Indonesian Journal of Global Health Research
Volume 8 Number 4, August 2026
e-ISSN 2715-1972; p-ISSN 2714-9749
https://jurnal2.globalhealthsciencegroup.com/index.php/IJGHR

THE POTENTIAL OF PROBIOTICS FROM FERMENTED RICE WATER ON FIBROBLAST PROLIFERATION AND MIGRATION: A SYSTEMATIC REVIEW

Nury Nur Melati Tanjung[1]*, Dian Widiyanti[2], Indra Kusuma[3], Dicky Budiman[4]
[1]Biomedical Doctoral Program, Graduate School, Universitas Yarsi, Jl. Letjen Suprapto Kav.13, Cemp. Putih Timur, Cemp. Putih, Jakarta Pusat, Jakarta 10510, Indonesia
[2]Department of Microbiology, Faculty of Medicine, Universitas Yarsi, Jl. Letjen Suprapto Kav.13, Cemp. Putih Timur, Cemp. Putih, Jakarta Pusat, Jakarta 10510, Indonesia
[3]Department of Physiology, Faculty of Medicine, Universitas Yarsi, Jl. Letjen Suprapto Kav.13, Cemp. Putih Timur, Cemp. Putih, Jakarta Pusat, Jakarta 10510, Indonesia
[4]Center for Environmental and Population Health, Griffith University, 170 Kessels Rd, Nathan, Queensland 4111, Australia
*nury.melati@yarsi01.onmicrosoft.com

ABSTRACT
Fermented rice water (FRW) has been traditionally used for skin care, but its biological mechanisms on fibroblasts, key cells in wound healing, have not been fully characterized. This systematic review aims to evaluate the efficacy of FRW on fibroblast proliferation and migration and to identify the molecular pathways involved. A literature search was conducted through PubMed, Scopus, and Google Scholar using the keywords "fermented rice water," "fibroblast," and "wound healing" in publications from 2015 to 2025. Studies were included if they evaluated the effects of FRW on fibroblasts in vitro or in vivo. Risk of bias was assessed using SYRCLE RoB (Risk Of Bias). Four studies met the inclusion criteria. FRW increased fibroblast viability by up to 116% and accelerated diabetic wound closure from 27% to 71% compared to controls. Molecular analysis showed upregulation of Collagen I mRNA by 17%, Collagen III by 47%, and Elastin by 159%. FRW activated the NRF2 pathway, which increased the expression of antioxidant enzymes (SOD, CAT, HO-1) and decreased inflammatory mediators including TNF-α, NF-κB, and MMP-1. Bioactive metabolites from Lactobacillus plantarum, Bacillus cereus, and Aspergillus oryzae played a role in these therapeutic effects. FRW shows potential as a fibroblast bio-stimulator through multi-pathway modulation involving extracellular matrix synthesis, antioxidant, and anti-inflammatory effects, with prospects for application in chronic wounds and anti-aging that require further clinical validation.

Keywords: fermented rice water; fibroblast; wound healing

How to cite (in APA style)
Tanjung, N. N. M., Widiyanti, D., Kusuma, I., & Budiman, D. (2026). The Potential of Probiotics from Fermented Rice Water on Fibroblast Proliferation and Migration: A Systematic Review. *Indonesian Journal of Global Health Research*, *8*(4), 251–260. https://doi.org/10.37287/ijghr.v8i4.1715.

INTRODUCTION

The skin wound healing process involves a series of complex, interconnected stages, ranging from hemostasis, inflammation, proliferation, to tissue remodeling.(Dermal fibroblasts play a crucial role in the proliferative phase through their ability to synthesize extracellular matrix (ECM) components, particularly type I and III collagen, and assist in cell contraction and migration to close the wound area.(Knoedler et al., 2023, Chen et al., 2024, Mathew-Steiner et al., 2021) Impairments in fibroblast proliferation and migration functions can delay wound healing and increase the risk of pathological scar formation. The use of probiotics and fermented products for dermatological applications has shown promising developments in the last decade. (Choudhury et al., 2025, Tsai et al., 2021, Yang et al., 2025) Fermented rice water, traditionally used in skin care in Asia, contains various probiotic microorganisms, mainly from the Lactic Acid Bacteria group, such as Lactobacillus plantarum, Lactobacillus fermentum, and Leuconostoc lactis.(The fermentation process produces bioactive metabolites including organic acids, antioxidant peptides, and polyphenolic compounds that have the potential to stimulate fibroblast cellular activity. (Mo et al., 2022, Lin et al., 2025)

Several studies have shown that probiotics from the Lactobacillus genus can increase type I collagen synthesis, decrease matrix metalloproteinase-1 (MMP-1) expression, and reduce oxidative stress induced by ultraviolet radiation. (Chen et al., 2024, Tsai et al., 2021, Jo et al., 2022)However, specific data on the efficacy of probiotics isolated from fermented rice water in promoting the proliferation and migration of human dermal fibroblasts are still limited. (Mo et al., 2022, Lin et al., 2025, Demir & Aslim, 2025). This study aims to evaluate the efficacy of probiotics from fermented rice water in enhancing the proliferation and migration of human dermal fibroblasts or in animal studies.

