International Journal of Medical Science and Public Health Research
ISSN : 2767-3774
SJIF: 2021: 5.456, 2022: 5.681, 2023: 6.591

TYPE Original Research
PAGE NO. 01-08

Check for updates

Investigating the therapeutic efficacy of sea cucumber protein extract on murine dermal wound healing and its anti-inflammatory modulatory pathways

Dr. Nur Aisyah Binti Razali

Department of Biomedical Sciences, Universiti Kebangsaan Malaysia (UKM), Kuala Lumpur, Malaysia

Dr. Jorge L. Mendoza

Institute of Marine Biomedicine, University of La Laguna, Tenerife, Spain

OPEN ACCESS

SUBMITTED 03 May 2025
ACCEPTED 02 June 2025
PUBLISHED 01 July 2025
VOLUME Vol.06 Issue07 2025

Abstract: Chronic and non-healing wounds pose significant global health challenges, necessitating the exploration of novel therapeutic agents that can accelerate tissue regeneration and mitigate excessive inflammation. This article conceptually investigates the therapeutic efficacy of a prepared sea cucumber protein extract on murine dermal wound healing and elucidates its potential anti-inflammatory mechanisms. Sea cucumbers are rich sources of bioactive compounds, including proteins, with reported regenerative and anti-inflammatory properties. This conceptual study outlines a methodology for preparing the protein extract, establishing a full-thickness dermal wound model in mice, and assessing wound closure rates, histological changes, and key inflammatory markers (e.g., pro-inflammatory cytokines, NF-κB pathway components). Hypothetical results anticipate accelerated wound closure, reduced inflammatory cell infiltration, and downregulation of inflammatory signaling pathways, particularly through the modulation of macrophages and related molecular cascades. The discussion explores how the unique protein composition of sea cucumber might contribute to these effects, proposing that its immunomodulatory actions facilitate a more favorable wound microenvironment for repair. This research direction holds substantial promise for developing new biomaterial-based dressings and therapeutic strategies

for challenging wound healing scenarios, leveraging natural marine resources.

Keywords: Sea cucumber, protein extract, wound healing, dermal repair, anti-inflammatory, murine model, NF-κB, macrophages, natural products.

Introduction: Wound healing is a complex biological process involving a coordinated cascade of cellular and molecular events, including inflammation, proliferation, and tissue remodeling [6, 47, 52]. While acute wounds typically heal efficiently, chronic wounds, often exacerbated by persistent inflammation, pose a significant burden on healthcare systems globally [2, 7]. Excessive or prolonged inflammation can impede the healing process, leading to delayed closure, scarring, and complications [7, 10, 50, 60]. Consequently, there is an urgent need for innovative therapeutic strategies that not only accelerate tissue regeneration but also effectively modulate the inflammatory response to create an optimal healing microenvironment [2, 3, 4, 10, 11].

The ocean, a vast reservoir of biodiversity, offers a rich source of novel bioactive compounds with diverse pharmacological properties [25]. Among marine organisms, sea cucumbers (Echinodermata: Holothuroidea) have gained increasing attention in traditional medicine and modern research due to their unique biochemical composition [30]. They are recognized for containing a variety of bioactive molecules, including proteins, polysaccharides, saponins, and peptides, which exhibit anti-inflammatory, antioxidant, immunomodulatory, and regenerative activities [25, 26, 27, 30]. Specifically, sea cucumber proteins have been reported to possess properties beneficial for tissue repair and anti-inflammatory effects [30]. For example, studies have indicated that certain marine-derived compounds can influence macrophage phenotype, which is crucial for orchestrating tissue development and healing [5, 13, 56, 57]. Macrophages play a dual role in wound healing, initially promoting inflammation to clear debris and later shifting to a pro-resolving phenotype essential for tissue repair and regeneration [5, 13, 50, 57].

The inflammatory phase of wound healing is tightly regulated, with key signaling pathways such as Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) playing a central role in driving the expression of pro-inflammatory cytokines and chemokines [19, 61, 62, 65]. Persistent activation of NF-κB can lead to chronic inflammation, hindering effective wound closure and promoting fibrotic responses [19, 46, 53, 63, 64]. Therefore, therapeutic agents that can modulate the NF-κB pathway hold significant promise for mitigating detrimental inflammation and promoting more efficient and scarless wound healing [10, 12, 19, 43].

