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Polynucleotide injectables in aesthetic medicine: A review of mechanisms, clinical uses, and comparative products with insights from the Egyptian market

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Abstract

Polynucleotides (PNs), derived primarily from purified trout or salmon DNA, have recently emerged as injectable biostimulatory agents in regenerative and aesthetic medicine. By enhancing hydration, stimulating fibroblast proliferation, modulating inflammation, and promoting collagen synthesis, PNs support tissue repair and skin rejuvenation. Several formulations including; Rejuran®, Nucleospire®, PhilArt®, and Plenhyage XL® have been introduced, each differing in composition, clinical applications, and market presence. This review provides a comparative overview of these products, emphasizing their mechanisms of action, clinical indications, regulatory status, and safety profiles. Beyond their use in dermatology and aesthetics, PN-based injectables show promise in dentistry, ophthalmology, and orthopedics, highlighting their expanding role in regenerative therapies. While accumulating evidence supports their efficacy, gaps remain in standardization, comparative clinical trials, and long-term safety evaluation.

Keyword: Polynucleotides; Rejuran; PhilArt; Plenhyage XL; Skin rejuvenation; Salmon DNA; Biostimulatory injectables

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Introduction

Polynucleotides (PNs) are long-chain nucleotide polymers derived from DNA or RNA, recognized for their regenerative and biostimulatory properties. These bioactive molecules have been widely applied in dermatology and aesthetic medicine due to their ability to stimulate cell repair, enhance hydration, and reduce inflammation. PNs are typically extracted from natural sources trout or salmon sperm DNA or synthesized through bioengineering techniques to ensure purity, reproducibility, and safety.[1-7]

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Source of polynucleotides

The predominant source of PNs in aesthetic medicine is trout and salmon DNA, which exhibits high biocompatibility and structural similarity to human DNA. The extraction process involves purification, enzymatic fragmentation, and stabilization, ensuring that the final product is safe, non-immunogenic, and free from contaminants. More recently, synthetic

formulations such as Nucleospire have been developed to mimic natural DNA structures, providing greater consistency and scalability.[8-10]

Constituents and properties

Polynucleotide-based injectables contain nucleotide chains, phosphate groups, and deoxyribose or ribose sugars. These molecular components underpin their biostimulatory effects, supporting cellular repair, extracellular matrix remodeling, angiogenesis, and hydration. Their strong water-binding properties further enhance skin elasticity and turgor.[11-13]

Mechanism of action at the cellular level

Polynucleotides function through multiple regenerative pathways.[6,7,10,11]

- *Fibroblast activation:* Stimulation of fibroblasts enhances collagen and elastin synthesis, restoring dermal density and reducing visible aging.
- *Wound healing:* PNs promote angiogenesis and tissue repair, aiding scar revision, post-procedure recovery, and chronic wound management.
- *Hydration and tissue remodeling:* Their high water-retention capacity improves tone, texture, and elasticity.
- *Anti-inflammatory and antioxidant effects:* By modulating cytokines and reducing oxidative stress, PNs are effective in sensitive skin, rosacea, *and post-laser recovery.*

Medical and dental applications

Polynucleotides (PNs) have been investigated in a range of medical fields, particularly dermatology and regenerative medicine. Their most established applications are in chronic wound healing, where clinical and preclinical studies have shown improved epithelialization, angiogenesis, and reduced scar formation. They have also been explored in post-surgical recovery and soft tissue repair, though large-scale clinical validation remains limited. In dentistry, the use of PNs is still in the early stages. Preclinical and pilot studies suggest potential benefits in periodontal regeneration, gingival healing, and oral mucosal repair, but robust randomized clinical trials are not yet available. This represents a promising but still experimental domain for translational research.[14-16]

Aesthetic applications

In aesthetic dermatology, PN-based injectables are more widely established and supported by clinical studies. Documented applications include.[12-15]

- *Skin Rejuvenation & biorevitalization:* clinical data demonstrate improvements in hydration, elasticity, and dermal thickness.
- *Scar and stretch mark management:* PNs may enhance collagen remodeling and tissue repair, with small-scale trials supporting efficacy.[17]
- *Post-procedure recovery:* used after laser resurfacing and chemical peels to accelerate re-epithelialization and reduce inflammation.
- *Hair restoration:* early studies suggest a potential role in promoting blood flow and nutrient supply, stimulating follicular activity, though evidence remains preliminary.

