

Review: Chemical profiles and therapeutic potentials of golden sea cucumber (*Stichopus hermanii*)

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Abstract. Aulia AA, Astuti AR, Wulandari AA, Nugroho GD, Setyawan AD. 2024. Review: Chemical profiles and therapeutic potentials of golden sea cucumber (*Stichopus hermanii*). *Cell Biol Dev* 8: 58-67. The golden sea cucumber (*Stichopus hermanii*) is a species of sea cucumber that has a unique chemical profile and significant therapeutic potential. Traditionally, sea cucumbers have been used in medicine in Southeast Asia for their properties which include anti-inflammatory, antioxidant and antimicrobial properties. The distribution of golden sea cucumbers is dominant in Southeast Asia and Northern Australia, but their populations are threatened due to excessive fishing. Conservation efforts through cultivation are being developed to restore wild stocks. This research aims to determine the hidden chemical profile and therapeutic potential of the golden sea cucumber by collecting information from various literature. Golden sea cucumbers have many chemical profiles, namely protein, saponin, triterpenoid, collagen, GAGs, flavonoid, mineral, glutathione, alkaloid, methanol, and hyaluronic acid. This species also have great potential as therapeutic agents, such as wound healing, antifungal properties, hipertriglyceridemia, hypercholesterolemia, diabetes, bone and tooth regeneration. This research brings various data that showed the importance of golden sea cucumbers in the field of health, such as the ability to increase insulin sensitivity, which is beneficial in the treatment of diabetes. Additionally, the high protein content in sea cucumbers provides additional nutritional value and supports antioxidant function. An in-depth understanding of the chemical composition and therapeutic benefits of golden sea cucumbers can encourage the development of biomedical products and support the economic well-being of coastal communities that depend on this resource. Therefore, conservation measures for this species must continue to be carried out so that it remains sustainable in nature and can be used wisely by humans.

Keywords: Chemical profile, golden sea cucumber, therapeutic potential

INTRODUCTION

The golden sea cucumber (*Stichopus hermanii* Semper, 1868) is a species of sea cucumber that has garnered attention in the health and medical fields due to its unique chemical profile and significant therapeutic potential. Research shows that the population of the golden sea cucumber has significantly declined due to overfishing and ineffective fisheries management (Brown et al. 2022). Conservation and restocking efforts through aquaculture are being developed to help restore wild stocks. Sea cucumbers also serve as a primary source of income for millions of small-scale fishers worldwide (Baker-Médard and Ohl 2019). However, sea cucumbers have become a premium product with high prices in international markets. Consequently, their exploitation has been excessive, disrupting their sustainability (Pangkey et al. 2012). Traditionally, sea cucumbers have been used in Southeast Asian medicine for their anti-inflammatory, antioxidant, and antimicrobial properties. Recent research has revealed the scientific basis behind these traditional claims,

highlighting that the bioactive components in sea cucumbers are promising as therapeutic agents. One of the key components in *S. hermanii* is Glycosaminoglycans (GAGs), which have anti-inflammatory activity and play a role in immune system modulation (Mulawarmanti et al. 2022). GAGs also contribute to wound healing and tissue regeneration, explaining their traditional use in wound care (Mondol et al. 2017). Additionally, the golden sea cucumber contains glycosaminoglycans such as heparan sulfate and chondroitin sulfate, which can benefit the wound healing process (Arundina et al. 2015).

Besides GAGs, this sea cucumber is also rich in other bioactive compounds like saponins, which exhibit anticancer activity (Wargasetia 2018). Research on saponins in *S. hermanii* has shown that these compounds can induce apoptosis, a process of programmed cell death crucial for cancer control. Sea cucumbers contain various bioactive compounds, including phenolics, polysaccharides, proteins (collagen and peptides), carotenoids, and saponins, which exhibit strong antioxidant activity and other therapeutic benefits (Hossain et al. 2022).