This article conceptually investigates the therapeutic efficacy of a prepared protein extract derived from sea cucumber on dermal wound healing in a murine model. Beyond assessing macroscopic wound closure, the study aims to delve into the potential anti-inflammatory mechanisms by exploring its effects on cellular infiltration and key molecular pathways, particularly those involving NF-κB. Such research could pave the way for novel wound dressings or pharmacological interventions based on natural marine resources, offering a promising alternative to current treatments [1, 11, 12, 23, 35, 37].

Research Questions:

1. Does the topical application of sea cucumber protein extract accelerate dermal wound healing in mice?
2. Does sea cucumber protein extract exhibit anti-inflammatory effects in the wound microenvironment of mice?
3. What are the potential molecular mechanisms, particularly involving the NF-κB signaling pathway and macrophage modulation, underlying the observed anti-inflammatory effects of sea cucumber protein extract in wound healing?

Literature Review

Wound healing is an intricate biological process, conventionally divided into four overlapping phases: hemostasis, inflammation, proliferation, and remodeling [6, 47, 52]. Each phase is orchestrated by a complex interplay of cellular components, growth factors, cytokines, and extracellular matrix remodeling [6, 52].

2.1 The Critical Role of Inflammation in Wound Healing

The inflammatory phase, initiated immediately after injury, is crucial for clearing debris, microorganisms, and damaged tissue, preparing the wound bed for subsequent repair [5, 50]. This phase is characterized by the infiltration of immune cells, primarily neutrophils and macrophages, into the wound site [50, 51]. While acute inflammation is essential, its dysregulation or persistence can be detrimental, leading to chronic non-healing wounds, excessive scarring, and poor functional outcomes [7, 10, 50, 60]. Cytokines, such as TNF-α, IL-1β, and IL-6, are key mediators of the inflammatory response [60].

Macrophages, specifically, play a pivotal and dual role in wound healing. Initially, pro-inflammatory (M1)

macrophages are recruited to phagocytose pathogens and cellular debris. Subsequently, these macrophages undergo a phenotypic switch to an anti-inflammatory (M2) phenotype, which is essential for promoting angiogenesis, collagen deposition, and tissue remodeling [5, 13, 50, 57]. Therapies that can modulate macrophage phenotype towards the M2 regenerative type are highly sought after [56, 57].

2.2 NF-κB Pathway and Inflammation

The Nuclear Factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathway is a central regulator of inflammatory and immune responses [19, 61, 62, 65]. Upon activation by various stimuli (e.g., bacterial products, pro-inflammatory cytokines), NF-κB translocates to the nucleus, where it induces the transcription of numerous genes encoding pro-inflammatory cytokines, chemokines, and adhesion molecules [19, 61, 62]. Persistent activation of the NF-κB pathway is implicated in chronic inflammatory conditions and can impede normal wound healing [19, 46, 63, 64]. Therefore, targeting NF-κB offers a promising strategy to attenuate excessive inflammation and promote beneficial wound resolution [10, 46, 63].

2.3 Natural Products and Wound Healing

Traditional medicine and modern pharmacology increasingly recognize the potential of natural products for wound healing due to their diverse biological activities [3, 23, 24, 35, 59]. Plant extracts, for instance, have shown promise in promoting wound healing through anti-inflammatory and antioxidant effects [3, 12, 18, 23, 24, 49]. Similarly, marine organisms represent an underexplored but rich source of bioactive compounds [25].

2.4 Sea Cucumber and Its Therapeutic Potential

Sea cucumbers are invertebrates rich in proteins, polysaccharides (e.g., fucoidans, sulfated polysaccharides), saponins (triterpene glycosides), and other bioactive molecules [25, 26, 27]. These compounds have demonstrated a wide array of pharmacological activities, including anti-inflammatory, antioxidant, immunomodulatory, anti-tumor, and regenerative properties [25, 26, 27, 30].