METHOD

This systematic review will be conducted in accordance with the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines. The literature search for this systematic review was conducted in major electronic databases, including PubMed, Scopus, and the Cochrane Library. The search was limited to articles published between January 1, 2015, and November 30, 2025. The search strategy was developed using *Boolean* operators (AND and OR) based on the PICOS (Population, Intervention, *Comparison*, *Outcome*, and *Study*) framework that we established. The keywords and search strings used for each database are presented in Table 1. Literature search results were managed using Rayyan.ai. In addition to database searches, the reference lists of all eligible studies were also manually checked to identify other relevant articles. Two reviewers independently screened the titles, abstracts, and full texts of the identified studies based on the predetermined inclusion and exclusion criteria. Disagreements between the two reviewers were resolved through discussion and, if necessary, by consulting a third independent reviewer to ensure that all relevant studies were included.

Table 1.
Literature Search Strategy

Electronic Databases	Search Strategy	Findings
PubMed	rice fermentation OR fermented rice AND Lactobacillus OR probiotic AND fibroblast AND proliferation OR migration	928
Scopus	rice fermentation OR fermented rice AND Lactobacillus	396
Cochrane Library	rice fermentation OR fermented rice AND Lactobacillus	119

Table 2.
PICOS Framework

Population	Human dermal fibroblasts (in vitro) or animal models studying the effects of dermal fibroblasts
Intervention	Probiotics derived from fermented rice water, fermented rice products, or rice-based probiotic formulations.
Comparison	Untreated control group or placebo control group
Outcome	Cell proliferation (primary), cell migration (primary).
Study	RCT/Cohort Study/Case-control study/Animal Study

Inclusion and Exclusion Criteria

All studies were evaluated using a predetermined PICOS framework to ensure systematic selection, with details listed in Table 2.

Population

Human dermal fibroblasts as an in vitro model (primary cell culture or *cell line* such as HDFa, HDF, Hs68, CCD986sk) or animal models that assess specific dermal fibroblast parameters through histological analysis or molecular markers related to fibroblast function.

Intervention

Probiotics or derived from fermented rice water, including *Lactobacillus* strains (*L. plantarum, L. fermentum*), *Bacillus*, or fermentative fungi (*Aspergillus oryzae*). The form of intervention can be live probiotics, *heat-killed*, fermentation filtrates, extracts, bioactive peptides, or *exopolysaccharides* resulting from rice fermentation.

Comparator
Untreated control group, *vehicle solution*, or placebo. Single-arm studies without controls may be included if they provide baseline data and outcome measurements at various time points that allow for the assessment of changes.

Outcome
Primary outcomes include fibroblast proliferation (MTT, CCK-8, BrdU assay, cell counting) and fibroblast migration (scratch assay, transwell assay). Secondary outcomes: collagen synthesis, ECM gene expression (COL1A1, COL3A1, elastin), protein expression, MMP activity, oxidative stress markers, collagen gel contraction.

Study Design
This review will include RCTs, prospective and retrospective cohort studies with a minimum of 5 subjects per group, and animal studies evaluating dermal fibroblasts. Exclusions include pilot studies, *case reports*, *case series <5 participants*, *systematic reviews*, *meta-analyses*, *conference abstracts* without *full text*, and non-mammalian preclinical studies.

Data Extraction
Two reviewers will extract data from all studies included in the period 2015–2025. The extracted information will be organized into two tables. The first table will record study characteristics, including the name of the first author and year of publication, study design, and specific details about the intervention and comparator. The second table will present the results of each study, including cell proliferation and cell migration, as well as mechanisms and ECM.

Study Bias Assessment
The risk of bias in all studies included in this research will be evaluated by two assessors, using *SYRCLE Risk of Bias* (SYRCLE RoB). This assessment will be used for animal experimental studies to assess potential bias across all predefined domains, including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other sources of bias relevant to animal research. During this process, any differences between the two independent assessors will be resolved through discussion; however, if consensus cannot be reached, a third assessor will be consulted to make a final decision, thereby ensuring accurate bias assessment prior to the data synthesis stage. All bias domains are visualized using RevMan 5.4.1.

RESULT
Study Selection and Inclusion Process
The studies included in this analysis are shown in Figure 1. Our initial search strategy identified a total of 1,443 studies from electronic databases. After removing 431 duplicates, 1012 studies were evaluated based on their titles and abstracts, leaving 6 studies that were then screened through the full text. Of these, 2 studies were excluded because they did not meet the inclusion criteria. After a careful screening process, we obtained 4 studies that were considered eligible and included in this final analysis.