The key advantage of PNs in aesthetics lies in their ability to restore skin quality without volumization, making them attractive for patients seeking subtle, natural outcomes.

Mechanism of action

PNs exert their biological effects through multiple overlapping pathways:

- *Fibroblast activation:* PNs stimulate fibroblast proliferation and migration, leading to increased collagen and elastin synthesis.
- *Hydration & tissue repair:* Promote prolonged, isosomotic moisturization and improve the overall condition of the skin matrix.

- *Anti-inflammatory modulation:* PNs reduce oxidative stress and down regulate pro-inflammatory cytokines, contributing to faster tissue recovery.

Cellular Interaction

- *Fibroblast activation:* Evidence suggests that PNs interact with cell surface and intracellular pathways, promoting fibroblast activation and extracellular matrix production.
- *Angiogenesis:* Preclinical studies indicate that PNs upregulate vascular endothelial growth factor (VEGF), supporting neovascularization and improved tissue oxygenation.
- *DNA support:* As nucleic acid precursors, PNs may contribute to DNA repair and replication in damaged cells, enhancing cellular survival and tissue regeneration.

Biochemical and signaling effects

- *Extracellular matrix remodeling:* PNs stimulate synthesis of glycosaminoglycans (GAGs) and hyaluronic acid, which enhance dermal hydration and elasticity.
- *Collagen synthesis:* Preclinical data indicate upregulation of transforming growth factor-beta (TGF-β), promoting collagen type I and III deposition.
- *Pathway modulation:* Experimental evidence implicates PN activity in the TGF-β, NF-κB, and MAPK/ERK signaling cascades, supporting fibroblast activation and reduced inflammatory mediator expression.

Histochemical changes

Histological analyses in animal and human studies consistently show:

- Increased fibroblast density, correlating with sustained collagen renewal and dermal thickening.
- Enhanced vascularization, improving nutrient and oxygen supply to regenerating tissues.
- Reduction in inflammatory markers such as TNF-α and IL-6, reported primarily in preclinical models, supporting an anti-inflammatory role.

Comparative analysis of polynucleotide brands in the Egyptian market

Polynucleotide (PN)-based injectables have gained increasing attention in aesthetic medicine and are being investigated in other medical fields, including wound healing, ophthalmology, orthopedics, and dentistry. The following section provides a comparative review of the currently available evidence for Rejuran, Nucleospire, PhilArt (Croma), and Plenhyage XL.

1. Rejuran

- *Aesthetic medicine*: Multiple clinical studies demonstrate that Rejuran improves skin hydration, elasticity, and fine lines. Histological findings confirm increased collagen deposition and dermal thickening following treatment.
- *Medical applications*: Evidence supports its role in wound healing, with accelerated re-epithelialization and improved scar quality reported in both preclinical and clinical contexts.
- *Dental applications*: Currently, published data on dental applications are limited. However, its regenerative properties suggest potential utility in periodontal and oral mucosal repair, warranting further investigation.

2. Nucleospire

- *Aesthetic medicine:* Clinical data remain scarce. Preliminary distributor reports and limited case-based experiences suggest improvements in hydration and texture, but peer-reviewed evidence is lacking.

Table 1 Comparative analysis of polynucleotide-based injectables.