Specific to wound healing, research suggests that sea cucumber components, particularly protein extracts, may directly promote tissue repair. Sun et al. [30] reported that oral administration of sea cucumber protein exerts wound healing effects via the PI3K/AKT/mTOR signaling pathway, which is known to be involved in cell proliferation, survival, and protein synthesis. While that study focused on oral administration, the potential for topical application as a wound dressing, perhaps in a paste or hydrogel format, is highly relevant [1, 11, 12, 21, 22, 33, 43]. Proteins, as biomolecules, play crucial roles in cell signaling, structural support, and enzymatic activity, making them attractive candidates for therapeutic applications [39, 40]. Essential amino acids, such as L-cysteine and L-arginine, which are components of proteins, also have known anti-inflammatory and wound healing properties [31, 32, 41, 42].

Given the comprehensive properties of sea cucumber constituents, investigating its protein extract directly on skin wound healing, with a focus on its anti-inflammatory mechanisms, represents a significant step towards developing new, naturally derived wound therapeutics. Understanding the molecular pathways, such as NF-κB modulation and macrophage reprogramming, through which these proteins act would provide valuable insights for optimizing their therapeutic application.

2.5 Safety and Pharmacokinetics

Prior to therapeutic application, the safety profile and potential adverse effects of novel compounds, especially on vital organs like the liver and kidney, must be considered [15, 16, 17]. While sea cucumber extracts are generally considered safe, any concentrated protein paste would require careful evaluation to ensure minimal systemic toxicity [17].

METHODS

This section outlines the conceptual methodology for investigating the therapeutic efficacy of sea cucumber protein extract on murine dermal wound healing and its potential anti-inflammatory mechanisms. This proposed methodology encompasses the preparation of the protein extract, establishment of a wound model, intervention protocol, and comprehensive assessment techniques.

Preparation of Sea Cucumber Protein Extract Paste

- **Sea Cucumber Sourcing and Pre-treatment**

Dried sea cucumbers (e.g., Stichopus japonicus) would be sourced from reputable suppliers. They would be thoroughly cleaned, rehydrated, and eviscerated. The body wall would then be minced and homogenized.

- **Protein Extraction**

The homogenized sea cucumber tissue would undergo a series of steps for protein extraction:

- Defatting: The homogenate would be defatted using an organic solvent (e.g., n-hexane) to remove lipids that could interfere with protein purity and stability.
- Protein Solubilization: The defatted material would be suspended in an appropriate buffer solution

(e.g., phosphate-buffered saline, PBS) with a suitable pH and temperature to facilitate protein solubilization. Enzymatic hydrolysis using food-grade proteases might be employed to obtain specific protein fractions or peptides, depending on the desired molecular weight profile [39].

- Centrifugation and Filtration: The mixture would be centrifuged to remove insoluble material, followed by filtration to clarify the protein solution.
- Protein Concentration and Purification: The protein solution would be concentrated using ultrafiltration or lyophilization. Further purification steps, such as dialysis or chromatographic techniques (e.g., size-exclusion chromatography, ion-exchange chromatography), could be performed to isolate specific protein fractions of interest based on their molecular weight or charge [39, 40].
- Characterization: The extracted protein would be characterized for its protein content (e.g., Bradford assay), amino acid composition (e.g., HPLC), molecular weight distribution (e.g., SDS-PAGE), and structural integrity (e.g., FTIR, CD spectroscopy) [39, 40].

Paste Formulation

The purified sea cucumber protein extract (in powdered or concentrated liquid form) would be formulated into a suitable paste for topical application. This would involve mixing the protein with a biocompatible hydrogel-forming material (e.g., chitosan, gelatin, hyaluronic acid, polyvinyl alcohol, carboxymethyl cellulose) to create a semi-solid consistency [1, 11, 21, 22, 33, 34, 35, 43]. The rheological properties and stability of the paste would be optimized to ensure ease of application and retention at the wound site.

Murine Dermal Wound Model

Animal Handling and Ethical Considerations

All animal procedures would be conducted in strict accordance with institutional animal care and use guidelines and ethical approvals. Male C57BL/6 mice (8-10 weeks old) would be chosen for their well-established use in wound healing research [8, 44, 49]. Animals would be housed under controlled environmental conditions with free access to food and water.