Study characteristics
This systematic review assessed four experimental studies consisting of in vitro tests on human dermal fibroblasts and in vivo experiments using diabetic mouse models or models that experienced aging due to sun exposure. The interventions studied included probiotics and bioactive metabolites derived from fermented rice water, specifically *Aspergillus oryzae* fermentation filtrate, *Bacillus cereus* strain, *Lactobacillus plantarum* polypeptide, and filtrate containing succinic acid. These

interventions were administered at varying concentrations, ranging from 0.25 mg/mL to 10 mg/mL in cell cultures, or via topical and oral routes in animal models. All studies assessed efficacy by comparing these interventions to untreated negative controls, *vehicles*, or stress-induced models. All study characteristics can be found in Table 3.

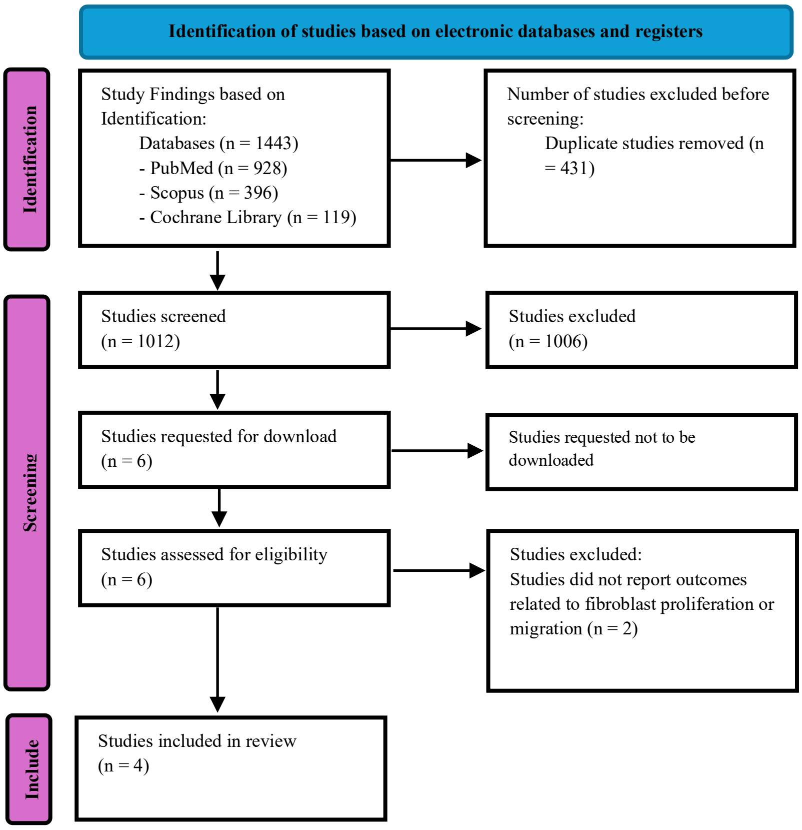

Figure 1. Study selection diagram based on PRISMA

Table 3.
Study Characteristics

Study (Author, Year)	Study Design	Population/Model	Intervention (Source & Concentration)	Comparator/Control
Chen et al. (2024)	In vitro experimental	Human Dermal Fibroblasts (FB)	RRFA (Red Rice *Aspergillus oryzae* Fermentation filtrate). Concentration: 1.25% & 3.00% (v/v)	• Negative Control (DMEM) • Positive Control (10% Calf Serum)
Choudhury et al. (2025)	In vivo experimental	Male Swiss Albino mice (Streptozotocin-induced diabetes model; Excision wound model)	Probiotic: *Bacillus* cereusBWN SC strain (isolated from fermented rice water). Synbiotic: Probiotic + Inulin. Dose: Topical & Oral (10^8 CFU)	• Diabetes Control (No treatment) • Non-diabetic control
Li et al. (2025)	In vitro experiment	Human Dermal Fibroblasts (HDFs) exposed to UVA	Maifuyin (Rice fermentation filtrate) & bioactive components (Succinic Acid, Choline). Concentration: 1.25–10 mg/mL	• Control (No treatment) • Model (UVA irradiation)
Mo et al. (2022)	In vitro and in vivo experiments	1. Human Skin Fibroblasts (HSFs) 2. Kunming Mice (UVA-induced damage model)	RFP (Rice Fermentation Polypeptides from *Lactobacillus plantarum*). Concentration: 0.31–20 g/L (*in vitro*); 1 g/L (*in vivo*)	• Control / UVA Model • Positive Control (GSH / Rice Peptide)

RRFA: Red Rice Fermentation by Aspergillus oryzae; RFP: Rice Fermentation Polypeptides; DMEM: Dulbecco's Modified Eagle Medium; CFU: Colony Forming Units; GSH: Glutathione (positive antioxidant control); v/v: volume/volume; UVA: Ultraviolet A radiation

