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The Effect of Salmon DNA Polynucleotide on Cell Migration Percentage and the Expression of Collagen Type 1 (*COL1A1*) and Elastin (*ELN*) Genes in Injured Fibroblast Cell Lines

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Abstract

Background: People with sensitive skin often have compromised barrier function, hindering the wound healing process. Collagen and elastin are essential in all wound healing stages, from hemostasis to tissue remodeling. Salmon DNA polynucleotide (PN) is increasingly used in beauty clinics for sensitive skin indications due to its regenerative properties. This study aimed to explore the salmon-derived PN as anti-aging agent and its impact on wound healing in scratch-induced fibroblast cell cultures by evaluating cell migration and the expression of type I collagen (*COL1A1*) and elastin (*ELN*) genes.

Methods: This study used BJ cell cultures from human skin fibroblasts. The cell migration was analyzed microscopically using ImageJ software, while *COL1A1* and *ELN* expression were measured by qRT-PCR.

Results: The IC_{50} of PN was 3.214%. The 0.78% PN concentration showed the highest cell migration, increasing by 33.80% at 48 *hr* post-scratch. PN also enhanced *COL1A1* and *ELN* expression, with the most effective concentration among the tested concentrations observed at 0.78%.

Conclusion: PN has been demonstrated to enhance fibroblast migration and increase COL1A1 and ELN gene expression in an in vitro scratch-injury model. Future studies to confirm these findings on experimental animals and human clinical trials are essential.

Keywords: Cell migration, COL1A1, ELN, Fibroblast, Polynucleotide
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Introduction

Sensitive skin can be described as a heightened sensory condition induced by contact-related or environmental stimuli, often occurring in the absence of clear clinical signs, yet characterized by exaggerated cutaneous responses such as erythema, pruritus, and irritation. This condition is commonly associated with compromised skin barrier integrity, which may negatively influence the physiological wound healing cascade [1]. Wound healing itself represents an intrinsic biological mechanism through which damaged tissue undergoes repair and restoration, involving a tightly regulated sequence of cellular and molecular events. Under normal circumstances, this process progresses through three interconnected phases, namely inflammation, re-epithelialization, and tissue remodeling [2]. Disruptions in any of these phases may arise from intrinsic or extrinsic factors, including aging, pharmacological treatment, obesity, alcohol intake, smoking habits, and nutritional status, ultimately delaying skin regeneration [3].

In individuals with sensitive skin, impaired barrier function may further compromise the wound healing response. Barrier dysfunction has been associated with delayed or suboptimal healing outcomes, as the skin's protective capacity is reduced [4]. Consequently, the key extracellular matrix components synthesis including collagen and elastin may be attenuated, increasing the likelihood of scar formation and diminished tissue elasticity [5]. Moreover, sensitive skin is frequently linked to exaggerated inflammatory or reactive responses during tissue repair, potentially intensifying symptoms such as redness, itching, and irritation at the

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wound site, which may further impede the healing trajectory [6]. Therefore, strategies aimed at preserving or restoring skin barrier function are essential to support effective wound repair in individuals with sensitive skin.

Collagen is the predominant structural protein in the skin and plays a fundamental role in maintaining tissue integrity and mechanical strength [7]. During wound repair, collagen serves as a scaffold for newly formed tissue, facilitates fibroblast migration, supports scar tissue development, promotes wound closure, and enhances tensile strength [2]. Its involvement spans all stages of wound healing, from hemostasis through to tissue remodeling [8]. In parallel, elastin contributes to the elastic and flexible properties of the skin [9]. Within the wound healing context, elastin not only provides mechanical resilience but also modulates cellular behaviour, gradually reducing wound contraction while supporting dermal regeneration. Adequate elastin synthesis during tissue regeneration is therefore critical for restoring elasticity and functional integrity of newly formed skin [10].

