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REVIEW ARTICLE

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High-Protein Composition of Freshwater Fish and Its Therapeutic Role in Chronic Infections and Burn Wound Healing

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ABSTRACT

Background: Freshwater fish are an affordable and accessible source of high-quality protein. Their amino acid profiles and bioactive compounds support tissue repair, immune modulation, and recovery from chronic infections and burns.

Objective: To explore the protein composition of commonly consumed freshwater fish species and their potential role in accelerating healing in chronic diseases and burn injuries.

Methods: This literature-based review compiles existing biochemical data on high-protein freshwater fish such as Clarias batrachus (catfish), Oreochromis niloticus (tilapia), and Pangasius hypophthalmus (pangasius), with emphasis on their protein structure, essential amino acid content, and therapeutic implications in healing processes.

Results: Freshwater fish species contain 18–24% high-quality protein. Key amino acids such as arginine, glutamine, glycine, and leucine are abundant, supporting collagen synthesis, immune responses, and tissue regeneration. These proteins have been shown to promote angiogenesis, fibroblast activity, and epithelialization in infected wounds and burn injuries.

Conclusion: Regular intake of freshwater fish with high protein content provides essential nutrients that significantly enhance wound healing and infection recovery. Their integration into clinical nutritional support should be encouraged for patients with chronic wounds or burn injuries.

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Introduction

Protein plays a pivotal role in numerous physiological processes, particularly in tissue regeneration, modulation of inflammatory pathways, and restoration of immune competence. These functions become critically important in patients suffering from chronic infections or extensive tissue injuries such as burns. Adequate protein intake has been shown to enhance wound healing outcomes, improve immune surveillance, and reduce the risk of infection-related complications during recovery phases [1,2]. In catabolic states such as severe trauma or infection, protein turnover increases significantly, necessitating a higher intake to support nitrogen balance and anabolic responses [3]. Additionally, sufficient dietary protein facilitates the synthesis of structural proteins like collagen and elastin, essential for dermal remodeling and angiogenesis [4].

Among the various dietary sources of protein, freshwater fish are increasingly recognized for their affordability, bioavailability, and nutritional completeness, making them a vital component in diets across many low- and middle-income regions [5]. Fish such as Clarias gariepinus (catfish), Oreochromis niloticus (tilapia), and Pangasius hypophthalmus (pangasius) are rich in high-quality proteins that contain all nine essential amino acids necessary for collagen synthesis, cellular regeneration, and enzymatic activity critical in wound repair [6]. These amino acids include leucine, isoleucine, lysine, methionine, phenylalanine, threonine, tryptophan, valine, and histidine—each playing a role in tissue regeneration and immune modulation [7].

Moreover, protein from freshwater fish is often accompanied by beneficial micronutrients such as selenium, zinc, and omega-3 fatty acids, which synergize in the healing process by reducing oxidative stress and enhancing epithelialization [6,8]. For instance, zinc acts as a cofactor in numerous metalloenzymes involved in DNA synthesis and cell proliferation, while selenium contributes to antioxidant defense via glutathione peroxidase activity [9]. Studies in burn patients have demonstrated that diets enriched with fish-derived protein accelerate granulation tissue formation, reduce infection rates, and shorten hospital stays [2,10]. In infection-related disorders, adequate protein intake supports leukocyte proliferation and immunoglobulin synthesis, improving the host's resistance to pathogens [1,7]. Furthermore, the anti-inflammatory properties of long-chain omega-3 fatty acids found in fish oil may help regulate cytokine responses and reduce systemic inflammation in critically ill patients [8,9].

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Considering these benefits, promoting the consumption of freshwater fish as a dietary strategy can offer significant advantages in public health nutrition, particularly in resource-limited settings where protein-energy malnutrition and infection burden remain high. Nutrition-based interventions that incorporate locally available, high-protein foods like freshwater fish can effectively address multiple health challenges, including delayed wound healing, immunosuppression, and prolonged recovery in both hospital and community contexts [5,10].

High-Protein Composition of Freshwater Fish

Freshwater fish are notable for their high biological value (BV) protein, meaning they are efficiently absorbed and utilized by the human body. Below is a breakdown of protein composition in selected freshwater species:

Fish Species	Protein Content (per 100g)	Key Amino Acids
Clarias batrachus	20.3 g	Arginine, Glutamine, Glycine, Leucine
Oreochromis niloticus	19.8 g	Lysine, Methionine, Valine
Pangasius hypophthalmus	18.5 g	Histidine, Isoleucine, Phenylalanine

Arginine plays a role in collagen formation and immune enhancement, while **glutamine** supports cell proliferation, especially in gut and skin tissues. **Glycine** is a major constituent of collagen, and **leucine** stimulates muscle protein synthesis.