Study Outcomes

Cell Proliferation

Studies included in this review consistently show that interventions derived from fermented rice significantly increase fibroblast proliferation. Chen et al. reported a significant increase in cell viability with *Aspergillus oryzae* fermentation filtrate, reaching up to 116% compared to the control group. Similarly, Mo et al. observed a dose-dependent proliferative effect with rice polypeptides, which maintained high cell viability even under UVA-induced stress. Li et al. further established cytoprotective capacity, showing that components such as Maifuyin and succinic acid effectively rescued cell viability suppressed by photoaging. These findings indicate that rice probiotic metabolites not only stimulate proliferation under normal conditions but also maintain fibroblast survival against oxidative reactions.

Migration and Wound Healing

Evidence from in vivo models strongly supports the effectiveness of using probiotics from rice water fermentation in accelerating wound healing, a process that depends on fibroblast migration. Choudhury et al. showed that diabetic mice treated with *Bacillus cereus* rice water synbiotics exhibited significantly faster wound contraction, reducing the remaining wound area to approximately 27% on day 14 compared to 71% in the untreated control group. Additionally, histological assessment by Mo et al. revealed that treatment with rice polypeptides resulted in smoother epidermis and denser dermal collagen organization in damaged skin. These macroscopic and microscopic improvements indicate that the intervention actively enhances fibroblast migration and tissue remodeling capabilities.

Mechanisms and Extracellular Matrix Synthesis

The regenerative effects are mediated through specific molecular mechanisms involving *Extracellular Matrix* (ECM) regulation and antioxidant defense. Chen et al. found a significant increase in the expression of mRNA proteins, including Collagen I, Collagen III, and Elastin. The use of probiotics from rice water fermentation as an intervention also alleviated cellular aging and oxidative stress. Li et al. reported a decrease in inflammatory pathways such as TNF and NF-κB, as well as a decrease in MMP-1 expression. Furthermore, Mo et al. found that activation of the NRF2 signaling pathway, which triggers nuclear translocation of transcription factors and increases the expression of endogenous antioxidant enzymes such as SOD and CAT, creates a favorable environment for fibroblast function.

All findings from the included studies can be seen in Table 4.

Table 4.
Study outcomes

Study	Cell Proliferation	Cell Migration / Wound Healing	Mechanism & ECM
Chen et al. (2024)	Significant Increase (+) RRFA significantly increased fibroblast proliferation compared to the control. • RRFA 1.25%: Viability 116.63%±6.04% • RRFA 3.0%: Viability 112.64%±4.65%	Not reported (*in vitro*)	ECM Synthesis: Upregulation of mRNA expression of *Collagen I* (17%↑), *Collagen III* (47%↑), and *Elastin* (159%↑). Antioxidant: Inhibition of ROS production post-UVA irradiation.
Choudhury et al. (2025)	Implied (*in vivo*) Accelerated wound healing indicates robust fibroblast proliferation in	Significant acceleration (+) Wound contraction rate	Tissue Repair: Re-epithelialization and collagen deposition improve.

Study	Cell Proliferation	Cell Migration / Wound Healing	Mechanism & ECM
	granulation tissue.	significantly increased on Day 14: • Synbiotic: 27.2% remaining wound area (most effective) • Diabetes control: 71.1% remaining wound area	Metabolic: Improvement in fasting glucose levels ( ) and renal parameters (Urea, Creatinine).
Li et al. (2025)	Cytoprotection/Rescue (+) • Maifuyin (2.5–10 mg/mL) enhances proliferation in normal cells. • Maifuyin & Succinic Acid restore cell viability reduced by UVA irradiation (rescue effect). Significant Increase (+)	Not reported (*in vitro*)	Anti-Senescence: Inhibition of SA-β-gal activity (senescence marker) and MMP-1 expression. Pathway: Downregulation of the TNF, MAPK, and NF-κB pathways, as well as inhibition of CXCL2 chemokine secretion.
Mo et al. (2022)	Significant increase (+) RFP (0.31–20 g/L) increased HSF proliferation in a dose-dependent manner and protected cells from UVA-induced death (viability >90% vs. model ~47%).	Structural Improvement (*in vivo*) Although cell migration was not measured directly, skin histology showed a denser dermal collagen structure and smoother epidermis (indicators of tissue remodeling).	Antioxidant Defense: Activation of the NRF2 pathway (nuclear translocation) and upregulation of antioxidant enzymes (HO-1, NQO1, SOD, CAT, GSH-Px).

