVs enriched with specific regulatory molecules. In particular, small RNAs and artificial microRNAs heterologously expressed in plants have been shown to be encapsulated within PDEVs and induce target gene silencing in recipient cells [12,13]. This combination of intrinsic biological activity, engineerable cargo, and delivery capability has generated considerable interest in the development of PDEVs as multifunctional nanoplatforms.

The cosmetic industry has become one of the most active areas of PDEV research. Increasing evidence suggests that PDEVs may promote skin regeneration, accelerate wound healing, enhance collagen synthesis, reduce oxidative stress, improve skin barrier function, regulate pigmentation, and protect against photoaging [14–16]. These properties are highly relevant to modern cosmeceutical development, where demand for biologically active, sustainable, and naturally derived ingredients continues to increase.

Despite rapidly growing interest in this field, the available evidence remains highly heterogeneous. Studies differ substantially in plant sources, isolation procedures, characterization methods, experimental models, dosing regimens, and outcome measurements. Although numerous reviews have summarized emerging applications of PDEVs, a quantitative assessment of their cosmetic and regenerative efficacy is currently lacking.

Therefore, the aim of the present review was to provide a comprehensive overview of the cosmetic and regenerative properties of plant-derived extracellular vesicles and to analyze current research trends in the field. Specifically, we sought to evaluate their effects on cellular proliferation and migration, wound healing, collagen synthesis, oxidative stress, inflammation, skin barrier function, pigmentation, and other skin-related biological outcomes relevant to cosmetic and dermatological applications.

## 2. Literature Search and Bibliometric Analysis

### *2.1. Data Source and Search Strategy*

A comprehensive literature search was conducted using the Web of Science Core Collection database to identify publications related to PDEVs and their applications in regenerative medicine, wound healing, cosmetology, cosmeceuticals, and drug delivery. The search covered the period from 1 January 2015 to 30 April 2026. The WoSCC database was selected because of its high-quality standardized bibliographic records and comprehensive citation indexing, which are particularly suitable for bibliometric and scientometric analyses. Furthermore, its structured metadata facilitate the construction of citation, co-authorship, and keyword co-occurrence networks.

The search was performed using the Topic Search (TS) field, which includes article titles, abstracts, author keywords, and Keywords Plus. The following search strategy was applied:

TS = ((“plant-derived extracellular vesicle” OR “plant extracellular vesicle” OR “plant-derived EV” OR “plant EV” OR “plant exosome” OR “plant-derived exosome” OR “exosome-like nanoparticle” OR “plant-derived exosome-like nanoparticle” OR “PELN” OR “PDEN” OR “plant nanovesicle” OR “plant-derived nanovesicle”) AND (“drug delivery” OR “drug carrier” OR “nanocarrier” OR “regenerative medicine” OR “tissue regeneration” OR “wound healing” OR “skin regeneration” OR “cosmetic” OR “cosmeceutical” OR “anti-aging” OR “anti-pigmentation”)).

Only peer-reviewed articles and review papers published in English were included. Conference proceedings, editorials, letters, notes, book chapters, and publications in languages other than English were excluded. Duplicate records and publications not directly related to the study topic were removed through manual screening. The literature search workflow is illustrated in Figure 1.

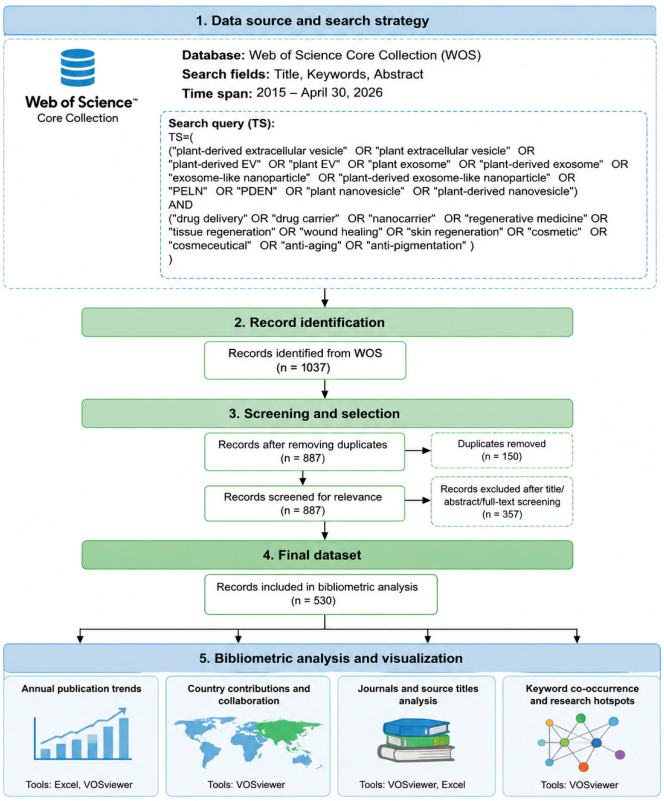


**Figure 1.** The research flow chart.

### *2.2. Bibliometric Analysis and Visualization*

Bibliometric analyses and data visualization were performed using R software (version 4.1.2), the Bibliometrix R package (version 3.0.3; https://www.bibliometrix.org; accessed on 28 September 2020), Microsoft Excel, and VOSviewer (version 1.6.18) [17]. These tools were used to evaluate annual publication trends, country contributions, journal productivity, citation patterns, and keyword co-occurrence relationships within the selected literature. Network visualization analyses were conducted using VOSviewer. For keyword co-occurrence analysis, the minimum occurrence threshold was set at 10. In country collaboration analyses, a minimum of three publications per country was required for inclusion. For citation analyses, only publications with at least 15 citations were included in the visualization. The resulting bibliometric networks were used to identify major research hotspots, collaboration patterns, and emerging trends in PDEVs research.

## 3. Results

### *3.1. Evolution of Research Activity over Time*

Figure 2 illustrates the annual publication output related to PDEVs in regenerative medicine, wound healing, cosmetology, cosmeceuticals, and drug delivery from 2015 to 2026. Overall, the number of publications demonstrated a pronounced upward trend throughout the study period, indicating rapidly growing scientific interest in this emerging research field. During the initial stage (2015–2020), publication activity remained relatively limited, with annual outputs generally below 35 papers. Although moderate fluctuations were observed, the overall growth rate was gradual, reflecting the exploratory phase of PDEVs research. Beginning in 2021, the field entered a period of accelerated development, with the annual number of publications increasing from 51 in 2021 to 80 in 2024. This growth coincided with expanding evidence regarding the therapeutic potential of plant-derived vesicles as natural bioactive agents and drug delivery platforms.