The fatty acids in sea cucumbers are known to have anti-inflammatory activity that can help manage chronic inflammatory conditions (Escobar-Sánchez et al. 2015). The high protein content in sea cucumbers provides additional nutritional value, with antioxidant activity that protects against oxidative damage and prevents degenerative diseases like Alzheimer's and Parkinson's (Shan et al. 2011). Sea cucumber extracts have shown antimicrobial properties effective against pathogens, including bacteria and fungi, presenting opportunities for natural antibiotics (Mnif et al. 2011). The golden sea cucumber is a natural marine biota containing proteins and active ingredients that function as antibacterial, anti-inflammatory, and antioxidant agents (Mulawarmanti et al. 2022). Extracts of *S. hermanii* can reduce hyphae count, neutrophils, and TNF- α levels through hyphae, neutrophils, and TNF- α pathways (Yudo et al. 2022). *S. hermanii* extracts contain antioxidants proven to alleviate oxidative stress conditions (Prawitasari et al. 2019). Furthermore, this sea cucumber has potential in diabetes treatment, with bioactive compounds that enhance insulin sensitivity and lower blood glucose levels (Oh et al. 2017). Research findings indicate that sea cucumbers can be developed as functional food products to help combat the onset of diabetes and its complications (Rahmadani 2023). The ability of sea cucumbers to produce bioactive metabolites stems from their response to various ecological pressures and predation avoidance (Telahigue et al. 2020). Sea cucumbers contain various bioactive compounds, including saponins and glycosaminoglycans, associated with their therapeutic properties (Bordbar et al. 2011). Sea cucumber aquaculture is an effective way to meet consumer demand and restore its resources (Ma et al. 2022). These findings suggest that adding sea cucumber polysaccharides or their low molecular weight derivatives to Baijiu has the potential to mitigate alcohol-induced liver damage (Song et al. 2024).

Overall, these marine-derived bioactive peptides have the ability to promote cell proliferation and can be further explored as cell growth-promoting agents for biomedical and bioprocess applications (Pilus et al. 2022). This research aims to determine the hidden chemical profile and therapeutic potential of the golden sea cucumber by collecting information from various literature. The literature review used search engines such as PubMed, Wiley, and Google Scholar with specific keywords. A total more than 100 articles were then selected and excluded. This research is motivated by the lack of unified data on chemical profile and therapeutic potential of the benefits of *S. hermanii*.

Stichopus hermanii

S. hermanii, commonly known as the golden sea cucumber, is named for its cucumber-like shape (Figure 1). *S. hermanii* belongs to the Phylum Echinodermata, Subphylum Echinozoa, and Class Holothuroidea. The golden sea cucumber sustains its life in the food chain by consuming organic matter in the sand, plankton, bacteria,

and aquatic organisms as supplements. Currently, the number of golden sea cucumber species has reached 2000 species with a wide area and distribution (Setiyowati et al. 2016).

S. hermanii is an invertebrate animal with spiny skin, forming a cylindrical and elongated shape. The spines on its skin are small and spread across the epidermal layer, visible under a microscope. Generally, the length of the golden sea cucumber ranges from 2.54 to 90 cm (Hartati et al. 2015). On the anterior part of its body, there is a mouth equipped with tentacles for capturing food, while the posterior part has an anus. According to Hartati et al. (2015), the identification of *S. hermanii* or golden sea cucumber reveals that this species has a trapezoidal or rectangular cross-section and is relatively large in size. The integument is smooth, with folds on the surface and structured papillae spread on both dorsolateral sides. The dorsal side is yellowish-brown with blackish papillae or wart-like protrusions.

The primary habitats of sea cucumbers are coral reefs and seagrass beds. Generally, the golden sea cucumber lives in coastal waters at depths of 1-40 meters. The golden sea cucumber thrives in waters with salinity levels between 30‰ and 33‰, with a seabed of fine sand and protective plants against wave action, such as detritus (decayed algae). In Indonesia, the distribution of the golden sea cucumber can be found in East Java, Madura, Sumba, Bali, Aceh, Lombok, Bangka, and Bengkulu (Pringgienies et al. 2018). The distribution spread across the world can be seen in the Figure 2.

