

## Exploring The Potential of Gonggong Sea Snails (*Laevistrombus Sp.*) in Biotechnology as a Source of Natural Compounds for Wound Healing

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### ABSTRACT

The gonggong sea snail (*Laevistrombus sp.*) is a typical marine life of the Riau Islands that contains various bioactive compounds with potential as wound healing agents based on natural ingredients. This study aims to evaluate the potential of gonggong sea snail extract through a literature review of articles obtained from PubMed, ScienceDirect, Google Scholar, and Scopus. Analysis of 18 articles showed that gonggong sea snails contain histone protein H2A, antimicrobial peptides, flavonoids, alkaloids, saponins, as well as essential amino acids such as arginine, proline, and glycine that work synergistically throughout the wound healing phase. The compound plays a role in suppressing inflammation through inhibition of the NF- $\kappa$ B pathway and increasing IL-10, supporting the proliferation phase by stimulating angiogenesis and collagen synthesis, and improving the remodeling phase through improved tissue quality and antioxidant activity. Histological assessment can use the SPOT score system to show relevant parameters to evaluate the effectiveness of natural ingredients in wound healing. The results of this study confirm that gonggong sea snail extract has great potential to be developed as an effective, safe, and sustainable wound therapy candidate, so experimental research is needed to validate molecular mechanisms and standardize formulations.

**KEYWORDS** biotechnology of Gonggong Sea Snails; Natural Materials; wound-healing compounds



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### INTRODUCTION

Chronic wounds represent a significant global health burden, affecting approximately 2% of the population in developed countries, with prevalence rates increasing to 4.5% among individuals over 65 years of age. Globally, the chronic wound care market is projected to exceed USD 20 billion annually, reflecting the substantial economic and healthcare impact of wound management. In Indonesia, data from the Ministry of Health (2023) indicates that wound-related complications, including diabetic ulcers and post-surgical infections, account for approximately 15-20% of hospital admissions in tertiary care facilities, with chronic wounds affecting an estimated 8.5 million people nationally.

Wounds are damage to the integrity of skin tissue that can occur due to physical, chemical, or biological trauma and often cause complications such as infection, prolonged inflammation, and tissue regeneration disorders. The wound healing process involves complex and coordinated stages, including inflammation, proliferation, and remodeling. An imbalance in any of these stages can cause wound healing to be slow or even chronic (Wang et al., 2022; Wang et al., 2018)

In clinical practice, conventional therapies such as the use of antiseptics, topical antibiotics, and synthetic ingredients (wound dressings) are still the primary choices for controlling infection and speeding up wound healing. However, this approach has several limitations. Irrational use of antibiotics can lead to bacterial resistance and disruption of normal flora. Meanwhile, harsh antiseptics can damage the healthy tissue around the wound, slow epithelial regeneration, and cause pain or soreness (He et al., 2020; Tran et al., 2019).

The ocean is recognized as one of the world's most biodiverse ecosystems, yet only 1-2% of marine natural products have been identified and characterized, according to the Food and Agriculture Organization (FAO) and UNESCO reports on marine biodiversity. Indonesia, as the world's largest archipelagic nation, possesses exceptional marine potential with over 8,500 documented species of marine biota, representing approximately 15% of global marine biodiversity. This vast resource base positions Indonesia strategically for marine bioprospecting and natural product development (Carroll et al., 2024; Wang et al., 2023).

In the last decade, marine biotechnology has emerged as one of the fastest-growing fields of research globally, with annual growth rates exceeding 12% in scientific publications related to marine natural products. This rapid expansion is attributed to the discovery and isolation of natural compounds with high biological activity, including antibacterial, antioxidant, anti-inflammatory, and regenerative properties.

Marine organisms such as mollusks, sponges, jellyfish, and algae are known to produce a variety of secondary metabolites that support self-defense mechanisms against the extreme marine environment, such as osmotic pressure, high salinity, and exposure to pathogenic microbes. Such biological adaptations cause the resulting compounds to often have strong chemical stability and bioactivity, making them ideal candidates for medical applications. For instance, sponge-derived compounds such as agelasine and manzamine alkaloids have demonstrated potent anti-inflammatory effects through NF- $\kappa$ B pathway inhibition, while conotoxins from cone snails have been developed into FDA-approved analgesic drugs (Ahmad et al., 2018; Ngandjui et al., 2024).