At present, salmon DNA polynucleotides (PN) are widely utilized in aesthetic clinical practice, particularly for managing sensitive skin conditions. Salmon-derived DNA exhibits anti-inflammatory effects through its interaction with adenosine A2A receptors, leading to suppression of mitogen-activated protein kinase (MAPK) and nuclear factor κB (NF-κB) signaling pathways, while simultaneously promoting Vascular Endothelial Growth Factor (VEGF) activity [11]. In addition, PN participates in the nucleotide salvage pathway by supplying nucleosides and nucleotides necessary for DNA synthesis, thereby reactivating cellular proliferation and growth associated with skin tissue regeneration [12]. Collectively, the biological activities of PN include stimulation of angiogenesis, enhancement of cellular metabolism, activation of collagen synthesis, modulation of inflammatory responses, inhibition of melanin production, and promotion of soft tissue regeneration, all of which contribute to skin revitalization [13]. Despite these reported benefits, scientific evidence specifically addressing the role of salmon DNA PN in accelerating wound healing in injured fibroblast cell cultures remains limited. Accordingly, the present study aims to analyze the potential of salmon DNA PN to enhance the wound repair-related process in injured fibroblast cell cultures, with a particular focus on cell migration as a key indicator of tissue repair.

Materials and Methods

Human fibroblast (BJ) cell culture

The sample used in this study is a Human fibroblast cell line (BJ, ATCC® CRL-2522™) obtained from Aretha Medika Utama, Bandung, Indonesia, with normal cell morphology (normal viability) after being cultured in BJ cell culture medium (10% FBS, 1% ABAM, 1% MEM Vit, 1% Fungizone, 1% Nanomycin, 0.1% Gentamicin, and basal MEM medium up to 100%) in an incubator at 37°*C* with 5% CO_2. Cells were maintained under standard culture conditions in T25 culture flasks and routinely monitored using an inverted microscope until approximately 70–80% confluence was achieved. Upon reaching the desired confluency, the spent medium was aspirated, and the cell layer was gently washed with 1× Phosphate-Buffered Saline (PBS). The detachment of the cell was initiated by the addition of 2 *ml* Trypsin–EDTA, followed by incubation for 5 *min* at 37°*C* with 5% CO_2. Detached cells were subsequently collected into a 15 *ml* centrifuge tube then centrifuged at 1600 *rpm* for 5 *min*. After removal of the supernatant, the resulting cell pellet was reconstituted in 1 *ml* fresh culture medium. The cell suspension was then evenly distributed into two T25 flasks and cultured at incubator in 37°*C* with 5% CO_2. For routine maintenance, the culture medium was refreshed or supplemented every 2-3 days [14].

Cytotoxicity assay

The cytotoxicity evaluation was performed following previously established protocols to define the appropriate concentration range for subsequent cell migration experiments [15]. Briefly, cells were quantified using a haemocytometer and seeded into 96-well culture plates at a density of 1×10^4 cells per well, then incubated at 37°*C* in a humidified atmosphere containing 5% CO_2 for 24 *hr*. After the initial incubation period, cells were exposed to \PN at graded concentrations of 50, 25, 12.5, 6.25, 3.13, 1.63, and 0.82%, respectively. Prior to treatment, the culture medium in each well was replaced with 90 *µl* of fresh medium, after which 10 *µl* of the corresponding PN solution was added. The treated cells were then incubated for 24 *hr* at 37°*C* in a humidified atmosphere containing 5% CO_2. After the treatment period, 10 *µl* of WST-8 reagent was added to each well, and the plates were further incubated for 3 *hr* at 37°*C* with 5% CO_2. Cell viability was subsequently assessed at 450 *nm* using a microplate spectrophotometer.

Cell treatment-cell migration assay

BJ fibroblast cultures were allocated into five experimental groups, each comprising five independent samples. Five wells per group were used within each experiment, and the entire experiment was independently repeated three times. The groups included: (I) non-wounded Negative Control (NC), consisting of BJ fibroblasts cultured in standard medium supplemented with DMSO without mechanical injury; (II) wounded Positive Control (PC), consisting of scratched BJ fibroblasts cultured in standard medium supplemented with DMSO; and three wounded treatment groups treated with salmon DNA PN: PN1 (12.5%), PN2 (3.13%), and PN3 (0.78%). The non-wounded NC was used as the physiological baseline for the fibroblasts, while the wounded PC was employed as the reference

group for evaluating the effects of PN following scratch injury. Cells were quantified using a haemocytometer and seeded into 24-well plates at a density of 6.8×10^3 cells per well, then incubated for 24 *hr* at 37°*C* in a humidified incubator containing 5% CO_2. Upon reaching approximately 70-80% confluence, as confirmed by inverted microscopic observation, a linear scratch was made across the center of each well using a sterile 1 *ml* blue pipette tip to simulate injury. The existing culture medium was subsequently aspirated and replaced with 500 *µl* of fresh medium containing the designated PN concentrations. The plates were then returned to the incubator under standard conditions. Wound closure was measured at 0, 24, and 48 *hr* following PN treatment, and the extent of BJ cell migration was quantitatively analyzed using ImageJ software [16].

