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Review

Polydeoxyribonucleotide (PDRN) from Diverse Biological Sources: Comparative Biochemistry, Biotechnological Production, and Translational Potential

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Abstract

Polydeoxyribonucleotide (PDRN) has emerged as a promising bioactive biomaterial with broad applications in regenerative medicine because of its anti-inflammatory, angiogenic, and tissue-repair properties. Traditionally obtained from salmonid sperm DNA, it has been reported to promote tissue regeneration primarily by activating adenosine A2A receptors and the nucleotide salvage pathway, thereby stimulating fibroblast proliferation, extracellular matrix remodeling, collagen synthesis, and angiogenesis. This review provides a comprehensive overview of the biochemical characteristics, mechanisms of action, extraction methods, and translational potential of PDRN from different biological sources. In addition to conventional animal-derived PDRN, recent advances have introduced plant-derived (PhytoPDRN) and microbial- or algae-derived alternatives, offering improved sustainability, scalability, and reduced environmental impact. Preliminary in vitro evidence suggests that these emerging sources may exhibit regenerative and antioxidant activities; however, differences in molecular characteristics, experimental models, and study designs currently preclude establishing biological or clinical equivalence with salmon-derived PDRN. Finally, the translational perspectives, industrial challenges, and future research directions are analyzed, highlighting the need for standardized manufacturing processes, comparative clinical trials, and sustainable production strategies. Overall, PDRN is a DNA-derived biomaterial of growing interest in regenerative medicine and cosmetic applications. At the same time, novel biological sources may contribute to the development of more sustainable and clinically effective next-generation PDRN-based therapies.

Keywords: polydeoxyribonucleotide; PDRN; adenosine A2A receptor; cosmetic applications; tissue regeneration; sustainable biotechnology

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Academic Editor: Jing Wang

Received: 4 August 2026
Revised: 29 August 2026
Accepted: 9 September 2026
Published: 11 September 2026

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1. Introduction

This work presents a narrative review of the available literature. The bibliographic search was conducted using several electronic databases, including PubMed/MEDLINE, Scopus, ScienceDirect, Google Scholar, and Google Patents. The search strategy combined the terms "PDRN" or "polydeoxyribonucleotide" with keywords related to the main topics addressed in this review, including "cosmetics," "dermatology," "pharmacology," "mechanism," "PhytoPDRN," "microbial PDRN," "encapsulation," "extraction," and "regulation."

Relevant studies addressing the clinical effects, mechanisms of action, pharmacokinetics, encapsulation strategies, extraction and production processes, and regulatory aspects of PDRN were considered. Studies were included regardless of the experimental model employed, encompassing in vitro, in vivo, and clinical investigations, as well as relevant narrative and systematic reviews. No restrictions were applied regarding publication date or language. Overall, 106 sources published up to the end of August 2026 were identified and reviewed. Polydeoxyribonucleotide (PDRN) is a linear biopolymer drug based on deoxyribonucleic acid (DNA), primarily derived from salmon sperm via a high-temperature extraction process to ensure a very high DNA content [1–3].

PDRN has chain lengths ranging from 80 to 2200 base pairs and a molecular weight between 50 and 1500 kDa. Structurally, each deoxyribonucleotide unit within PDRN comprises three essential components: a phosphate group, a pentose sugar (deoxyribose), and a nitrogenous base (purine or pyrimidine) linked via a β-N-glycosidic bond at the C1′ position of the sugar (Figure 1) [4–6].

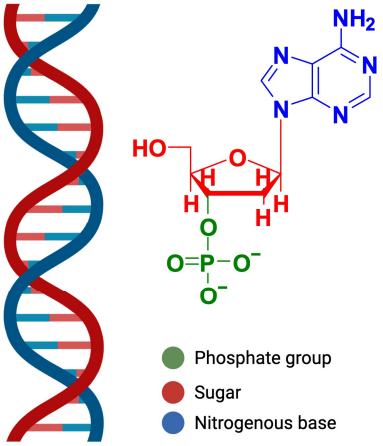


Figure 1. PDRN structure. Created in BioRender. magallon, O. (2026) https://BioRender.com/0aw1bmw. The corresponding BioRender Academic Open Access Publication License (dated 19 October 2026) is supplied separately.

The term PDRN first appeared in the scientific literature during the 1960s, when researchers used it to describe DNA polymers synthesized or processed by enzymatic systems. Early studies by Birnie and Fox demonstrated that DNA polymerases could generate PDRN chains from defined substrates, while Sarkar was the first to use the term PDRN in investigations concerning DNA degradation and nuclease activity. At that time, the term referred primarily to nucleic acid polymers and was not associated with the therapeutic biomaterials currently recognized as PDRN preparations [7–9].

Interest in PDRN as a bioactive and regenerative compound emerged several decades later. During the 1980s and 1990s, studies demonstrated that DNA-derived preparations could promote tissue repair and cellular regeneration. Bianchini et al. reported the pharmacological properties of placental-derived PDRN and developed extraction and purification

strategies to produce biologically active PDRN fractions suitable for therapeutic applications [10,11].

Subsequent investigations revealed that PDRN stimulates fibroblast proliferation, enhances extracellular matrix remodeling, and accelerates tissue repair processes. These biological effects were later associated, at least in part, with activation of adenosine A2A receptors and the salvage pathway of nucleotide synthesis, mechanisms that contribute to angiogenesis, anti-inflammatory responses, and wound healing [12,13].

The development of reproducible extraction and purification procedures enabled the clinical translation of PDRN-based products. In Italy, PDRN formulations were approved for the treatment of tissue injuries, skin ulcers, and dystrophic connective tissue disorders. During the early 1990s, Mastelli Srl (Sanremo, Italy) introduced Placentex®, one of the first commercial PDRN-based medicinal products, which became widely used in regenerative medicine and wound care [10,14,15].

Over the following decades, the therapeutic applications of PDRN expanded considerably. Clinical studies demonstrated benefits in burn injuries, chronic wounds, diabetic ulcers, orthopedic disorders, and postoperative tissue repair [13]. More recently, PDRN-based formulations have gained significant attention in esthetic dermatology, particularly in East Asian countries such as South Korea, where injectable products are increasingly employed to improve skin hydration, elasticity, texture, and overall skin rejuvenation [16–18].

In parallel with the growing clinical use of nucleic acid-derived biomaterials, a broader category of polynucleotides (PNs) has emerged. Although the terms PDRN and PN are frequently used interchangeably in the scientific and commercial literature, important differences exist regarding molecular-weight distribution, manufacturing processes, biological properties, and clinical applications. These distinctions have become an active area of investigation in regenerative medicine and esthetic dermatology. Both terms are used to designate a polymer composed of multiple deoxyribonucleotide units. Marques et al. propose distinguishing between them by using the term PN exclusively for longer deoxyribonucleotide chains (>1500 kDa), while reserving the term PDRN for short and medium-length deoxyribonucleotide chains (<1500 kDa) [7,8].

In this review, the term "DNA-derived materials" is used as a broader descriptor for nucleic acid-based preparations whose molecular characteristics do not allow their unequivocal classification as PDRN or PN; source-specific terms such as Phyto-DNA are retained when they align with the terminology used in the original study.

Historically, commercial PDRN products were initially obtained from human placenta and, later, from salmonid fish species. However, increasing demand, sustainability concerns, ethical considerations, and the need for standardized production have stimulated research into alternative biological sources and novel manufacturing strategies. Consequently, the exploration of diverse PDRN sources has become a rapidly evolving field with significant implications for future biomedical, pharmaceutical, and cosmetic applications.