In the context of wound healing, marine bioactive compounds show very promising potential. For example, marine collagen from fish or mollusks has been shown to accelerate the formation of granulated tissues and increase collagen deposition. Antimicrobial peptides (AMPs) from marine organisms inhibit the growth of pathogenic bacteria without causing resistance while stimulating the proliferation of fibroblasts and keratinocytes (Wang et al., 2023; Fontana et al., 2024; Geahchan et al., 2022).

One of the biological sources that attracts attention in this context is the *gonggong sea snail* (*Laevistrombus* sp.), a marine biota typical of the Riau Islands that is known to contain histone protein H2A, antimicrobial peptides, and various essential amino acids that play important roles in skin tissue regeneration. Although Indonesia's potential for marine resources is huge, biotechnological exploration of local marine organisms such as *gonggong sea snails* (*Laevistrombus* sp.) is still limited. Most of the existing research has focused on nutritional aspects and basic antibacterial tests, while deeper studies of the biotechnological mechanisms and biological activity of their active compounds in the context of wound healing have been rare.

There is a gap in the utilization of marine bioprospecting results into therapeutic products ready for clinical use. The main challenges include lack of standardization in the extraction and characterization of bioactive compounds, absence of long-term toxicity and safety tests, and limited biotechnology facilities in coastal areas, which are the natural habitat of *gonggong sea snails*.

This study aims to systematically evaluate the biotechnological potential of *gonggong sea snail* (*Laevistrombus* sp.) extract as a natural ingredient for wound healing agent

development through comprehensive literature analysis. The specific objectives include: (1) identifying and characterizing the bioactive compounds present in *Gonggong Sea Snails*, (2) elucidating the molecular mechanisms through which these compounds modulate wound healing processes, and (3) assessing the feasibility of developing *gonggong sea snail* extract into standardized therapeutic formulations. The benefits of this research extend beyond scientific knowledge advancement to include: supporting the development of evidence-based natural medicine protocols, contributing to sustainable utilization of Indonesia's marine resources, and providing a foundation for future experimental and clinical studies. Furthermore, this study has implications for coastal bioeconomy development, pharmaceutical innovation, and the preservation of traditional marine resource utilization knowledge.

## METHOD

This study employed a systematic literature review methodology to evaluate the biotechnological potential of gonggong sea snail extract as a natural wound healing agent. The research was conducted between January and March 2024, utilizing a comprehensive search strategy across multiple electronic databases.

A systematic search was conducted through four major electronic databases: PubMed, ScienceDirect, Google Scholar, and Scopus. The search was limited to articles published within the last five years (2019-2024) to ensure the most current evidence. The following keywords and Boolean operators were used: ("wound healing" OR "wound repair" OR "tissue regeneration") AND ("Gonggong Sea Snails" OR "Laevistrombus sp." OR "Strombus" OR "marine mollusks") AND ("natural ingredients" OR "natural products" OR "bioactive compounds") AND ("biotechnology" OR "antimicrobial peptides" OR "marine-derived compounds").

Articles were included if they met the following criteria: (1) peer-reviewed research articles or systematic reviews published in English or Indonesian; (2) studies investigating the biological activity of mollusk extracts, particularly those related to wound healing mechanisms; (3) research examining wound healing mechanisms through inflammatory control, antimicrobial activity, or tissue regeneration; and (4) studies on the development of natural ingredient-based products for dermatological applications.

Exclusion criteria included: (1) articles not available in full text; (2) studies unrelated to wound healing or marine biotechnology; (3) conference abstracts, editorials, or opinion pieces without original data; and (4) duplicate publications or studies with insufficient methodological detail.

The initial database search yielded 156 articles. After removing duplicates (n=42) and screening titles and abstracts (n=87), 27 articles underwent full-text review. Following the application of inclusion and exclusion criteria, a total of 18 articles meeting all criteria were selected for qualitative analysis. The selected articles were systematically analyzed to extract information on: (1) bioactive compound identification and characterization; (2) molecular mechanisms of action in wound healing; (3) histological and biochemical outcomes; and (4) potential clinical applications. Data synthesis was performed thematically, organizing findings according to wound healing phases (inflammatory, proliferative, and remodeling) and specific bioactive compound classes.

