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A novel innovative polysaccharide ingredient combination for skin repair and healing based on glycobiology

Yue Sun[1,*], Hongling Kan[1], Feng Li[1], Fengtong Shen[1], BaiXiu Chen[1], and Shaoqing Lu[1]

[1] Research and Development Centre, BLOOMAGE BIOTECHNOLOGY CORPORATION LIMITED., Jinan, China

1. Introduction

The evolving aesthetic landscape, driven by shifting societal ideals and advancements in medical technology, has precipitated an 8%–12% annual growth in demand for minimally invasive to invasive cosmetic procedures over the past decade, reflecting public prioritization of self-image enhancement while catalyzing technological innovation. Postoperative recovery, however, constitutes a critical determinant of therapeutic efficacy in cosmetic medicine, as inadequate management may compromise skin repair mechanisms, diminish treatment outcomes, and precipitate complications that undermine aesthetic results. Consequently, systematic investigation of postoperative skin regeneration mechanisms and refinement of evidence-based nursing protocols are imperative to optimizing procedural safety, efficacy, and overall quality in aesthetic medical practice.

Skin wound repair is a dynamic endogenous process involving coordinated interactions among repair cells, growth factors, and the extracellular matrix following injury, progressing sequentially through hemostasis, inflammation, cellular proliferation and differentiation, and scar remodeling. The rate and efficacy of healing are modulated by local and systemic determinants: local factors, such as temperature fluctuations, infection, and oxidative stress levels [1-3], directly impair repair mechanisms, whereas systemic conditions, including pathological, psychological, and physiological states, govern the body's reparative capacity. These interrelated variables collectively dictate healing trajectories—either accelerating tissue regeneration through optimized cellular signaling or delaying repair via dysregulated inflammatory or metabolic pathways—thereby identifying them as pivotal therapeutic targets to enhance clinical outcomes.

As a key component of cell and skin barrier, sugar molecules play an indispensable role in maintaining life activities and skin health. At the cellular level, sugar molecules are not only important components of glycoproteins and glycolipids on the cell membrane surface but also mediate precise cell communication by specifically binding with sugar molecules on the surface of adjacent cells, thereby regulating cell growth, differentiation, and migration. Many studies have shown that the structural changes of glycoproteins on the cell surface can affect cell-cell signaling. For example, in tumor cells, abnormal glycoprotein glycochains alter cell communication and promote tumor development. In the skin, sugar molecules are an important part of the skin barrier. They can bind with water molecules to form a moisturizing

network, effectively preventing the loss of skin moisture and maintaining the skin's moisture state. At the same time, these sugar molecules also participate in the recognition process of immune cells, playing a key role in the immune response and helping the skin resist the invasion of external pathogens. In addition, mannose receptors, as sugar-binding proteins on the surface of immune cells, can recognize pathogen surface sugar molecules and initiate immune responses. When the skin is damaged, sugar molecules activate the relevant repair mechanism, promote the synthesis of collagen and elastic fibers, and accelerate wound healing. Studies have shown that after skin damage, specific sugar molecules can stimulate fibroblast proliferation, increase collagen synthesis, and help wound repair.

Hyaluronic acid (HA), a pivotal component of the extracellular matrix, plays a multifunctional role in skin repair, hydration, and anti-aging processes [4]. Based on molecular weight, HA can be categorized into three distinct types: high molecular weight HA (>1000 kDa), which remains localized on the skin surface to exert anti-inflammatory, immunomodulatory, and lubricating effects [5,6]; medium molecular weight HA (200-1000 kDa), penetrating the dermis to promote cellular repair and proliferation [7,8]; and low molecular weight HA (<200 kDa), which infiltrates deeper skin layers to enhance cell migration and collagen synthesis [9,10]. Through receptor-mediated interactions, HA activates key signaling pathways critical for tissue regeneration. Binding to CD44 triggers the PI3K/Akt pathway, enhancing cell survival, proliferation, and oxidative stress resistance [11], while RHAMM engagement stimulates the ERK pathway to improve cell motility and accelerate tissue repair [12,13]. Furthermore, HA mitigates cellular senescence and strengthens skin barrier function via free radical scavenging, NF-κB pathway inhibition, and epidermal barrier reinforcement. During wound healing, HA accelerates fibroblast proliferation and extracellular matrix deposition (including collagen), thereby shortening repair timelines [14].