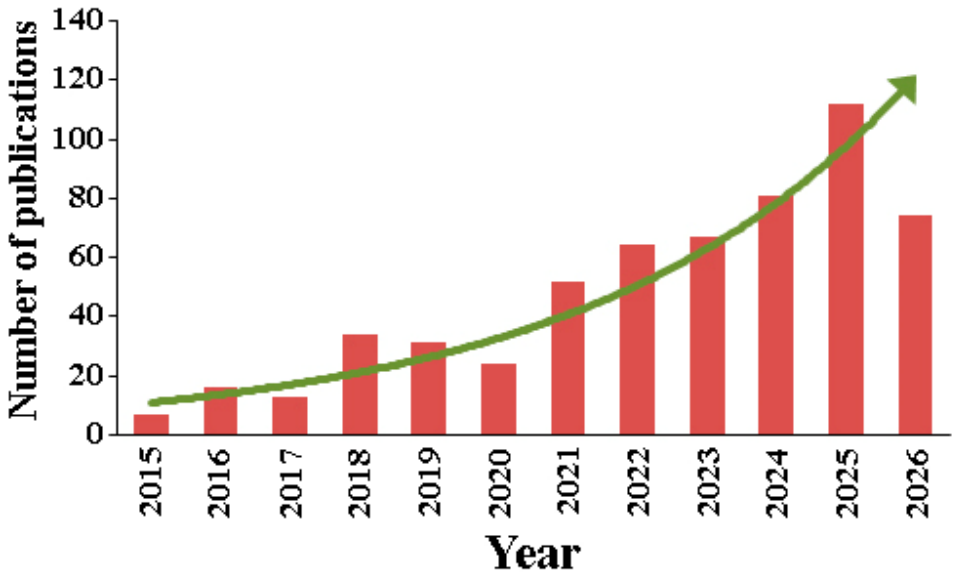


**Figure 2.** Annual publication trends in research on plant-derived extracellular vesicles for regenerative medicine, wound healing, cosmetology, cosmeceuticals, and drug delivery from 2015 to 2026. The green arrow schematically indicates the overall upward trend in the annual number of publications.

A particularly notable increase occurred between 2024 and 2025, when the publication output rose from 80 to 111 articles, representing the highest annual productivity within the analyzed period. This surge suggests that PDEVs have become an important research focus in regenerative medicine, tissue repair, skin rejuvenation, and nanomedicine. The growing

interest may also be attributed to increasing recognition of their favorable biocompatibility, low immunogenicity, and potential applications in targeted drug delivery and cosmetic formulations. Although a lower number of publications was recorded for 2026 (74 articles), this value reflects incomplete indexing of publications for the current year rather than a genuine decline in research activity. The fitted growth curve further demonstrates a strong and sustained upward trajectory, indicating that research on plant-derived extracellular vesicles is expected to continue expanding in the coming years.

### *3.2. Global Distribution of Research Output*

Researchers from numerous countries and regions contributed to the advancement of PDEV research, reflecting the growing global interest in its applications in regenerative medicine, wound healing, cosmetics, cosmeceuticals, and drug delivery. China, the United States, and Italy were the leading contributors in terms of publication volume, while South Korea, India, and Spain also demonstrated significant research activity (Figure 3A). The distribution of publications shows that research efforts are concentrated in a relatively small number of highly productive countries, with China accounting for the largest share of published literature (Figure 3B). China contributed approximately 43.6% of all publications, followed by the United States (13.9%) and Italy (10.8%). Together, these three countries accounted for more than two-thirds of the total publication volume, highlighting their important contributions to the advancement of PDEV research.

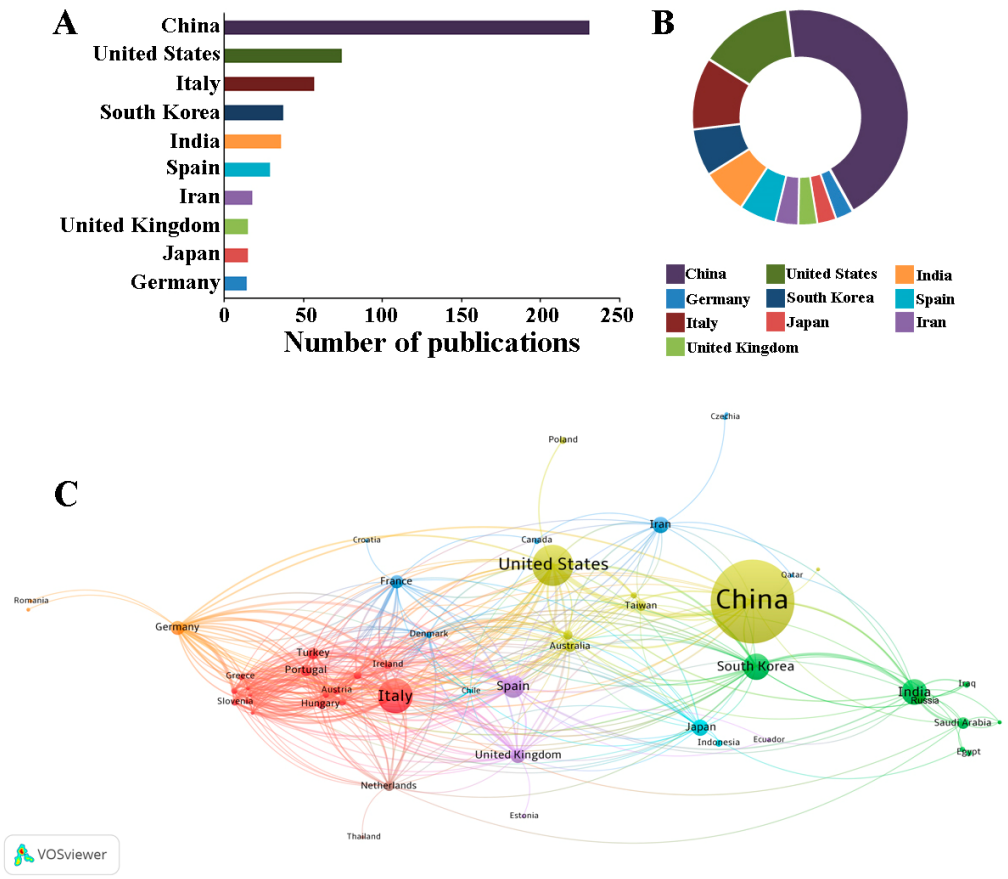


**Figure 3.** Global distribution and collaboration patterns of countries involved in PDEV research. (**A**) Top 10 countries ranked by publication output. (**B**) Proportional contribution of publications by country. (**C**) International collaboration network among countries; node size represents publication output, and link thickness indicates the strength of collaborative relationships.