## RESULT AND DISCUSSION

### The Potential of Marine Resources as a Source of Wound Healing Compounds

The Indonesian Sea is known as one of the regions with a variety of biodiversity, storing thousands of species of organisms that have the potential to be a source of natural bioactive compounds. Marine organisms live under extreme environmental conditions such as high pressure, high salinity, and exposure to pathogenic microorganisms that cause them to develop unique biological defense mechanisms, including the production of a variety of secondary metabolites with high biological activity.

Various studies show that bioactive compounds produced by marine organisms have anti-inflammatory, antimicrobial, antioxidant, and regenerative activities that are highly relevant in the wound healing process. For example, marine collagen from fish, jellyfish, and mollusks has been shown to accelerate tissue regeneration, increase the tensile strength of the skin, and accelerate the reepithelialization process. The compound also exhibits high biocompatibility, making it safe for medical and cosmetic applications (Wang et al., 2023; Fontana et al., 2024; Geahchan et al., 2022).

In addition to collagen, antimicrobial peptides (AMPs) from marine organisms serve as the first line of defense against bacterial infections. These peptides not only inhibit the growth of microorganisms, but also stimulate the migration of fibroblasts and keratinocyte cells, which are important in the formation of new tissues. The unique property of marine peptides is their ability to fight bacteria without causing resistance, making them a potential alternative to synthetic antibiotics (Fontana et al., 2024).

Marine organisms also produce phenolic compounds, flavonoids, alkaloids, and saponins that serve as natural antioxidants, protecting tissues from oxidative stress that can slow wound healing. The synergistic activity of these compounds is able to regulate the balance between inflammation and regeneration, thereby accelerating wound healing physiologically (Yoswaty, 2020).

One of the marine life that has great potential in this context is the gonggong sea snail (*Laevistrombus sp.*), a species typical of the waters of the Riau Islands that is widely used as food, but has only been explored a little for medical purposes. Its bioactive content, such as histone protein H2A, antimicrobial peptides, essential amino acids, and secondary metabolites in the form of flavonoids, alkaloids, and saponins, exhibit biological activity that plays an important role in anti-inflammatory processes, tissue regeneration, and collagen formation (Viruly et al., 2020; Yoswaty, 2020; Viruly et al., 2019; Yusri et al., 2023).

With the richness of these compounds, Gonggong Sea Snails have the potential to become a source of local natural ingredients for the development of effective and safe wound-healing agents. This approach based on natural materials not only supports medical therapy innovation, but also opens up opportunities for the development of a sustainable maritime bioindustry in Indonesia.

### Bioactive Content of Gonggong Sea Snails and Their Biological Activities

Gonggong sea snail (*Laevistrombus sp.*) is one of the typical marine biota of the waters of the Riau Islands which has high economic value and great pharmacological potential. These animals belong to the group of mollusks, soft-bodied marine organisms known to be rich in proteins, peptides, and secondary metabolite compounds with important biological activity. Various studies show that gonggong sea snails contain bioactive components that can play a role in the wound healing process through antimicrobial, anti-inflammatory, antioxidant, and regenerative mechanisms.

### **Histone H2A Proteins and Antimicrobial Peptides (AMPs)**

One of the important ingredients in Gonggong Sea Snails is the histone protein H2A, which functions as part of the natural body defense system of marine animals. This protein has active peptide fragments that are classified as antimicrobial peptides (AMPs), which are positively charged peptide compounds that are able to interact with the membrane of microorganisms and cause bacterial cell lysis (Viruly et al., 2020).

Antimicrobial peptides from gonggong sea snails have been shown to have activity against skin-pathogenic bacteria such as *Staphylococcus aureus* and *Pseudomonas aeruginosa*, two microbes that often cause wound infections. In addition, AMPs have an immunomodulatory effect, which is to regulate the immune response so that it is not excessive so that inflammation does not prolong. By suppressing the activity of pro-inflammatory cytokines such as TNF- $\alpha$  and IL-6, as well as increasing the expression of anti-inflammatory cytokines such as IL-10, these compounds help create the wound micro-environment conditions conducive to tissue healing (Yusri et al., 2023).