The distribution of *S. hermanii*, marked with yellow-orange dots on a world map, showed a predominant presence in Southeast Asia and Northern Australia, indicating a preference for warm tropical waters (Figure 2). Their presence in East Africa confirms the global range of this species, which may be influenced by international trade. This information is crucial for ecological studies, conservation efforts, and the development of sustainable aquaculture, providing insights into marine ecosystem health and the role of sea cucumbers in bioturbation. Therefore, understanding this distribution can aid in conservation efforts and in selecting suitable aquaculture locations that match the natural conditions of the golden sea cucumber.



Figure 1. *Stichopus hermanii* (inaturalist.org)

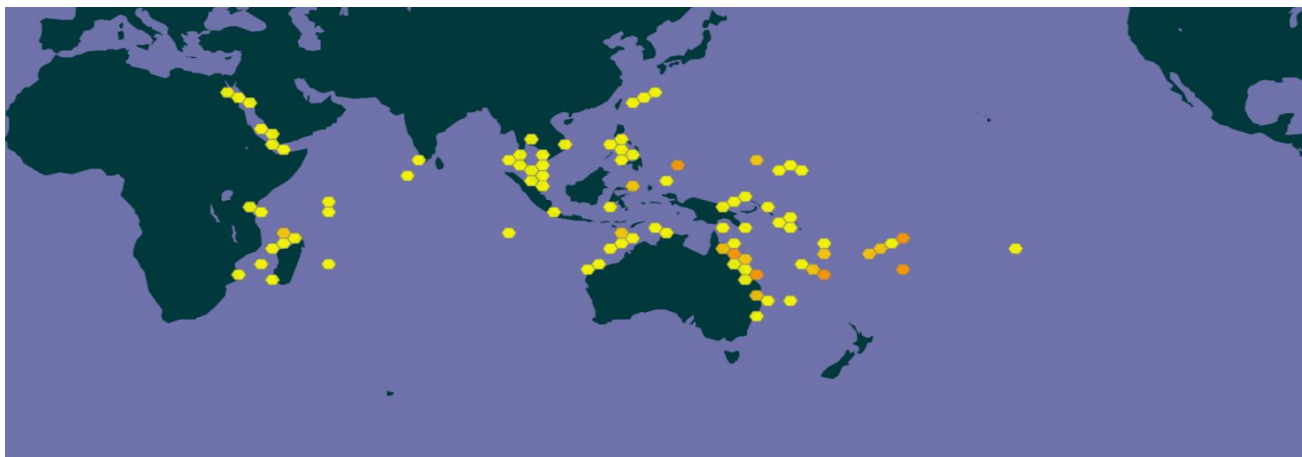


Figure 2. Distribution of golden sea cucumber in the world in 2024 (gbif.org). Note: The more orange the color indicates that the species' presence coordinate points are more numerous and dense in that area

CHEMICAL PROFILES

Protein

S. hermanii contains various beneficial components, one of which is protein (Table 1). The protein in this species is highly beneficial for the body (Prameswari et al. 2020; Safithri et al. 2022a; Taurina and Andrie 2022). The protein content in the golden sea cucumber reaches 86%, which is easily soluble in pepsin enzyme (Rasyid 2018). The golden sea cucumber is considered a marine animal rich in protein and low in lipids, with a large amount of sulfated glycosaminoglycans (De Fretes et al. 2020). Due to its beneficial proteins, the sea cucumber is also known to be used as medicine and is very effective in healing various diseases. It can help with anti-inflammatory, antiviral, and antioxidant processes (Oktaviani et al. 2018; Yatmasari et al. 2021; Rusmini et al. 2023), antimicrobial (Pringgenies et al. 2018), prevent blood clotting, prevent arthritis, accelerate wound healing, serve as a high-protein food source, boost the immune system, combat fatigue, and prevent cancer (Nurwidodo et al. 2018; Rusmini et al. 2023).