The international collaboration network is presented in Figure 3C. Node size reflects publication volume, and connections indicate collaboration between countries. China

demonstrated the highest publication volume and maintained extensive ties with the United States, South Korea, India, Japan, and several European countries. The United States also occupied a central position in the collaboration network, connecting research groups across Asia, Europe, and Oceania. Italy demonstrated strong ties with several European countries, including Portugal, Greece, Austria, and Germany, forming an active regional collaboration cluster. Overall, countries with higher publication volumes tended to demonstrate greater international collaboration and network connectivity. The dense connections between leading participants indicate that research on plant-derived extracellular vesicles is increasingly supported by international partnerships and interdisciplinary collaboration.

### *3.3. Analysis of Publication Sources and Journal Citation Networks*

The distribution of publications by journal demonstrates the interdisciplinary nature of research in drug and cosmeceutical development, encompassing nanotechnology, drug delivery, biomaterials, regenerative medicine, and sustainable plant science (Figure 4). Figure 4B shows that the most productive journals were the International Journal of Molecular Sciences and the Journal of Nanobiotechnology, each publishing 28 articles. They are followed by the International Journal of Nanomedicine (23 publications), Pharmaceutics (16 publications), and Molecules (16 publications). Other notable journals include Scientific Reports, Biomaterials, Frontiers in Bioengineering and Biotechnology, Journal of Controlled Release, and Plants.

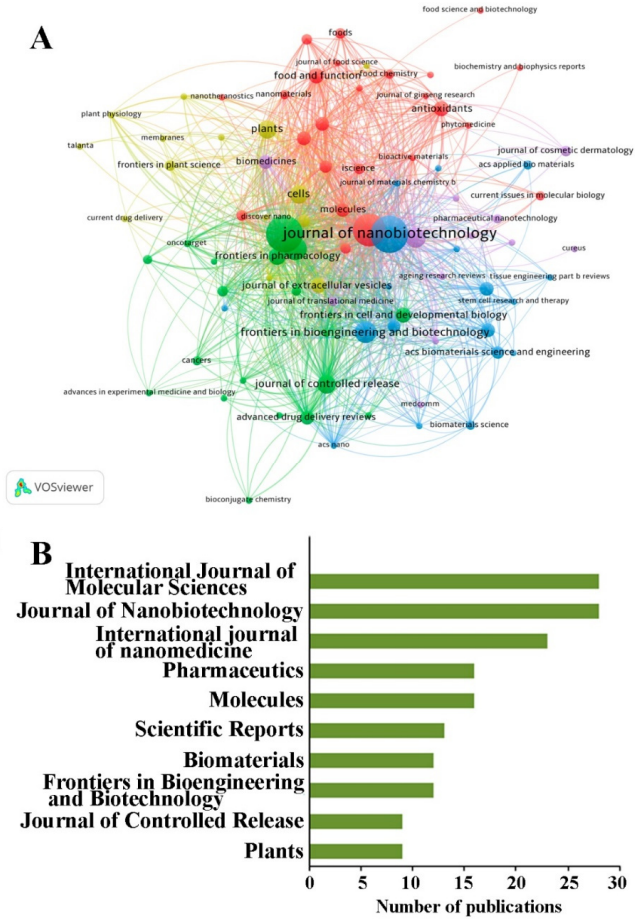


**Figure 4.** Journal analysis of publications on plant-derived extracellular vesicles (PDEVs). (**A**) Journal citation network generated using VOSviewer; node size represents citation impact, and links indicate citation relationships between journals. Different colors denote journal clusters representing related research areas. (**B**) Top 10 journals ranked by publication output.

The journal citation network is presented in Figure 4A. Node size reflects citation impact, while links indicate citation relationships among journals. Journal of Nanobiotechnology occupied a central position within the network and exhibited extensive connections with journals specializing in nanomedicine, extracellular vesicles, biomaterials, and drug delivery. Several highly interconnected clusters were identified, representing major research directions within the field. The red cluster was primarily associated with food science, plant biology, and bioactive compounds, whereas the green cluster was linked to pharmacology, drug delivery systems, and extracellular vesicle research. The blue cluster mainly comprised journals focused on biomaterials, tissue engineering, and regenerative medicine.

Notably, highly cited journals were predominantly concentrated in the fields of nanotechnology, biomaterials, and pharmaceutical sciences, highlighting the increasing recognition of PDEVs as multifunctional nanoplatforms for therapeutic and drug delivery applications. The strong interconnections among journals further indicate substantial knowledge exchange across traditionally distinct disciplines, reflecting the multidisciplinary evolution of this research area.

### *3.4. Keyword Density Analysis and Research Trends*

The keyword density visualization revealed the major research hotspots and thematic concentrations within the field of PDEVs (Figure 5). Areas highlighted in yellow represent topics with the highest occurrence frequency and strongest interconnections, whereas green and blue regions indicate less frequently occurring but still relevant research themes.




**Figure 5.** Density visualization map of keyword co-occurrence in publications. Warmer colors (yellow) indicate higher keyword occurrence density and stronger thematic concentration, whereas cooler colors (green to blue) represent lower-density research topics.

The most frequently encountered keywords were “drug delivery”, “inflammation”, and “wound healing”, forming the central core of the research landscape [1–3,5,7,13]. Their high density and close spatial proximity indicate that the therapeutic application of PDEVs for the treatment of inflammatory conditions and tissue repair is one of the most intensively researched areas in the field. The frequent co-occurrence of these terms indicates a strong focus on exploiting the inherent anti-inflammatory properties of plant-derived vesicles and their potential as natural nanocarriers for targeted delivery of therapeutic drugs.

Another widely represented topic was “plant-derived extracellular vesicles”, which occupied a central position and was closely associated with terms associated with regenerative medicine, including “stem cells”, “cell biology”, “regeneration”, and “fibroblasts” [5–7]. These associations reflect the growing interest in the role of plant-derived extracellular vesi-

cles in tissue regeneration and cellular repair processes. The emergence of keywords such as "anti-aging", "anti-pigmentation", "anti-scarring", and "scars" further highlights the growing importance of plant-derived extracellular vesicles in cosmetic and cosmeceutical applications [14–16].