Full-Thickness Dermal Wound Creation

Mice would be anesthetized (e.g., with isoflurane). The dorsal hair would be shaved and the skin disinfected. A full-thickness excisional wound (e.g., 6,mm diameter) would be created using a sterile biopsy punch on the dorsal midline, ensuring removal of the epidermis, dermis, and subcutaneous fat down to the panniculus carnosus [8].

Treatment Groups

Mice would be randomly assigned to different treatment groups:

- Control Group: No treatment or application of a placebo paste (e.g., vehicle hydrogel without protein).
- Positive Control Group: Application of a known wound healing agent (e.g., commercially available wound dressing, silver sulfadiazine, or a growth factor) [1, 11, 12, 23, 57].
- Sea Cucumber Protein Paste Group(s): Topical application of the formulated sea cucumber protein paste at varying concentrations or dosages to the wound site, once or twice daily.

Wound Healing Assessment

Macroscopic Wound Closure

Wound healing would be monitored daily by photographing the wound using a digital camera with a scale bar. The wound area would be measured using image analysis software (e.g., ImageJ) [8, 24]. The percentage of wound closure would be calculated relative to the initial wound area. Time to complete epithelialization would also be recorded.

Histological Analysis

At predetermined time points (e.g., day 3, 7, 14, 21 post-wounding), mice would be euthanized, and full-thickness skin samples encompassing the wound and surrounding healthy tissue would be harvested. Tissues would be fixed in formalin, embedded in paraffin, sectioned, and stained with:

- Hematoxylin and Eosin (H&E): To assess general tissue morphology, inflammatory cell infiltration, re-epithelialization, granulation tissue formation, and angiogenesis [8, 47].
- Masson's Trichrome: To visualize collagen deposition and assess collagen organization, indicating the quality of scar formation [8, 10].
- Immunohistochemistry (IHC): For specific cellular markers:
  - Macrophages: CD68 (general macrophage marker), iNOS (M1 pro-inflammatory marker), CD206 (M2 anti-inflammatory/pro-resolving marker) [5, 13, 50, 56, 57].
  - Fibroblasts/Myofibroblasts: α-SMA (alpha-smooth muscle actin) [45].
  - Proliferation: Ki67 [49].
  - Angiogenesis: CD31 [6].

Assessment of Anti-inflammatory Mechanism

Cytokine Analysis

At early inflammatory time points (e.g., 24h, 48h, 72h, 3

days post-wounding), wound tissue homogenates or wound exudates would be collected. Pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6) and anti-inflammatory cytokines (e.g., IL-10, TGF-β) would be quantified using ELISA or multiplex cytokine arrays [8, 10, 56, 60].

Molecular Pathway Analysis (NF-κB)

Wound tissue samples would be collected at relevant time points (e.g., 1 day, 3 days) for molecular analysis:

- Western Blotting: To assess the protein expression levels of key components of the NF-κB signaling pathway, including IκBα, phosphorylated IκBα, and NF-κB p65 (total and phosphorylated) [19, 46, 61, 63, 64, 65].
- Quantitative Real-Time PCR (qRT-PCR): To quantify the mRNA expression levels of genes regulated by NF-κB, such as those encoding pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6), and enzymes involved in inflammation (e.g., iNOS, COX-2) [19, 46, 61, 62, 63, 64].
- Immunofluorescence/Confocal Microscopy: To visualize the nuclear translocation of NF-κB p65 in wound cells, indicating NF-κB activation [19, 63, 64].

Safety Evaluation

To assess potential systemic toxicity, at the endpoint of the study, blood samples would be collected for liver and kidney function tests (e.g., AST, ALT, creatinine, BUN) [17]. Histological examination of liver and kidney tissues would also be performed to check for any organ damage [15, 16, 17, 32].

Statistical Analysis

All quantitative data would be expressed as mean ± standard deviation (SD) or standard error of the mean (SEM). Statistical comparisons between groups would be performed using appropriate statistical tests, such as one-way ANOVA followed by post-hoc tests (e.g., Tukey's or Dunnett's), or repeated measures ANOVA for time-dependent data. A p-value less than 0.05 would be considered statistically significant.

RESULTS (HYPOTHETICAL ILLUSTRATIONS)

This section presents hypothetical results, derived from the outlined methodology and consistent with existing literature on bioactive compounds and wound healing, to illustrate the anticipated findings from the investigation of sea cucumber protein extract on murine dermal wound healing and its anti-inflammatory mechanisms.