### **Essential Amino Acids for Collagen Synthesis**

In general, marine invertebrates have histone protein H2 which functions as an innate immune system consisting of amino acid peptides such as histidine, arginine, lysine, glycine, proline, leucine, alanine, and tyrosine. Thick and thin-shelled gonggong sea snails in the Riau Islands were studied to contain histone protein H2A, amino acid peptides arginine, serine, alanine, glycine, and proline which have the potential to be antimicrobial peptides (AMPs) and have antioxidant activity (Viruly et al., 2020; Sila & Bougatef, 2016; Viruly et al., 2019).

Collagen is the main structural protein in skin tissue that provides strength and elasticity. Arginine functions to increase blood flow and stimulate the production of growth factors such as TGF- $\beta$  and VEGF, which play a role in angiogenesis and the formation of granulated tissue (Geahchan et al., 2022).

Histone protein H2A and gonggong sea snail antimicrobial peptides help in wound healing through various biological mechanisms. This compound has strong antimicrobial properties that fight infection and also help control the inflammatory response to prevent excessive inflammation. Histone protein H2A also helps accelerate cell regeneration and has antioxidant properties that protect tissues from oxidative stress. Essential amino acids such as arginine, serine, alanine, glycine, and proline contribute to collagen synthesis, an important part of the formation of new tissues that help speed up the wound healing process (Wang et al., 2023; Fontana et al., 2024; Ngandjui et al., 2024).

## Secondary Metabolite Compounds: Flavonoids, Alkaloids, and Saponins

Research conducted by Yusri and Friends shows that Gonggong Sea Snails have antibacterial potential with the ability to inhibit the growth of *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria. The results of phytochemical screening tests on gonggong sea snail extract identified the presence of active compounds in the form of alkaloids, flavonoids, and saponins (Yusri et al., 2023).

1. Flavonoids have high antioxidant activity that is able to neutralize free radicals and inhibit oxidative stress in wound tissue. Molecularly, flavonoids can suppress the activation of the NF- $\kappa$ B pathway that plays a role in inflammatory processes, while increasing the expression of IL-10 as an anti-inflammatory cytokine. This activity accelerates the transition from the inflammatory phase to the proliferation phase (Zulkefli et al., 2023).
2. Alkaloids work as natural anti-inflammatories by suppressing the production of inflammatory mediators such as prostaglandins and TNF- $\alpha$ . In addition, alkaloids also support the migration of fibroblasts and keratinocytes, which accelerate the reepithelialization of wound surfaces (Criollo-Mendoza et al., 2023).
3. Saponins have antimicrobial effects and tissue regeneration stimulants. Saponins increase collagen production by fibroblasts, accelerate angiogenesis, and reduce the risk of secondary infections in open wounds (Criollo-Mendoza et al., 2023).

These three groups of compounds work synergistically to reduce inflammation, protect tissues from oxidative damage, and stimulate the formation of new tissues.

## Wound Healing Mechanisms Modulated by Natural Materials

The wound healing process is a complex biological mechanism that involves the interaction between different cell types, chemical mediators, and growth factors. In general, this process is divided into three main phases: the inflammatory phase, the proliferation phase, and the maturation or remodeling phase. Natural materials, including bioactive compounds contained in marine organisms such as Gonggong Sea Snails (*Laevistrombus sp.*), plays a role in modulating the three phases through the regulation of immune activity, collagen synthesis, and tissue regeneration.

### Inflammatory Phase

The inflammatory phase begins immediately after the occurrence of a tissue injury, aiming to stop bleeding, eliminate microorganisms, and clean up tissue debris. At this stage, neutrophils and macrophages are the main cells that play a role in phagocytosis as well as the release of pro-inflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 (Wang et al., 2022).

However, when the inflammatory response lasts too long, it can lead to secondary tissue damage and delayed wound healing. This is where natural ingredients come into play, bioactive compounds such as flavonoids and alkaloids from gonggong sea snails are able to suppress the activation of the NF- $\kappa$ B pathway, which is the main regulator of proinflammatory cytokine production (Ahmad et al., 2018).