Therapeutic Role in Chronic Infections and Burns

In Chronic Infections

- Proteins from freshwater fish provide substrates for immunoglobulin and cytokine production.
- Amino acids like arginine enhance nitric oxide production, which aids immune cells in pathogen elimination
- Increased dietary protein improves serum albumin levels, critical for infection recovery.

In Burn Wound Healing

- Burns lead to hypermetabolic states and protein catabolism. Freshwater fish protein:
- Enhances **collagen deposition**, improving wound tensile strength.
- Promotes **angiogenesis** and **epithelialization**, speeding skin regeneration
- Reduces inflammation via anti-inflammatory amino acids like glycine
- Clinical studies have demonstrated faster wound closure and reduced hospital stay in patients supplemented with high-protein diets from fish.

Methods

This study employed a **randomized controlled trial (RCT)** design to evaluate the effectiveness of freshwater fish protein intake in accelerating wound healing among patients with chronic or post-surgical wounds. A total of **240 participants** were selected using **simple random sampling** from several healthcare facilities in South Sulawesi and divided into two groups: an intervention group (n = 120), which received daily freshwater fish as the primary protein source, and a control group (n = 120), which received protein from non-fish sources.

The intervention group was provided with **Channa striata (snakehead fish)** or **Clarias gariepinus (catfish)** as the main protein source, administered **three times daily (morning, afternoon, and evening)** in servings of 3**00–500 grams per meal.** The fish preparation methods were alternated daily to maintain palatability and adherence, including **grilled, fried, and boiled cooking styles**. Participants consumed their meals under supervision at the health facility or during home visits by trained community nurses.

The study was conducted over a **9-month period**, from **January to September 2023**, with **weekly monitoring and evaluation**. Each participant underwent a physical assessment by clinical nurses and research staff, focusing on the following wound characteristics:

- **Wound Size** (length, width, depth)
- **Wound Bed Condition** (necrotic tissue, granulation, exudate)
- **Wound Edges** (adhesion, epithelialization)
- **Pain at the Wound Site**
- **Signs of Infection**
- **Wound Color and Moisture**

These parameters were documented using a **standardized wound evaluation** checklist adapted from WHO wound care guidelines and contextualized for use in local clinical practice. This checklist enabled consistent weekly tracking of wound healing progression. Additional data were collected on daily dietary intake, body weight, hemoglobin levels, and serum albumin levels to monitor participants' nutritional and immune status.

Prior to the study, **ethical approval** was granted by the **Health Research Ethics Committee of Poltekkes Kemenkes Makassar** under approval number **387/2023**. Written informed consent was obtained from all participants. The study followed the ethical principles outlined in the **Declaration of Helsinki** and ensured confidentiality, voluntary participation, and the right to withdraw at any time.

This investigation was conducted based on the hypothesis that **fish-based protein**, particularly from commonly available freshwater species, can significantly enhance wound healing outcomes through its nutritional and immunological benefits, as suggested by existing literature [11].

Results

A total of 240 participants completed the 5-week intervention and weekly evaluations without significant dropout. Both groups were comparable in terms of baseline demographics, nutritional status, and wound type.

Weekly Wound Evaluation

Over the 5-week observation period, participants in the **intervention group** (receiving freshwater fish protein)

demonstrated **significantly faster wound healing** compared to the control group. Improvements were observed in wound size reduction, granulation tissue formation, epithelialization, and reduction in signs of infection.

- **Week 1:** Minimal changes were observed in both groups; however, 28.3% of participants in the intervention group showed early granulation formation versus 15.8% in the control group.
- **Week 2:** Significant improvement in wound bed granulation and reduced exudate in the intervention group ($p<0.05$).
- **Week 3:** Wound size in the intervention group had reduced by an average of 35.6%, compared to 18.2% in the control group.
- **Week 4:** 62.5% of the intervention group had epithelialization initiated, compared to 37.5% in the control group.
- **Week 5:** 84.2% of the intervention group achieved >75% wound closure with no infection signs, while the control group reached only 51.7% ($p<0.01$).

These findings align with previous evidence highlighting the role of high-quality protein and amino acids from freshwater fish in enhancing tissue repair mechanisms and modulating inflammation [12].

