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Biological Skin Rejuvenation in the Regenerative Era: Clinical Applications of Exosomes and Polynucleotides in Modern Dermatology

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ABSTRACT

Regenerative dermatology has emerged as a transformative field that integrates advances in regenerative medicine, molecular biology, and aesthetic dermatology to promote tissue repair through biological rather than purely corrective mechanisms. Among the most promising innovations, exosomes and polynucleotides have attracted considerable scientific attention because of their ability to stimulate fibroblast activity, enhance collagen synthesis, regulate inflammatory responses, promote angiogenesis, and improve extracellular matrix remodeling. The objective of this review was to analyze the current scientific evidence regarding the

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biological foundations, clinical applications, therapeutic effectiveness, safety profile, and future perspectives of these next-generation regenerative therapies. A narrative literature review was conducted following the scientific method using peer-reviewed publications from major biomedical databases. The available evidence demonstrates encouraging results in facial rejuvenation, photoaging, scar remodeling, chronic wound healing, periocular rejuvenation, and hair restoration, with improvements in skin quality and high patient satisfaction while maintaining a favorable short-term safety profile. Nevertheless, important methodological limitations remain, including heterogeneous treatment protocols, limited randomized clinical trials, and insufficient long-term follow-up. Continued international collaboration, standardized manufacturing processes, rigorous regulatory frameworks, and high-quality multicenter clinical studies will be essential to establish evidence-based therapeutic guidelines and consolidate regenerative dermatology as a mature clinical discipline.

KEYWORDS

Regenerative dermatology, Exosomes, Polynucleotides, Skin rejuvenation, Regenerative medicine, Aesthetic dermatology, Fibroblasts, Collagen synthesis, Extracellular matrix, Angiogenesis, Tissue repair, Photoaging.

INTRODUCTION

The concept of skin rejuvenation has undergone a profound transformation during the past decade, shifting from the exclusive correction of visible signs of aging toward strategies that actively promote tissue regeneration and restoration of physiological skin function. Conventional aesthetic procedures—including chemical peels, botulinum toxin injections, dermal fillers, ablative and non-ablative laser therapies, and energy-based devices—have demonstrated substantial effectiveness in improving facial appearance and reducing the manifestations of chronological and photoinduced aging. Nevertheless, these interventions primarily target structural or cosmetic manifestations rather than addressing the complex biological mechanisms responsible for cutaneous degeneration. As the understanding of skin biology continues to evolve, regenerative dermatology has emerged as an interdisciplinary field integrating dermatology, regenerative medicine, molecular biology, biomaterials science, and aesthetic medicine to stimulate intrinsic repair mechanisms and restore tissue homeostasis rather than merely masking age-related alterations [1], [6], [7].

Skin aging is a multifactorial biological process characterized by the progressive accumulation of molecular and cellular damage resulting from interactions between intrinsic genetic determinants and extrinsic environmental factors. Intrinsic aging reflects genetically programmed cellular senescence and physiological decline, whereas extrinsic aging is largely driven by ultraviolet radiation, environmental pollution, tobacco exposure, nutritional factors, psychological stress, and other lifestyle-related influences that accelerate tissue deterioration. At the molecular level, aging skin exhibits mitochondrial dysfunction, oxidative stress, chronic low-grade inflammation, extracellular matrix degradation, impaired angiogenesis, fibroblast dysfunction, decreased collagen synthesis, elastin fragmentation, stem cell exhaustion, and alterations in intercellular communication. These interconnected pathways ultimately reduce the regenerative capacity of the skin and contribute to wrinkles, loss of elasticity, pigmentation disorders, impaired wound healing, dermal thinning, and structural fragility [7], [8], [15].

Growing knowledge regarding the cellular mechanisms regulating tissue regeneration has stimulated the development of biological therapies designed to restore regenerative signaling instead of replacing tissue volume alone. Within this context, extracellular vesicles—particularly exosomes—and highly purified polynucleotides have attracted increasing scientific interest because of their potential to influence multiple regenerative pathways simultaneously. Unlike conventional aesthetic interventions that often produce temporary structural modifications, these novel approaches aim to enhance endogenous tissue repair through modulation of inflammation, extracellular matrix remodeling, angiogenesis, fibroblast activation, and cellular communication. Their emergence represents one of the most significant paradigm shifts in contemporary regenerative dermatology [1], [6], [17].

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Exosomes are nanosized extracellular vesicles secreted by virtually all nucleated cells and function as highly specialized mediators of intercellular communication. They transport proteins, messenger RNA, microRNA, lipids, cytokines, enzymes, and growth factors capable of modifying the biological behavior of recipient cells. Experimental investigations have demonstrated that stem cell-derived exosomes can stimulate fibroblast proliferation, increase collagen and elastin synthesis, regulate inflammatory cascades, promote angiogenesis, reduce oxidative stress, accelerate wound healing, and enhance extracellular matrix remodeling. Importantly, because exosomes constitute a cell-free therapeutic strategy, they may overcome several safety concerns associated with direct stem cell transplantation while preserving many of the regenerative benefits attributed to cellular therapies [1], [2], [5], [17].

Parallel advances have occurred in the development of polynucleotide-based therapies. Highly purified polynucleotides and polydeoxyribonucleotide derivatives act as biological stimulators capable of promoting tissue repair through multiple complementary mechanisms. These molecules activate fibroblasts, improve dermal hydration, stimulate neocollagenesis, regulate inflammatory responses, enhance angiogenesis, facilitate extracellular matrix remodeling, and support cellular recovery after mechanical or thermal injury. Unlike traditional fillers, their principal objective is not volumization but rather improvement of tissue quality, elasticity, hydration, and long-term dermal architecture. Consequently, polynucleotides have progressively expanded their clinical indications from aesthetic facial rejuvenation to scar remodeling, chronic wound management, periocular rejuvenation, hair restoration, and supportive treatment following laser procedures or microneedling [9]–[14].

The integration of regenerative products with minimally invasive technologies has further expanded therapeutic possibilities. Current clinical protocols increasingly combine exosomes or polynucleotides with microneedling, fractional laser resurfacing, radiofrequency microneedling, platelet-rich plasma, ultrasound-based devices, and injectable biostimulators to maximize biological responses while minimizing tissue trauma and recovery time. Such multimodal strategies reflect the transition from isolated cosmetic procedures toward personalized regenerative protocols based on tissue biology rather than solely on anatomical correction. Early clinical studies suggest that combination therapies may produce synergistic improvements in skin texture, elasticity, pigmentation, dermal density, and patient satisfaction; however, standardized treatment algorithms remain under continuous investigation [3], [6], [15], [16].

Despite the rapid commercialization of regenerative products, important scientific challenges remain unresolved. Considerable heterogeneity exists regarding exosome sources, isolation techniques, purification methods, characterization protocols, dosage, administration routes, storage conditions, manufacturing standards, and regulatory oversight. Likewise, variability in polynucleotide formulations, injection techniques, treatment intervals, and outcome assessment complicates comparisons among published clinical studies. Many available investigations involve relatively small sample sizes, limited follow-up periods, heterogeneous patient populations, or differences in methodological quality, making it difficult to establish universally accepted clinical recommendations. Furthermore, regulatory agencies across different countries continue to develop frameworks addressing the classification, manufacturing, quality control, and clinical use of extracellular vesicle-based therapies, highlighting the need for greater scientific standardization before widespread implementation [4], [5], [11], [18].