Analysis of COL1A1 and ELN gene expressions

Cells were harvested and lysed using TRI reagent (300 *µl*), after which the lysates were subjected to centrifugation. The clarified lysate was mixed with an equal volume (300 *µl*) of absolute ethanol and gently inverted to ensure uniform dispersion. The resulting solution was transferred onto a Zymo-Spin IIICG column and centrifuged at 10,000×*g* for 30 *s* to allow RNA adsorption to the column matrix. For column purification, 400 *µl* of Direct-zol RNA PreWash was added and centrifuged at 10,000×*g* for 30 *s*, and the eluate was discarded. This washing procedure was performed twice. Subsequently, the column was rinsed with 700 *µl* of RNA Wash Buffer and centrifuged again at 10,000×*g* for 30 *s*. The column was then placed into a fresh RNase- and DNase-free collection tube. RNA was recovered by applying 100 *µl* of DNase/RNase-free water directly to the column membrane, followed by centrifugation at 10,000×*g* for 180 *s*. The concentration and purity of the isolated RNA were determined spectrophotometrically by measuring absorbance at 260 and 280 *nm*. First-strand complementary DNA (cDNA) synthesis was performed using the SensiFAST cDNA Synthesis Kit (Meridian Bioscience, BIO-65054). Quantitative real-time PCR (RT-qPCR) was conducted using SsoFast™ Evergreen Supermix (Bio-Rad, 1725200) following the manufacturers' instructions [17].

Data analysis

Quantitative data are presented as the mean value with corresponding mean and standard deviation (SD) derived from three independent experimental repeats. Data visualization was performed using GraphPad Prism (version 8.0.244). Statistical comparisons between groups were carried out using one-way ANOVA, and significant differences were further examined using Tukey's HSD post hoc analysis. A probability value below 0.05 ($p<0.05$) was considered indicative of statistical significance. All statistical analyses were executed using SPSS software (version 23.0; SPSS Inc., USA).

Results

Cytotoxicity analysis and migration assay

The cytotoxicity test was conducted on final concentrations of PN in BJ cell medium at 50, 25, 12.5, 6.25, 3.13, 1.63, and 0.82%, respectively. The results of the cytotoxicity test are presented in figure 1. Based on the cytotoxicity test results, the IC_{50} value of PN was evaluated in BJ cell cultures. We found that the IC_{50} of PN obtained from this WST-8 assay is 3.214%. Therefore, in subsequent pharmacological testing, three concentrations above IC_{50}, at IC_{50}, and below IC_{50} were used, namely, 12.5, 3.13, and 0.78%, respectively.

Cell migration in this study was tested using the scratch method, which involves creating an artificial wound or scratch on a confluent layer of cells in culture. Cell migration assays were performed on groups with final concentrations of 12.5, 3.13, and 0.78% in BJ cell medium, respectively. The results showed that the best migration potential was demonstrated by the 0.78% concentration of PN, which increased cell migration to 33.80% at 48 *hr* post-scratch