(+) = Positive effect/statistically significant increase; ↑ = Increase/upregulation; ROS = Reactive Oxygen Species; ECM = Extracellular Matrix; MMP-1 = Matrix Metalloproteinase-1; SA-β-gal = Senescence-Associated β-galactosidase; NRF2 = Nuclear factor erythroid 2-related factor 2; HO-1 = Heme Oxygenase-1; NQO1 = NAD(P)H Quinone Oxidoreductase 1; SOD = Superoxide Dismutase; CAT = Catalase; GSH-Px = Glutathione Peroxidase

Study Bias Risk

Overall, the studies showed a low risk of bias in most key domains, particularly in terms of *baseline characteristics*, *blinding* of *caregivers* and *outcome assessors*, *random outcome assessment*, completeness of outcome data, and selective reporting of outcomes. However, there were consistent methodological weaknesses in the domains *of sequence generation*, *allocation concealment*, and *random housing*, where the majority of studies (75%) had unclear risk of bias due to inadequate methodological information in the publications. Choudhury et al. (2025) demonstrated the best methodological quality with only two domains *of unclear risk*, while Chen et al. (2024) and Li et al. (2024) each had four domains of unclear risk. The "*other sources of bias*" domain also showed unclear risk in 75% of studies, indicating potential additional bias that could not be definitively assessed from the available information. The visualization of bias risk can be seen in Figure 2.

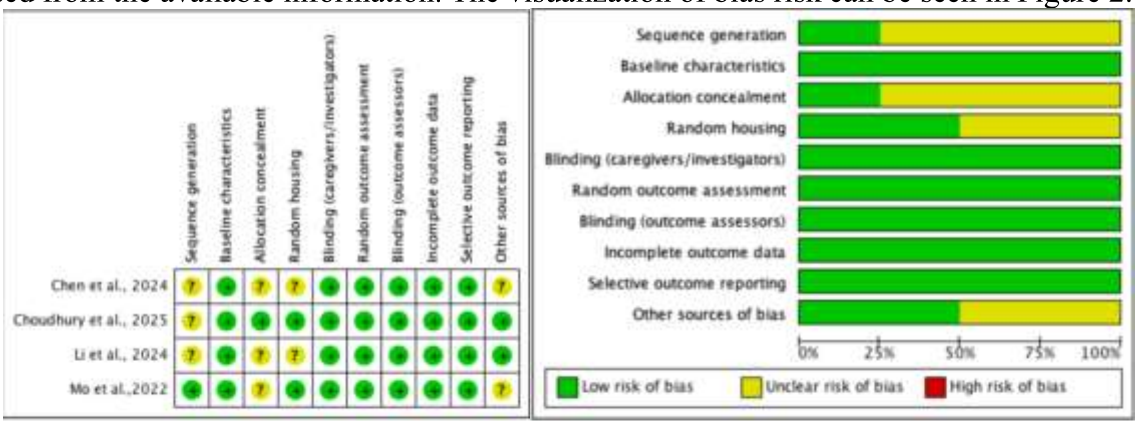

Figure 2. RoB using *SYRCLE Risk of Bias* for animal studies

DISCUSSION

This systematic review confirms that fermented rice water (FRW) has a strong biological basis for enhancing fibroblast proliferation and migration, rather than being merely an empirical treatment without a clear mechanism. (Li et al., 2025). Quantitative data show an increase in fibroblast viability of up to 116% and accelerated wound closure in a diabetic model from 27% to 71% compared to controls. (Chen et al., 2024, Choudhury et al., 2025) Underscoring that fibroblasts play a major role as effector cells in the tissue proliferation process.(Bioactive metabolites produced by fermentation by microorganisms such as Aspergillus oryzae and Bacillus cereus appear to interact with specific receptors on the surface of fibroblast cells, rather than just providing non-specific hydration effects as may occur with ordinary rice water. Research shows that collagen is a key component of the extracellular matrix that regulates various phases of wound healing, from hemostasis and inflammation to tissue remodeling, and optimal collagen synthesis is highly dependent on healthy fibroblast function.(FRW appears to be able to modulate the fibroblast microenvironment through several interrelated molecular pathways, creating conditions conducive to efficient tissue regeneration.(Choudhury et al., 2025, Mo et al., 2022, Li et al., 2025)

The upregulation of collagen mRNA observed in these studies, with increases of 17% for Collagen I, 47% for Collagen III, and 159% for Elastin, provides important insights into how FRW affects the architecture of the extracellular matrix. (Chen et al., 2024, Li et al., 2025). The ratio of Collagen I to Collagen III is critical in determining the final quality of wound healing and scar formation.(In the early stages of healing, Collagen III is synthesized first as a temporary scaffolding that provides initial structure, then gradually replaced by Collagen I, which provides maximum tensile strength to the healing tissue. (Mathew-Steiner et al., 2021, Rodrigues et al., 2019, Stewart et al., 2025). This transition process is crucial because an imbalanced ratio can lead to keloid or hypertrophic scar formation.(A dramatic increase in elastin expression is also noteworthy, as elastin is responsible for maintaining skin elasticity and preventing the formation of rigid, inflexible scar tissue. Histological analysis shows that fibroblasts exposed to FRW produce denser and better-organized collagen, unlike the fragmented and disorganized collagen often found in chronic wounds or aging skin.(FRW can be considered a superior extracellular matrix bio-stimulator due to the complexity of its fermented metabolites that work synergistically, unlike single synthetic peptides that may only target one specific pathway. (Choudhury et al., 2025, Mo et al., 2022, Mathew-Steiner et al., 2021)