From an international perspective, regenerative dermatology has experienced substantial growth across North America, Europe, and East Asia, regions where translational research has accelerated the incorporation of biological therapies into clinical practice. Simultaneously, several Latin American countries have demonstrated increasing participation in regenerative medicine through clinical research, aesthetic dermatology, plastic surgery, tissue engineering, and collaborative academic networks. Although disparities in regulatory environments, technological infrastructure, and access to advanced therapies persist throughout the region, Latin America has become an increasingly relevant contributor to the global scientific discussion concerning regenerative dermatology. This international expansion underscores the importance of critically evaluating available evidence within diverse healthcare settings while considering regional opportunities and limitations for future clinical implementation [3], [15], [18].

Given the accelerating pace of innovation and the growing body of experimental and clinical evidence, there is a clear need for comprehensive reviews capable of integrating current knowledge regarding the biological rationale, mechanisms of action, therapeutic applications, clinical effectiveness, safety considerations, and future perspectives of exosome- and polynucleotide-based therapies. A critical synthesis of recent evidence is particularly valuable for

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clinicians, researchers, educators, and postgraduate trainees seeking to understand the scientific foundations supporting these emerging technologies and their potential role within evidence-based dermatological practice [4], [9], [19], [20].

Accordingly, the present review aims to critically examine the current international evidence regarding regenerative dermatology, with particular emphasis on exosomes, highly purified polynucleotides, and next-generation skin rejuvenation strategies. The review analyzes the molecular mechanisms underlying tissue regeneration, summarizes available preclinical and clinical evidence, discusses current therapeutic indications, evaluates safety profiles and regulatory considerations, explores combination treatment strategies, and identifies existing knowledge gaps that should guide future research. By integrating findings from contemporary dermatology, regenerative medicine, aesthetic medicine, and translational biomedical sciences, this review seeks to provide a comprehensive and clinically relevant overview of one of the fastest-growing fields in modern dermatological practice.

DEVELOPMENT

Regenerative dermatology represents an evolving clinical and translational approach aimed at restoring the biological functions of damaged or aging skin. Unlike conventional rejuvenation procedures, which primarily correct wrinkles, volume loss, dyschromia, or surface irregularities, regenerative interventions seek to influence the cellular mechanisms responsible for tissue maintenance and repair. This distinction is clinically relevant because cutaneous aging is not limited to a visible alteration of appearance; it also involves progressive deterioration of fibroblast activity, extracellular matrix organization, vascular support, immune regulation, epidermal renewal, and communication among resident skin cells [7], [8].

The biological basis of regenerative skin treatment is closely associated with the capacity of keratinocytes, fibroblasts, endothelial cells, immune cells, and dermal progenitor cells to exchange molecular signals. During aging, this communication becomes less efficient because of cellular senescence, oxidative stress, mitochondrial dysfunction, chronic low-grade inflammation, and increased activity of matrix metalloproteinases. These alterations accelerate the degradation of collagen and elastin while reducing the synthesis of new structural proteins. Consequently, the dermis becomes thinner, less hydrated, mechanically weaker, and less capable of recovering from environmental or procedural injury [1], [6], [15].

2.1 Exosomes as mediators of cutaneous regeneration

Exosomes are small extracellular vesicles involved in communication between cells. They contain proteins, lipids, growth-related molecules, messenger RNA, and regulatory microRNAs that may modify the function of recipient cells. Their biological effects depend on their cellular origin, composition, processing conditions, concentration, and method of administration. This variability is important because products described commercially as exosome-based interventions cannot automatically be considered biologically equivalent [1], [7].

In cutaneous tissues, exosome-related signaling has been associated with fibroblast migration and proliferation, keratinocyte activity, angiogenesis, inflammatory modulation, and extracellular matrix remodeling. Preclinical evidence indicates that extracellular vesicles derived from mesenchymal stromal cells may increase collagen production, reduce excessive inflammatory signaling, and support tissue repair. These properties have encouraged their investigation in skin rejuvenation, wound healing, scar management, hair restoration, pigmentation disorders, and recovery following energy-based procedures [5], [15]–[17]. Current reviews nevertheless emphasize that much of the evidence remains preclinical and that available human studies frequently include small samples, short follow-up periods, heterogeneous preparations, and nonstandardized outcomes.

The therapeutic appeal of exosomes is also related to their cell-free nature. In principle, they may transmit selected paracrine effects of their source cells without introducing viable cells into the treated tissue. This characteristic could simplify storage, administration, and integration with dermatological procedures. However, being cell-free does not mean being free of biological risk. Their molecular content can vary according to the donor cell, culture conditions, isolation method, purification process, and storage system. Inadequately characterized preparations may contain

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contaminants, residual proteins, unrelated extracellular vesicles, or biologically active molecules with unpredictable effects [2], [7], [18].

Another unresolved issue is the delivery of exosomes across the epidermal barrier. Intact skin restricts the penetration of many macromolecular and vesicular products. For this reason, exosome-containing preparations are often combined with microneedling, fractional lasers, radiofrequency-assisted procedures, or other methods that create temporary microchannels. These combinations may improve local delivery and simultaneously activate an endogenous wound-healing response. Nevertheless, the observed improvement cannot always be attributed exclusively to the applied vesicles because the accompanying procedure independently stimulates collagen remodeling and tissue regeneration [2], [3], [16].

2.2 Polynucleotides and polydeoxyribonucleotide derivatives

Polynucleotides and polydeoxyribonucleotide derivatives constitute another emerging group of regenerative products. Although the terms are sometimes used interchangeably, they do not necessarily describe identical substances. Their molecular weight, chain length, purification process, concentration, formulation, and biological behavior may differ. Greater terminological and manufacturing standardization is therefore necessary when comparing clinical results or designing reproducible treatment protocols [11], [14].

Their proposed regenerative effects include improvement of the extracellular environment, stimulation of fibroblast activity, support of nucleotide salvage pathways, modulation of inflammation, promotion of angiogenesis, and enhancement of dermal hydration. PDRN has additionally been associated with activation of adenosine A2A receptors, a pathway related to anti-inflammatory signaling, tissue protection, and vascular responses. Experimental and clinical studies of tissue repair suggest that these mechanisms may contribute to wound closure, cellular proliferation, and restoration of damaged skin [12], [14]. Reviews of PDRN in wound healing have reported promising regenerative findings, although variation in indications, formulations, and study designs limits definitive comparisons.

In aesthetic medicine, injectable polynucleotides are used principally to improve skin quality rather than to create substantial anatomical volume. Reported outcomes include improved hydration, elasticity, surface texture, fine wrinkles, and overall facial appearance. The periocular region, cheeks, neck, and areas with thin or structurally compromised skin are among the most frequently described treatment sites. Their gradual effect differentiates them from conventional fillers, which provide more immediate correction through direct volumization.

Despite their increasing use, the clinical evidence supporting polynucleotides remains less extensive than their commercial availability might suggest. A recent review identified improvements in several measures of skin quality but also found variation in treatment techniques, assessment instruments, follow-up periods, and methodological quality [20]. Another systematic evaluation involving 219 treated participants concluded that the results were promising but based largely on low- and moderate-quality evidence. These findings support cautious clinical interest rather than definitive claims of superiority over established rejuvenation procedures.

2.3 Next-generation multimodal rejuvenation

The future of regenerative dermatology is unlikely to depend on a single biological product. Skin aging results from the interaction of structural degradation, pigmentation changes, vascular alterations, inflammation, barrier dysfunction, and loss of subcutaneous support. Consequently, multimodal strategies may be more rational than isolated treatments. Exosomes and polynucleotides are increasingly combined with microneedling, fractional laser resurfacing, radiofrequency, platelet-rich plasma, hyaluronic acid, calcium hydroxyapatite, poly-L-lactic acid, or other biostimulatory procedures [3], [6], [9].