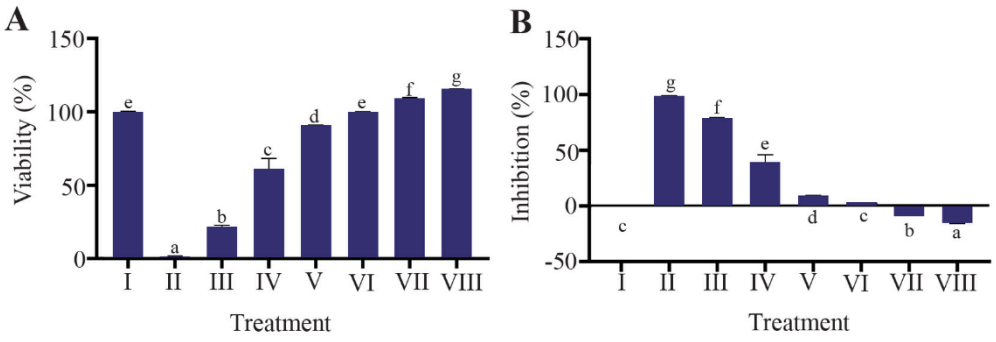

Figure 1. Viability (A) and inhibition (B) of BJ cells after PN treatment.
I: Negative Control (NC: BJ cells no treatment), II: PN 50 (BJ cells+PN 50%), III: PN 25 (BJ cells+PN 25%), IV: PN 12.5 (BJ cells+ PN 12.5%), V: PN 6.25 (BJ cells+PN 6.25%), VI: PN 3.13 (BJ cells+PN 3.13%), VII: PN 1.63 (BJ cells+PN 1.63%), VIII: PN 0.82 (BJ cells+PN 0.82%). The data is presented as mean±SD. According to Tukey HSD post hoc test, same superscripts indicate that treatments are not significantly different, various superscript marks (a, b, c, d, e, f, g) revealed significant differences between concentrations ($p<0.05$).

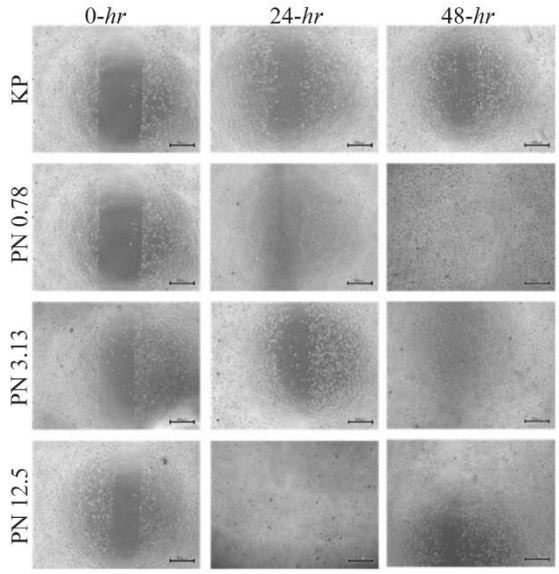

Figure 2. BJ cell migration (40x magnification).

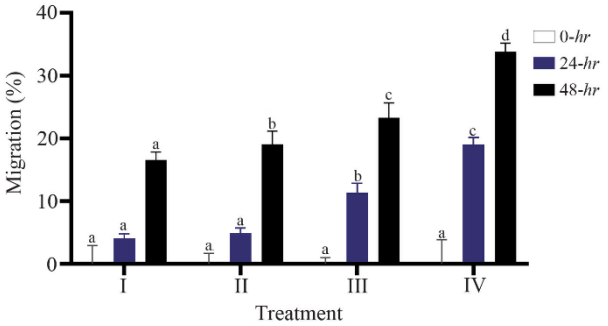

Figure 3. Effects of PN on the migration of BJ cell.
I: Negative Control (NC: BJ cells no treatment), II: PN 12.5 (BJ cells+PN 12.5%), III: PN 3.13 (BJ cells+PN 3.13%), IV: PN 0.78 (BJ cells+PN 0.78%). The data is presented as mean±SD. According to Tukey HSD post hoc test, same superscripts indicate that treatments are not significantly different, various superscript marks (a, b, c, d) revealed significant differences between concentrations ($p<0.05$).

(Figures 2 and 3). The migration percentages observed in the groups subjected to PN treatment were primarily compared to the wounded vehicle control group (PC).

The expression of COL1A1 and ELN

The expression of collagen type 1 (*COL1A1*) and elastin (*ELN*) genes in injured fibroblast cells was tested using qRT-PCR. The results showed that the scarring method can reduce the expression of the *COL1A1* and *ELN* genes, and administration of PN reversed these effects. The greatest increase in *COL1A1* and *ELN* gene expression resulted from administration of PN at a concentration of 0.78% (Figure 4).

Discussion

Based on the cell viability assessment, salmon DNA PN serum demonstrated a favorable safety profile, particularly at lower concentrations, indicating minimal cytotoxic effects on BJ fibroblast cells. Evaluation using the WST-8 assay revealed that the IC_{50} value of PN in BJ cells was 3.214%. This finding aligns with previous studies conducted on human dermal fibroblasts (CCD-25SK) and murine fibroblast cell lines (L929), which reported that PN exposure at low concentrations (0.1–1 *µg/ml*) did not adversely affect cell viability [18]. Similarly, investigations involving primary gingival fibroblasts derived from mice showed that PN concentrations up to 100 *µg/ml* supported cell survival and proliferation, as assessed by MTT and CellTiter-Glo® assays [19]. Comparable observations were reported in studies using human articular chondrocyte cell lines (HC-a), where PN treatment at concentrations up to 1000 *µg/ml* did not reduce viability, and lower doses were even associated with enhanced cellular viability [20].