Several keywords were associated with methodological and technological aspects of this field. Terms such as "hydrogel", "drug carriers", "small RNA", and "microRNA" indicate active research into delivery systems, characterization of bioactive substances, and vesicle isolation methods. The presence of specific plant sources, including apple, pomegranate, citrus, tomato, rose, and *Ginkgo biloba*, suggests that research is increasingly focusing on identifying plant species with beneficial biological activity and therapeutic potential.

Interestingly, keywords related to disease treatment and mechanistic research, such as "myocardial infarction", "autophagy", "metastasis", and "immunomodulation", were found in lower-density regions of the map. This pattern suggests that, although these topics are evolving and expanding, they remain less developed compared to the more established fields of wound healing and drug delivery. Overall, the density distribution indicates that current PDEV research is largely driven by translational applications in regenerative medicine and nanomedicine. The growing prominence of keywords related to hydrogels, small RNAs, and cosmetic applications suggests a gradual shift from fundamental characterization studies toward the development of advanced therapeutic platforms, engineered delivery systems, and next-generation cosmeceutical formulations. The strong interconnection between biological, pharmaceutical, and biomaterial-related terms further demonstrates the multidisciplinary nature of the field and highlights its potential for future clinical and commercial translation.

## 4. Cosmetic and Regenerative Properties of Plant-Derived Extracellular Vesicles

The studies included in this review collectively demonstrate that PDEVs exert a broad range of biological activities relevant to cosmetic and regenerative applications. Despite substantial differences in plant sources, isolation methods, and experimental models, the reported effects consistently converge on the promotion of skin regeneration, protection against oxidative stress, improvement of skin barrier function, regulation of pigmentation, and enhancement of hair growth (Table 1).

**Table 1.** Summary of the cosmetic and regenerative activities of PDEVs.

| Plant Species | Source of PDEVs | Activity | References |
|---|---|---|---|
| *Triticum aestivum* | Grass juice | Proliferation and migration of endothelial cells, epithelial cells, and dermal fibroblasts; type I collagen expression; anti-apoptotic and angiogenic effects | [18] |
| *Citrus × paradisi* | Juice | Keratinocyte migration; angiogenesis; wound healing | [19] |
| *Aloe vera* | Peels | Keratinocyte and fibroblast migration; wound healing | [20] |
| *Panax ginseng* | Roots and callus cultures | Endothelial cell proliferation; fibroblast migration; angiogenesis; healing of diabetic wounds; skin regeneration; UVB protection; anti-aging effects | [21–23] |
| *Iris germanica* | Rhizomes | Anti-senescence; restoration of wound-healing capacity; keratinocyte differentiation | [24] |

**Table 1.** *Cont.*

| Plant Species | Source of PDEVs | Activity | References |
|---|---|---|---|
| *Dendrobium officinale* | Plant homogenate | Collagen synthesis; skin elasticity; cytoskeletal organization; UV protection; anti-aging effects | [25] |
| *Tetraselmis chuii* | Conditioned medium | UVB protection; reduced oxidative stress and senescence; modulation of melanogenesis; depigmentation | [26] |
| *Centella asiatica* | Plant juice and tissue cultures | Skin regeneration; wrinkle reduction; enhancement of the skin barrier; modulation of melanin biosynthesis; antioxidant and photoprotective activities; repair of UV-damaged skin | [27,28] |
| *Pinus densiflora, Zanthoxylum piperitum, Lagerstroemia indica* | Homogenates from flowers, fruits, or needles | Reduced IL-6 levels; procollagen synthesis; hyaluronic acid production; inhibition of collagenase and elastase; moisturizing and barrier-enhancing effects | [29] |
| *Solanum tuberosum* | Potato juice | Wound closure; expression of skin barrier-related genes; improved skin elasticity; wrinkle reduction; skin-whitening effects | [30] |
| *Phalaenopsis aphrodite* | Plant homogenate | Anti-melanogenic activity; reduced *Tyrp1* expression; protection against oxidative damage; skin-conditioning effects | [31] |
| *Polygonum multiflorum* | Plant homogenate | Hair growth; modulation of androgen receptor signaling; activation of Wnt/β-catenin signaling | [32] |
| *Rosa damascena* | Callus culture-conditioned medium | Hair regeneration; improvement in androgenetic alopecia and alopecia areata; hair repigmentation | [33–35] |

One of the most extensively investigated applications of PDEVs is the stimulation of skin regeneration and wound healing [6,11,14–16,36]. Early studies demonstrated that wheat-derived nanovesicles significantly enhanced the proliferation and migration of endothelial, epithelial, and dermal fibroblast cells, increased collagen type I expression, reduced apoptosis, and promoted angiogenic activity [18]. Similar regenerative effects were later reported for grapefruit-derived extracellular vesicles, which stimulated keratinocyte migration, reduced intracellular oxidative stress, and enhanced angiogenesis in wound-healing models [19]. Aloe vera-derived extracellular vesicles also promoted keratinocyte and fibroblast migration while activating antioxidant defense mechanisms through the Nrf2 signaling pathway [20]. Additional evidence was provided by ginseng-derived vesicles, which restored endothelial cell proliferation, migration, and tube formation under hyperglycemic conditions and accelerated vascular regeneration in diabetic wound models [21]. Furthermore, extracellular vesicles isolated from non-edible ginseng callus cultures stimulated fibroblast migration and activated the TGF-β/SMAD signaling pathway, resulting in increased expression of collagen synthesis-related genes and enhanced regenerative capacity [22].

Another major area of research concerns the anti-aging and photoprotective properties of PDEVs. Ginseng root-derived exosome-like nanoparticles protected keratinocytes against UVB-induced damage and oxidative stress, reducing ROS accumulation, apoptosis, inflammatory signaling, and the expression of matrix metalloproteinases associated with skin aging [23]. Similar anti-senescence effects were observed for *Iris germanica* rhizome-derived exosomes, which reduced oxidative stress, restored wound-healing capacity, decreased cellular senescence markers, and normalized keratinocyte differentiation [24]. Particularly strong evidence was reported for *Dendrobium officinale*-derived extracellular vesicles, which

enhanced collagen synthesis, improved cytoskeletal organization, increased skin elasticity, reduced UV-induced damage, and demonstrated beneficial effects in three-dimensional skin models as well as in human volunteer studies [25]. More recently, extracellular vesicles isolated from the microalga *Tetraselmis chuii* were shown to protect skin cells from UVB-induced damage, reduce oxidative stress and senescence, and modulate melanogenesis, further expanding the range of potential cosmetic sources beyond terrestrial plants [26].