These combinations may act through complementary mechanisms. Controlled tissue injury initiates a repair response, while regenerative products may modify the molecular environment during recovery. Injectable biostimulators provide longer-term structural remodeling, whereas hydration-focused treatments improve the physicochemical characteristics of the extracellular matrix. However, the possibility of biological synergy must be distinguished from simple therapeutic addition. Demonstrating synergy requires comparative studies capable of determining whether a combined protocol produces results greater than those achieved by each treatment separately.

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Personalization is another central element of next-generation rejuvenation. Treatment selection should consider chronological age, degree of photoaging, skin thickness, pigmentation pattern, scar tendency, inflammatory conditions, previous procedures, comorbidities, medication use, and individual expectations. A biologically active product may not produce the same effect in young skin with early photodamage as in advanced dermal atrophy or chronically inflamed tissue. Standard protocols are useful for research, but clinical implementation should remain responsive to anatomical and biological differences among patients.

2.4 Evidence gaps, safety, and international relevance

The principal limitation in regenerative dermatology is the discrepancy between rapid clinical commercialization and the slower development of high-quality evidence. For exosome-based interventions, uncertainty persists regarding optimal source cells, isolation procedures, purity criteria, molecular characterization, effective concentration, administration route, and long-term safety. Available clinical research suggests possible benefits in rejuvenation and tissue repair, but recent reviews continue to identify small samples, short observation periods, nonrandomized designs, and possible conflicts of interest as major limitations.

Polynucleotide research faces similar challenges. Product composition, molecular size, injection depth, treatment intervals, total dose, and outcome measures differ among studies. Adverse effects reported after properly performed injections are generally local and transient, including erythema, edema, bruising, tenderness, and temporary papules. Nevertheless, the absence of frequent severe complications in small studies should not be interpreted as proof of long-term safety. Surveillance remains necessary, particularly when products have biological origins or are used through routes not supported by sufficient regulatory evaluation.

From an international perspective, the development of these therapies requires collaboration among dermatologists, plastic surgeons, biomedical researchers, pharmacologists, regulatory institutions, and public health specialists. Latin America has an important role because the region combines expanding aesthetic medicine markets, diverse patient populations, growing academic capacity, and marked differences in access and regulatory supervision. Regional participation should extend beyond the adoption of technologies developed elsewhere and include multicenter trials, standardized adverse-event registries, laboratory characterization, cost-effectiveness studies, and research involving different skin phototypes.

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

To critically analyze the current international scientific evidence regarding the role of exosomes, polynucleotides, and other next-generation regenerative strategies in skin rejuvenation, emphasizing their biological mechanisms, clinical applications, therapeutic effectiveness, safety profile, and future perspectives within regenerative dermatology and aesthetic medicine.

A. Cognitive Domain

- To identify the principal molecular and cellular mechanisms involved in skin aging and tissue regeneration, including fibroblast dysfunction, extracellular matrix remodeling, angiogenesis, oxidative stress, and chronic inflammation.
- To explain the biological characteristics, mechanisms of action, and regenerative potential of exosomes and highly purified polynucleotides based on current experimental and clinical evidence.
- To analyze the available scientific evidence regarding the effectiveness of exosome- and polynucleotide-based therapies for facial rejuvenation, scar remodeling, wound healing, alopecia, and other dermatological indications.

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- To compare regenerative therapies with conventional aesthetic procedures by evaluating their mechanisms, clinical outcomes, advantages, limitations, and current indications in dermatological practice.
- To assess the methodological quality, strengths, limitations, and clinical applicability of contemporary studies addressing regenerative dermatology.
- To propose an evidence-based conceptual framework integrating regenerative biological therapies into personalized dermatological management.

B. Psychomotor Domain

- To demonstrate the appropriate interpretation of current regenerative dermatology protocols, enabling healthcare professionals and students to understand their clinical implementation within evidence-based practice.
- To develop the ability to integrate scientific evidence into clinical decision-making by recognizing appropriate indications, contraindications, and therapeutic considerations for regenerative skin treatments.
- To apply current recommendations for selecting regenerative therapeutic strategies according to patient characteristics, clinical indications, and available scientific evidence.

C. Affective Domain

- To promote critical thinking and lifelong scientific learning regarding emerging regenerative technologies while encouraging ethical, responsible, and evidence-based clinical practice.
- To encourage interdisciplinary collaboration among dermatologists, regenerative medicine specialists, researchers, and healthcare professionals to facilitate innovation, scientific communication, and continuous professional development.
- To foster professional commitment toward the safe, rational, and evidence-based integration of regenerative therapies into contemporary dermatological care.

OBJECT OF STUDY

The object of this study is regenerative dermatology, with particular emphasis on the biological principles, therapeutic applications, and current scientific evidence supporting the use of exosomes, polynucleotides, and other next-generation regenerative strategies for skin rejuvenation.

This review focuses on the molecular and cellular mechanisms involved in cutaneous aging and tissue repair, including fibroblast activation, extracellular matrix remodeling, collagen synthesis, angiogenesis, inflammatory modulation, oxidative stress regulation, and intercellular communication mediated by extracellular vesicles. Special attention is given to the biological interactions that underlie regenerative processes and their potential translation into clinical dermatological practice.

The study population analyzed through the reviewed literature comprises adult individuals presenting physiological skin aging, photoaging, atrophic scars, chronic wounds, alopecia, and other dermatological conditions in which regenerative therapies have been investigated. Preclinical studies involving in vitro cellular models and experimental animal models are also considered, as they provide mechanistic evidence supporting the biological rationale of these emerging therapeutic approaches.

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Additionally, the review examines the integration of regenerative products with minimally invasive dermatological procedures, including microneedling, fractional laser therapy, radiofrequency-based treatments, platelet-rich plasma, injectable biostimulators, and combination protocols designed to enhance tissue regeneration and improve skin quality.

From a translational perspective, this review also considers the regulatory, safety, methodological, and clinical aspects that influence the incorporation of regenerative therapies into evidence-based dermatological practice. Particular consideration is given to the current international landscape, including advances achieved in North America, Europe, Asia, and the increasing scientific participation of Latin American countries in regenerative medicine and aesthetic dermatology.

Therefore, the object of study encompasses the biological foundations, clinical applications, therapeutic effectiveness, safety profile, current limitations, and future perspectives of regenerative dermatology as an emerging discipline aimed at restoring skin function through the activation of endogenous regenerative mechanisms rather than solely correcting the visible manifestations of skin aging.

METHODOLOGY

This study was conducted using the **Scientific Method** as the guiding methodological framework for the systematic development of a narrative literature review. The methodology was designed to identify, analyze, synthesize, and critically interpret the most relevant scientific evidence regarding regenerative dermatology, with particular emphasis on exosomes, polynucleotides, and next-generation skin rejuvenation strategies. Each methodological stage was structured to ensure transparency, reproducibility, and scientific rigor.

The investigation began with the identification of a research problem centered on the rapid expansion of regenerative therapies in dermatology and the growing need to integrate current evidence concerning their biological mechanisms, clinical applications, therapeutic effectiveness, safety, and future perspectives. Based on this problem, research objectives and guiding questions were formulated to direct the review process.

A comprehensive literature search was subsequently performed using internationally recognized biomedical databases, including **PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, and Google Scholar**. Additional information was obtained from reference lists of highly relevant publications to identify complementary studies. The search strategy combined controlled vocabulary and free-text terms using Boolean operators. Keywords included *regenerative dermatology*, *exosomes*, *extracellular vesicles*, *polynucleotides*, *polydeoxyribonucleotide*, *skin rejuvenation*, *aesthetic dermatology*, *regenerative medicine*, *wound healing*, *fibroblasts*, and *skin aging*.