The antioxidant pathway mediated by Nuclear factor erythroid 2-related factor 2 (NRF2) emerges as an important protective mechanism in the context of oxidative stress that often accompanies tissue damage.(Studies show that bioactive peptides from Lactobacillus plantarum and Maifuyin components can restore the viability of fibroblasts exposed to UVA radiation, which normally causes significant cell dysfunction.(NRF2 functions as a master transcription factor that regulates the expression of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and heme oxygenase-1 (HO-1), which collectively reduce the burden of reactive oxygen species (ROS) in cells.(UV exposure and chronic inflammatory conditions induce excessive ROS production, causing fibroblasts to undergo cell cycle arrest, inhibiting the proliferation and migration necessary for wound healing.(FRW metabolites appear capable of breaking this destructive cycle by activating the NRF2 pathway, allowing fibroblasts to remain functional even in toxic and free radical-rich environments.(This is highly relevant for clinical conditions such as chronic wounds in diabetes or photoaging, where fibroblasts must function optimally amidst a microenvironment saturated with persistent inflammatory mediators and oxidative stress.(Li et al., 2025, Liu, Yang, et al., 2021, Feng et al., 2024, Liu, Guo, et al., 2025)

Inflammatory modulation through the reduction of tumor necrosis factor-alpha (TNF-α), nuclear factor kappa B (NF-κB), and inhibition of matrix metalloproteinase-1 (MMP-1) indicates that FRW is capable of transforming the wound environment from a chronic inflammatory state to one that supports active regeneration.(In diabetic wounds and photoaged skin, fibroblasts often enter a phase of senescence (cellular aging) and begin to secrete a senescence-associated secretory phenotype (SASP), a mixture of pro-inflammatory cytokines, proteases, and other bioactive molecules that actually inhibit healing.(Senescent fibroblasts not only lose their ability to proliferate, but also actively secrete MMPs that degrade newly formed collagen, creating a destructive cycle in which inflammation triggers senescence, and senescence further exacerbates inflammation.(Excessive TNF-α has been shown to inhibit wound healing by increasing NF-κB activity, which in turn induces more inflammatory mediators and proteases. Succinic acid and other bioactive metabolites in FRW appear to have a dual-action effect by inhibiting collagen degradation through MMP-1 suppression while simultaneously suppressing chronic inflammatory pathways through TNF-α and NF-κB modulation.(This intervention opens a therapeutic window that allows fibroblasts to return to the proliferative and migratory mode necessary for effective tissue regeneration, transforming stagnant wounds into actively healing wounds.(Choudhury et al., 2025, Ashcroft et al., 2000, Han et al., 2001)

Variations in microbial strains within FRW, ranging from Lactobacillus plantarum, Bacillus cereus, to Aspergillus oryzae, produce distinct metabolite profiles with varying biological activities.(The fermentation process produces bioactive polypeptides and organic acids that are not present in non-fermented rice water, explaining why FRW has significantly higher efficacy compared to regular rice water.(Studies show that administering synbiotics (a combination of probiotics with prebiotics such as inulin) produces superior outcomes compared to probiotics alone, indicating a synergistic effect between microorganisms and fermented substrates.(The biological effects of FRW are highly dependent on strain-specific characteristics and the type of substrate used; brown rice versus white rice can produce different antioxidant peptide profiles due to differences in initial nutrient content.(Research on topical and oral probiotics indicates that certain Lactobacillus strains can enhance wound healing by modulating the immune response, reducing pathogenic bacterial colonization, and promoting re-epithelialization without causing harmful immune reactions.((29,30,31,32,40) These findings are important for the development of standardized clinical protocols, where the selection of microbial strains, fermentation methods, and final formulations must be optimized to achieve reliable therapeutic consistency.(Bădăluță et al., 2024, Knackstedt et al., 2020, Yu et al., 2019)

Although preclinical evidence shows promising results, the majority of studies reviewed are still limited to in vitro and animal models, with a risk of bias assessed as "unclear" , especially in terms of allocation concealment. Heterogeneity in the doses used, fermentation duration, and preparation methods makes it difficult to directly compare results between studies and complicates efforts to standardize clinical applications. Human RCTs are needed to validate the efficacy of FRW in a real-world clinical setting, with standardized topical formulations and clear application protocols. Key challenges include determining the optimal dose, appropriate application frequency, effective duration of therapy, and characterization of specific microbial strains for particular dermatological conditions whether strains effective for diabetic wounds are the same as those optimal for anti-aging or other inflammatory skin conditions. Nevertheless, the cumulative evidence supports the conclusion that FRW has great potential as a cost-effective, accessible, and natural-based adjuvant therapy for various pathological wound conditions and anti-aging applications. Future research should focus on transitioning, bridging traditional medicine with modern molecular dermatology through research and evidence-based approaches.