Accelerated Dermal Wound Closure

Topical application of sea cucumber protein paste would hypothetically lead to significantly accelerated wound closure compared to the control and placebo groups.

- Macroscopic Observation: Gross observation would show a visibly smaller wound area and faster epithelialization in the sea cucumber-treated groups from early time points (e.g., day 3-7) onward (Figure 1a).
- Wound Area Reduction: Quantitative analysis would demonstrate a statistically significant reduction in wound area percentage from day 3 through day 14 in the sea cucumber group(s) compared to controls. For instance, by day 7, the sea cucumber group might show 60% wound closure, while the control group only shows 40% (Figure 1b).
- Time to Closure: The median time required for complete epithelialization would be significantly shorter in the sea cucumber-treated animals (e.g., 14 days) compared to the control group (e.g., 21 days).

Improved Histological Features of Wound Healing

Histological examination of wound tissues would reveal superior healing characteristics in mice treated with sea cucumber protein paste.

- Reduced Inflammation: H&E staining would show decreased infiltration of inflammatory cells (neutrophils and macrophages) in the early phases (e.g., day 3) in the sea cucumber group compared to controls. This indicates an attenuated inflammatory response, consistent with an anti-inflammatory effect (Figure 1c).
- Enhanced Granulation Tissue Formation: By day 7, the sea cucumber group would exhibit more robust and organized granulation tissue, characterized by increased angiogenesis (more blood vessels, confirmed by CD31 IHC) and fibroblast proliferation (confirmed by Ki67 IHC).
- Improved Re-epithelialization: H&E staining would show faster and more complete re-epithelialization, with a thicker and more mature epidermal layer in the sea cucumber-treated wounds by day 14.
- Superior Collagen Deposition: Masson's Trichrome staining at later time points (e.g., day 14, 21) would reveal denser, more organized collagen fibers in the sea cucumber group, indicating a higher quality of tissue remodeling and potentially reduced scar formation (Figure 1d), consistent with research on scarless healing [12].

Anti-inflammatory Mechanism: Macrophage Modulation and NF-κB Pathway Downregulation

Molecular and immunohistochemical analyses would elucidate the anti-inflammatory mechanisms of the sea cucumber protein paste.

- Macrophage Phenotype Shift: Immunohistochemistry for macrophage markers (CD68,

iNOS, CD206) would show a shift in macrophage polarization in the wound microenvironment. In the early inflammatory phase, the sea cucumber group would exhibit a relatively lower proportion of pro-inflammatory M1 macrophages (iNOS+) and a higher proportion of anti-inflammatory M2 macrophages (CD206+) compared to controls. This suggests that the sea cucumber protein actively modulates macrophage phenotype towards a pro-resolving, regenerative state [5, 13, 50, 56, 57].

- Reduced Pro-inflammatory Cytokine Expression: ELISA or multiplex assays of wound homogenates would show a significant reduction in the levels of key pro-inflammatory cytokines, such as TNF-α, IL-1β, and IL-6, in the sea cucumber-treated groups at early time points (e.g., 24-72 hours post-wounding) (Figure 1e). Conversely, there might be an increase in anti-inflammatory cytokines like IL-10. This aligns with a dampened inflammatory response [8, 10, 60].

- NF-κB Pathway Inhibition: Western blotting and qRT-PCR analyses would demonstrate the inhibitory effect of sea cucumber protein on the NF-κB signaling pathway. In the sea cucumber-treated groups, there would be:

o Reduced phosphorylation and degradation of IκBα (the inhibitor of NF-κB).

o Reduced phosphorylation and nuclear translocation of NF-κB p65 (Figure 1f) [19, 46, 61, 62, 63, 64, 65].

o Consequently, a downregulation of mRNA expression of NF-κB target genes, including pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and inflammatory enzymes (iNOS, COX-2). This suggests that the sea cucumber protein directly interferes with the activation of this central inflammatory pathway, thereby mediating its anti-inflammatory effects.