Table 1 summarizes the baseline demographic and clinical characteristics of the participants enrolled in the study, comparing the intervention and control groups prior to the administration of the dietary protein intervention using freshwater fish. The analysis shows no statistically significant differences between the two groups across all measured variables ($p>0.05$), confirming that both groups were comparable at baseline and ensuring the validity of subsequent outcome comparisons.

Table 1: Baseline Characteristics of Participants

Variable	Intervention (n = 120)	Control (n = 120)	p-value
Age (mean ± SD)	46.2 ± 9.3 years	45.7 ± 10.1 years	0.712
Male (%)	54 (45.0%)	57 (47.5%)	0.682
BMI (mean ± SD)	22.8 ± 1.9 kg/m²	22.6 ± 2.0 kg/m²	0.549
Albumin (mean ± SD, g/dL)	3.4 ± 0.5	3.5 ± 0.6	0.434
Wound Type (Post-op / Chronic)	64 / 56	66 / 54	0.787

Age Distribution

The mean age of participants in the intervention group was **46.2 ± 9.3 years,** while in the control group it was **45.7 ± 10.1 years** ($p=0.712$). This indicates that the age distribution between both groups was statistically similar, reducing the risk of age-related confounding effects on wound healing outcomes.

Sex Distribution

In terms of gender, **45.0%** of participants in the intervention group were male, compared to **47.5%** in the control group ($p=0.682$). This near-equal distribution of sexes ensures that gender-related biological variability does not skew the results of the nutritional intervention.

Body Mass Index (BMI)

The average BMI of participants was **22.8 ± 1.9 kg/m²** in the intervention group and **22.6 ± 2.0 kg/m²** in the control group ($p=0.549$), indicating that both groups were within the normal BMI range, with no significant difference in nutritional status at baseline. Adequate BMI is a known contributor to optimal wound healing and metabolic stability.

Serum Albumin Levels

Albumin levels were measured as an indicator of nutritional and inflammatory status. The mean serum albumin was **3.4 ± 0.5 g/dL** in the intervention group and **3.5 ± 0.6 g/dL** in the control group ($p=0.434$), suggesting comparable protein status prior to intervention. Hypoalbuminemia is a known risk factor for delayed wound healing, and the similar levels in both groups eliminate it as a confounder.

Wound Type Distribution

Participants were evenly distributed in terms of wound type, with 64 post-operative and 56 chronic wound cases in the intervention group, compared to 66 post-operative and 54 chronic wound cases in the control group ($p=0.787$). This even distribution is essential to ensure that differences in healing trajectory due to wound chronicity do not affect comparative outcomes.

Table 2 presents the weekly percentage reduction in wound size for both the intervention and control groups over a 5-week observation period. The intervention group received a high-protein diet based on freshwater fish (Clarias gariepinus or Channa striata) administered three times daily, while the control group received a standard diet without additional fish-based protein.

Table 2: Mean Wound Size Reduction (%) By Week

Week	Intervention Group (%)	Control Group (%)	p-value
1	4.3	2.9	0.102
2	14.7	7.3	0.031*
3	35.6	18.2	0.002*
4	58.4	34.1	0.001*
5	79.5	51.6	0.000*

*Statistically significant at $p < 0.05$

Week 1

During the first week, both groups demonstrated a modest reduction in wound size. The intervention group showed an average reduction of **4.3%**, compared to **2.9%** in the control group ($p = 0.102$). Although the difference was not statistically significant, it suggests an early trend favoring the protein-enriched

fish-based diet. The lack of significant difference may reflect the initial inflammatory phase of wound healing, where visible wound contraction is still limited.

Week 2

By the second week, a **statistically significant difference** emerged, with the intervention group experiencing a **14.7% reduction** versus **7.3%** in the control group (p = 0.031). This finding indicates a more rapid transition into the proliferative phase of healing in the intervention group, likely facilitated by improved protein availability and essential amino acids supporting fibroblast activity, collagen synthesis, and granulation tissue formation.

Week 3

In the third week, wound healing in the intervention group accelerated substantially, showing a **35.6% mean reduction**, compared to only **18.2%** in the control group (p = 0.002). This marked improvement aligns with the critical role of dietary protein and micronutrients (e.g., zinc, selenium) in cell proliferation, angiogenesis, and matrix remodeling. The intervention group's doubled healing rate reinforces the therapeutic benefit of consistent intake of bioavailable animal protein in tissue regeneration.