PDRN research is directed toward two main lines: the development of new extraction sources and the development of controlled release systems (encapsulation). In developing new extraction sources, the focus is on successfully extracting plant-derived PDRN (PhytoPDRN) from broccoli and Artemisia [19]. Likewise, there is a more recent extraction source dating to 2025, in which microbially derived PDRN is reported for the first time, specifically from *Lactobacillus rhamnosus* [4]. On the other hand, regarding the development of release systems, which involve encapsulating PDRN within micro- or nanostructures to improve delivery bioavailability and increase its regenerative potential, recent examples include the use of titanium nanoparticles, photosynthesizable polysaccharide-based hydrogels, and exosomes [20–23].

PDRN has emerged as a multifunctional bioactive compound with broad therapeutic potential in regenerative medicine, dermatology, orthopedics, ophthalmology, and esthetic medicine. Numerous studies have demonstrated its ability to promote tissue repair and wound healing, stimulate fibroblast proliferation, enhance extracellular matrix remodeling, accelerate corneal epithelial regeneration, and modulate cytokine signaling pathways involved in collagen synthesis and angiogenesis, all through its mechanisms of action [24–38].

The main biological mechanism of PDRN largely involves it acting as an agonist at the adenosine A2A receptor (A2AR), which regulates the inflammatory stress response and increases the secretion of growth factors involved in tissue repair [20,39]. Adenosine, a ubiquitous purine nucleoside, can be formed intracellularly from ATP, ADP, or AMP, or extracellularly from ATP or ADP, playing a key role in numerous physiological and pathological processes mediated by four distinct receptors, namely A1, A2A, A2B, and A3, which modulate adenylate cyclase activity in either an inhibitory or a stimulatory manner (A1, A3 inhibitory; A2A, A2B stimulatory) [1,4,6,16,39,40]. The A2A receptor is mainly involved in regulating myocardial blood flow, suppressing immune cell activation, and regulating glutamate and dopamine release [4,24].

Through binding to the A2A receptor, PDRN mediates three main activities:

- Inflammation Resolution: The resulting reaction leads to decreased levels of pro-inflammatory cytokines and increased anti-inflammatory counterparts [10,41].
- Proliferation: Nucleotides promote increased VEGF expression, stimulating blood vessel formation (neoangiogenesis), as well as cell and fibroblast migration and growth [10,41–44].
- Remodeling: Reduced inflammation, increased blood flow, and stimulated cell growth create favorable conditions for extracellular matrix remodeling, including collagen and elastin production, thereby supporting tissue repair [10,42,43].

Additionally, it promotes phosphorylation of focal adhesion kinase (FAK) and protein kinase B (AKT), which is fundamental for cell and fibroblast proliferation and migration, contributing to wound healing and improved skin barrier function [4,45,46].

Furthermore, it stimulates nucleic acid synthesis by serving as a source of pyrimidines and purines, including angiogenesis-promoting, anti-ischemic, and tissue repair activities [1,16].

In this sense, this review critically compares conventional and emerging PDRN production platforms to identify the most promising strategies for next-generation regenerative biomaterials.

2. Molecular Structure and Physicochemical Properties of PDRN

The structure of PDRN contains a mixture of deoxyribonucleotides with molecular weights ranging from 50 to 1500 kDa, obtained through a controlled process of DNA purification and sterilization that allows recovery of a substance more than 95% pure, free of proteins or intact DNA to avoid immunogenicity. Among its key structural properties are low viscosity, thermal resistance, and biocompatibility, similar to the properties of human mitochondria [10,47,48].

The chemical structure of PDRN consists of a DNA fraction, which is composed of a linear polymer of deoxyribonucleotides, which are linked by phosphodiester bonds, whose monomeric units are purine and pyrimidine nucleotides. These chains join sterically to form a double helix [6]. The polymeric unit of the PDRN chain is the deoxyribonucleotide, composed of three components: a pentose sugar, phosphoric acid, and a purine or pyrimidine base bound to the pentose at position 1 by a β-N-glycosidic bond [16,49].

Currently, there are three extraction sources: animal- and plant-derived, and others such as algae and microorganisms.

3. Sources of PDRN Extraction

3.1. Animal-Derived PDRN: Classical Sources

Animal-derived DNA remains the most established and commercially relevant source of PDRN. Currently, the gonads of salmonid fish, particularly chum salmon (*Oncorhynchus keta*) and rainbow trout (*Oncorhynchus mykiss*), are the predominant raw materials used for industrial PDRN production. These tissues provide highly purified DNA fragments that have demonstrated regenerative, anti-inflammatory, anti-apoptotic, and tissue-repair activities in numerous preclinical and clinical studies [4,6,48–50].

The widespread use of salmonid-derived PDRN is supported by its favorable safety profile, standardized extraction processes, and extensive clinical validation. Nevertheless, dependence on marine resources has limitations, including seasonal availability, production costs, supply chain fluctuations, and environmental sustainability concerns associated with large-scale harvesting and aquaculture practices [49].

The semen collection process is performed manually by holding the salmon at a slight angle on a clean surface. Then, a gentle, continuous pressure is applied from the upper abdomen toward the cloaca to extract the semen. The ejaculate is then collected in a clean tube or container, and later diluted or frozen [51,52].

Some PDRN extraction methods involve chemical or non-organic approaches. In the first of these, the chemical approach is characterized by being low-cost and easy to implement at scale. The process starts with sperm thawing, cell lysis, sterilization, molecular-weight reduction, precipitation, and dry granulation. The second non-organic method is distinctive for its ease of use and preparation; it consists of cell lysis, centrifugation, precipitation, and molecular-weight reduction (Figure 2) [19,49–54].

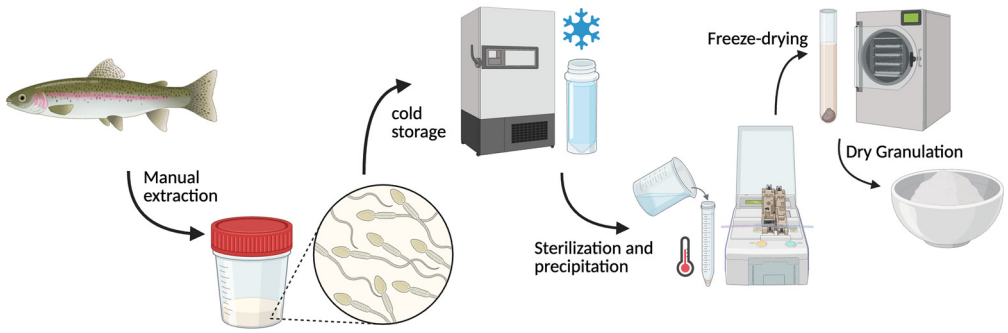


Figure 2. Method of extraction of animal-derived PDRN. Created in BioRender. magallon, O. (2026) https://BioRender.com/0aw1bmw. The corresponding BioRender Academic Open Access Publication License (dated 19 October 2026) is supplied separately.

PDRN has been reported to exhibit sufficient thermal resistance to withstand conventional moist-heat sterilization procedures, including autoclaving at 121 °C. High-temperature treatments may also be incorporated into extraction and purification processes to facilitate the removal of proteins and other biological contaminants, contributing to the production of highly purified PDRN preparations (>90%) [6,26,48,55,56]. Nevertheless, processing conditions should be carefully controlled because excessive thermal exposure may compromise DNA integrity and molecular-weight distribution, both of which are relevant quality attributes of the final PDRN product.