Ulva lactuca polysaccharide is a water-soluble acidic polysaccharide found in the cell walls of Ulva lactuca. It is primarily composed of sulfated rhamnose, uronic acids (including glucuronic acid and iduronic acid), and xylose [15]. As the main active component of Ulva lactuca, this polysaccharide exhibits diverse biological activities, such as immune regulation, anti-inflammatory activity, anticoagulant effect, anti-tumor activity, antioxidant capacity, anti-hyperlipidemic effect, and plant growth-promoting activity. Consequently, Ulva lactuca polysaccharide holds promising application prospects in medicine, cosmetics, food, and healthcare products [16–18].

Studies have confirmed that polysaccharides from Ulva fasciata and Ulva lactuca possess antioxidant activity in vitro, capable of scavenging superoxide radicals, hydroxyl radicals, and ABTS radicals, and enhancing reducing power. Li et al.[19] demonstrated that Ulva pertusa polysaccharide significantly improves antioxidant capacity in vivo, as evidenced by increased superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GSH-Px) levels in mouse liver tissue, alongside reduced malondialdehyde (MDA) content. Furthermore, Ulva lactuca polysaccharide has been shown to ameliorate oxidative stress in SAMP8 mice, decreasing serum levels of pro-inflammatory cytokines including interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), and interleukin-6 (IL-6) [20] .Notably, Jiang et al.[21] developed three low-molecular-weight Enteromorpha prolifera polysaccharides (LMPs) via acid hydrolysis, which exhibited elevated sulfate content and potent anti-inflammatory effects in vitro. Label-free quantitative proteomics revealed that the most bioactive LMP (LPEP) downregulated nitric oxide (NO), IL-1β, IL-6, and TNF-α by suppressing the NF-κB, PKC/ERK/MAPK, and PI3K/Akt signaling pathways. In vivo, LPEP application accelerated full-thickness skin wound healing in rats by reducing local inflammatory factor expression.

Sodium DNA (polydeoxyribonucleotide), a bioactive polynucleotide mixture with molecular weights ranging from 50 to 1500 kDa, exhibits no antigenic properties or systemic toxicity [22,23], and its mechanisms of action are primarily attributed to two pathways: first, through the salvage pathway, where Sodium DNA is synthesized from purine and pyrimidine bases derived from dietary or metabolic sources via phosphorylation, thereby maintaining cellular nucleic acid homeostasis; second, as an agonist of the adenosine A_2 A receptor (A_2 A), Sodium DNA binds to A_2 A receptors to activate the PI3K/Akt pathway, promoting cell survival and proliferation, while simultaneously stimulating the cAMP-PKA pathway to regulate gene transcription and inhibiting the MAPK pathway, which attenuates inflammatory responses by suppressing NF-κB, PKC/ERK/MAPK, and PI3K/Akt signaling cascades.

Under oxidative stress, excessive reactive oxygen species (ROS) upregulate transcription factors activator protein 1 (AP-1) and nuclear factor E2-related factor 2 (Nrf2) while activating mitogen-activated protein kinase (MAPK) and nuclear factor-kappa B (NF-κB) pathways, which collectively induce matrix metalloproteinase (MMP)-1, -3, and -9 expression, leading to elastic fiber and collagen degradation and accelerating wrinkle formation and aging. Kim et al. demonstrated that Sodium DNA potently inhibited elastase activity in vitro in a dose-dependent manner through 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging and suppressed MMP-1 gene expression in human skin fibroblasts, thereby attenuating oxidative stress [24]. Conversely, other studies suggest Sodium DNA inhibits MAPK by blocking extracellular signal-regulated kinase (ERK) phosphorylation via A_2 A receptor activation, reducing MMP-1, -3, and -9 expression and promoting skin regeneration.