Notably, the determination of an IC_{50} value of 3.214% for PN in BJ fibroblast cultures represents a novel contribution to the current literature. These findings are further supported by studies employing polydeoxyribonucleotide (PDRN), in which no cytotoxic effects were observed in human chondrocyte cultures

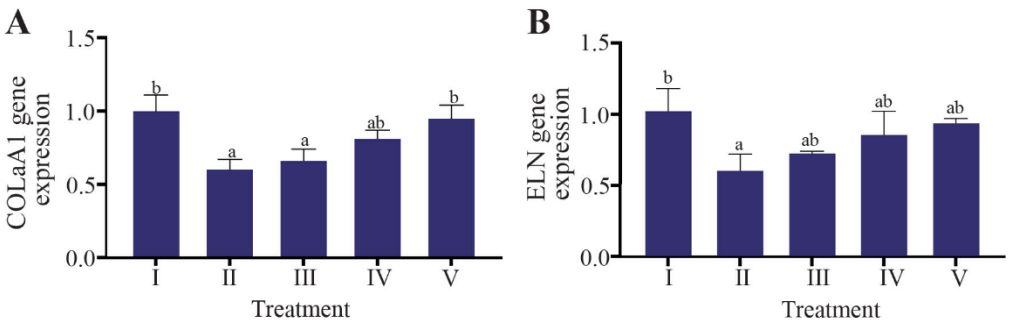

Figure 4. Effects of PN on the expression of COL1A1 and ELN.
I: Negative Control (NC: BJ cells no treatment), II: PN 12.5 (BJ cells+PN 12.5%), III: PN 3.13 (BJ cells+PN 3.13%), IV: PN 0.78 (BJ cells+PN 0.78%). The data is presented as mean±SD. According to Tukey HSD post hoc test, same superscripts indicate that treatments are not significantly different, various superscript marks (a, b, ab) revealed significant differences between concentrations ($p<0.05$).

(CHON-001) treated with PDRN at concentrations ranging from 6.3 to 100 *µg/ml* [21]. Although organism-level toxicity data specific to PN remain limited, the safety of PDRN has been well established. Two independent studies confirmed that both acute and chronic PDRN administration did not induce mortality or toxicity in vital organs, such as the liver, lungs, brain, heart, and skeletal muscle [22,23].

The IC_{50} value of 3.214% suggests that salmon DNA PN serum can be considered relatively safe for therapeutic or regenerative applications. This observation is consistent with previous reports highlighting the capacity of polynucleotides to enhance cellular functions essential for tissue repair [24]. Polynucleotides derived from salmon DNA have been shown to exert anti-inflammatory effects while promoting tissue regeneration. In the present study, PN administration at a concentration of 0.78% significantly enhanced the migratory capacity of injured fibroblasts, resulting in an increase in cell migration of up to 33.80%. This enhancement corroborates existing evidence emphasizing the stimulatory effects of polynucleotides on fibroblast proliferation and migration, which are critical steps in tissue repair [25]. Mechanistically, these effects are thought to be mediated through the activation of adenosine receptors, which contribute to regulating cellular responses during wound healing [26]. This interaction highlights the potential of polynucleotides as key components in advanced therapeutic strategies aimed at optimizing wound repair and tissue regeneration, particularly when combined with other bioactive molecules [27].

Further evaluation of migration and regenerative capacity using a scratch assay demonstrated that salmon DNA PN serum at a concentration of 0.78% exhibited the highest migratory potential, increasing wound closure by 33.80% at 48 *hr* post-scratch. These results suggest a strong potential role for PN in accelerating the *in vitro* wound healing process. Comparable outcomes have been reported in primary gingival fibroblast cultures derived from scratch-induced murine models, where PN treatment at 100 *µg/ml* promoted wound closure after 96 *hr* [19]. *In vivo* studies have also demonstrated that intraperitoneal administration of PDRN accelerates wound healing in ischemic skin models by upregulating VEGF and Hypoxia-Inducible Factor-1α (HIF-1α) [28]. Similar therapeutic benefits were observed in diabetic mouse models, where PDRN treatment enhanced angiogenesis and expedited wound repair [29]. Additionally, improved healing outcomes following intraperitoneal PDRN administration have been reported in murine models of deep second-degree dermal burns [22]. Clinical evidence further supports these findings, as PDRN injections administered to muscles and tissues surrounding wound sites in humans have been shown to improve healing at skin graft donor sites [30] and accelerate recovery in patients with pressure ulcers while reducing hospitalization duration and additional care requirements [23].