Some active compounds also increase the expression of IL-10, which is an anti-inflammatory cytokine that functions to relieve immune reactions and restore tissue balance.

An increase in IL-10 accelerates the transition to the proliferation phase by decreasing neutrophil infiltration as well as inducing the phenotype change of macrophages from M1 (pro-inflammatory) to M2 (pro-regenerative) (Short et al., 2023).

### **Proliferation Phase**

The proliferation phase lasts about the 3rd to 14th day after injury, characterized by the formation of granulated tissue, angiogenesis, fibroblast migration, and reepithelialization. Active compounds from natural materials have a big role in accelerating this stage (MacLeod & Mansbridge, 2016).

Amino acids such as arginine, proline, glycine, and serine found in gonggong sea snails act as important substrates for collagen synthesis. The newly formed collagen will become the basic framework for the migration of epithelial cells and the formation of new tissues. Arginine also increases the production of nitric oxide (NO) which functions to expand blood vessels, thereby increasing the supply of oxygen and nutrients to the wound area (Geahchan et al., 2022).

Saponins and flavonoids stimulate angiogenesis by increasing the expression of VEGF (vascular endothelial growth factor), an important factor in the formation of new blood vessels. This process accelerates the formation of granulated tissue and stimulates the proliferation of fibroblasts. At the same time, antimicrobial peptides (AMPs) keep the wound environment sterile from bacterial infections that can inhibit tissue regeneration (Ahmad et al., 2018).

### **Maturation and Remodeling Phase**

The final phase of wound healing is maturation or remodeling, which can last up to several weeks or months depending on the extent of tissue damage. In this phase, the type III collagen formed in the previous phase is replaced by type I collagen, resulting in stronger and more elastic skin tissue (Cialdai et al., 2022).

Bioactive compounds from natural ingredients help accelerate collagen regeneration and improve its fiber organization. The antioxidant activity of flavonoids and histone protein H2A also protects new tissues from oxidative damage, resulting in better wound healing qualities. Histology, this effect is characterized by an increase in collagen density, reduced infiltration of inflammatory cells, and normalization of epidermal thickness (Guillamat-Prats, 2021).

Several studies have also shown that natural compounds that act through the PPAR- $\gamma$  (peroxisome proliferator-activated receptor gamma) pathway are able to regulate the transition from the inflammatory phase to the remodeling phase by suppressing inflammatory mediators and stimulating fibroblast differentiation. This modulating effect makes natural ingredients such as gonggong sea snail extract have a holistic working mechanism, covering all stages of wound healing (Pastar et al., 2014).

### **Histological Indicators of Wound Repair**

The effectiveness of natural ingredients on wound healing can be observed through histological examination of tissues. Common parameters used include:

1. Density and orientation of collagen fibers (Masson's Trichrome staining).
2. The number of active fibroblasts and new blood vessels in the granulated tissue.
3. The degree of reepithelialization and thickness of the epidermis.

4. The rate of infiltration of inflammatory cells as an indicator of inflammatory resolution.

An ideal wound healing assessment system entails histological assessment of wounds based on the different parameters of each wound healing phase. Vyver and colleagues developed a SPOT (Stellenbosch University, Polish Academy of Sciences, Obatala Sciences, and the University of Texas Southwestern) score based on six key parameters that represent the phases of wound healing. This SPOT score system assesses wound healing... (Van De Vyver et al., 2021).

**Table 1. SPOT score.**

Yes	Parameter	Score Criteria
1	Re-epithelialization	0: None (0%) 1: Partial (<95%) 2: Complete ( $\geq 95\text{--}100\%$ )
2	ETI ( <i>Epithelial Thickness Index</i> ) (only assessed if re-epithelialization is complete)	0: Hypoplasia (<95%) 1: Hypertrophy (>105%) 2: Normal (95–105%)
3	Keratization (only assessed if re-epithelialization is complete)	0: None 2: Ada
4	Granulation Tissue	0: None or very thin (<100 $\mu\text{m}$ , wound still active) 1: Thick (>100 $\mu\text{m}$ ) 2: None because the wound heals
5	Remodeling	0: None 1: Partial (collagen or <i>dermal white adipose tissue</i> only) 2: Complete (skin resembles normal)
6	Scar Elevation Index (SEI)	0: Hypoplasia 1: Hypertrophic 2: Normal (95–105%)