Several studies have demonstrated the ability of PDEVs to improve skin barrier function, hydration, and overall skin quality. Comparative transcriptomic analyses revealed that *Centella asiatica*-derived exosomes induced stronger activation of genes associated with skin regeneration, wrinkle reduction, and skin barrier enhancement than conventional plant extracts [27]. Additional studies using extracellular vesicles obtained from *Centella asiatica* tissue cultures demonstrated antioxidant, anti-inflammatory, anti-melanogenic, and photoprotective activities in both cellular assays and UV-damaged animal models [28]. Similar skin-conditioning effects were reported for extracellular vesicles isolated from *Pinus densiflora*, *Zanthoxylum piperitum*, and *Lagerstroemia indica*, which reduced inflammatory IL-6 expression, enhanced procollagen synthesis, stimulated hyaluronic acid production, and inhibited collagenase and elastase activities [29]. Potato-derived extracellular vesicles further expanded this evidence by promoting wound closure, enhancing skin barrier-related gene expression, reducing oxidative stress, and improving skin elasticity, wrinkle appearance, and whitening parameters in human skin tests [30].

Regulation of pigmentation and skin tone represents another emerging application of PDEVs. *Centella asiatica* exosomes were predicted to modulate genes associated with melanin biosynthesis through their miRNA cargo, while experimental studies confirmed reductions in melanin content and tyrosinase activity [27,28]. Likewise, PDEVs derived from *Phalaenopsis aphrodite* inhibited melanogenesis, reduced Tyrp1 expression, and protected keratinocytes from oxidative damage while exhibiting no irritation in reconstructed epidermal and corneal models [31]. Similar depigmenting effects were recently reported for microalgal extracellular vesicles, which significantly reduced UV-induced melanogenesis and melanin accumulation [26]. These findings suggest that plant-derived vesicles may represent a novel class of natural skin-whitening and pigmentation-modulating agents.

Although most studies focused on skin-related applications, several recent reports have extended the potential use of PDEVs to hair care and scalp regeneration. Exosome-like nanoparticles isolated from Polygoni Multiflori Radix promoted hair growth through miRNA-mediated modulation of androgen receptor signaling and activation of the Wnt/β-catenin pathway, outperforming minoxidil in an experimental androgenetic alopecia model [32]. Clinical case reports further described improvements in androgenetic alopecia, alopecia areata, and hair repigmentation following treatment with rose stem cell-derived exosomes [33–35], suggesting that plant-derived vesicles may represent a promising platform for future trichological applications.

Overall, the available evidence indicates that PDEVs possess multifunctional biological activities relevant to skin and hair care. Despite differences among studies, the most consistently reported effects include stimulation of cellular proliferation and migration, promotion of wound healing, enhancement of collagen synthesis, reduction in oxidative stress and inflammation, protection against photoaging, improvement of skin barrier function, modulation of pigmentation, and promotion of hair regeneration. These findings collectively support the growing interest in PDEVs as next-generation cosmetic and cosmeceutical ingredients.

## 5. Translational and Commercial Perspectives of Plant-Derived Extracellular Vesicles

An important aspect emerging from the current literature is the substantial difference between the prospects for therapeutic and cosmetic translation of PDEVs. Although PDEVs have demonstrated considerable potential as regenerative agents, bioactive nanotherapeutics, and delivery platforms, their translation into clinical practice remains constrained by multiple scientific, technological, and regulatory challenges [37].

One of the major obstacles is the absence of harmonized regulatory frameworks governing extracellular vesicle-based products. Similar concerns have been widely discussed for mammalian exosome therapeutics, where difficulties associated with vesicle classification, manufacturing standardization, quality control, batch-to-batch variability, and safety assessment continue to limit clinical translation [15,38]. In addition, large-scale production remains technically challenging because extracellular vesicle yield, composition, and biological activity are strongly influenced by the source material, isolation method, and storage conditions. These issues are particularly important for pharmaceutical applications, which require strict reproducibility and extensive preclinical and clinical validation.

In contrast, cosmetic applications appear to provide a substantially more accessible route toward commercialization (Figure 6). The cosmetics sector generally operates under less restrictive regulatory requirements than the pharmaceutical industry while simultaneously benefiting from increasing consumer demand for natural, sustainable, and biologically active ingredients. As a result, PDEVs have rapidly attracted interest as next-generation cosmeceutical ingredients capable of combining intrinsic biological activity with nanocarrier functionality [39].