Furthermore, Sodium DNA exhibits efficacy in treating skin wounds; in a drug-induced diabetic mouse model, it accelerated diabetic foot ulcer (DFU) healing [25], and Kim et al. reported that intramuscular Sodium DNA administration post-debridement in type 2 diabetic patients with DFU undergoing initial surgery reduced peripheral tissue hypoxia, enhanced angiogenesis and granulation tissue formation, improved inflammation, and achieved 100% healing rates, validating its safety and efficacy in DFU management [26]. Additionally, Sodium DNA has demonstrated therapeutic potential for burn wounds: in a mouse model of deep second-degree scalding, it significantly increased microvessel density and neovascularization marker CD31 expression while decreasing the anti-inflammatory marker TNF-α, accelerated re-epithelialization, and shortened wound closure time [27]. Collectively, these findings underscore Sodium DNA's promising applications in treating diverse skin lesions.

The growing demand for aesthetic medicine to enhance appearance underscores the critical importance of post-treatment recovery in skin restoration and the durability of surgical outcomes. In this study, we employed a glycomics-driven approach to pioneer the integration of glycan-based skincare with regenerative medicine, developing a novel polysaccharide formulation comprising sodium DNA complexed with hyaluronic acid, Ulva lactuca-derived polysaccharides, and Laminaria japonica extracts. Through integrated in vivo and in vitro investigations, we demonstrate that this formulation enhances skin hydration—a cornerstone for maintaining epidermal integrity — while stimulating collagen neogenesis, accelerating cellular proliferation and migration, and activating tissue remodeling and wound healing cascades. These synergistic effects collectively support cutaneous homeostasis and establish a transformative therapeutic strategy for optimizing postoperative recovery in aesthetic medicine populations.

2. Materials and Methods

1-Evaluation of the combination on stimulating the proliferation of skin cells

1.1-Keratinocyte Proliferation Assay Using MTT Test

The proliferation of human keratinocytes has been studies by using MTT test after 24h and 48h cultivation. The internal environment of proliferating cells is more reduced than that of non-proliferating cells This reduced state is measured using tetrazolium salts such as MTT [3-(4,5-dimethylethiazol-2-yl)-2,5-diphenyltetrazolium bromide].

1.2-Normal Human Fibroblast Proliferation Assay by BrdU Labeling Method

The proliferation of normal human fibroblasts was studied by incubating cells with BrdU at a density of 10,000 cells per well.

2-Evaluation of the combination on increasing the synthesis of total collagens

2.1-Procedure for Collagen Synthesis Evaluation in Fibroblasts

To assess the effect of the combination of 0.1% and 0.2% on collagen synthesis, fibroblasts were treated with collagenases, followed by centrifugation and chemical treatments. Ophthaldehyde acid was used to prevent interference, and NBD-Cl was applied to label hydroxyproline, the major amino acid in collagen.

2.2-Quantification of Collagen Content Using HPLC

The labeled hydroxyproline was then measured by fluorescence using reverse-phase HPLC, which quantifies the total collagen content.

3-Evaluation of the combination on Wound Healing

3.1-Evaluation of Wound Healing in Human Fibroblast Monolayer via Scratch Assay Model

The scratch assay was performed using normal human fibroblasts, which were cultured to confluence in 6-well plates. A sterile pipette tip was used to create a uniform scratch across the cell monolayer, mimicking a wound. The cells were then treated with the combination at specified concentrations and incubated at 37°C with 5% CO_2 for a set period, typically 24 to 48 hours. Control groups were treated with the same medium but without the combination.