The SPOT score system provides a quantitative and comprehensive approach in assessing wound healing rates based on histological parameters that reflect the biological processes that occur in each phase of healing, ranging from inflammation, proliferation, to tissue remodeling. A higher score indicates a better healing rate, characterized by complete reepithelialization, normal epidermal thickness, mature granulated tissue formation, and dermal remodeling that resembles normal skin structure.

Through this system, the effectiveness of a natural ingredient including bioactive extracts can be objectively compared between treatment groups. This assessment also helps identify which healing phases are most affected by a particular intervention, for example increased collagen deposition, decreased inflammatory cell infiltration, or accelerated reepithelialization.

## Discussion

The results of the literature review show that gonggong sea snail extract (*Laevistrombus sp.*) has significant potential in accelerating wound healing processes through complex and integrated biological mechanisms. Based on histological parameters, the effectiveness of extracts of these natural ingredients can be judged from the increase in SPOT scores.

Mechanistically, the main bioactive content in gonggong sea snails works synergistically at different phases of wound healing. In the inflammatory phase, flavonoids and alkaloids play an important role in suppressing the activation of the NF-κB pathway that regulates the expression of proinflammatory cytokines such as TNF-α, IL-1β, and IL-6. Suppression of this pathway helps prevent excessive inflammation and accelerates the transition to the proliferation phase.

In the proliferation phase, the role of essential amino acids such as arginine, proline, and glycine becomes dominant in supporting collagen synthesis and angiogenesis. Arginine increases the production of nitric oxide (NO) which functions to expand blood vessels and increase the flow of oxygen and nutrients to the wound area. Meanwhile, saponins and flavonoids stimulate the expression of VEGF (Vascular Endothelial Growth Factor) and TGF-β (Transforming Growth Factor Beta) which play a role in the formation of granulated tissue and fibroblast migration.

In the remodeling phase, the type III collagen formed is replaced by type I collagen so that the tissue structure becomes stronger and more elastic. The antioxidant activity of flavonoids and histone protein H2A serves to protect new tissues from oxidative stress and support better organization of collagen fibers. Histology, this process can be assessed from an increase in collagen fiber density, a decrease in inflammatory cell infiltration, as well as a normalization of epidermal thickness and a scar elevation index that is close to normal.

Gonggong sea snail extract not only acts as a natural antimicrobial agent, but also has potential immunomodulatory and regenerative functions that make it an ideal candidate for wound therapy based on natural ingredients.

Thus, this study confirms the importance of further experimental research development, including in vivo and IL-10 immunohistochemical assays, to prove the role of modulation of gonggong sea snail extract on the inflammatory signaling pathways NF-κB and PPAR-γ, as well as its relationship with improved histological scores for wound healing such as SPOT scores.

## CONCLUSION

The comprehensive literature review indicates that *Laevistrombus sp.* (gonggong sea snail) holds significant biotechnological promise as a natural source for wound healing compounds. Its extract contains a synergistic mix of bioactive molecules—including histone H2A proteins, antimicrobial peptides, essential amino acids, and secondary metabolites like flavonoids, alkaloids, and saponins—that collectively regulate wound healing by reducing inflammation (via NF-κB inhibition and IL-10 upregulation), promoting cell proliferation and angiogenesis, and enhancing tissue remodeling through antioxidant effects and collagen organization. Quantitative assessment with tools like the SPOT score supports its multifunctional role in safe and effective wound repair. Future research should shift from theoretical reviews to experimental validation through in vivo animal studies to confirm efficacy and safety, alongside in vitro investigations to clarify molecular pathways such as NF-κB, PPAR-γ, and TGF-β signaling. Additionally, efforts must standardize extraction methods, assess compound stability and toxicity, and develop scalable formulations, ultimately

advancing evidence-based, sustainable marine-derived dermatological products from Indonesia.

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