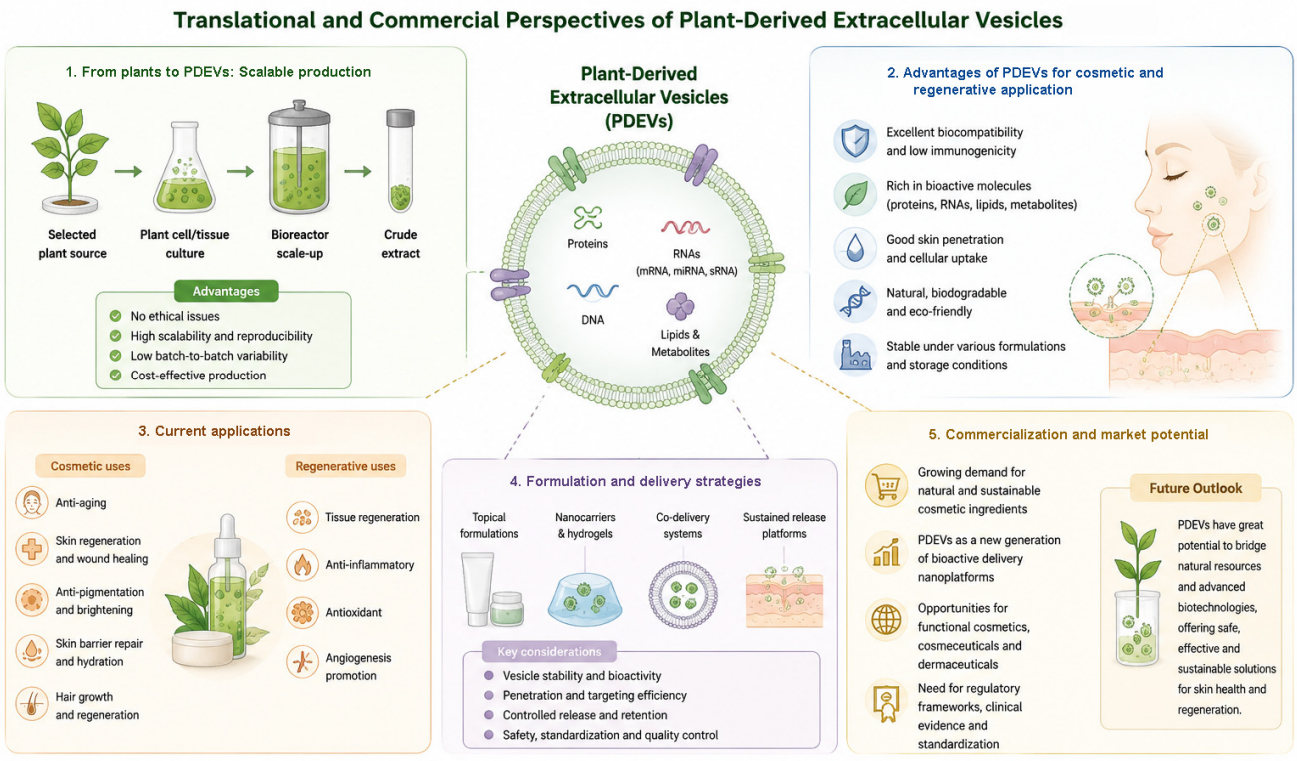


**Figure 6.** Schematic overview of the translational and commercial perspectives of plant-derived extracellular vesicles.

Importantly, the last several years have witnessed a rapid increase in scientific publications, patent applications, industrial developments, and commercial products utilizing the use of plant-derived extracellular vesicles or exosome-like nanovesicles. Recent reviews

focusing on cosmetic dermatology and cosmeceutical applications have noted that the cosmetics sector is currently the most active area of extracellular vesicle commercialization and may become the first industry to achieve widespread implementation of plant-derived vesicle technologies [14,16].

Another important trend is the growing interest in controlled production systems based on plant tissue and callus cultures. Unlike agricultural raw materials, plant cell cultures enable standardized cultivation conditions, year-round biomass production, and reduced seasonal variability. Recent studies demonstrated successful production of extracellular vesicles from ginseng callus cultures [22], *Centella asiatica* tissue cultures [28], and *Vitis vinifera* callus [40]. Such systems may facilitate scalable manufacturing, improve batch reproducibility, and support the development of more standardized production processes, which remains one of the central challenges for the industrial implementation of extracellular vesicle technologies.

Taken together, current evidence suggests that cosmetics may represent the most realistic near-term pathway for the commercial adoption of PDEVs. Their natural origin, favorable biocompatibility profile, multifunctional biological activity, and compatibility with consumer trends toward sustainable and biologically active ingredients provide significant advantages for cosmeceutical development. At the same time, advances achieved through cosmetic applications may help establish manufacturing standards, safety assessment strategies, and regulatory frameworks that could ultimately facilitate future therapeutic and clinical translation of plant-derived extracellular vesicle technologies.

## 6. Conclusions

This review demonstrates that plant-derived extracellular vesicles (PDEVs) represent a promising class of natural bioactive nanomaterials with considerable potential for cosmetic and regenerative applications. Across diverse experimental models, PDEVs consistently promoted skin regeneration by enhancing cellular proliferation and migration, accelerating wound healing, stimulating collagen synthesis, reducing oxidative stress, and suppressing inflammatory responses. Additional benefits included photoprotection, improved skin barrier function and hydration, anti-aging activity, pigmentation control, and hair growth promotion.

The quantitative synthesis of available studies revealed a significant overall positive effect of PDEVs on cosmetic and regenerative outcomes. These activities have been reported for vesicles isolated from diverse sources, including edible plants, medicinal herbs, microalgae, and plant cell cultures, suggesting that the beneficial properties of PDEVs are broadly distributed across the plant kingdom.

Despite these encouraging findings, the current evidence remains dominated by in vitro studies, while animal experiments and especially clinical investigations are still limited. Moreover, methodological heterogeneity in plant sources, isolation procedures, vesicle characterization, and experimental design complicates direct comparisons among studies.

Importantly, while the clinical translation of PDEVs remains constrained by regulatory, manufacturing, and standardization challenges, cosmetic applications provide a more accessible route toward commercialization. The rapid growth of PDEV-based cosmetic products and industrial developments observed in recent years suggests that the cosmetics sector may become the first large-scale adopter of plant extracellular vesicle technologies.

Overall, PDEVs are emerging as multifunctional natural nanoplatforms with strong potential for next-generation cosmetic and regenerative products. Future progress will depend on methodological standardization, mechanistic studies, scalable production systems, and well-designed clinical trials.