PDRN has achieved advances in the preclinical and clinical areas, involved in advances such as treatment of skin ulcers and connective tissue disorders; post-surgical healing;

corneal regeneration; treatment of venous ulcers; support for bone regeneration; treatment of periimplantitis and osteoarthritis; and in dermatology for rejuvenation to address issues such as wrinkles, hyperpigmentation and elasticity. Likewise, it has demonstrated capabilities for the treatment of diabetic ulcers, in TMD disorders and for neuropathic pain relief [16,17,47,55–61].

The quality of polydeoxyribonucleotide (PDRN) depends strongly on the biological source and the extraction, purification, depolymerization, and sterilization processes. The biological source can significantly affect purity and reproducibility. Studies comparing fish-derived DNA have reported purities ranging from approximately 73% to 93%, with residual proteins and lipids varying by species and extraction method [55–61]. Batch-to-batch consistency remains insufficiently characterized in the available literature [55–61]. Variations in fish species, tissue composition, endogenous nuclease activity, and processing conditions may modify DNA concentration and molecular-weight distribution. Consequently, PDRN quality control should include DNA purity, molecular-weight profile, residual proteins and lipids, endotoxins, microbial contamination, residual solvents, and, where applicable, sterility and biological activity. Regarding scalability, fish-derived tissues represent an abundant source of DNA, but industrial production requires stringent control of raw materials and downstream processing to minimize biological variability.

3.2. Plant-Derived PDRN: Emerging Alternative Platforms

In recent years, plant-derived nucleic acid preparations have attracted attention as potential alternatives to conventional animal sources. Extracts obtained from plants such as Korean ginseng (*Panax ginseng*), Artemisia species, *Hibiscus sabdariffa* callus, *Gynostemma pentaphyllum* callus, *Paeonia lactiflora*, roses, *Chrysanthemum coronarium*, Misticanza, *Raphanus sativus*, *Ipomoea aquatica*, *Sedum sarmentosum*, *Brassica oleracea* and *Aloe vera* have demonstrated biological activities associated with wound healing, antioxidant protection, anti-inflammatory responses, and skin regeneration [49,62–68]. These extraction sources are known as PhytoPDRN or vegan PDRN.

Several authors have reported a similar extraction procedure. Briefly, a 100 g fresh-weight sample is combined with two volumes (200 mL) of DNA extraction buffer containing 0.5 M sodium chloride and 8.75 mL of a 5% detergent solution. The sample is frozen in liquid nitrogen for cell lysis; then, homogenization is performed by triturating the sample with 200 µL of RNase using a blender, and the mixture is incubated in water at 65 °C for 1 h. The lysate is centrifuged at 13,000 rpm for 10 min or at 4500 rpm for 20 min, and the supernatant is filtered through Miracloth. Subsequently, for DNA extraction, an equal volume of 99.9% ethanol is added, and the mixture is incubated at −80 °C for 12 h. The resulting DNA precipitate is recovered after centrifugation at 13,000 rpm for 20 min, then 5 mL of 80% ethanol is added to the precipitate and the mixture is centrifuged for 2 min at the same speed. The DNA precipitate is air-dried and then resuspended in nuclease-free water. Sonication is applied to fragment genomic DNA into smaller fragments using a PULSE device, with amplification adjusted to 40% and sonication for eight cycles. The resulting PDRN is confirmed by gel electrophoresis (Figure 3) [63,64,67,69,70]. Nevertheless, further optimization and standardization of this extraction process are required.

Although plant-derived nucleic acid fractions represent a promising and sustainable approach, their structural equivalence, molecular composition, and biological comparability with conventional salmon-derived PDRN require further investigation and standardization before widespread clinical adoption [62,64,70].

The development of plant-derived PDRN may improve raw-material sustainability and supply scalability; future manufacturing strategies should therefore adopt standardized critical quality attributes, validated purification and sterilization processes, molecular-

weight profiling, contaminant testing, stability assessment, and batch-release criteria. Such standardization will be essential to ensure reproducibility and safety.

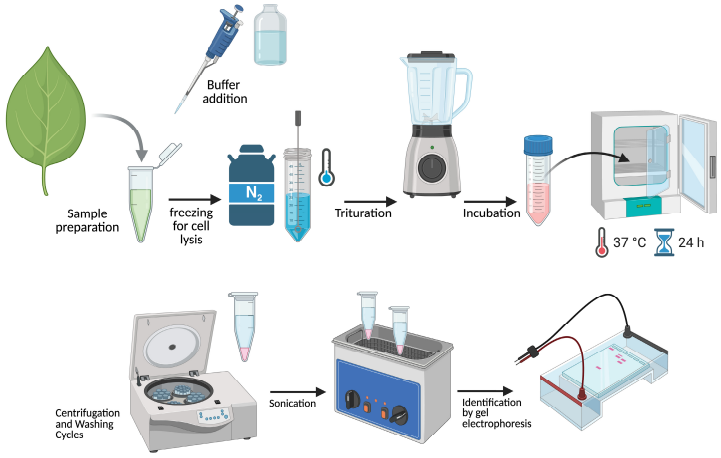


Figure 3. Method of extraction of plant-derived PDRN. Created in BioRender. magallon, O. (2026) https://BioRender.com/0aw1bmw. The corresponding BioRender Academic Open Access Publication License (dated 19 October 2026) is supplied separately.

3.3. PDRN Derived from Other Sources: Biotechnological Production Platforms

Recent advances in biotechnology have enabled the development of microbial-based and algal approaches for the production of nucleic acid-derived biomaterials. Compared with animal and plant sources, microbial systems offer several advantages, including rapid growth rates, year-round production, scalability, lower environmental impact, and reduced dependence on natural resources [71–74].

Among these emerging sources, probiotic microorganisms such as *Lactobacillus rhamnosus* have shown considerable promise [4]. The first report of microbial PDRN extraction dates back to 2025, describing that extracting PDRN from these microorganisms required a process of multiple inoculations and incubations, followed by collection of bacterial cells via centrifugation and washing with saline solution to obtain purified bacterial cells [4]. The extraction involved using the purified bacterial cells and resuspending them in tridistilled water (AD) to prepare the PDRN extraction. The suspension was placed in an incubator with shaking at 45 °C and 100 rpm and left to react for 30 min. To extract the PDRN, the bacterial cells were subjected to thermal pressure crushing at 121 °C and 0.2 MPa. The extract was immediately cooled to 4 °C and then centrifuged to separate the supernatant containing PDRN from the cellular remains. The collected supernatant was filtered through a 0.45 µm PES filter to eliminate particles and residues; sodium acetate was added to the filtered solution, adjusting its concentration to 0.3 M to facilitate precipitation with ethanol. Then ethanol was added to the solution until the concentration reached 70%, and the mixture was incubated at −20 °C overnight to allow PDRN to precipitate. After incubation, the precipitated mixture was centrifuged at 4 °C and 15,000 rpm for 20 min, and the supernatant was discarded; the precipitate was washed with 70% ethanol, cooled to −20 °C, and centrifuged again under the same conditions. The final purified precipitate was collected for subsequent processing [4]. For the recovery of PDRN, the purified precipitate was dissolved in 1× TE buffer to ensure complete dissolution; the resulting solution was then filtered through a vacuum glass filtration system equipped with 0.45 µm and 0.20 µm PES membrane filters (Figure 4) [4]. Currently, this extraction process has not been optimized.