Wound healing is known as a complex physiological process involving molecular components and coordinated cellular events aimed at restoring damaged tissue. This process typically progresses through three overlapping phases, including inflammation, re-epithelialization, and tissue remodeling [2]. Aging has been shown to significantly impair wound healing by prolonging the inflammatory phase and increasing oxidative stress, thereby shifting the balance toward protein degradation and increasing the risk of chronic, non-healing wounds [31]. Within this context, PN appears to facilitate the migration and regeneration of injured BJ fibroblasts, largely due to its anti-inflammatory properties. Previous studies demonstrated that PDRN demonstrates anti-inflammatory effects in models of CCl_4-induced acute liver injury by binding to adenosine A2A receptors, subsequently inhibiting MAPK and NF-κB signaling pathways while activating VEGF expression [11]. Moreover, PN supports the nucleotide salvage pathway by supplying nucleotides and nucleosides necessary for DNA synthesis, thereby reactivating cell proliferation and promoting tissue regeneration [12]. Collectively, the biological activities of PN include stimulation of angiogenesis, enhancement of cellular metabolism, activation of collagen synthesis, modulation of inflammatory responses, inhibition of melanin synthesis, and regeneration of soft tissue, contributing to overall skin revitalization [13].

In vivo wound environments are characterized by the release of multiple mediators from damaged tissue, including ATP and DNA fragments derived from necrotic or apoptotic cells, which contribute as Damage-Associated Molecular Patterns (DAMPs) and play critical roles in initiating repair responses [32]. PN may partially mimic these endogenous signals while simultaneously providing essential substrates for cell replication and tissue reconstruction [19].

The present study also demonstrated that scratch-induced injury in BJ fibroblast cultures resulted in reduced expression of *COL1A1* and *ELN* genes, whereas PN treatment significantly upregulated the expression of both genes. The most pronounced increases in *COL1A1* and *ELN* expression were observed following treatment with PN at a concentration of 0.78%. These findings are consistent with reports by Colangelo *et al*, who observed increased expression of collagen-related genes, including *COL1A1* and *COL3A1*, in primary rat gingival fibroblasts treated with PN 96 *hr* post-injury [19]. Similarly, Kim *et al* reported that PN treatment at 0.5 *µg/ml* significantly enhanced gene expression in human dermal fibroblast cultures (CCD-25SK), with up to a threefold increase observed [18]. The anti-inflammatory and regenerative effects of PN are believed to be mediated through modulation of multiple signaling pathways, including

adenosine receptor activation, which may influence the expression of Extracellular Matrix (*ECM*)-related genes such as *COL1A1* and *ELN* [33]. Upregulation of *COL1A1* is essential for collagen deposition and ECM integrity, both of which are fundamental for effective wound healing and tissue regeneration [34]. Concurrent modulation of *ELN* expression may further enhance the elastic properties of repaired tissue, thereby supporting functional recovery following injury.

The present study has several limitations that should be considered when interpreting the findings. First, this study was conducted using an in vitro scratch-injury model with a monoculture of BJ fibroblasts, which does not fully represent the complexity of wound healing *in vivo*. Second, the molecular evaluation was limited to the expression of *COL1A1* and *ELN* without protein-level validation or mechanistic investigations. Third, although the scratch assay is widely used to assess wound closure, the observed effects may reflect both cell migration and proliferation. In addition, only a limited range of PN concentrations was evaluated. Therefore, further dose-response studies are required to determine the optimal concentration range. Furthermore, the availability of archived experimental records was restricted, which limited the extent of methodological details and material characterization that could be further presented in this revised manuscript. Therefore, the present findings should be regarded as preliminary and interpreted with caution. Further studies involving standardized experimental documentation, comprehensive PN characterization, protein expression analyses, animal models, and clinical investigations are required to confirm the biological effects and translational relevance of PN.