3.2- Assessment of Wound Healing by Monitoring Wound Closure and Quantification

The wound closure was monitored and photographed at various time points using a phase-contrast microscope. The images were analyzed to measure the wound area. The percentage of wound closure was calculated by comparing the initial and final wound areas using the formula:Wound closure (%) = [(Initial wound area - Final wound area) / Initial wound area] × 100%.

This method quantitatively assesses the extent of cell migration and wound healing induced by the treatment.

4-Clinical testing

4.1-Assessment of skin hydration

Hydration is important to preserve skin integrity and tone. The loss of water from the stratum corneum induces dry and scaly skin.Moreover , a hydrated and luminous epidermis helps accelerate skin repair.This in vivo study has been performed on 10 volunteers (30-70 years old) with very dry skin, the basic Carbopol gels containing the combination (5%) or the corresponding placebo, are applied under controlled conditions (single application of 0.2ml on an area of 35cm^2 on the leg). The moisturizing efficacy of the combination is determined using a corneometer Courage & Khazaka CM 825. Readings are taken at regular intervals.

4.2-Restoration of smoother feeling

This in vivo study has been performed on 5 volunteers (30-70 years old) with very dry and cracked skin, a basic Carbopol gel containing the combination (5%) has been applied twice daily during 4 days on the leg.

4.3-Improvement of superficial skin imperfections

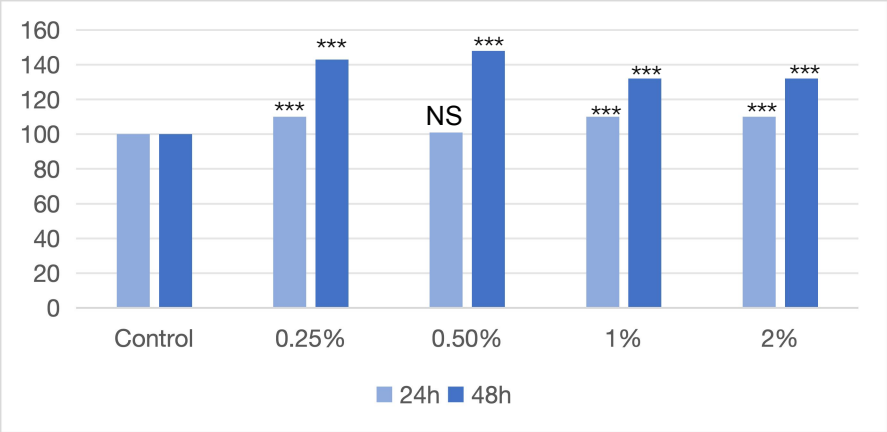
Xerosis typically causes scaly and cracked skin, which can result from factors like thickened calluses, aging, exposure to dry and cold weather, alcohol, irritants, harsh chemicals, and certain diseases (e.g., diabetes and peripheral vascular disease). Cracked skin most commonly occurs around the heels, but can also appear on knuckles and fingertips. Skin may

also be damaged by abrasions, cuts, or deep fissures, which can lead to infection. Once the skin is cut, cracked, or damaged, the repair process begins.This in vivo study has been performed on 5 volunteers (30-70 years old) with very dry and cracked skin, a basic Carbopol gel containing the combination (5%) has been applied twice daily during several days on the heel to evaluate whether the combination can effectively repair skin damage of the heel.