Additionally, the use of algae as a source of PDRN extraction has been proposed in various articles; from this extraction source, we can find recent advances in PDRN derived from *Chlorella protothecoides* and *Porphyra* sp. [71–77].

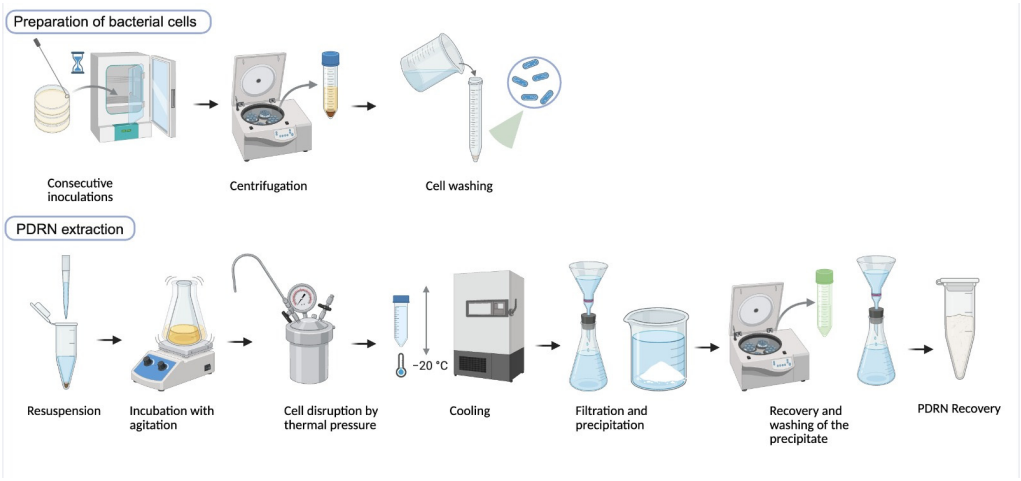


Figure 4. Method of extraction of microbial-derived PDRN. Created in BioRender. magallon, O. (2026) https://BioRender.com/0aw1bmw. The corresponding BioRender Academic Open Access Publication License (dated 19 October 2026) is supplied separately.

The method of PDRN extraction from algae has a Korean patent; this method is based on washing three times with running water to eliminate adhered epiphytes, residual salts, and sand, and thorough rinsing with clean water; the clean material is stored at −20 °C; after lyophilization, it is homogenized to obtain a dry powder. An ecological mixed solution is prepared for protein dissolution, composed of 10% soy by weight, 10% Job's tears by weight, 20% green tea extract by weight, 20% soy fatty acids by weight, 20% tocopherol by weight, cocamidopropyl betaine, and 20% olive oil carboxylate by weight, to eliminate and decompose the proteins from marine algae. After protein lysis, the mixture is centrifuged to remove residues, filtered, and dried at room temperature for 1 h. Purified water and fermented acetic acid are added to the dry product, and the mixture is treated with a reaction and sonication for 10 min to obtain the final low-molecular-weight PDRN [71–77].

Experimental studies have reported that microbial-derived and algae-derived PDRN preparations exhibit antioxidant activity, free-radical scavenging capacity, enhanced cell migration, accelerated wound closure, and potential immunomodulatory effects. Preliminary in vitro studies have reported regenerative, antioxidant, and immunomodulatory activities for these emerging preparations; however, differences in molecular characteristics, purity, experimental models, and study designs currently limit direct comparison with salmon-derived PDRN, and additional in vivo and clinical studies are required to establish comparative efficacy [4,62–65].

As research progresses, microbial biotechnology may provide a sustainable and highly controllable platform for future PDRN production, potentially overcoming many of the limitations associated with traditional extraction sources [71–74].

Beyond extraction yield, the suitability of PDRN production methods should be evaluated according to critical quality attributes that directly influence the reproducibility, safety, and biological performance of the final product. These include DNA purity and molecular-weight distribution, batch-to-batch consistency, sterility, stability, and the presence of residual proteins, lipids, cellular debris, solvents, salts, endotoxins, or other source-dependent contaminants. Such considerations become particularly important when comparing animal-, plant-, microbial-, and algae-derived PDRN, since differences in the

biological matrix and extraction procedures may result in distinct impurity profiles and purification requirements.

From a manufacturing perspective, scalable production also requires standardized raw materials, reproducible extraction and purification processes, validated contaminant removal and sterilization procedures, and appropriate quality control criteria. These manufacturing-related variables are particularly relevant because differences in extraction, purification, and sterilization procedures may directly affect the physicochemical and biological characteristics of the final PDRN product. Therefore, although emerging biological sources offer promising alternatives for PDRN production, the lack of harmonized manufacturing processes and quality-control specifications remains a significant challenge to ensuring batch-to-batch consistency and to comparing PDRN preparations from different biological sources. The implications of these limitations for the clinical and commercial translation of PDRN are further discussed in Section 11.

4. Biological Mechanisms

The mechanisms proposed for PDRN differ substantially in their level of experimental support. Adenosine A2A receptor-mediated signaling and the nucleotide salvage pathway represent the most widely described and experimentally supported mechanisms underlying the regenerative and anti-inflammatory effects of PDRN. In contrast, the potential involvement of nucleic acid-sensing pathways, including TLR9 and cGAS–STING, remains less well established in the specific context of PDRN and is supported mainly by indirect or emerging evidence. Therefore, these pathways should currently be considered potential complementary mechanisms rather than established primary mechanisms of PDRN action (Figure 5).

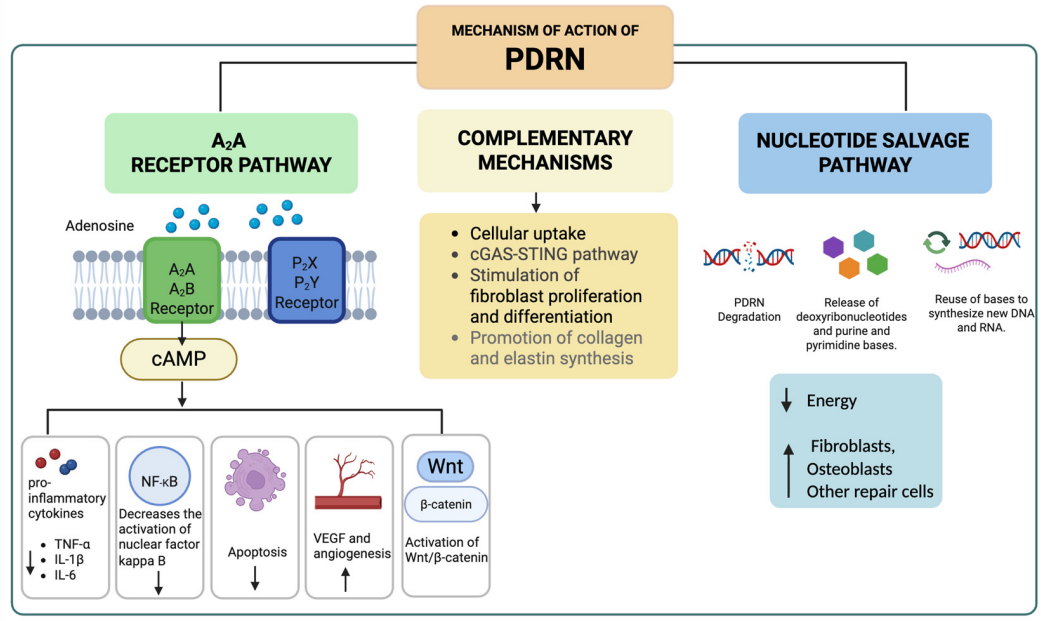


Figure 5. Proposed mechanisms of action of PDRN. Adenosine A2A receptor-mediated signaling and the nucleotide salvage pathway represent the better-established mechanisms, whereas the potential involvement of TLR9 and cGAS–STING signaling remains less well established and requires further experimental validation. Created in BioRender. magallon, O. (2026) https://BioRender.com/0aw1bmw. The corresponding BioRender Academic Open Access Publication License (dated 19 October 2026) is supplied separately.