Week 4

By the fourth week, wounds in the intervention group had reduced by **58.4%**, significantly more than the **34.1%** observed in the control group (p = 0.001). This phase typically involves enhanced re-epithelialization and contraction, processes that appear to be notably augmented by the intervention. The sustained difference between the groups suggests cumulative biological benefits of fish-based dietary protein on wound healing mechanisms.

Week 5

At the end of the five-week period, the intervention group achieved a **mean wound size reduction of 79.5%**, compared to **51.6%** in the control group (p = 0.000). This represents a highly significant outcome, indicating nearly complete wound closure in many patients within the intervention group. The nutritional intervention appears to have accelerated all key healing stages—from inflammation through proliferation to remodeling—resulting in a faster recovery trajectory.

The results across all five weeks demonstrate a consistent and statistically significant advantage of the protein-rich fish diet in promoting wound healing, beginning from week two onward. The pattern of increasing divergence between the groups suggests that early and sustained intake of high-quality dietary protein plays a vital role in enhancing cellular repair mechanisms. This is especially relevant in populations at risk for malnutrition or impaired healing, such as patients with chronic wounds or post-surgical complications.

These findings support previous evidence highlighting the importance of adequate protein intake in clinical wound management strategies and suggest that locally sourced freshwater fish may serve as an accessible and cost-effective nutritional intervention to improve recovery outcomes in diverse patient populations [12].

Table 3 presents the comparative clinical indicators of wound healing between the intervention and control groups at **week 5**, reflecting the cumulative effects of the dietary protein intervention involving freshwater fish (Channa striata or Clarias gariepinus) administered three times daily. The data show s**tatistically significant improvements** across all measured wound healing parameters in the intervention group compared to the control group ($p < 0.05$), indicating the efficacy of fish-based protein supplementation in accelerating wound repair and reducing complications.

Table 3: Clinical Indicators of Wound Healing at Week 5

Indicator	Intervention (%)	Control (%)	p-value
Granulation tissue present	100.0	88.3	0.003*
Epithelialization observed	84.2	59.1	0.000*
Signs of infection absent	92.5	67.5	0.000*
Pain score reduced by ≥50%	81.7	55.0	0.001*
Wound closure ≥75%	84.2	51.7	0.000*

* Statistically significant at $p < 0.05$

Granulation Tissue Formation

At week 5, **100%** of participants in the intervention group exhibited robust **granulation tissue**, compared to **88.3%** in the control group (p = 0.003). This indicator reflects early proliferative phase activity, with granulation tissue serving as a key matrix for re-epithelialization and angiogenesis. The universal presence of granulation tissue in the intervention group suggests an optimal microenvironment for tissue regeneration, likely facilitated by the high-quality amino acids and micronutrients in the fish-based diet [12].

Epithelialization

Epithelialization, a marker of wound resurfacing, was observed in **84.2%** of the intervention group, significantly higher than the **59.1%** in the control group ($p = 0.000$). The higher epithelialization rate among participants receiving fish protein may be attributed to enhanced collagen synthesis, improved cellular migration, and tissue hydration—processes closely linked to protein adequacy and zinc availability in fish [12].

Absence of Infection

The absence of **clinical signs of infection** was reported in **92.5%** of the intervention group versus **67.5%** in the control group (p = 0.000). Protein intake has been linked to better immune modulation, with improved leukocyte function and immunoglobulin production contributing to a more efficient antimicrobial response. The presence of omega-3 fatty acids and selenium in the intervention diet may also have anti-inflammatory and antimicrobial effects [12].

Pain Reduction

A ≥**50% reduction in pain scores** from baseline was achieved by **81.7%** of the intervention group, compared to **55.0%** in the control group (p = 0.001). This improvement is likely multifactorial—linked to decreased infection, reduced inflammation, and more rapid tissue regeneration. The nutritional completeness of fish protein, especially in modulating prostaglandin pathways, may play a role in perceived pain reduction [12].

Wound Closure ≥75%

A significant proportion **(84.2%)** of the intervention group achieved ≥**75% wound closure** at week 5, compared to only **51.7%** in the control group (p = 0.000). This metric is a critical endpoint in wound care, directly reflecting the pace of tissue contraction and re-epithelialization. The superior outcomes in the intervention group affirm the potential of fish-derived proteins in supporting all stages of wound healing, from inflammation to remodeling [12].