Conclusion

Salmon DNA PN serum IC_{50} is 3.214%. The administration of polynucleotides can enhance the migration of injured fibroblast cells, with the most effective concentration being 0.78%, which can increase cell migration by up to 33.80%. PN also upregulated *COL1A1* and *ELN* gene expression in a BJ fibroblast scratch-injury model. These findings suggest a potential role of PN in supporting cellular processes associated with wound repair. Further research on animal models (including rats, mice, guinea pigs, or rabbits) with injuries is necessary to validate the PN effectiveness in an *in vivo* experimental setting. Additionally, clinical trials are needed to monitor the effectiveness of PN in the wound healing process in humans.

Ethics approval

Ethical approval was not required because this study exclusively utilized commercially available established cell lines and did not involve human participants or animal experiments.

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Conflict of Interest

The authors have no conflict of interest.

References

1. Duarte I, Silveira JEPS, Hafner MFS, Toyota R, Pedroso DMM. Sensitive skin: review of an ascending concept. An Bras Dermatol 2017 Jul-Aug;92(4):521-525.
2. Mathew-Steiner SS, Roy S, Sen CK. Collagen in wound healing. Bioengineering (Basel) 2021;8:63.
3. Chen Y, Wu Y, Xiong F, Yu W, Wang T, Xiong J, et al. Construction of a collagen-like protein based on elastin-like polypeptide fusion and evaluation of its performance in promoting wound healing. Molecules 2023;28(19): 6773.
4. Wikramanayake TC, Stojadinovic O, Tomic-Canic M. Epidermal differentiation in barrier maintenance and wound healing. Adv Wound Care (New Rochelle) 2014; 3(3):272-280.
5. Spada F, Lui AH, Barnes TM. Use of formulations for sensitive skin improves the visible signs of aging, including wrinkle size and elasticity. Clin Cosmet Investig Dermatol 2019;12:415–425.
6. Chen L, Zheng J. Does sensitive skin represent a skin condition or manifestations of other disorders? J Cosmet Dermatol 2021;20(7):2058-2061.
7. Barnes M. Update on collagens: what you need to know and consider. Plast Surg Nurs 2019;39(4):112-115.
8. Zhang Y, Wang Y, Li Y, Yang Y, Jin M, Lin X, et al. Application of collagen-based hydrogel in skin wound healing. Gels 2023;9(3):185.
9. Almine JF, Wise SG, Weiss AS. Elastin signaling in wound repair. Birth Defects Res C Embryo Today 2012;96(3):248-257.
10. Baumann L, Bernstein EF, Weiss AS, Bates D, Humphrey S, Silberberg M, et al. Clinical relevance of elastin in the structure and function of skin. Aesthet Surg J Open Forum 2021 May 14;3(3):ojab019.
11. Ko IG, Jin JJ, Hwang L, Kim SH, Kim CJ, Han JH, et al. Polydeoxyribonucleotide exerts protective effect against CCl_4-induced acute liver injury through inactivation of NF-κB/MAPK signaling pathway in mice. Int J Mol Sci 2020;21(21):7894.