Safety Profile

Systemic safety evaluation would indicate that topical application of the sea cucumber protein paste does not induce significant systemic toxicity. Liver and kidney function tests (AST, ALT, creatinine, BUN) in the treated mice would remain within normal physiological ranges, and histological examination of these organs would show no signs of inflammation or damage [15, 16, 17, 32]. This would confirm the local action and safety of the topical treatment.

DISCUSSION

The hypothetical findings from this conceptual study strongly suggest that sea cucumber protein extract, formulated into a topical paste, holds significant therapeutic potential for accelerating dermal wound healing in mice, primarily through its potent anti-inflammatory mechanisms. These results, if empirically confirmed, would align with and significantly expand upon existing research regarding the bioactive properties of marine-derived compounds and the critical role of inflammation in wound repair.

The observed acceleration in wound closure, coupled with improved re-epithelialization and collagen organization, directly indicates the regenerative capacity of the sea cucumber protein. This would support the notion that active components within the extract contribute to the proliferation and migration of keratinocytes and fibroblasts, which are essential for wound contraction and tissue formation [49, 52]. The enhanced quality of collagen deposition, indicative of reduced scar formation [12], is particularly important for functional and aesthetic outcomes in wound healing, potentially suggesting that the sea cucumber extract promotes a more regenerative rather than fibrotic repair process [53].

Crucially, the hypothetical anti-inflammatory effects provide a mechanistic explanation for the improved healing. The reduction in inflammatory cell infiltration and the downregulation of pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) in the early wound phases are key indicators of effective inflammation modulation [10, 60]. This suggests that the sea cucumber protein helps to transition the wound from an acute inflammatory state to a pro-resolving phase more efficiently. The proposed shift in macrophage polarization from pro-inflammatory M1 to pro-resolving M2 phenotypes is a critical finding, as M2 macrophages are known to orchestrate tissue repair, angiogenesis, and extracellular matrix remodeling [5, 13, 50, 56, 57]. This immunomodulatory action positions sea cucumber protein as a promising agent for fine-tuning the immune response in the wound bed, thereby creating a more conducive environment for regeneration [57].

The hypothesized inhibition of the NF-κB signaling pathway directly explains the anti-inflammatory effects. NF-κB is a central mediator of inflammation [19, 61, 62, 65], and its downregulation (evidenced by reduced IκBα phosphorylation/degradation and decreased NF-κB p65 nuclear translocation) would directly lead to a decrease in the expression of various pro-inflammatory genes. This precise molecular targeting suggests that the sea cucumber protein components act at a fundamental level of the inflammatory cascade, preventing excessive or prolonged inflammatory responses that would otherwise impede healing [10, 46, 63, 64]. This mechanism is distinct from simply reducing bacterial load; it actively modulates the host's inflammatory machinery.

The safety profile, demonstrating no systemic toxicity to liver or kidney, is paramount for the translational potential of this natural product [15, 16, 17]. It indicates that the therapeutic effects are localized to the wound site, minimizing undesirable systemic side effects often associated with conventional drug therapies [37, 38, 39].

The specific protein composition of sea cucumber is likely responsible for these multi-faceted effects. Sea cucumbers contain a diverse range of proteins, including collagen, lectins, and various enzymes, which could contribute to tissue regeneration, antimicrobial activity, and immunomodulation. For example, certain amino acids found abundantly in proteins, such as L-arginine and L-cysteine, are known to support wound healing and exhibit anti-inflammatory properties [31, 32, 41, 42]. The precise combination and interaction of these protein components within the sea cucumber extract warrant further detailed investigation. The formulation into a paste also offers practical advantages for topical application, ensuring direct contact with the wound bed and potentially providing a moist healing environment [1, 11, 21, 22, 33, 43].

Limitations

As a conceptual study, the primary limitation is the hypothetical nature of its results. The findings are based on a synthesis of existing literature and assumed common biological responses rather than empirical data collected from actual animal experiments. Therefore, the generalizability and specific quantitative outcomes are speculative. An actual empirical study would need to rigorously perform the described experiments, potentially optimizing concentrations, application frequencies, and time points, and validate the proposed mechanisms through further in-depth molecular studies. Furthermore, the complexity of a natural extract means that identifying the precise bioactive protein(s) responsible for the effects would require further fractionation and purification steps.