PDRN can therefore be considered a DNA-derived preparation whose biological effects are primarily associated with two complementary mechanisms: adenosine A2A receptor-mediated signaling and the provision of nucleotides through the salvage pathway [60].

4.1. Adenosine A2A Receptor-Mediated Signaling

Following administration, PDRN is progressively degraded by endogenous nucleases into smaller oligonucleotides and nucleotides. Purine metabolites derived from nucleotide degradation may contribute to extracellular adenosine availability and purinergic signaling. Among these pathways, activation of the adenosine A2A receptor is considered one of the best-established mechanisms underlying the anti-inflammatory and regenerative effects associated with PDRN [10,60,61].

Activation of A2A receptors increases intracellular cyclic adenosine monophosphate (cAMP) and modulates downstream signaling pathways involved in inflammation and tissue regeneration. A2A receptor signaling suppresses the production of proinflammatory mediators while promoting a cellular environment favorable for tissue repair. In addition, PDRN-mediated A2A receptor signaling has been associated with increased vascular endothelial growth factor (VEGF) expression, thereby supporting angiogenesis and wound healing [60,61,78].

PDRN-mediated A2A receptor signaling has also been associated with modulation of signaling pathways involved in inflammation, cell survival, and tissue regeneration. These effects collectively contribute to the resolution of inflammation and promotion of tissue repair [60,61].

4.2. Nucleotide Salvage Pathway

Following enzymatic degradation, PDRN provides deoxyribonucleotides and purine and pyrimidine bases that can be reutilized by cells through nucleotide salvage pathways. These pathways allow cells to synthesize nucleotides required for DNA and RNA production without relying exclusively on energetically demanding de novo nucleotide synthesis [60,61].

The nucleotide supply provided by PDRN may be particularly relevant under conditions of cellular stress, ischemia, or tissue injury, in which nucleotide demand increases to support DNA synthesis, cell proliferation, and tissue repair. By providing substrates that can be recycled through salvage pathways, PDRN may support the proliferation and metabolic activity of fibroblasts and other cells involved in tissue regeneration [60,61].

4.3. Proposed Complementary and Emerging Mechanisms

In addition to A2A receptor-mediated signaling and nucleotide salvage, cellular responses and DNA-sensing pathways have been proposed to contribute to the biological effects of PDRN. However, the strength of evidence supporting these mechanisms is heterogeneous. In particular, direct mechanistic evidence demonstrating activation of TLR9 or cGAS–STING by PDRN remains limited. Consequently, these pathways should currently be considered hypothetical or emerging mechanisms rather than established primary mechanisms of PDRN action.

4.4. Potential Involvement of TLR9 Signaling

TLR9 is an intracellular pattern-recognition receptor that recognizes DNA containing unmethylated CpG motifs, particularly those associated with microbial DNA, within endosomal compartments. Its activation initiates signaling through molecules including MyD88, IRAK1, and TRAF6, resulting in downstream activation of transcription factors such as NF-κB and AP-1 and modulation of inflammatory and immune responses [79–81]. Given the DNA-derived nature of PDRN, a potential interaction with DNA-sensing pathways

such as TLR9 may be hypothesized. However, direct experimental evidence demonstrating PDRN-mediated TLR9 activation and establishing its contribution to the biological effects of PDRN remains insufficient. Therefore, TLR9 should currently be regarded as a hypothetical complementary mechanism requiring further experimental validation.

4.5. Potential Involvement of the cGAS–STING Pathway

The cGAS–STING pathway represents an intracellular DNA-sensing mechanism in which cytosolic DNA can be recognized by cyclic GMP–AMP synthase (cGAS), leading to cyclic GMP–AMP (cGAMP) production, STING activation, and downstream signaling involving TBK1 and IRF3 [80,81]. Because PDRN is a DNA-derived material, an interaction with this pathway may be theoretically plausible. Nevertheless, direct experimental evidence demonstrating activation of cGAS–STING by PDRN and establishing its contribution to PDRN-mediated biological effects remains insufficient. Therefore, the involvement of this pathway should currently be considered hypothetical and requires specific experimental validation.

4.6. Fibroblast Proliferation and Extracellular Matrix Remodeling

PDRN has been experimentally associated with increased fibroblast proliferation and migration, as well as enhanced collagen accumulation [82]. In human skin fibroblasts, these effects have been associated with modulation of ERK signaling, supporting a role for this pathway in PDRN-mediated cellular responses [61]. However, these effects are better interpreted as downstream regenerative responses associated with PDRN treatment rather than independent primary mechanisms of action.

5. Pharmacokinetics

The available pharmacokinetic data for PDRN are primarily derived from systemic administration studies and should therefore be interpreted according to the specific route, dose, and experimental model. Following a single intraperitoneal administration of PDRN at 8 mg/kg in rats, measurable plasma levels were detected within 15 min, with peak concentrations occurring approximately 1 h after administration and a reported bioavailability of approximately 90%. Plasma concentrations subsequently declined, although PDRN remained detectable 6 h after administration, with a reported half-life of approximately 3 h [47].

In healthy human volunteers, pharmacokinetic evaluation following intramuscular administration of 5.625 mg PDRN showed a similar temporal profile, with peak plasma concentrations at approximately 1 h, a half-life of approximately 3.5 h, and reported bioavailability of 80–90% [47]. Following systemic administration, PDRN circulates predominantly in an unbound form, and its tissue distribution is influenced by local blood flow. It is primarily degraded by plasma and cell membrane-associated nucleases into oligo- and mononucleotides rather than undergoing hepatic metabolism, with approximately 65% of PDRN fragments reported to be excreted in the urine [47].

These systemic pharmacokinetic parameters should not be extrapolated to topical PDRN formulations. Unlike systemic administration, validated human pharmacokinetic data for topical PDRN remain limited. Therefore, topical administration should be considered primarily in terms of local cutaneous delivery, including skin penetration, permeation, and tissue retention, rather than using the systemic pharmacokinetic parameters described above. The limited cutaneous penetration of PDRN has also encouraged the investigation of different formulation and delivery strategies designed to improve local skin delivery [16,49,83].

PDRN preparations may exhibit different physicochemical and biological characteristics depending on their molecular-weight distribution. Within the terminology adopted in this review, PDRN refers to DNA-derived polymers with molecular weights below 1500 kDa, whereas longer DNA polymers (≥1500 kDa) are classified as polynucleotides (PNs) [18,83–85]. Low-molecular-weight PDRN (<50 kDa) has been explored for topical formulations such as gels and creams. In contrast, medium-molecular-weight PDRN (50–1500 kDa) has been investigated for injectable preparations and hydrogel-based delivery systems.