3. Results

3.1. Study of the combination on stimulating the proliferation of skin cells

3.1.1. Study on human keratinocytes

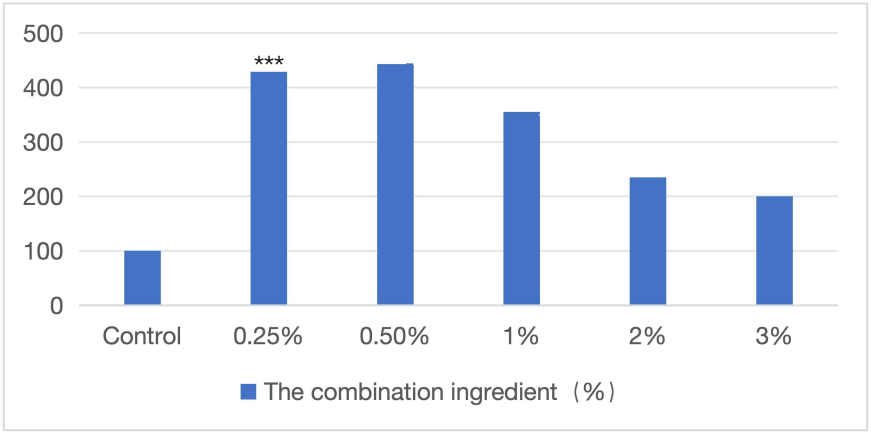


Figue 1- Stimulates the proliferation of Keratinocyte

***p < 0.001 vs control

The results are shown in the figure1.The combination ingredient is able to increase keratinocytes proliferation and viability；After 48 hours of cultivation, the proliferation of human keratinocytes increased by 143% with 0.25% combination and by 148% with 0.5% combination.

3.1.2. Study on normal human fibroblasts

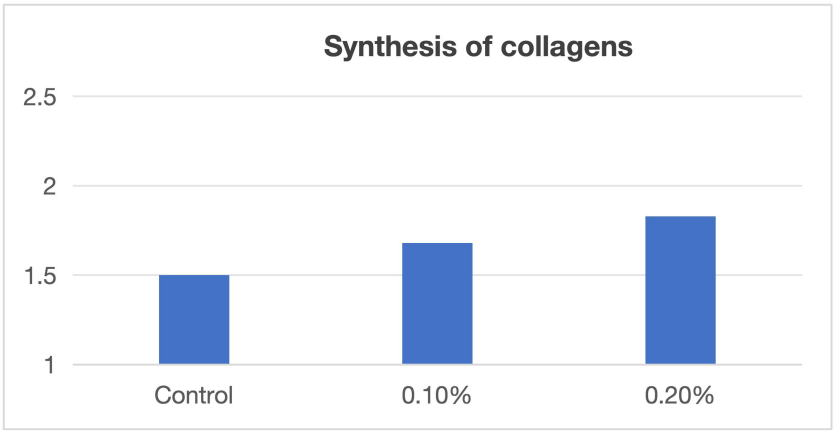


Figue 2- Stimulates the proliferation of normal human fibroblasts

***p < 0.001 vs control

The results are shown in the figure2.With 10,000 cells per well, the proliferation of normal human fibroblasts increased by 429% with 0.25% combination ingredient and 443% with 0.5% combination ingredient.