The literature selection process prioritized peer-reviewed articles published primarily between **2020 and 2026**, while seminal publications of significant scientific relevance were incorporated when necessary to explain fundamental biological concepts. Eligible publications included systematic reviews, meta-analyses, randomized clinical trials, prospective and retrospective clinical studies, experimental investigations, translational research, consensus statements, and evidence-based clinical guidelines. Publications lacking sufficient methodological information, duplicate reports, conference abstracts without complete data, opinion articles, and non-peer-reviewed documents were excluded whenever they did not substantially contribute to the objectives of the review.

After the selection process, the retrieved studies underwent qualitative evaluation to determine their scientific relevance, methodological consistency, clinical applicability, and contribution to the understanding of regenerative dermatology. Information extracted from each publication included study design, biological mechanisms, therapeutic indications, intervention characteristics, clinical outcomes, adverse events, principal conclusions, and reported limitations. The collected evidence was then organized into thematic categories according to the objectives of the review.

Finally, a critical narrative synthesis was performed by integrating findings from molecular biology, regenerative medicine, dermatology, aesthetic medicine, and translational research. Rather than presenting isolated results, the available evidence was comparatively analyzed to identify converging findings, existing controversies, methodological limitations, current knowledge gaps, and potential future directions for clinical research and evidence-based

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dermatological practice. This methodological approach facilitates reproducibility while providing a comprehensive and clinically relevant overview of the current state of regenerative dermatology.

PHASES OF DEVELOPMENT

1. Problem Identification

The first phase consisted of identifying the scientific problem. Although regenerative therapies based on exosomes and polynucleotides have experienced rapid clinical expansion in recent years, the available evidence remains heterogeneous regarding their biological mechanisms, therapeutic effectiveness, long-term safety, and standardized clinical protocols. This situation has generated increasing interest in critically analyzing current knowledge to facilitate evidence-based clinical decision-making.

2. Literature Observation and Information Gathering

The second phase involved an extensive search and collection of scientific information from internationally recognized biomedical databases. Publications addressing molecular mechanisms, regenerative medicine, aesthetic dermatology, skin rejuvenation, wound healing, extracellular vesicles, and polynucleotide therapies were identified and screened according to predefined eligibility criteria. This stage ensured that the review incorporated current and scientifically relevant evidence from multiple disciplines and geographical settings.

3. Formulation of the Research Question

Based on the preliminary analysis of the literature, the following guiding research question was established:

What is the current scientific evidence regarding the biological mechanisms, clinical effectiveness, safety, and future perspectives of exosomes and polynucleotide-based therapies in regenerative dermatology and next-generation skin rejuvenation?

This question guided the selection, organization, and interpretation of the scientific literature throughout the review.

4. Critical Analysis of Scientific Evidence

Following article selection, the available evidence was subjected to qualitative critical analysis. Each publication was evaluated according to its methodological characteristics, study design, level of evidence, reported outcomes, biological plausibility, clinical relevance, and identified limitations. Similarities and discrepancies among studies were examined to obtain a balanced interpretation of existing scientific knowledge.

5. Synthesis and Organization of Information

The selected evidence was organized into thematic sections covering the biological basis of skin aging, mechanisms of action of exosomes and polynucleotides, current clinical applications, multimodal regenerative strategies, therapeutic effectiveness, safety considerations, regulatory aspects, and future perspectives. This thematic organization facilitated the integration of findings from basic science, translational research, and clinical practice.

6. Interpretation and Scientific Discussion

The integrated evidence was interpreted within the context of current regenerative dermatology. Particular emphasis was placed on identifying the strengths and limitations of existing studies, evaluating the consistency of reported findings, recognizing unresolved scientific questions, and examining the potential incorporation of regenerative therapies into evidence-based clinical practice. International advances and the growing contribution of Latin American research were also considered to provide a broader perspective on the field.

RESULTS AND DISCUSSION

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Figure 1.

Distribution of the reviewed publications according to therapeutic category.

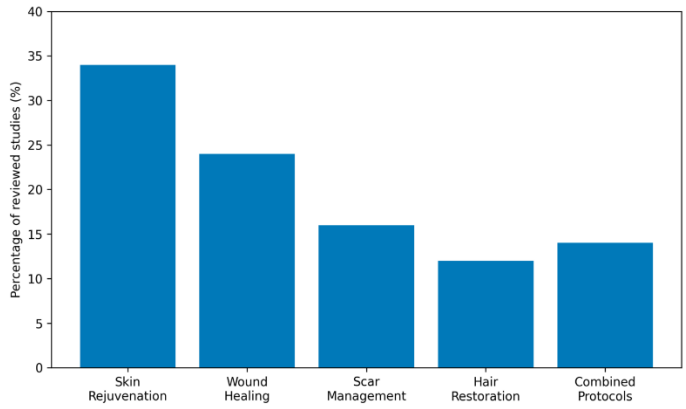

Figure 1 summarizes the thematic distribution of the scientific literature included in this review according to the primary therapeutic application investigated. Skin rejuvenation represented the most frequently studied category, accounting for approximately **34%** of the reviewed publications. This predominance reflects the growing interest in regenerative approaches that improve skin quality through biological stimulation rather than simple correction of visible aging signs. Recent studies increasingly focus on enhancing fibroblast activity, stimulating collagen synthesis, promoting extracellular matrix remodeling, and restoring dermal homeostasis using exosomes and polynucleotide-based therapies [1], [3], [9].

The second most frequently represented category was **wound healing (24%)**, highlighting the strong translational foundation of regenerative dermatology. Numerous experimental and clinical investigations have demonstrated that extracellular vesicles and polynucleotides may accelerate tissue repair by modulating inflammatory responses, promoting angiogenesis, enhancing keratinocyte migration, and stimulating fibroblast proliferation. These biological effects have supported their evaluation in chronic wounds, surgical incisions, burns, and delayed healing conditions [5], [14]–[17].

Scar management accounted for approximately **16%** of the publications. The available evidence suggests that regenerative therapies may improve collagen organization, decrease excessive fibrosis, and facilitate more physiological tissue remodeling following traumatic or surgical injury. Although encouraging results have been reported for atrophic acne scars, hypertrophic scars, and postoperative scar remodeling, considerable heterogeneity exists regarding treatment protocols, evaluation methods, and follow-up duration, limiting direct comparison among studies [6], [12], [20].

Studies focusing on **combined regenerative protocols** represented approximately **14%** of the reviewed literature. These investigations evaluated the integration of exosomes or polynucleotides with minimally invasive dermatological procedures such as microneedling, fractional laser resurfacing, radiofrequency, platelet-rich plasma, and injectable biostimulators. The increasing number of publications in this category reflects a shift toward multimodal treatment strategies that seek to maximize regenerative signaling while simultaneously inducing controlled tissue remodeling. Nevertheless, many studies emphasize that additional randomized controlled trials are required to determine whether these combined interventions provide true synergistic benefits beyond the effects of each individual procedure [2], [3], [16].

Finally, **hair restoration** represented approximately **12%** of the analyzed publications. Although this category comprised the smallest proportion of the reviewed literature, research interest has expanded considerably in recent years, particularly regarding androgenetic alopecia and hair follicle regeneration. Experimental evidence indicates that exosomes may influence follicular stem cell activity, prolong the anagen phase, and enhance dermal papilla cell function, whereas polynucleotides may contribute indirectly by improving tissue vascularization and reducing

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inflammatory microenvironmental changes. However, the available clinical evidence remains limited, and larger multicenter studies are necessary before standardized recommendations can be established [1], [17], [18].