To increase the regenerative potential of PDRN, recent research has explored its combination with nanomaterials, hydrogels, liposomes, and exosomes to overcome certain limitations of traditional administration routes, such as the short half-life of PDRN under physiological conditions, and to reduce the need for invasive needle-based administration. Each encapsulation method offers distinct advantages (Table 1) [86–89].

Table 1. Encapsulation method.

Encapsulation System	Advantages	References
Nanoparticles	High swelling capacity Efficient encapsulation Suitable for local administration Stability Prolonged local bioavailability	[20,83,88]
Hydrogels	Improved swelling Degradation kinetics Strong proliferation Cell migration and angiogenic growth factors Improves the effectiveness of wound healing	[21,22,50,86]
Exosomes	Wound healing efficacy Improved delivery of PDRN to the wound site Protection of DNA fragments from degradation by nucleases	[87]
Liposomes	Improved permeability Sustained release Improved stability Improved skin retention	[89]

6. Comparative Biochemical Analysis of PDRN Sources

Performing a comparative analysis of the various sources of PDRN extraction, while noting their similarities, allows us to identify the characteristics that stand out among these sources (Table 2).

Each PDRN extraction source offers specific advantages: the animal-derived extraction source is the most described in the literature, so its extraction processes and mechanisms of action are well documented and standardized. In contrast, plant-derived and microbial/algal extraction sources are more recent; although there are patents that explain their extraction processes and some articles that describe their mechanisms of action, further research is still needed to verify whether all possible extraction sources will produce the same results [4,67,68,85,90].

Table 2. Comparative analysis of PDRN sources.

PDRN Extraction Source	Salmon Sperm	PhytoPDRN	Microbiological/ Algae PDRN
Molecular weight	50–1500 kDa; predominant fraction 80–200 kDa (peak ≈ 132 kDa). In a comparative electrophoretic study: 200–800 bp	Source-dependent; Panax PDRN: slightly <100 bp	Lactobacillus-derived PDRN: <100 bp; size may vary among strains Algae-derived PDRN: insufficient standardized molecular-size data
Mode of action	Activation of adenosine A2A receptors Rescue pathway	Activation of adenosine A2A receptors Phosphorylation of FAK, AKT, and MAPK Promoted proliferation of keratinocytes and fibroblasts by increasing expression of fibronectin, filaggrin, Ki-67, Bcl-2, inhibin beta A, and cyclin D1 Specific involvement of CLDN1, FLG, and IVL	Activation of adenosine A2A receptors Exclusively phosphorylates p38 and ERK independently of FAK
Quantitative characteristics	50–1500 kDa; predominant fraction 80–200 kDa; peak ≈ 132 kDa Commercial PDRN generally reported in the 50–1500 kDa range Yield ranges from 50 to 150 milligrams per gram of raw material Purity > 95%	PDRN fragments reported at approximately <100 bp in the experimental preparation Biological activity evaluated at 5 µg/mL in skin-related experimental models 5–30 milligrams per gram of raw material (dependent on species and extraction method)	PDRN fragments approximately <100 bp PDRN characterized as a low-MW DNA-derived bioactive 10–40 10–40 milligrams per gram of raw material (dependent on species of algae and extraction method) Microbiological purity A260/A280 = 1.91, consistent with high-purity DNA 89
Advantages	High purity Composition similar to human DNA	Abundant extraction sources Low molecular weight Sustainable	Abundant source High purity Scalable Eco-friendly
Disadvantages	High price Dependence on the breeding season	Expensive extraction methods Further research is needed to understand all its modes of action and potential extraction sources	Further research into modes of action and potential sources of extraction
References	[47–61]	[62–70]	[4,71–77]

7. Translational and Clinical Potential

PDRN has strong translational potential as a drug with regenerative and anti-inflammatory modulatory activity across multiple specialties. In preclinical studies, it has shown accelerated wound healing, vascularization, and epithelization in in vitro and in vivo models of ulcers and cutaneous lesions; likewise, it has been beneficial in treating skin and connective tissue injuries associated with dystrophic and ulcerative diseases such as diabetic foot, venous ulcers, and bone regeneration. In clinical applications, however, it has primarily emerged in periodontics, tendinopathies, and esthetic procedures [87–93]. Nonetheless, certain translational opportunities remain, such as standardization of the product obtained from recent sources and evaluation of interactions with other regenerative therapies; these would support the standardization of formulations, the design of trials comparing PDRN with standard treatments, and the definition and measurement of mechanistic biomarkers [10,16,55,91–100].

Importantly, the available evidence supporting the biological effects of PDRN varies considerably according to its biological source and experimental model. Salmonid-derived and conventional PDRN preparations are supported by a broader body of experimental and clinical evidence, whereas most emerging plant-, microbial-, and algae-derived preparations

have been evaluated primarily in vitro, with only selected studies extending to animal models, ex vivo systems, reconstructed-skin models, or early human application studies. Therefore, findings obtained from different experimental levels should not be interpreted as equivalent evidence of efficacy. Table 3 summarizes representative studies according to the source or type of DNA-derived preparation, experimental model, level of evidence, and principal biological outcomes.

As shown in Table 3, the strength and type of evidence are unevenly distributed among PDRN sources. Conventional PDRN has been investigated across in vitro and in vivo models and is supported by a broader body of clinical literature, whereas the evidence for emerging biological sources remains more heterogeneous. Plant-derived preparations are supported predominantly by in vitro studies, although reconstructed-skin models and early human application studies have recently been reported for selected preparations. Algae-derived PDRN has been investigated in both in vitro and in vivo models, with limited human application evidence reported for selected marine-derived preparations, whereas microbial-derived PDRN remains supported primarily by in vitro studies. Importantly, positive findings obtained in cellular, ex vivo, reconstructed-skin, or animal models should not be interpreted as demonstrating clinical equivalence among PDRN sources. Direct comparative studies and well-designed randomized clinical trials using standardized preparations are still required to establish whether emerging PDRN sources provide efficacy and safety comparable to those of established PDRN preparations.

Table 3. Experimental and clinical evidence supporting the biological activities of conventional and emerging PDRN and related DNA-derived preparations.

Source/Material	Experimental Model	Level of Evidence	Main Biological Activity/Outcome	Ref.
Salmon-derived PDRN	Human skin keratinocytes and fibroblasts	In vitro	Increased proliferation and migration; differential ERK modulation; increased collagen accumulation in fibroblasts; and modulation of inflammatory mediators in keratinocytes	[61]
Development of PDRN (source not specified) formulation heterogeneity	Genetically diabetic mice with cutaneous wounds	In vivo	Increased VEGF expression and angiogenesis and improved wound-healing parameters	[42]
Panax ginseng-derived PDRN	Keratinocytes, fibroblasts, and reconstructed human skin model	In vitro/reconstructed-skin model	Increased skin-cell proliferation and improvement of skin-regeneration and barrier-related responses	[62]
Hibiscus sabdariffa callus-derived PDRN	Human keratinocytes	In vitro	Enhanced wound-healing responses and modulation of Nrf2- and wound-healing/antioxidant-related markers	[63]
Gynostemma pentaphyllum callus-derived PDRN	Skin-cell models	In vitro	Antioxidant, anti-inflammatory, and wound-healing effects; increased FLG, IVL, and CLDN1	[64]
Paeonia lactiflora-derived PDRN	Skin-cell models and human topical evaluations	In vitro + human study	Increased proliferation and migration; modulation of ECM/barrier-related genes; reduced oxidative/inflammatory responses; improved barrier recovery and periorbital elasticity	[65]