CONCLUSION

Pre-clinical evidence suggests that fermented rice water has promising biological potential in enhancing fibroblast proliferation and migration through multi-pathway modulation involving extracellular matrix synthesis, NRF2 activation, and chronic inflammation suppression. Although quantitative data from in vitro and animal studies show promising results, evidence for clinical application still requires validation through human RCTs with standardized protocols. FRW has the potential to be a cost-effective and accessible adjuvant therapy for pathological wound management and anti-aging, bridging traditional medicine with modern molecular dermatology approaches.

REFERENCES

Knoedler S, Broichhausen S, Guo R, Dai R, Knoedler L, Kauke-Navarro M, et al. Fibroblasts – the cellular choreographers of wound healing. Front Immunol. 2023 Aug 14;14:1233800.

Chen M, Sun Y, Zhu L, Li L, Zhao Y. Study on the Skincare Effects of Red Rice Fermented by Aspergillus oryzae In Vitro. Molecules. 2024 Apr 30;29(9):2066.

Golebiewska EM, Poole AW. Platelet secretion: From haemostasis to wound healing and beyond. Blood Rev. 2015 May;29(3):153–62.

Mathew-Steiner SS, Roy S, Sen CK. Collagen in Wound Healing. Bioengineering. 2021 May 11;8(5):63.

Gharbia FZ, Abouhashem AS, Moqidem YA, Elbaz AA, Abdellatif A, Singh K, et al. Adult skin fibroblast state change in murine wound healing. Sci Rep. 2023 Jan 17;13(1):886.

Xue M, Jackson CJ. Extracellular Matrix Reorganization During Wound Healing and Its Impact on Abnormal Scarring. Adv Wound Care. 2015 Mar;4(3):119–36.

Choudhury S, Saha I, Bandyopadhyay B, Banerjee P. Probiotic and Synbiotic Isolates From Whey Water and Fermented Rice Water Exert Compelling Wound‐Healing Efficacy in a Diabetic Mouse Model. Biotechnol Appl Biochem. 2025 June 18;bab.70013.

Tsai WH, Chou CH, Chiang YJ, Lin CG, Lee CH. Regulatory effects of Lactobacillus plantarum - GMNL6 on human skin health by improving skin microbiome. Int J Med Sci. 2021;18(5):1114–20.

Yang F, Hu Y, Wu M, Guo M, Wang H. Biologically Active Components and Skincare Benefits of Rice Fermentation Products: A Review. Cosmetics. 2025 Feb 13;12(1):29.

Mo Q, You S, Fu H, Wang D, Zhang J, Wang C, et al. Purification and Identification of Antioxidant Peptides from Rice Fermentation of Lactobacillus plantarum and Their Protective Effects on UVA−Induced Oxidative Stress in Skin. Antioxidants. 2022 Nov 25;11(12):2333.

Lin S, Tang L, Xu N. Research progress and strategy of FGF21 for skin wound healing. Front Med. 2025 Mar 31;12:1510691.

Jo CS, Myung CH, Yoon YC, Ahn BH, Min JW, Seo WS, et al. The Effect of Lactobacillus plantarum Extracellular Vesicles from Korean Women in Their 20s on Skin Aging. Curr Issues Mol Biol. 2022 Jan 21;44(2):526–40.

Demir A, Aslim B. Investigation of the multifaceted wound healing effect of exopolysaccharide (EPS) produced from the probiotic strain Lactiplantibacillus plantarum GD2 in vitro and in ovo. Sci Rep. 2025 Oct 21;15(1):36512.

Li Y, Guo M, Li L, Yang F, Xiong L. Effects of rice fermentation and its bioactive components on UVA‐induced oxidative stress and senescence in dermal fibroblasts. Photochem Photobiol. 2025 Mar;101(2):392–403.

Mathew-Steiner SS, Roy S, Sen CK. Collagen in Wound Healing. Bioengineering. 2021 May 11;8(5):63.

Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound Healing: A Cellular Perspective. Physiol Rev. 2019 Jan 1;99(1):665–706.

Gardeazabal L, Izeta A. Elastin and collagen fibers in cutaneous wound healing. Exp Dermatol. 2024 Mar;33(3):e15052.