3.2. Study of the combination on increasing the synthesis of total collagens

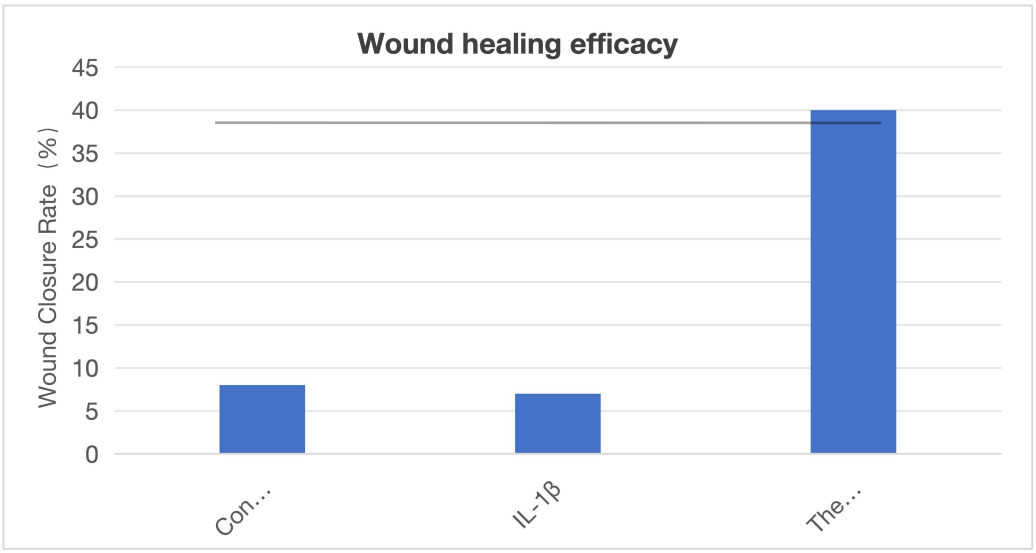


Figue 3- Stimulation of synthesis of total collagens by the combination ingredient

*p < 0.05 vs control

Results of the study on collagens synthesis have demonstrated that the combination ingredient at 0.1% and 0.2% significantly increases the synthesis of total collagens respectively by 12% and 22%.

3.3. Study of the efficacy on Wound Healing



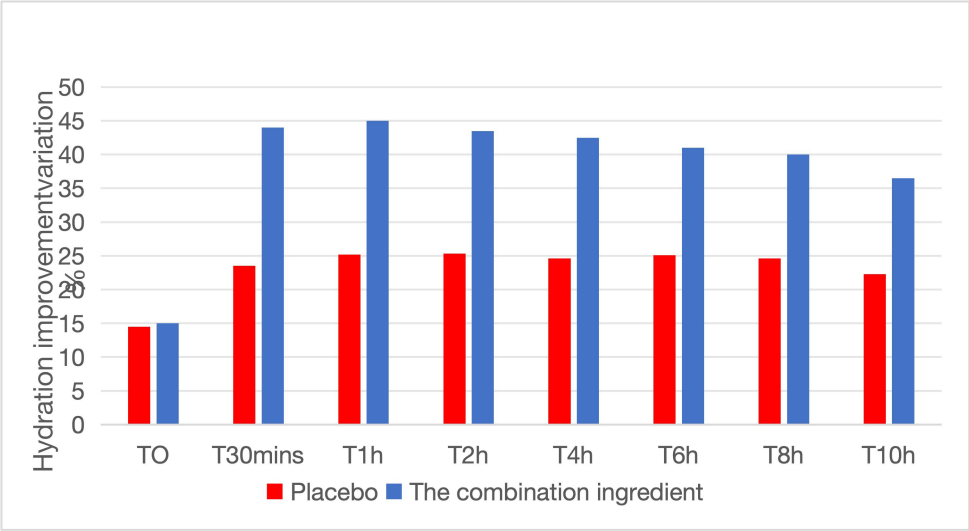
Figue 4-Acceleration of wound closure by the combination ingredient

***p < 0.001 vs control

A cell scratch assay demonstrated that after 36 hours of treatment, the wound healing rate in the the combination ingredient-treated group reached 40%, compared to less than 10% in the control group.