12. Squadrito F, Bitto A, Irrera N, Pizzino G, Pallio G, Minutoli L, et al. Pharmacological activity and clinical use of PDRN. Front Pharmacol 2017;8:224.
13. Khan A, Wang G, Zhou F, Gong L, Zhang J, Qi L, et al. Polydeoxyribonucleotide: A promising skin anti-aging agent. Chinese Journal of Plastic and Reconstructive Surgery 2022 Dec 1;4(4):187-93.
14. Utami S, Endrini S, Batubara L, Rahmah NA, Syarif I, Nafik S, et al. Cytotoxicity of combination doxorubicin and Garcinia picrorrhiza fruit extract on fibroblast cell. GMHC 2023 Dec 23;11(3):195-9.
15. Girsang E, Lister IN, Ginting CN, Nasution SL, Suhartina S, Munshy UZ, et al. Antioxidant and anti-inflammatory activity of chlorogenic acid on lead-induced fibroblast cells. In: Journal of Physics: Conference Series 2019 Nov 1 (Vol. 1374, No. 1, p. 012006). IOP Publishing.
16. Radstake WE, Gautam K, Van Rompay C, Vermeesen R, Tabury K, Verslegers M, et al. Comparison of in vitro scratch wound assay experimental procedures. Biochem Biophys Rep 2023;33:101423.
17. Pujimulyani D, Suryani CL, Setyowati A, Handayani RAS, Arumwardana S, Widowati W, et al. Cosmeceutical potentials of Curcuma mangga Val. extract in human BJ fibroblasts against MMP1, MMP3, and MMP13. Heliyon 2020;6(9):e04921.
18. Kim JH, Kwon TR, Lee SE, Jang YN, Han HS, Mun SK, et al. Comparative evaluation of the effectiveness of novel hyaluronic acid–polynucleotide complex dermal filler. Sci Rep 2020;10(1):5127.
19. Colangelo MT, Belletti S, Govoni P, Guizzardi S, Galli C. A biomimetic polynucleotides–hyaluronic acid hydrogel promotes wound healing in a primary gingival fibroblast model. Appl Sci 2021;11:4405.
20. Kuppa SS, Kim HK, Kang JY, Lee SC, Yang HY, Sankaranarayanan J, et al. Polynucleotides suppress inflammation and stimulate matrix synthesis in an in vitro cell-based osteoarthritis model. Int J Mol Sci 2023;24(15):12282.
21. Ra HJ, Oh MY, Kim HJ, Lee SY, Eom DW, Lee SK, et al. Effects of salmon DNA fraction in vitro and in a monosodium iodoacetate-induced osteoarthritis rat model. Korean J Physiol Pharmacol 2018;22(2):163-72.
22. Bitto A, Galeano M, Squadrito F, Minutoli L, Polito F, Dye JF, et al. Polydeoxyribonucleotide improves angiogenesis and wound healing in experimental thermal injury. Crit Care Med 2008;36(5):1594-1602.
23. Kim CS, Pak JH, Park JH, Jeong JH, Heo CY. Effects of polydeoxyribonucleotide in the treatment of pressure ulcers. J Korean Med Sci 2014;29 Suppl 3(Suppl 3): S222-7.
24. Chiuman L, Ongko NX, Tarigan SB. Dermapen Treatments for Healing Pockmarked Skin in Male Wistar Rats (Rattus norvegicus): A Study Comparing Platelet-Rich Plasma with Salmon DNA Serum. Jurnal Penelitian Pendidikan IPA 2023 Dec 20;9(12):10733-9.
25. Galeano M, Pallio G, Irrera N, Mannino F, Bitto A, Altavilla D, et al. Polydeoxyribonucleotide: a promising biological platform to accelerate impaired skin wound healing. Pharmaceuticals (Basel) 2021 Oct 29;14(11): 1103.
26. Rho N. A survey on the cosmetic use of injectable polynucleotide: the pattern of practice among Korean dermatologists. J Cosmet Dermatol 2023;23(4):1243-1252.
27. Araco A, Raichi M. Clinical efficacy and safety of polynucleotides highly purified technology (PN-HPT®) and cross-linked hyaluronic acid for moderate to severe nasolabial folds. J Cosmet Dermatol 2022;22(1):146-155.
28. Polito F, Bitto A, Galeano M, Irrera N, Marini H, Calò M, et al. Polydeoxyribonucleotide restores blood flow in an experimental model of ischemic skin flaps. J Vasc Surg 2012;55(2):479-488.
29. Galeano M, Bitto A, Altavilla D, Minutoli L, Polito F, Calò M, et al. Polydeoxyribonucleotide stimulates angiogenesis and wound healing in the genetically diabetic mouse. Wound Repair Regen 2008;16(2):208-217.
30. De Aloe G, Rubegni P, Biagioli M, Taddeucci P, Fimiani M. Skin graft donor site and use of polydeoxyribonucleotide as a treatment for skin regeneration: a randomized, controlled, double-blind, clinical trial. Wounds-A compendium of clinical research and practice 2004 Aug 1;16(8):258-63.
31. Khalid KA, Nawi AFM, Zulkifli N, Barkat MA, Hadi H. Aging and wound healing of the skin: a review of clinical and pathophysiological hallmarks. Life (Basel) 2022 Dec 19;12(12):2142.
32. Vénéreau E, Ceriotti C, Bianchi ME. DAMPs from cell death to new life. Front Immunol 2015;6:422.
33. Kim TH, Heo SY, Oh GW, Heo SJ, Jung WK. Applications of Marine Organism-Derived Polydeoxyribonucleotide: Its Potential in Biomedical Engineering. Mar Drugs 2021 May 22;19(6):296.
34. Pan X, Chen Z, Huang R, Yao Y, Ma G. Transforming growth factor β1 induces the expression of collagen type I by DNA methylation in cardiac fibroblasts. PLoS One 2013;8(4):e60335.