Future Research Directions:

Future empirical research should focus on:

1. Experimental Validation: Conduct rigorous in vivo studies in murine models to experimentally validate the hypothesized wound healing and anti-inflammatory effects, optimizing the sea cucumber protein extract concentration and paste formulation.

2. Mechanism Elucidation: Delve deeper into the specific molecular targets and signaling pathways involved, potentially using omics approaches (e.g., proteomics, transcriptomics) to identify other affected pathways beyond NF-κB.

3. Active Compound Isolation: Isolate and identify the specific protein(s) or peptides within the sea cucumber extract responsible for the observed therapeutic effects. This would allow for standardized production and targeted therapeutic development.

4. Comparative Studies: Compare the efficacy of sea cucumber protein paste with existing commercial wound dressings and other natural product-based treatments.

5. Scarring and Long-term Outcomes: Evaluate the long-term effects of the treatment on scar quality, tensile strength, and functional restoration of the healed skin.

6. Safety and Toxicology: Conduct comprehensive toxicological studies to confirm the safety of the extract for human use, including acute and chronic toxicity, allergenicity, and potential drug interactions.

7. Different Wound Types: Explore the efficacy of sea cucumber protein paste on other types of wounds, such as diabetic wounds or burn injuries [8, 44].

CONCLUSION

This article has conceptually outlined the compelling potential of sea cucumber protein extract, formulated as a topical paste, to accelerate dermal wound healing in mice, primarily through its potent anti-inflammatory modulatory properties. The hypothetical results suggest that this natural marine-derived product could significantly enhance wound closure, improve tissue regeneration, and effectively mitigate excessive inflammation by modulating macrophage phenotypes and inhibiting key inflammatory pathways, particularly NF-κB. This precise control over the inflammatory microenvironment is crucial for achieving high-quality, potentially scarless, wound repair. While rigorous empirical validation is essential, this conceptual framework provides a strong scientific rationale for further investigating sea cucumber protein as a promising, naturally derived therapeutic agent for advanced wound care, offering a novel approach to addressing the persistent challenges of chronic and non-healing wounds.

REFERENCES

Cui H, Cai J, Hanjiao H, Ding S, Long Y and Lin S 2023 Tailored chitosan/glycerol micropatterned composite dressings by 3D printing for improved wound healing Int. J. Biol. Macromol. 255 127952

Freedman B R, Hwang C, Talbot S, Hibler B, Matoori S and Mooney D J 2023 Breakthrough treatments for accelerated wound healing Sci. Adv. 9 7007

He X, Liu L, Gu F, Huang R, Liu L, Nian Y, Zhang Y and Song C 2024 Exploration of the anti-inflammatory, analgesic, and wound healing activities of Bletilla Striata

polysaccharide Int. J. Biol. Macromol. 261 129874

Gowtham A and Kaundal R K 2024 Exploring the ncRNA landscape in exosomes: insights into wound healing mechanisms and therapeutic applications Int. J. Biol. Macromol. 292 139206

Mass E 2023 Human macrophages choreograph tissue development Trends Immunol. 44 865–7

Peña O A and Martin P 2024 Cellular and molecular mechanisms of skin wound healing Nat. Rev. Mol. Cell. Biol. 25 599–616

Zanoli L et al 2020 Vascular consequences of inflammation: a position statement from the ESH Working Group on Vascular Structure and Function and the ARTERY Society J. Hypertens. 38 1682–98

Ban E, Jeong S, Park M, Kwon H, Park J, Song E J and Kim A 2020 Accelerated wound healing in diabetic mice by miRNA-497 and its anti-inflammatory activity Biomed. Pharmacother. 121 109613

Gao W, Wu X, Wang Y, Lu F and Liu F 2025 Brazilin-rich extract from Caesalpinia sappan L. Attenuated the motor deficits and neurodegeneration in MPTP/p-induced Parkinson's disease mice by regulating gut microbiota and inhibiting inflammatory responses ACS Chem. Neurosci. 16 181–94

Zhao C C, Zhu L, Wu Z, Yang R, Xu N and Liang L 2020 Resveratrol-loaded peptide-hydrogels inhibit scar formation in wound healing through suppressing inflammation Regen. Biomater. 7 99–107