The findings clearly demonstrate that participants receiving **freshwater fish-based dietary protein interventions** exhibited **faster, more complete wound healing** across all key clinical indicators. The statistically significant improvements in granulation, epithelialization, infection control, pain reduction, and wound closure not only highlight the biological value of fish protein but also suggest a practical, low-cost nutritional intervention for patients with tissue injuries, particularly in resource-limited settings. These results support the integration of locally sourced fish proteins into therapeutic diets for wound management and rehabilitation [12].

Discussion

The present study demonstrated that dietary intervention with freshwater fish protein significantly enhanced multiple clinical indicators of wound healing over a five-week period compared to the control group. These findings corroborate the growing body of evidence supporting the critical role of high-quality protein intake in promoting tissue regeneration, immune function, and infection control among patients with wounds or chronic injuries [13].

The universal presence of granulation tissue in the intervention group at week 5 (100%) compared to 88.3% in controls highlights the accelerated proliferative phase induced by fish protein consumption. Granulation tissue formation is essential for creating a scaffold that supports new capillary growth and fibroblast activity, and the amino acid profile of fish protein—particularly leucine, lysine, and methionine—provides necessary substrates for collagen synthesis and cellular proliferation [14]. Similar studies have reported improved granulation and wound bed preparation with enhanced dietary protein intake in burn and surgical patients, emphasizing the importance of nutritional support in wound management [15].

Epithelialization rates were also significantly higher in the intervention group (84.2% vs. 59.1%), indicating faster re-epithelial coverage of wounds. This outcome aligns with prior research demonstrating that sufficient protein intake accelerates keratinocyte migration and differentiation, processes essential for restoring the skin barrier [16]. Moreover, the micronutrients co-present in freshwater fish, such as zinc and selenium, have been shown to stimulate epithelial cell function and antioxidant defense, further facilitating wound closure [17].

Infection control was markedly improved, with 92.5% of the intervention group showing absence of infection signs compared to 67.5% in controls. Protein plays a pivotal role in immune competence, including leukocyte proliferation and immunoglobulin synthesis, which are critical for pathogen clearance [18]. The anti-inflammatory and immunomodulatory properties of omega-3 fatty acids found in fish may also contribute to lowering infection risk by modulating cytokine production and reducing excessive inflammation.

Pain reduction, an important clinical outcome, was significantly greater in the intervention group. Reduced pain may result from decreased inflammatory mediators and improved tissue oxygenation associated with better nutritional status. Additionally, the rapid wound closure observed in the intervention group (≥75% closure in 84.2% vs. 51.7% in controls) further reflects the combined benefits of fish protein and associated micronutrients in supporting all phases of wound healing from inflammation through remodeling [13].

These findings are particularly relevant in low- and middle-income settings where protein-energy malnutrition and infection burden complicate wound care. Promoting the inclusion of affordable and nutrient-dense sources such as freshwater fish can provide a practical dietary strategy to enhance healing outcomes and reduce healthcare burdens.

Limitations

Despite the promising results, this study has several limitations that should be considered when interpreting the findings. First, the study design did not include biochemical analyses of specific amino acid levels, micronutrient status, or inflammatory markers, which could have provided more detailed insights into the mechanisms by which freshwater fish protein influences wound healing. Second, while wound care procedures were standardized as much as possible, variability in individual patient compliance and clinical management could have influenced healing outcomes. Third, the study duration of five weeks for primary outcome assessment may not fully capture long-term effects or potential late complications related to wound healing. Fourth, the generalizability of these findings may be limited to similar populations with comparable nutritional status and types of wounds, and may not extend to patients with more complex comorbidities or different cultural dietary habits. Finally, the study did not control for other dietary intake outside the intervention, which may have affected nutritional status and healing processes.

Future research should incorporate biochemical markers, longer follow-up periods, and a broader range of wound types to strengthen the evidence and clarify the pathways involved in protein-mediated wound healing.

Conclusion

This study demonstrates that dietary supplementation with freshwater fish protein significantly improves clinical indicators of wound healing, including granulation tissue formation, epithelialization, infection control, pain reduction, and wound closure. The intervention offers a practical and effective nutritional strategy to enhance recovery in patients with wounds, particularly in resource-limited settings where protein deficiency and infection risks are prevalent. Incorporating freshwater fish into the diet

can be a valuable adjunct to standard wound care, supporting tissue regeneration and immune function. Further studies are recommended to explore the underlying biological mechanisms and to evaluate long-term outcomes.

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