Table 3. *Cont.*

Source/Material	Experimental Model	Level of Evidence	Main Biological Activity/Outcome	Ref.
Rose-derived PDRN	Primary human keratinocytes and ex vivo human skin explants	In vitro + ex vivo	Protection of mitochondrial function, attenuation of oxidative stress, modulation of autophagy/mitophagy, and preservation of collagen-related parameters	[66]
Chrysanthemum coronarium- and *Brassica oleracea*-derived PDRN	Cell-based wound-healing assays	In vitro	Significant stimulation of wound-healing activity	[67]
Aloe vera-derived Phyto-DNA	DPPH assay, fibroblasts, HaCaT cells, wound-healing assay, and human topical application	In vitro + human application study	Antioxidant activity, mitigation of blue-light-associated cytotoxicity, modulation of barrier-related factors, and improved epidermal barrier recovery	[68]
Chlorella protothecoides-derived PDRN	Keratinocytes and fibroblasts	In vitro	Increased proliferation and migration, collagen synthesis, VEGF expression, and ERK/AKT/β-catenin/STAT3 signaling	[71]
Porphyra sp.-derived PDRN	LPS-stimulated RAW264.7 macrophages and human dermal fibroblasts	In vitro	Anti-inflammatory activity through modulation of NO/iNOS and p38/ERK signaling and increased fibroblast proliferation/collagen production	[72]
Porphyra sp.-derived PDRN	LPS-induced acute lung injury in mice	In vivo	Reduced pulmonary inflammation, inflammatory cytokines, edema, and histopathological damage	[73]
Marine plant-derived PDRN	DPPH assay, RAW264.7 cells, CCD-986sk fibroblasts, 3D skin model, and human application test	In vitro + reconstructed-skin model + human application study	Antioxidant and anti-inflammatory activity, increased procollagen production, and improvement of facial wrinkles	[74]
Lactobacillus rhamnosus-derived PDRN	Cell-based antioxidant, wound-healing, and immunological assays	In vitro	Antioxidant, cell-migration/wound-healing, and immunomodulatory activities compared with salmon-derived PDRN	[4]
PN/PDRN clinical evidence	Seven randomized clinical trials summarized in a systematic review	Randomized clinical evidence	Skin rejuvenation, postoperative scar prevention, and wound-healing outcomes	[96]

8. Sustainability and Industrial Perspectives

The industrial objective in obtaining PDRN is to convert it into a safe, stable, and processable input at large scale. The inherent characteristics of PDRN make it of interest for transitioning research to an industrial scale, as has previously been demonstrated; however, if new extraction sources continue to be sought, its industrial sustainability will depend on the extraction source, the efficiency of extraction processes, purification processes, and the purity achieved in the final product. Likewise, from an industrial perspective, the production process must minimize waste, ensure traceability, and optimize and control product stability and processes [4,10,17,48,55,70,93–102].

9. Cosmetic and Esthetic Applications of PDRN

PDRN has emerged as an active ingredient of growing interest in cosmetic and esthetic dermatology for its regenerative and bioactive properties. Consequently, it has been investigated for applications including skin rejuvenation, wound repair, and scar prevention. Although PDRN is currently used in cosmetic and esthetic applications, the available clinical evidence remains limited, making rigorous evaluation difficult. This limitation is evident in the systematic review conducted by Alhussain et al. in 2026 [96], which evaluated clinical trials and identified seven studies involving 183 participants whose results could be compared. These studies constituted the evidence base for assessing esthetic skin rejuvenation, scar prevention, and wound repair.

The findings of this review are significant because they demonstrated consistent improvements in wrinkle-related parameters, wound healing, and other healing outcomes. In particular, PDRN accelerated re-epithelialization and reduced healing times, with no serious adverse events reported. These results are promising; however, the main limitations included small sample sizes, protocol heterogeneity, and variability in outcome measures. Therefore, greater standardization of clinical protocols and outcome measures is required. To enable more meaningful comparisons of the effects of PDRN, several factors should be considered, including conducting more rigorous trials with larger sample sizes, evaluating different molecular weights and purity levels, and assessing potential synergies with other bioactive compounds and delivery systems [96]. Addressing these gaps in the clinical evidence is essential for consolidating the role of PDRN in regenerative cosmetics.

Other studies have also investigated the potential cosmetic and esthetic benefits of PDRN. In the context of skin rejuvenation and wrinkle reduction, PDRN has been associated with improvements in wrinkle-related parameters, skin texture, elasticity, and firmness. Although formulations, routes of administration, and treatment protocols vary across studies, the available evidence suggests that PDRN may promote dermal repair and extracellular matrix remodeling, potentially contributing to improvements in visible signs of skin aging. Nevertheless, differences in study design and outcome assessment currently limit direct comparisons among studies [65,96,97].

Skin hydration and barrier function represent additional areas of cosmetic interest for PDRN. Improvements in skin hydration have been reported in esthetic applications of PDRN-based preparations [16–18]. Experimental studies using plant-derived PDRN have provided additional evidence of effects on epidermal regeneration and barrier function. PDRN isolated from *Panax ginseng* adventitious roots has been associated with skin regeneration and barrier improvement [62], whereas PDRN derived from *Gynostemma pentaphyllum* callus has demonstrated beneficial effects on skin barrier function, including modulation of key barrier-related proteins [64]. Similarly, a mineral-cation Phyto-DNA preparation obtained from *Aloe vera* adventitious roots showed in vivo skin barrier recovery activity [68]. Collectively, these findings suggest that PDRN-based preparations may contribute to the maintenance or restoration of epidermal homeostasis; however, further clinical studies are required to determine the magnitude and consistency of these effects on skin hydration and barrier function.

The potential influence of PDRN on skin pigmentation has also attracted interest within esthetic dermatology, particularly regarding post-procedural skin recovery. Pigmentation-related outcomes, including melanogenesis, have been evaluated in clinical studies involving PDRN following esthetic procedures. However, compared with the evidence available for wound healing and skin regeneration, direct evidence supporting a specific effect of PDRN on melanogenesis remains limited. Therefore, pigmentation should currently be considered an emerging cosmetic outcome. Further, mechanistic and controlled

clinical studies are required to determine whether PDRN directly modulates melanogenesis and to establish its potential relevance to the management of hyperpigmentation [103].

Another emerging application of PDRN in esthetic medicine is post-procedure skin recovery. Minimally invasive and energy-based esthetic procedures, including laser resurfacing, chemical peeling, microneedling, and radiofrequency, induce controlled tissue injury and transient inflammatory responses as part of the remodeling process. In this context, the regenerative and anti-inflammatory properties attributed to PDRN have generated interest in its use as an adjunctive strategy to support tissue repair following esthetic interventions. Available evidence suggests that PDRN may promote re-epithelialization and improve post-procedural erythema and scarring. Nevertheless, the available clinical evidence remains heterogeneous, with differences in treatment protocols, PDRN formulations, routes of administration, and outcome measures. Therefore, although post-procedure recovery represents a promising esthetic application of PDRN, standardized prospective clinical trials are still required to establish its efficacy, optimal administration protocols, and long-term safety [103].

10. Regulatory Status

The regulatory status and clinical use of PDRN vary according to jurisdiction, route of administration, intended use, and product classification [16,47]. This distinction is particularly relevant because PDRN-containing preparations have been developed for different therapeutic, dermatological, and esthetic applications.