Feature	*Rejuran*	*Nucelospire*	*PhilArt (Croma)*	*Plenhyage XL*
Source	Salmon-derived PN (polydeoxyribonucleotide)	DNA–RNA complex (PDRN; formulations 1% and 2% available)	Trout-derived PN	Polymerised PN from wild salmon sperm DNA
Concentration	Varies by product line (e.g., Rejuran Healer, Rejuran S)	1% and 2% formulations (e.g., Nucleospire DNA-RNA 2%)	40 mg/2 ml	Medium: 20 mg/ml; Strong: 25 mg/ml
Molecular Weight	Not specified by manufacturer	Not specified by manufacturer	Not specified by manufacturer	Not specified by manufacturer
Viscosity	Not specified by manufacturer	Not specified by manufacturer	Not specified by manufacturer	Not specified by manufacturer
Injection Technique	Needle, cannula (protocol-dependent)	Needle (protocol-dependent)	Needle, cannula	Needle, cannula
Indications	Skin rejuvenation, scar repair	Hydration, elasticity (limited published data)	Biorevitalization, fine lines	Skin regeneration, post-procedure recovery
Injection Depth	Superficial–mid dermis (varies by protocol)	Superficial dermis	Superficial–deep dermis	Mid–deep dermis
Longevity	~6–9 months (clinical reports)	Limited published data	~4–6 months (clinical reports)	~6–12 months (clinical reports)
Safety Profile	Well-tolerated, minimal side effects	Limited clinical data; generally safe in distributor reports	Clinically tested, good tolerability	Mild swelling; rare hypersensitivity
Clinical Data	Extensive (Asia, now EU)	Limited peer-reviewed studies	Moderate (EU clinical use)	Growing clinical use (EU)
Regulatory Status	MFDS (Korea) medical device; CE-MDR certified in EU	Registered in Russia (RZN 2014/2065); not CE-marked	CE-marked (EU)	CE-marked (CE 0373, EU)

- *Medical and dental applications:* At present, no robust published studies document Nucleospire's role in medical or dental fields. Controlled clinical trials are required to validate its efficacy and safety.

3. PhilArt

- *Aesthetic medicine:* PhilArt has been applied in biorevitalization protocols, with European clinical practice and early studies showing enhanced hydration and elasticity. Patient satisfaction is generally high.
- *Medical applications:* Improving wound healing. Randomized study shows that highly purified polynucleotide in contrast to placebo in treatment of moderate to severe acne scars is very effective.[17]
- *Dental applications:* No peer-reviewed studies are currently available.

4. Plenhyage XL

- *Aesthetic medicine:* Plenhyage XL, containing polymerised polynucleotides, is utilized in protocolsaimed at skin regeneration and post-procedure recovery. Clinical reports describe improved healing and reduced downtime, although high-quality trials remain limited.
- *Medical applications:* Its regenerative potential is under exploration for soft tissue repair; however, data from controlled studies are insufficient.
- *Dental applications:* To date, no clinical research has been published on its application in dentistry.

Clinical applications and evidence

Polynucleotide injectables are primarily used in skin rejuvenation, scar management, and tissue repair. Independent studies support the efficacy of Rejuran and PhilArt, and, to a lesser extent, Plenhyage XL. Clinical evidence for Nucleospire is currently insufficient.

Our group has investigated PN injectables for lip

hydration, and ongoing work is evaluating hybrid formulations combining PNs with non-cross-linked hyaluronic acid and exosomes. Early observations suggest that PNs provide hydration without volumization, making them suitable for subtle rejuvenation. We have also introduced a four-point cannula injection technique for lip treatment to optimize distribution.

Safety and adverse effects

Available evidence indicates that PN-based injectables have a favorable safety profile when administered by trained professionals. Reported adverse effects are generally mild and transient, including erythema, swelling, and discomfort at the injection site. To date, no severe adverse events have been documented in the literature.

Future perspectives

Research into PNs is ongoing, with growing interest in their use in combination therapies (e.g., with hyaluronic acid, growth factors, or regenerative biomaterials). Expanding indications include hair restoration and deeper tissue regeneration. High-quality, comparative, randomized controlled trials are needed to establish standardized protocols and evaluate long-term safety and efficacy across different brands.

Conclusion

PN-based injectables represent a valuable innovation in regenerative and aesthetic medicine. Among available formulations, Rejuran has the strongest clinical evidence, particularly for aesthetic and wound-healing applications. PhilArt demonstrates promising results in biorevitalization, while Plenhyage XL shows potential for post-procedure recovery and skin regeneration. Nucleospire remains under-studied, and further peer-reviewed clinical research is required. Evidence supporting dental and broader medical uses is currently limited but represents an important avenue for future investigation. This review underscores the need for well-designed comparative studies to clarify product-specific benefits and guide evidence-based clinical decision-making.

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Author's contribution

NA,AG,NS,MG: Have made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data. Have been involved in drafting the manuscript and revising it critically for important intellectual content.

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