Stewart DC, Brisson BK, Yen WK, Liu Y, Wang C, Ruthel G, et al. Type III Collagen Regulates Matrix Architecture and Mechanosensing during Wound Healing. J Invest Dermatol. 2025 Apr;145(4):919-938.e14.

Zhang J, Yu H, Man MQ, Hu L. Aging in the dermis: Fibroblast senescence and its significance. Aging Cell. 2024 Feb;23(2):e14054.

Hiebert P, Werner S. Regulation of Wound Healing by the NRF2 Transcription Factor—More Than Cytoprotection. Int J Mol Sci. 2019 Aug 8;20(16):3856.

Wang M xuan, Zhao J, Zhang H, Li K, Niu L zhi, Wang Y ping, et al. Potential Protective and Therapeutic Roles of the Nrf2 Pathway in Ocular Diseases: An Update. Oxid Med Cell Longev. 2020 Mar 23;2020:1–22.

Liu T, Lv YF, Zhao JL, You QD, Jiang ZY. Regulation of Nrf2 by phosphorylation: Consequences for biological function and therapeutic implications. Free Radic Biol Med. 2021 May;168:129–41.

Saha S, Buttari B, Panieri E, Profumo E, Saso L. An Overview of Nrf2 Signaling Pathway and Its Role in Inflammation. Molecules. 2020 Nov 23;25(22):5474.

Liu Y, Yang X, Liu Y, Jiang T, Ren S, Chen J, et al. NRF2 signaling pathway: New insights and progress in the field of wound healing. J Cell Mol Med. 2021 July;25(13):5857–68.

Feng C, Chen X, Yin X, Jiang Y, Zhao C. Matrix Metalloproteinases on Skin Photoaging. J Cosmet Dermatol. 2024 Dec;23(12):3847–62.

Liu C, Guo J, Guan L, Li J, Xu B, Zhao H. Protective effects of melatonin on stroke in diabetic mice: central and peripheral inflammation modulation. Stroke Vasc Neurol. 2025 Oct;10(5):582–93.

Ashcroft GS, Lei K, Jin W, Longenecker G, Kulkarni AB, Greenwell-Wild T, et al. Secretory leukocyte protease inhibitor mediates non-redundant functions necessary for normal wound healing. Nat Med. 2000 Oct;6(10):1147–53.

Mahmoud NN, Hamad K, Al Shibitini A, Juma S, Sharifi S, Gould L, et al. Investigating Inflammatory Markers in Wound Healing: Understanding Implications and Identifying Artifacts. ACS Pharmacol Transl Sci. 2024 Jan 12;7(1):18–27.

Quan T, Xia W, He T, Calderone K, Bou-Gharios G, Voorhees JJ, et al. Matrix Metalloproteinase-1 Expression in Fibroblasts Accelerates Dermal Aging and Promotes Papilloma Development in Mouse Skin. J Invest Dermatol. 2023 Sept;143(9):1700-1707.e1.

Buruiană A, Gheban BA, Gheban-Roșca IA, Georgiu C, Crișan D, Crișan M. The Tumor Stroma of Squamous Cell Carcinoma: A Complex Environment That Fuels Cancer Progression. Cancers. 2024 Apr 29;16(9):1727.

Wyles S, Brandt E, Nelson T. Stem Cells: The Pursuit of Genomic Stability. Int J Mol Sci. 2014 Nov 14;15(11):20948–67.

Liu T, Zhang L, Joo D, Sun SC. NF-κB signaling in inflammation. Signal Transduct Target Ther. 2017 July 14;2(1):17023.

Han YP, Tuan TL, Wu H, Hughes M, Garner WL. TNF-α stimulates activation of pro-MMP2 in human skin through NF-κB mediated induction of MT1-MMP. J Cell Sci. 2001 Jan 1;114(1):131–9.

Bădăluță VA, Curuțiu C, Dițu LM, Holban AM, Lazăr V. Probiotics in Wound Healing. Int J Mol Sci. 2024 May 24;25(11):5723.

Knackstedt R, Knackstedt T, Gatherwright J. The role of topical probiotics on wound healing: A review of animal and human studies. Int Wound J. 2020 Dec;17(6):1687–94.

Yu Y, Dunaway S, Champer J, Kim J, Alikhan A. Changing our microbiome: probiotics in dermatology. Br J Dermatol. 2019 July 28;bjd.18088.

Umekar M, Chaudhary AA, Manghani M, Shidhaye S, Khajone P, Mahore J, et al. Probiotics in Nanotechnology-Driven Wound Healing: From Mechanistic Insight to Clinical Promise. Pharmaceutics. 2025 June 21;17(7):805.

Nami Y, Abdullah N, Haghshenas B, Radiah D, Rosli R, Yari Khosroushahi A. A newly isolated probiotic Enterococcus faecalis strain from vaginal microbiota enhances apoptosis of human cancer cells. J Appl Microbiol. 2014 Aug;117(2):498–508.