3.4. Clinical testing

3.4.1. Increase of skin hydration

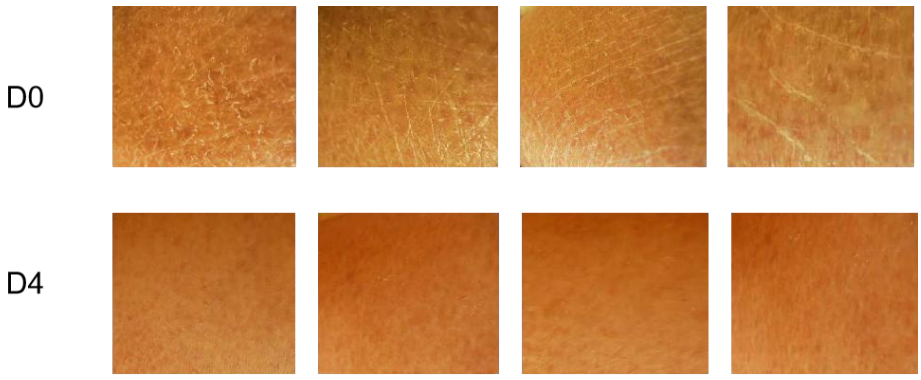


Figue 5- Increase of skin hydration

Compared to placebo, the combination ingredient of 5% cause a noticeable immediate moisturizing effect of the outer layers of the skin that is maintained for at least 10 hours.Hydration is important to recover skin integrity.

3.4.2. Restoration of smoother feeling

At day 0, the very dry skin of volunteers appears scaly and striped. At day 4, after 4 days twice daily application of a gel with the combination ingredient of 5% , their skin appears smoother and more hydrated.



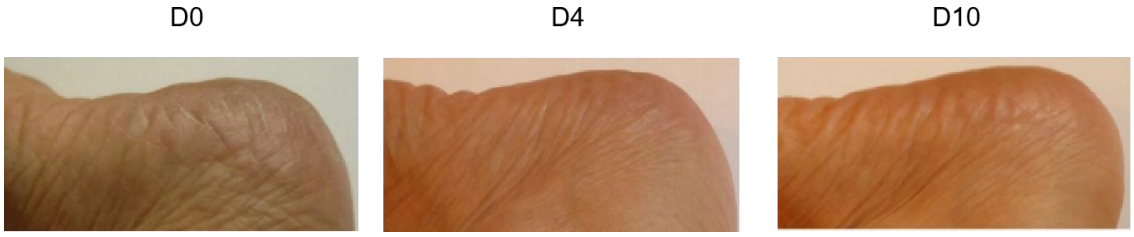
Figue 6- Photographs of volunteers-Keep smoother and more hydrated

In conclusion, the combination ingredient restores the skin to a healthier state, bringing a feeling of suppleness and comfort.

3.4.3. Improvement of superficial skin imperfections

At Day 0, the heel shows small cracks, which progressively disappear after twice-daily application of a gel containing 5% of the combination ingredient. The combination effectively

reduces minor scratches and provides an efficient solution for repairing superficial skin injuries.



Figue 7- Photographs of volunteers-Restore and heal the skin

In conclusion, the combination ingredient favours skin repair and promotes a healthy skin.

4. Discussion

This study demonstrates the promising potential of a glycobiology-based ingredient combination in promoting skin repair and regeneration. The significant improvements in cell proliferation, collagen synthesis, and wound healing observed in vitro, combined with enhanced skin hydration and visible improvement in clinical tests, suggest strong applicability in post-aesthetic procedure care. These findings highlight the synergistic effects of the multi-components and underscore the importance of glycobiology in advancing next-generation skincare and regenerative solutions.

5. Conclusion

In this study, we used glycobiology as the research pathway and, for the first time, integrated glycobiology-based skincare with skin regeneration medicine to develop an innovative polysaccharide ingredient combination designed for rapid skin repair and healing. This unique combination primarily consists of an acidic polysaccharide — hyaluronic acid — along with polysaccharide components extracted from Ulva lactuca and Laminaria saccharina, and is further enhanced with sodium DNA, known for its bioactive properties.

Through a series of in vivo and in vitro studies, we demonstrated that this combination ingredient significantly promotes skin hydration, which is essential for restoring skin barrier integrity. Simultaneously, it stimulates collagen regeneration, accelerates cell proliferation and migration, and activates tissue reconstruction and wound closure, thus supporting the regeneration of healthy skin.

More importantly, this glycobiology - driven approach offers a safe, effective, and cutting - edge solution for post - aesthetic procedure recovery, showing promising clinical potential and market value. It represents a new frontier in skin repair science and paves the way for future innovations in both cosmetic and medical dermatology.

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