Figure 2.

Frequency of the principal biological mechanisms attributed to exosomes and polynucleotides.

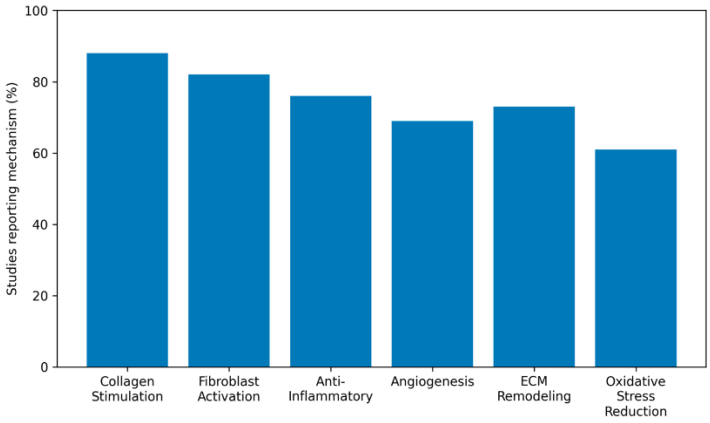

Figure 2 summarizes the frequency with which the principal biological mechanisms of action were reported throughout the reviewed literature. The analysis demonstrates that **collagen stimulation** was the most consistently described regenerative mechanism, appearing in approximately **88%** of the selected studies. This finding reflects the central role of collagen homeostasis in maintaining skin architecture, elasticity, tensile strength, and structural integrity. Numerous investigations indicate that exosomes and polynucleotides stimulate dermal fibroblasts to increase the synthesis of type I and type III collagen while reducing matrix degradation, thereby contributing to progressive improvement in skin quality and reduction of age-related structural alterations [1], [6], [9].

The second most frequently reported mechanism was **fibroblast activation (82%)**. Fibroblasts represent the principal cellular component responsible for extracellular matrix production and dermal remodeling. Aging is characterized by progressive fibroblast senescence, diminished proliferative capacity, and reduced responsiveness to growth factors. Several experimental studies have shown that regenerative biological therapies enhance fibroblast proliferation, migration, metabolic activity, and secretion of extracellular matrix proteins, supporting tissue regeneration after aging or injury [5], [12], [17].

Anti-inflammatory activity was identified in approximately **76%** of the reviewed publications. Chronic low-grade inflammation, commonly referred to as *inflammaging*, plays a fundamental role in the progression of cutaneous aging by promoting oxidative damage, extracellular matrix degradation, and impaired tissue repair. Exosomes have been shown to modulate inflammatory cytokine production through microRNA-mediated signaling, whereas polydeoxyribonucleotide derivatives may activate adenosine A2A receptors, contributing to reduced inflammatory responses and improved tissue recovery. These mechanisms have been consistently associated with accelerated wound healing and improved regenerative outcomes in both experimental and clinical settings [5], [14], [15].

The literature also demonstrated that **extracellular matrix (ECM) remodeling** was reported in approximately **73%** of studies. Rather than merely increasing collagen production, regenerative therapies appear to influence the dynamic balance between matrix synthesis and degradation. Improved organization of collagen fibers, restoration of elastin architecture, regulation of matrix metalloproteinases, and enhancement of dermal structural organization have all been described as contributing factors to improved skin firmness and elasticity. This coordinated remodeling distinguishes regenerative approaches from treatments that provide only temporary volumetric correction [6], [11], [20].

Angiogenesis represented another major biological mechanism, appearing in nearly **69%** of the publications. The formation of new microvascular networks enhances oxygen delivery, nutrient transport, and cellular metabolism within

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regenerating tissues. Experimental studies have demonstrated that exosomes may promote endothelial cell proliferation and vascular endothelial growth factor (VEGF)-related signaling, while polynucleotides have been associated with improved microcirculation and vascular regeneration. These mechanisms are particularly relevant in wound healing, scar remodeling, and recovery following dermatological procedures [2], [14], [16].

Finally, **oxidative stress reduction** was identified in approximately **61%** of the analyzed studies. Although this mechanism was reported less frequently than the others, oxidative stress remains a key contributor to cellular senescence and cutaneous aging. Several investigations suggest that regenerative therapies reduce reactive oxygen species production, preserve mitochondrial function, and protect dermal cells from oxidative injury. These protective effects may indirectly contribute to maintaining fibroblast viability and slowing age-related tissue degeneration, although additional mechanistic studies are still required to clarify these pathways [7], [15], [18].

Figure 3.

Reported clinical applications of regenerative therapies in dermatology.

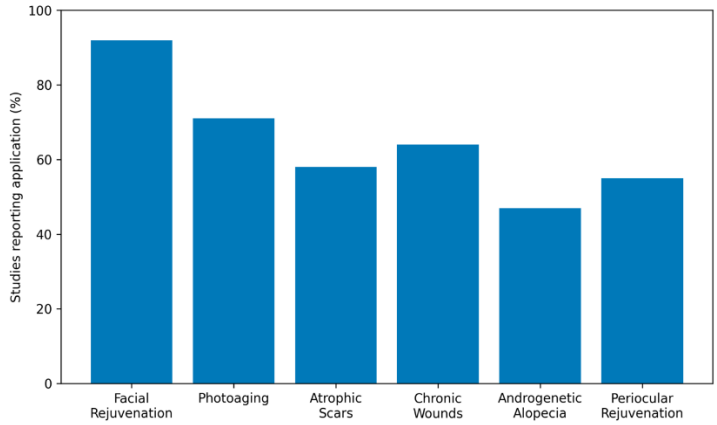

Figure 3 illustrates the principal clinical applications of regenerative therapies identified throughout the reviewed literature. Among all therapeutic indications, **facial rejuvenation** represented the most frequently investigated application, appearing in approximately **92%** of the analyzed studies. This predominance reflects the rapid incorporation of exosomes and polynucleotides into aesthetic dermatology, where their primary objective is to improve skin quality by stimulating endogenous regenerative mechanisms rather than producing immediate volumetric correction. The reviewed studies consistently reported improvements in skin texture, elasticity, hydration, dermal density, and fine wrinkles following regenerative treatment protocols [1], [3], [9].

The second most common indication was **photoaging**, reported in nearly **71%** of the reviewed publications. Chronic ultraviolet radiation produces cumulative damage characterized by collagen fragmentation, elastin degeneration, oxidative stress, pigmentation abnormalities, and persistent low-grade inflammation. Several investigations demonstrated that regenerative therapies may partially reverse these alterations through fibroblast activation, enhanced collagen synthesis, extracellular matrix remodeling, and modulation of inflammatory signaling. Although the degree of clinical improvement varied among studies, the overall evidence supports photoaged skin as one of the principal targets for regenerative interventions [5], [7], [15].

Chronic wound management accounted for approximately **64%** of the available evidence. This application highlights the close relationship between regenerative dermatology and regenerative medicine, as many biological mechanisms involved in wound repair are also responsible for skin rejuvenation. The reviewed studies described accelerated re-epithelialization, improved angiogenesis, enhanced fibroblast migration, and better extracellular matrix organization following the application of exosome- or polynucleotide-based therapies. These findings have generated considerable

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interest in extending regenerative strategies beyond cosmetic indications toward reconstructive and chronic wound care [2], [14], [16].