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## References

1. Huang, D.; Chen, J.; Zhao, M.; Shen, H.; Jin, Q.; Xiao, D.; Peng, Z.; Chen, T.; Zhang, Y.; Rao, D.; et al. Plant-Derived Extracellular Vesicles: Composition, Function and Clinical Potential. *J. Transl. Med.* **2025**, *23*, 1065. [CrossRef] [PubMed]
2. Lo, K.J.; Wang, M.H.; Ho, C.T.; Pan, M.H. Plant-Derived Extracellular Vesicles: A New Revolutionization of Modern Healthy Diets and Biomedical Applications. *J. Agric. Food Chem.* **2024**, *72*, 2853–2878. [CrossRef] [PubMed]
3. Shkryl, Y.; Tsydeneshieva, Z.; Degtyarenko, A.; Yugay, Y.; Balabanova, L.; Rusapetova, T.; Bulgakov, V. Plant Exosomal Vesicles: Perspective Information Nanocarriers in Biomedicine. *Appl. Sci.* **2022**, *12*, 8262. [CrossRef]
4. Subha, D.; Harshnii, K.; Madhikiruba, K.G.; Nandhini, M.; Tamilselvi, K.S. Plant-Derived Exosome-Like Nanovesicles: An Updated Overview. *Plant Nano Biol.* **2023**, *3*, 100022. [CrossRef]
5. Jin, Z.; Na, J.; Lin, X.; Jiao, R.; Liu, X.; Huang, Y. Plant-Derived Exosome-Like Nanovesicles: A Novel Nanotool for Disease Therapy. *Heliyon* **2024**, *10*, e30630. [CrossRef] [PubMed]
6. Amin, A.; Park, S. Mechanistic Insights into Plant-Derived Exosomes, Their Cross-Kingdom Effects, and Potential Biomedical Applications in Skin Wounds Repair. *Plants* **2026**, *15*, 1286. [CrossRef] [PubMed]
7. Liu, D.; Gao, J.; Wu, X.; Han, L. Plant-Derived Exosome-Like Nanoparticles as Promising Biotherapeutic Tools: Recent Advances and Challenges. *Smart Mater. Med.* **2025**, *6*, 285–304. [CrossRef]
8. Sha, A.; Luo, Y.; Xiao, W.; Wang, Y.; Sun, X.; Li, Z.; Zhang, H.; Chen, J.; Liu, Y.; Zhao, Q. Plant-Derived Exosome-Like Nanoparticles: A Comprehensive Overview of Their Composition, Biogenesis, Isolation, and Biological Applications. *Int. J. Mol. Sci.* **2024**, *25*, 12092. [CrossRef] [PubMed]
9. Gao, Z.; Li, J.; Yang, W.; Wang, X.; Zhang, Y.; Liu, H.; Chen, R.; Zhao, L.; Sun, Q.; Xu, M. Plant-Derived Exosome-Like Nanoparticles: Innovative Nanomedicine for Therapeutic Applications. *Food Sci. Nutr.* **2025**, *13*, e70974. [CrossRef] [PubMed]
10. Zuo, Y.; Zhang, J.; Wang, X.; Sun, B.; Tian, S.; Miao, M. Engineered Plant-Derived Extracellular Vesicles: A Novel Strategy for Tumor-Targeted Therapy. *Pharmaceutics* **2026**, *18*, 577. [CrossRef] [PubMed]
11. Li, Y.; Wang, Y.; Zhao, H.; Pan, Q.; Chen, G. Engineering Strategies of Plant-Derived Exosome-Like Nanovesicles: Current Knowledge and Future Perspectives. *Int. J. Nanomed.* **2024**, *19*, 12793–12815. [CrossRef] [PubMed]
12. Ravet, A.; Zervudacki, J.; Singla-Rastogi, M.; Charvin, M.; Thiebeauld, O.; Perez-Quintero, A.L.; Courgeon, L.; Candat, A.; Lebeau, L.; Fortunato, A.E.; et al. Vesicular and Non-Vesicular Extracellular Small RNAs Direct Gene Silencing in a Plant-Interacting Bacterium. *Nat. Commun.* **2025**, *16*, 3533. [CrossRef] [PubMed]
13. Shkryl, Y.; Tsydeneshieva, Z.; Gorpenchenko, T.; Kazarin, V.; Kudinova, O.; Bulgakov, V.; Yugay, Y. Artificial MicroRNA Delivery and Gene Silencing via Extracellular Vesicles Derived from Molecularly Modified Tobacco. *Protoplasma* **2026**, *263*, 875–891. [CrossRef] [PubMed]