In Italy, PDRN-containing medicinal products, including Placentex®, are listed by the Agenzia Italiana del Farmaco (AIFA) [14]. The pharmacological literature has also described PDRN as a proprietary and registered DNA-derived drug with established applications in tissue repair and regenerative medicine [47].

Regulatory status and clinical applications may differ among countries. For example, the recent literature describes PDRN-containing pharmaceutical preparations used in Italy and South Korea, with formulations and indications varying according to product type and route of administration [16]. These differences highlight the importance of considering the specific regulatory classification and intended use of each PDRN-containing product rather than extrapolating the regulatory status of one preparation to all PDRN-based products.

Overall, the regulatory landscape of PDRN remains heterogeneous and closely associated with product classification, intended use, route of administration, and jurisdiction [16,47]. Continued development of PDRN for cosmetic, esthetic, and therapeutic applications will therefore require careful consideration of the regulatory requirements applicable to each specific product and market.

11. Future Directions and Limitations

Due to PDRN's properties, its future prospects focus on several areas, including its continued development as a therapeutic agent in regenerative medicine, given the existing evidence supporting its potential applications in complex wound management and reconstructive procedures. Another important future direction is the standardization of formulations, doses, and delivery methods, together with the need for additional clinical trials to confirm efficacy and safety, optimize controlled-release strategies, and investigate new biological sources and mechanisms of action. From an industrial perspective, future development should also focus on ensuring stable, safe, reproducible, scalable, and traceable products, while promoting more sustainable production processes and reducing dependence on animal-derived sources [4,7,48,55,62,70,100–106].

The existing limitations can be grouped into four fundamental aspects, as follows:

Clinical evidence: Although clinical evidence is available for selected PDRN and PN applications, much of the evidence for emerging PDRN sources remains based on preclinical, in vitro, or animal studies. Available clinical trials frequently involve relatively small sample sizes, heterogeneous treatment protocols, and limited follow-up periods, restricting conclusions regarding long-term efficacy and safety [96,103].

Definition: The terms "PDRN" and "PN" are frequently used interchangeably in the literature, despite differences in their reported chain lengths and molecular-weight distributions. Although molecular-weight-based classifications have been proposed to distinguish these materials, universally standardized criteria remain lacking, complicating comparisons among studies and formulations [7,8].

Manufacturing: PDRN characteristics may be affected by extraction, purification, sterilization, and formulation conditions, which may influence DNA integrity and molecular-weight distribution and contribute to batch-to-batch variability. Animal-derived production may also depend on biological raw-material availability, while emerging plant, algal, and microbial sources still require comparative validation in terms of purity, composition, consistency, and safety [6,26,48,55,56].

Regulatory status: The regulatory status of PDRN varies according to jurisdiction, intended use, route of administration, and product classification. Consequently, requirements related to efficacy, manufacturing, labeling, and post-market surveillance may differ among PDRN-containing products and markets [14,16,47].

12. Conclusions

Current evidence gathered in this review positions PDRN as a biomaterial of growing interest in regenerative medicine, given that various studies have reported its ability to modulate processes such as tissue repair, resolution of inflammation, stimulation of angiogenesis, cell proliferation, and extracellular matrix remodeling. This is underpinned by its biological activity, mediated primarily by activation of the adenosine A2A receptor and the nucleotide salvage pathway; together, these mechanisms foster a functional, pro-regenerative environment for healing injured tissues.

However, translation to broader therapeutic scenarios is constrained by limitations related to the heterogeneity of PDRN sources and variability in extraction and purification processes. Nested within this is insufficient standardization among commercial and experimental products, which limits clinical translation. Importantly, the level of evidence and technological maturity differ substantially among PDRN sources. Salmon-derived PDRN currently represents the most mature platform, supported by established extraction and purification approaches, commercial availability, and a broader body of in vitro, in vivo, and clinical evidence. In contrast, plant-derived PDRN represents an emerging platform supported mainly by experimental and early preclinical evidence. Microbial- and algal-derived platforms remain at an earlier stage of technological development, with current evidence predominantly focused on proof-of-concept production, molecular characterization, and in vitro biological activity. Therefore, the more limited evidence available for these emerging sources should not necessarily be interpreted as indicating lower biological potential, but rather in the context of their more recent development and lower technological readiness. Nevertheless, functional equivalence among these sources still requires deeper investigation and standardization, as they differ in molecular weight, purity, and nucleotide composition, potentially leading to meaningful variations in bioavailability, biological activity, and pharmacological behavior. Consequently, future research on PDRN depends not only on identifying new extraction sources but also on optimizing controlled-release systems. Therefore, standardized direct comparative studies, in vivo validation, and

well-designed clinical trials are required to determine whether emerging PDRN sources can achieve efficacy and safety profiles comparable to those of conventional salmon-derived PDRN. In parallel, harmonizing molecular characterization, manufacturing processes, and regulatory criteria will be essential for successful clinical translation.

Author Contributions: J.d.J.R.-A.: conceptualization, writing—review and editing. O.M.-C.: supervision, editing, visualization. J.N.-P.: editing, visualization. L.F.B.-M.: editing, visualization. E.J.L.-N.: investigation, writing—original draft, validation. J.A.R.-L.: investigation, writing—original draft, validation. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Acknowledgments: J.J.-R. (2209187) thanks SECIHTI-México for the scholarship.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

The following abbreviations are used in this manuscript:

PDRN	Polydeoxyribonucleotide
DNA	Deoxyribonucleic acid
kDa	Kilodalton
PNs	Polynucleotides
ATP	Adenosine triphosphate
ADP	Adenosine diphosphate
AMP	Adenosine monophosphate
VEGF	Vascular endothelial growth factor
ECM	Extracellular matrix
FAK	Focal adhesion kinase
AKT	Protein Kinase B
°C	Celsius
TMD	Temporomandibular disorders
g	Grams
mL	Milliliter
M	Molar
µL	Microliter
h	Hour
min	Minute
rpm	Revolutions per minute
MPa	Megapascal
µm	Micrometer
NF-κB	Nuclear Factor kappa
GMP	Guanosine monophosphate
cGAS	Cyclic GMP-AMP synthase
STING	Stimulator of interferon genes
TLRs	Toll-like receptors
MyD88	Myeloid differentiation primary response 88
IRAK1	Interleukin-1 receptor-associated kinase 1
TRAF6	Tumor necrosis factor receptor-associated factor 6
TBK1	TANK-binding kinase 1

IRF3	Interferon Regulatory Factor 3
FGF	Fibroblast growth factor
PI3K	Phosphoinositide 3-kinase
MAPK	Mitogen-activated protein kinase
TGF-β	Transforming growth factor-beta
PDGF	Platelet-derived growth factor
mg	Milligram
kg	Kilogram
nm	Nanometer
bp	Base pairs
ERK	Extracellular Signal-Regulated Kinase
Bcl-2	B-cell lymphoma 2
CLDN1	Claudin-1
FLG	Filaggrin
IVL	Involucrin
FDA	Food and Drug Administration
AIFA	Agenzia Italiana del Farmaco
MFDS	Ministry of Food and Drug Safety
CSAR	Cosmetics Supervision and Administration Regulation
IECIC	Inventory of Existing Cosmetic Ingredients in China
CPSR	Cosmetic Product Safety Report
EMA	European Medicines Agency

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