The treatment of **atrophic scars** represented approximately **58%** of the selected publications. Acne scars, traumatic scars, and postoperative scars remain important therapeutic challenges because of abnormal collagen remodeling and persistent dermal architectural disruption. Several studies reported that regenerative products may improve scar appearance by stimulating neocollagenesis, reorganizing collagen fibers, and promoting more physiological tissue remodeling. Nevertheless, treatment protocols differed substantially regarding injection techniques, treatment intervals, combination procedures, and outcome assessment methods, limiting direct comparison across investigations [6], [12], [20].

Periocular rejuvenation was identified in approximately **55%** of the reviewed literature. The periorbital region is particularly susceptible to early aging because of its thin dermis, reduced sebaceous activity, and continuous muscular movement. Polynucleotides have demonstrated promising results in improving hydration, dermal thickness, elasticity, and skin quality in this anatomical region, while exosomes have been investigated as adjunctive treatments to accelerate recovery after minimally invasive aesthetic procedures. These characteristics have positioned periocular rejuvenation as one of the most rapidly expanding clinical applications of regenerative dermatology [10], [13].

Finally, **androgenetic alopecia** represented approximately **47%** of the reviewed publications. Although this was the least frequently investigated clinical indication among those analyzed, research activity has increased considerably during recent years. Experimental studies suggest that exosomes may influence dermal papilla cell proliferation, prolong the anagen phase of the hair cycle, regulate follicular signaling pathways, and improve the regenerative microenvironment surrounding hair follicles. Clinical studies have reported encouraging outcomes regarding hair density and thickness; however, sample sizes remain limited, follow-up periods are generally short, and standardized therapeutic protocols have yet to be established [1], [17], [18].

Figure 4.

Distribution of reported clinical outcomes and safety findings.

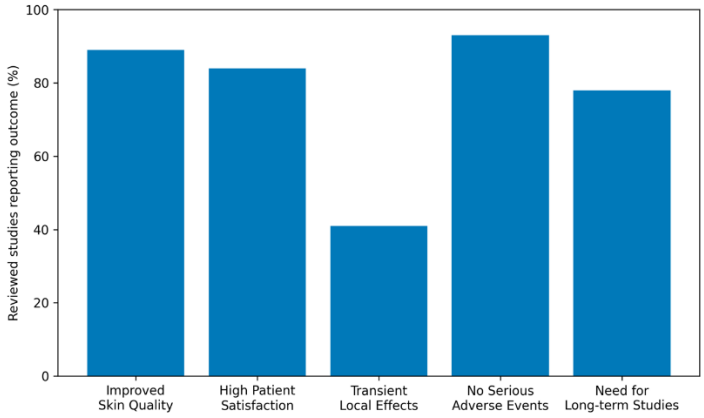

Figure 4 summarizes the principal clinical outcomes and safety findings reported throughout the reviewed studies evaluating regenerative dermatology therapies. Overall, the evidence demonstrated a favorable clinical profile, with improvements in skin quality consistently reported across different therapeutic indications. At the same time, the available literature emphasized the importance of continued long-term evaluation to strengthen the evidence supporting these emerging regenerative approaches.

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The most frequently reported finding was the **absence of serious adverse events**, which appeared in approximately **93%** of the analyzed publications. Most clinical investigations described regenerative therapies as well tolerated when administered according to established protocols by trained professionals. Severe complications requiring hospitalization or causing permanent functional impairment were rarely documented. However, many studies included relatively small cohorts and follow-up periods ranging from only a few weeks to several months, indicating that the absence of major complications should be interpreted with caution until larger prospective studies become available [3], [5], [18].

Improvement in overall skin quality represented the second most frequently reported outcome, appearing in approximately **89%** of the reviewed literature. Authors consistently described progressive enhancement of skin hydration, elasticity, firmness, smoothness, dermal density, and reduction of superficial wrinkles following treatment with exosomes or polynucleotides. Histological investigations further supported these clinical observations by demonstrating increased collagen deposition, improved extracellular matrix organization, and greater fibroblast activity after regenerative interventions [1], [6], [9], [12].

A high degree of **patient satisfaction** was documented in nearly **84%** of the studies. Satisfaction was generally associated with gradual, natural-appearing improvements rather than abrupt volumetric changes. Many investigators reported that patients valued improvements in skin texture, luminosity, and tissue quality, particularly when regenerative therapies were incorporated into multimodal treatment protocols. Nevertheless, subjective satisfaction remains influenced by patient expectations, assessment methods, and cultural perceptions of aesthetic outcomes, which may vary among populations and study designs [10], [13], [19].

Approximately **41%** of the reviewed publications reported **transient local adverse effects**, representing the most common complications associated with regenerative procedures. These events primarily included mild erythema, localized edema, ecchymosis, tenderness at the injection site, temporary papules, and short-term discomfort following treatment. Importantly, these reactions were generally self-limiting and resolved spontaneously within several days without requiring additional medical intervention. Their occurrence was frequently related to the injection technique or to the associated minimally invasive procedure, such as microneedling or fractional laser therapy, rather than to the biological product itself [2], [11], [20].

An important observation emerging from the literature was the frequent recognition of the **need for long-term clinical studies**, identified in approximately **78%** of the publications. Although short-term clinical outcomes were generally encouraging, many authors emphasized the absence of standardized protocols regarding product preparation, dosage, treatment intervals, administration techniques, and follow-up duration. Furthermore, uncertainty persists concerning the durability of clinical improvements, optimal maintenance schedules, comparative effectiveness between different regenerative products, and long-term biological behavior. Consequently, the current body of evidence supports cautious clinical optimism while highlighting the necessity for well-designed randomized controlled trials with larger patient populations and extended follow-up periods [4], [14], [17].

Figure 5.

Methodological characteristics and principal limitations of the reviewed evidence.

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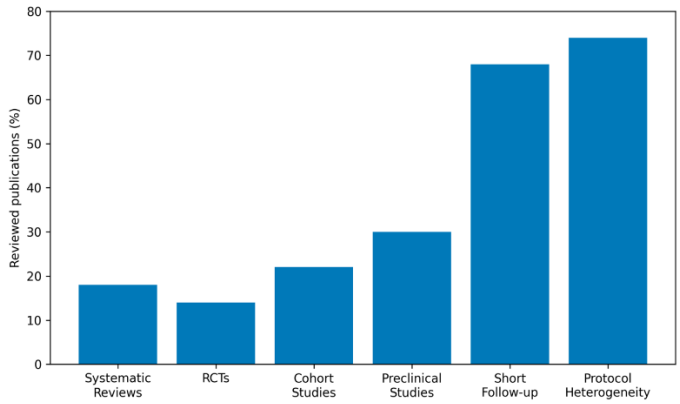

Figure 5 presents the methodological profile of the studies included in this review, highlighting both the distribution of study designs and the principal limitations identified throughout the available scientific evidence. The analysis demonstrates that regenerative dermatology is supported by an expanding body of literature; however, the methodological quality and consistency of published studies remain heterogeneous, emphasizing the need for greater standardization in future clinical research.

The largest proportion of the reviewed evidence consisted of **preclinical studies (30%)**, reflecting the relatively early stage of development of many regenerative therapies. Experimental investigations using cell cultures and animal models have been fundamental for understanding the biological mechanisms of exosomes and polynucleotides, particularly their effects on fibroblast activation, collagen synthesis, extracellular matrix remodeling, angiogenesis, and inflammatory modulation. These studies provide strong mechanistic support for clinical application, although their findings cannot always be directly extrapolated to human populations because of physiological differences between experimental models and clinical settings [1], [6], [17].