14. Flores Rodríguez, J.C.; Toledo Avelar, L.E.; Yi, K.; Merino Arellano, R.; López Rodríguez, J.A.; Garza Vargas, M.S. Efficacy of Exosome-Based Therapies for Skin Rejuvenation: A Systematic Review of Human Studies. *Cureus* **2026**, *18*, e104182. [CrossRef] [PubMed]
15. Haykal, D.; Wyles, S.; Garibyan, L.; Cartier, H.; Gold, M. Exosomes in Cosmetic Dermatology: A Review of Benefits and Challenges. *J. Drugs Dermatol.* **2025**, *24*, 12–18. [CrossRef] [PubMed]
16. Bai, G.; Truong, T.M.; Pathak, G.N.; Benoit, L.; Rao, B. Clinical Applications of Exosomes in Cosmetic Dermatology. *Ski. Health Dis.* **2024**, *4*, e348. [CrossRef] [PubMed]
17. van Eck, N.J.; Waltman, L. Software Survey: VOSviewer, a Computer Program for Bibliometric Mapping. *Scientometrics* **2010**, *84*, 523–538. [CrossRef] [PubMed]
18. Şahin, F.; Koçak, P.; Güneş, M.Y.; Özkan, İ.; Yıldırım, E.; Kala, E.Y. In Vitro Wound Healing Activity of Wheat-Derived Nanovesicles. *Appl. Biochem. Biotechnol.* **2019**, *188*, 381–394. [CrossRef] [PubMed]
19. Savcı, Y.; Kırbaş, O.K.; Bozkurt, B.T.; Abdik, E.A.; Taşlı, P.N.; Şahin, F.; Abdik, H. Grapefruit-Derived Extracellular Vesicles as a Promising Cell-Free Therapeutic Tool for Wound Healing. *Food Funct.* **2021**, *12*, 5144–5156. [CrossRef] [PubMed]
20. Kim, M.K.; Choi, Y.C.; Cho, S.H.; Choi, J.S.; Cho, Y.W. The Antioxidant Effect of Small Extracellular Vesicles Derived from *Aloe vera* Peels for Wound Healing. *Tissue Eng. Regen. Med.* **2021**, *18*, 561–571. [CrossRef] [PubMed]
21. Tan, M.; Liu, Y.; Xu, Y.; Yan, G.; Zhou, N.; Chen, H.; Jiang, Z.; Peng, L. Plant-Derived Exosomes as Novel Nanotherapeutics Contrive Glycolysis Reprogramming-Mediated Angiogenesis for Diabetic Ulcer Healing. *Biomater. Res.* **2024**, *28*, 0035. [CrossRef] [PubMed]
22. Park, H.Y.; Kang, M.H.; Lee, G.; Kim, J.W. Enhancement of Skin Regeneration through Activation of TGF-β/SMAD Signaling Pathway by *Panax ginseng* Meyer Non-Edible Callus-Derived Extracellular Vesicles. *J. Ginseng Res.* **2025**, *49*, 34–41. [CrossRef] [PubMed]
23. Choi, W.; Cho, J.H.; Park, S.H.; Kim, D.S.; Lee, H.P.; Kim, D.; Kim, H.S.; Kim, J.H.; Cho, J.Y. Ginseng Root-Derived Exosome-Like Nanoparticles Protect Skin from UV Irradiation and Oxidative Stress by Suppressing Activator Protein-1 Signaling and Limiting the Generation of Reactive Oxygen Species. *J. Ginseng Res.* **2024**, *48*, 211–219. [CrossRef] [PubMed]
24. Kim, J.-S.; Lee, H.-J.; Yoon, E.-J.; Lee, H.; Ji, Y.; Kim, Y.; Park, S.-J.; Kim, J.; Bae, S. Protective Effect of Iris germanica L. Rhizome-Derived Exosome against Oxidative-Stress-Induced Cellular Senescence in Human Epidermal Keratinocytes. *Appl. Sci.* **2023**, *13*, 11681. [CrossRef]
25. Zhang, Y.; Zhao, B.; Wang, J.; Shen, M.; Zhang, Z.; Ren, C.; Li, M.; Liu, M.; You, Z.; Li, P. Novel Exosome-Like Vesicles from *Dendrobium officinale*: Unraveling a Pioneering Extraction Protocol and Their Skin Anti-Aging Potentials. *Extracell. Vesicles* **2025**, *6*, 100090. [CrossRef]
26. Gargano, P.; Picciotto, S.; Paterna, A.; Raccosta, S.; Rao, E.; Romancino, D.P.; Smeraldi, G.; Manno, M.; Salamone, M.; Zarovni, N.; et al. Extracellular Vesicles from Microalgae as Natural Bioactive Agents for UVB Protection, Anti-Aging, and Skin Depigmentation. *Biomed. Pharmacother.* **2026**, *194*, 118961. [CrossRef] [PubMed]
27. Kim, M.H.; Yoon, E.J.; Kim, J.S.; Park, S.J.; Lee, H. Comparative Analysis of the Transcriptome and Efficacy of Bioactive *Centella asiatica* Exosomes on Skin Cells. *Res. Sq.* **2023**, *preprint*. [CrossRef] [PubMed]
28. Chang, T.-M.; Wu, C.-C.; Huang, H.-C.; Wang, S.-S.; Chuang, C.-H.; Kao, P.-L.; Tang, W.-H.; Liu, L.T.-C.; Qiu, W.-Y.; Percec, I.; et al. In Vitro Characterization of *Centella asiatica* Extracellular Vesicles and Their Skin Repair Effects in a UVB-Irradiated Mouse Model. *Int. J. Mol. Sci.* **2025**, *26*, 8982. [CrossRef] [PubMed]
29. Kim, H.-R.; Lee, S.-H.; Bae, W.B.; Shin, M.-J.; Kim, S.-Y.; Jung, Y.O.; Park, M.H. Skin Barrier Enhancement and Moisturizing Effects of Exosome Extracts Derived from *Pinus densiflora*, *Zanthoxylum piperitum*, and *Lagerstroemia indica* Plants. *Biology* **2026**, *15*, 249. [CrossRef] [PubMed]
30. Lee, Y.; Mohamed, R.W.; Yang, S. Safety Profile of *Solanum tuberosum*-Derived Exosomes: Evidence from In Vitro Experiments and Human Skin Tests. *Pharmaceuticals* **2025**, *18*, 458. [CrossRef] [PubMed]
31. Chuang, K.-A.; Li, K.-C.; Yao, H.-J.; Tsai, P.-Y.; Lu, I.H.; Lin, C.H.; Umbreen, H.; Lin, C.-C.; Pan, I.-H. Unveiling the Potential of Plant-Derived Exosome-Like Extracellular Vesicles from *Phalaenopsis aphrodite* as Skin-Conditioning Ingredients in Cosmetic Applications. *Cosmetics* **2026**, *13*, 15. [CrossRef]
32. Li, S.; Zhang, Y.; Liu, X.; Su, H.; Cao, H.; Xuan, H.; Cui, Y.; Lu, Z.; Zhang, Q.; Li, Y.; et al. Cross-Kingdom Delivery and Putative Gene Modulation of Androgen Pathways by Plant-Derived Exosome-Like Nanoparticles from *Polygoni multiflori* Radix Promotes Hair Growth via miRNA Cargo. *Pharmacol. Res.* **2025**, *222*, 108033. [CrossRef] [PubMed]
33. Bento, E.B.; Matos, C.; Ribeiro Junior, H.L. Successful Treatment of Hair Loss and Restoration of Natural Hair Color in Patient with Alopecia Areata Due to Psychological Disorder Using Exosomes: Case Report with 6-Month Follow-Up. *Cosmetics* **2025**, *12*, 97. [CrossRef]
34. Lueangarun, S.; Cho, B.S.; Tempark, T. Rose Stem Cell-Derived Exosomes for Hair Regeneration Enhancement via Noninvasive Electroporation in Androgenetic Alopecia. *J. Cosmet. Dermatol.* **2024**, *23*, 3791–3794. [CrossRef] [PubMed]

35. Lueangarun, S.; Cho, B.S.; Tempark, T. Hair Repigmentation of Poliosis Circumscripta in Androgenetic Alopecia Patient Treated with Exosomes and Fractional Picosecond Laser. *J. Cosmet. Dermatol.* **2024**, *23*, 2307–2311. [CrossRef] [PubMed]
36. Xu, P.; Wang, X.; Chen, W.; Mao, Y.; Zhu, H.; Zhang, J.; Jiang, M.; Zhang, X.; Wang, Y. Plant-Derived Exosomes in Skin Wound Repair: Biological Properties, Extraction, Characterization, and Therapeutic Mechanisms. *Mol. Pharm.* **2026**, *23*, 6–27. [CrossRef] [PubMed]
37. Domaszewska-Szostek, A.; Krzyżanowska, M.; Polak, A.; Puzianowska-Kuźnicka, M. Effectiveness of Extracellular Vesicle Application in Skin Aging Treatment and Regeneration: Do We Have Enough Evidence from Clinical Trials? *Int. J. Mol. Sci.* **2025**, *26*, 2354. [CrossRef] [PubMed]
38. Ferroni, L.; Zavan, B. Plant-Derived Extracellular Vesicles in Cosmetics: Building a Framework for Safety, Efficacy, and Quality. *Cosmetics* **2025**, *12*, 252. [CrossRef]
39. Liu, H.; Dong, T.; Dong, C.; Yang, F.; Zhou, Q.; Guan, C.; Wang, W. Plant-Derived Exosome-Like Nanovesicles: A Novel Therapeutic Perspective for Skin Diseases. *J. Nanobiotechnol.* **2025**, *23*, 640. [CrossRef] [PubMed]
40. Shkryl, Y.; Tsydeneshieva, Z.; Menchinskaya, E.; Rusapetova, T.; Grishchenko, O.; Mironova, A.; Bulgakov, D.; Gorpenchenko, T.; Kazarin, V.; Tchernoded, G.; et al. Exosome-Like Nanoparticles, High in Trans-δ-Viniferin Derivatives, Produced from Grape Cell Cultures: Preparation, Characterization, and Anticancer Properties. *Biomedicines* **2024**, *12*, 2142. [CrossRef] [PubMed]


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