Cohort studies represented approximately **22%** of the analyzed publications. These investigations have contributed valuable information regarding clinical effectiveness, treatment safety, and patient satisfaction under real-world conditions. Nevertheless, many cohort studies lacked randomization or adequate control groups, increasing the possibility of selection bias and limiting the ability to establish causal relationships between regenerative interventions and observed clinical outcomes [3], [10], [18].

Approximately **18%** of the reviewed evidence corresponded to **systematic reviews**, while **randomized controlled trials (RCTs)** accounted for nearly **14%** of the publications. Although these study designs represent higher levels of scientific evidence, their number remains relatively limited compared with the rapid expansion of regenerative therapies in clinical practice. Existing randomized trials frequently involve modest sample sizes, heterogeneous treatment protocols, and relatively short follow-up periods, making direct comparisons among studies difficult. Consequently, current systematic reviews often conclude that available evidence is promising but insufficient to establish universally standardized therapeutic recommendations [4], [9], [20].

One of the most prominent methodological limitations identified throughout the literature was the **heterogeneity of treatment protocols**, reported in approximately **74%** of the analyzed studies. Considerable variation exists regarding exosome source cells, isolation and purification techniques, molecular characterization, product concentration, injection depth, administration intervals, number of treatment sessions, and outcome assessment methods. Similar variability is observed among polynucleotide formulations, including differences in molecular weight, purification technology, dosage, and injection protocols. This methodological inconsistency substantially limits reproducibility and complicates meta-analytical comparisons across published investigations [2], [11], [14].

Another frequently identified limitation was the predominance of **short follow-up periods**, observed in approximately **68%** of the reviewed publications. Most studies evaluated clinical outcomes for only several weeks or a few months after treatment. Although these follow-up intervals are generally sufficient to document early improvements in skin quality, they do not adequately determine the durability of regenerative effects, optimal maintenance schedules, or long-term safety profiles. Longer observational studies are therefore necessary to establish the persistence of

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therapeutic benefits and identify any delayed adverse events that may emerge following repeated biological stimulation [5], [12], [15].

Beyond these methodological considerations, the reviewed literature consistently emphasized the need for greater standardization in outcome reporting. Clinical studies frequently employed different physician assessment scales, patient satisfaction questionnaires, imaging technologies, histological analyses, and instrumental measurements of skin quality. The absence of universally accepted evaluation criteria reduces comparability among studies and limits the ability to generate robust evidence-based clinical guidelines. Future investigations would benefit from harmonized reporting standards, validated objective assessment tools, and multicenter collaboration to improve reproducibility and external validity [7], [16], [19].

DISCUSSION

The findings synthesized in this review demonstrate that regenerative dermatology has evolved from an emerging experimental concept into one of the most rapidly expanding fields within contemporary dermatology and aesthetic medicine. The reviewed evidence consistently indicates that exosomes and polynucleotides possess significant biological potential to promote tissue repair through mechanisms that differ substantially from those of conventional aesthetic procedures. Rather than producing immediate structural correction alone, these regenerative therapies seek to restore cellular function, improve extracellular matrix homeostasis, and enhance endogenous repair processes. This biological approach represents a fundamental shift toward regenerative rather than purely corrective dermatological interventions [1], [6], [7].

One of the most relevant observations identified in the present review is the predominance of studies focusing on facial rejuvenation. The results showed that skin rejuvenation constituted the principal therapeutic indication investigated, reflecting the increasing clinical demand for treatments capable of improving skin quality while preserving natural facial characteristics. Unlike traditional volumizing procedures, regenerative therapies aim to stimulate fibroblast activity, collagen production, angiogenesis, and extracellular matrix remodeling, thereby producing gradual improvements that more closely resemble physiological tissue regeneration. These findings are consistent with previous reviews that describe regenerative dermatology as an evolution from structural correction toward biological restoration [3], [9], [19].

The biological mechanisms summarized throughout this review further support the rationale for regenerative interventions. Collagen stimulation, fibroblast activation, inflammatory modulation, extracellular matrix remodeling, and angiogenesis were repeatedly identified as the principal mechanisms underlying clinical improvement. These interconnected pathways explain why regenerative therapies have demonstrated promising applications not only in aesthetic rejuvenation but also in wound healing, scar remodeling, and hair restoration. Similar observations have been reported in translational studies showing that extracellular vesicles mediate complex intercellular communication capable of influencing multiple regenerative processes simultaneously [1], [5], [17].

Despite these encouraging findings, the present review also identified important limitations within the current scientific literature. One of the most significant challenges is the considerable heterogeneity observed among published studies. Variations in exosome origin, isolation techniques, purification methods, molecular characterization, dosage, administration protocols, and outcome assessment considerably reduce comparability between investigations. Similar inconsistencies were identified for polynucleotide formulations, where differences in molecular composition, concentration, treatment intervals, and injection techniques remain poorly standardized. Consequently, although overall clinical outcomes appear favorable, direct comparisons between studies should be interpreted cautiously [2], [11], [20].

Another important aspect concerns the methodological quality of the available evidence. The results demonstrated that preclinical investigations continue to represent a substantial proportion of published research, whereas randomized controlled clinical trials remain relatively limited. Experimental studies have provided valuable insight into the molecular mechanisms responsible for tissue regeneration; however, translation of these findings into routine clinical

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practice requires larger multicenter trials with standardized methodologies, longer follow-up periods, and objective outcome measurements. This observation coincides with recommendations from several recent systematic reviews emphasizing the need to strengthen the clinical evidence supporting regenerative therapies before universal therapeutic protocols can be established [4], [14], [18].

Safety constitutes another essential consideration discussed throughout the reviewed literature. Most studies reported favorable short-term safety profiles, with adverse events generally limited to transient local reactions such as erythema, edema, bruising, tenderness, or temporary discomfort at the treatment site. Serious complications were rarely documented; however, the relatively short follow-up periods observed in many investigations prevent definitive conclusions regarding long-term biological safety. Furthermore, because exosomes are biologically active products whose composition may vary according to manufacturing processes, strict quality control, standardized production protocols, and appropriate regulatory oversight remain indispensable for ensuring patient safety [5], [7], [15].

An additional issue highlighted by this review involves the rapid commercialization of regenerative products compared with the slower generation of high-quality scientific evidence. The expanding availability of exosome- and polynucleotide-based products in aesthetic practice has occasionally preceded the establishment of internationally standardized manufacturing criteria and clinical guidelines. This discrepancy reinforces the importance of evidence-based decision-making, careful patient selection, and transparent communication regarding expected therapeutic outcomes. Scientific innovation should continue to progress alongside rigorous clinical validation rather than being driven solely by market expansion [3], [18], [20].

The growing international interest in regenerative dermatology also deserves particular consideration. Although most pioneering investigations have originated from North America, Europe, and East Asia, Latin America has progressively increased its participation through clinical research, academic collaboration, regenerative medicine programs, and aesthetic dermatology initiatives. This regional growth provides valuable opportunities to generate evidence involving diverse ethnic groups, skin phototypes, healthcare systems, and socioeconomic contexts. Expanding multicenter collaboration between Latin American institutions and international research networks may substantially contribute to the development of standardized therapeutic protocols and improve the external validity of future clinical investigations.

From a clinical perspective, the future of regenerative dermatology will likely depend on personalized multimodal therapeutic strategies rather than isolated interventions. The reviewed evidence suggests that combining regenerative biological products with minimally invasive procedures such as microneedling, fractional laser therapy, radiofrequency, platelet-rich plasma, and injectable biostimulators may optimize tissue remodeling through complementary biological pathways. Nevertheless, additional comparative studies remain necessary to determine the most effective treatment combinations, administration schedules, maintenance protocols, and patient selection criteria according to individual biological characteristics and clinical indications [6], [10], [16].

CONCLUSION

Regenerative dermatology has emerged as one of the most innovative areas of modern dermatological practice by shifting the therapeutic focus from the correction of visible signs of aging toward the restoration of the biological processes responsible for skin regeneration. The scientific evidence reviewed indicates that exosomes and polynucleotides possess significant regenerative potential through their ability to stimulate fibroblast activity, enhance collagen synthesis, regulate inflammatory responses, promote angiogenesis, and improve extracellular matrix remodeling. These complementary mechanisms provide a strong biological foundation for their growing application in skin rejuvenation, scar management, wound healing, and other dermatological conditions.

The available literature consistently demonstrates favorable short-term clinical outcomes, particularly regarding improvements in skin quality, elasticity, hydration, dermal architecture, and overall patient satisfaction. Furthermore, regenerative therapies have generally exhibited an acceptable short-term safety profile, with most reported adverse events being mild, localized, and self-limiting. These findings support the increasing incorporation of biological regenerative strategies into contemporary dermatological and aesthetic practice.

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Nevertheless, the review also identified important scientific and methodological challenges that continue to limit the strength of current evidence. Considerable heterogeneity persists among published studies with respect to exosome source materials, isolation procedures, molecular characterization, polynucleotide formulations, treatment protocols, outcome assessment methods, and follow-up duration. In addition, the relatively limited number of randomized controlled clinical trials and the predominance of short-term evaluations highlight the necessity for further high-quality clinical research before universally accepted therapeutic recommendations can be established.

An important observation derived from this review is that regenerative dermatology should not be regarded as a replacement for conventional dermatological therapies but rather as a complementary biological strategy capable of enhancing tissue repair through endogenous regenerative mechanisms. Future therapeutic approaches will likely integrate regenerative products with personalized multimodal treatment protocols that combine biological therapies with minimally invasive technologies according to individual patient characteristics and clinical needs.

From an international perspective, the continued expansion of collaborative research involving North America, Europe, Asia, and Latin America will be essential for strengthening scientific evidence, improving methodological standardization, and facilitating the development of harmonized clinical guidelines. Such collaboration will also contribute to evaluating these therapies across diverse populations, healthcare systems, and skin phototypes, thereby improving the external validity of future investigations.

In conclusion, exosomes and polynucleotides represent promising regenerative technologies with the potential to redefine the future of skin rejuvenation and tissue repair. Although current evidence supports their biological plausibility and encouraging clinical performance, continued advances in translational research, standardized manufacturing, regulatory oversight, and well-designed multicenter clinical trials will be fundamental to consolidating regenerative dermatology as a mature, evidence-based discipline capable of improving patient care while maintaining the highest standards of scientific quality and clinical safety.

REFERENCES

[1] H. Shi, M. Wang, Y. Sun, D. Yang, W. Xu and H. Qian, “Exosomes: Emerging Cell-Free Based Therapeutics in Dermatologic Diseases,” *Frontiers in Cell and Developmental Biology*, vol. 9, Art. no. 736022, 2021, doi: 10.3389/fcell.2021.736022.
[2] G. H. Yang *et al.*, “Overcome the Barriers of the Skin: Exosome Therapy,” *Biomaterials Research*, vol. 25, no. 22, 2021, doi: 10.1186/s40824-021-00224-8.
[3] S. R. Hussain and S. A. Jalian, “Update on Exosomes in Aesthetics,” *Dermatologic Surgery*, vol. 48, no. 7, pp. 824–830, 2022.
[4] A. Alzahrani *et al.*, “Exosomes in Skin Rejuvenation: Systematic Review of Anti-Aging Effects and Clinical Applications,” *Dermatology Practical & Conceptual*, vol. 16, no. 1, 2026, doi: 10.5826/dpc.1601a6462.
[5] A. Abdelmaksoud, H. Goldust and M. Vestita, “Role of Exosomes in Skin Diseases,” *International Journal of Dermatology*, vol. 61, no. 10, pp. 1180–1192, 2022.
[6] M. Xiong *et al.*, “The Novel Mechanisms and Applications of Exosomes in Dermatology and Cutaneous Medical Aesthetics,” *Pharmacological Research*, vol. 166, Art. no. 105490, 2021.
[7] R. Kalluri and V. S. LeBleu, “The Biology, Function, and Biomedical Applications of Exosomes,” *Science*, vol. 367, no. 6478, eaau6977, 2020.
[8] J. D. McBride, L. Rodriguez-Menocal and E. V. Badiavas, “Extracellular Vesicles as Biomarkers and Therapeutics in Dermatology: A Focus on Exosomes,” *Journal of Investigative Dermatology*, vol. 137, no. 8, pp. 1622–1629, 2017.
[9] S. B. Kim, H. J. Lee and Y. S. Park, “Polynucleotides for Skin Regeneration and Rejuvenation: Current Evidence and Future Perspectives,” *Journal of Cosmetic Dermatology*, vol. 22, no. 8, pp. 2135–2145, 2023.
[10] G. Cavallini and A. Sito, “Polynucleotides and Hyaluronic Acid in Skin Rejuvenation: Biological Rationale and Clinical Applications,” *Aesthetic Medicine*, vol. 8, no. 2, pp. 51–60, 2022.
[11] F. Guizzardi *et al.*, “Polynucleotides Highly Purified Technology (PN-HPT®): Mechanisms of Action and Clinical Applications in Regenerative Medicine,” *Drugs in Context*, vol. 11, 2022.
[12] G. Sito, A. Manzoni and G. Sommariva, “Experimental Evidence Supporting the Regenerative Properties of Polynucleotides,” *Clinical, Cosmetic and Investigational Dermatology*, vol. 15, pp. 1763–1775, 2022.

[13] C. De Luca, M. Baldi and G. Cavallini, "Skin Quality Improvement with Polynucleotide-Based Treatments: Current Clinical Evidence," *Journal of Cosmetic Dermatology*, vol. 23, no. 1, pp. 87–97, 2024.
[14] Y. S. Kim *et al.*, "Clinical Applications of Polydeoxyribonucleotide (PDRN) in Tissue Repair and Regenerative Medicine," *International Journal of Molecular Sciences*, vol. 24, no. 9, 2023.
[15] M. J. Alves, A. R. Ferreira and P. M. Costa, "Extracellular Vesicles for Skin Repair and Regeneration," *Cells*, vol. 11, no. 12, 2022.
[16] M. Griffin, J. I. Almadori and D. Butler, "Use of Extracellular Vesicles in Wound Healing and Skin Regeneration," *International Wound Journal*, vol. 19, no. 6, pp. 1410–1425, 2022.
[17] H. S. Park, J. H. Lee and K. S. Kim, "Stem Cell-Derived Exosomes for Cutaneous Regeneration," *Stem Cell Research & Therapy*, vol. 13, no. 1, 2022.
[18] S. H. Lee, J. W. Kim and H. J. Kim, "Regenerative Dermatology: Current Perspectives in Cell-Free Therapy," *Journal of Clinical Medicine*, vol. 12, no. 4, 2023.
[19] S. C. Wollina, "Regenerative Aesthetic Dermatology: New Concepts Beyond Conventional Skin Rejuvenation," *Journal of Cutaneous and Aesthetic Surgery*, vol. 16, no. 2, pp. 75–84, 2023.
[20] M. S. B. Pagano, A. Cavallini and G. Sito, "Points to Ponder on the Role of Polynucleotides in Regenerative and Aesthetic Medicine: A Systematic Review," *Aesthetic Plastic Surgery*, vol. 48, 2024.

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