Saponin

S. hermanii is known to contain various bioactive compounds, including saponins (Zhafira 2016; Wang and Wang 2017; Pringgenies et al. 2018; Windari et al. 2019; Prameswari et al. 2020; Setianingsih et al. 2020; Monika et al. 2021; Adam et al. 2023a). Initially discovered in sea cucumbers, saponins are classified as holothurins, identified for their broad spectrum of physiological activities. Saponins in *S. hermanii* are found in the skin, flesh, and tubular Cuvierian organs. These high concentrations of saponins act as a defense mechanism against predators and serve as antimicrobial agents. Pure sea cucumber extract tends to contain holotoxins, which exhibit effects similar to antimycin at doses of 6.25-25 µg/mL (Pringgenies et al. 2018). The saponins in golden sea cucumbers stimulate cell regeneration and possess high antioxidant content. Additionally, saponins provide antibacterial functions (Cushnie et al. 2014; Irfan et al.

2014). Safithri et al. (2020b) highlighted that *S. hermanii* contains triterpene glycosides, known antioxidants that can improve hyperlipidemia and hyperglycemia conditions in tested animals like rats. Saponins act as antibacterial agents by breaking down cytoplasmic membranes and killing cells (Cankaya and Somuncuoglu 2021). The antioxidant activity in *S. hermanii* derives from compounds like riboflavin, flavonoids, saponins, tannins, and omega-3. Saponins are a primary component of the antimicrobial properties in *S. hermanii* (Pringgenies 2013).

Triterpenoid

S. hermanii contains triterpenoids that function as antibacterial agents (Cushnie et al. 2014; Irfan et al. 2014). This species has various triterpenoids, particularly holostane types, which possess significant biological activities. Akerina and Sangaji (2019) reinforced that many marine organisms with triterpenoids benefit the body by providing antibacterial, antifungal, and anticancer properties. Zhafira (2016) also confirmed that *S. hermanii* contains triterpenoids, which can reduce blood cholesterol, Low-Density Lipoprotein (LDL), and Triacylglycerol (TAG) levels. Triterpenoids enhance antioxidant functions in plasma and serum, reducing DNA damage, inflammation, and oxidative stress (Han and Bakovic 2015). Testing triterpenoids involves dissolving extracts in 0.5 mL chloroform, adding 0.5 mL acetic anhydride, and 2 mL H₂SO₄ (Anggraeni et al. 2014).

Collagen

All animals contain collagen, a structural protein component in bones, tendons, skin, blood vessels, and the cornea (Marks et al. 2014). Collagen has antioxidant properties and can inhibit tyrosinase activity in melanogenesis. Sea cucumbers are an alternative source of collagen (Safithri et al. 2018). According to Sari et al. (2017) and Siahaan (2017a), sea cucumbers, including *S. hermanii*, are rich in collagen (Sari et al. 2012; Shahrulazua et al. 2013). Additionally, omega-3 and glycosaminoglycans in golden sea cucumbers aid in healing by increasing collagen levels (Damaiyanti et al.

2019). Collagen content in *S. hermanii* can reach 70% of the total protein in the body (Siahaan et al. 2017b). Pringgenies et al. (2018) confirmed that the highest collagen content in *S. hermanii* is in amino acids, chondroitin, and glucosamine. This extracellular collagen is beneficial for dental support tissues (Ratri et al. 2017), shortening the healing time for diseases (Shahrulazua et al. 2013)

GAGs

S. hermanii is rich in Glycosaminoglycans (GAGs) (Sari et al. 2012; Damaiyanti et al. 2019; De Fretes et al. 2020). GAGs in *S. hermanii* offer health benefits such as anti-inflammatory, anticoagulant, and wound healing properties. GAGs enhance skin health by maintaining moisture and elasticity and supporting cell regeneration. They also have potential in repairing connective tissues and cartilage, useful in treating conditions like osteoarthritis and other joint diseases (Rusmini et al. 2023). GAGs

include heparin sulfate and chondroitin sulfate. Heparin sulfate, a complex polysaccharide involved in various biological processes, is found in golden sea cucumbers and has anticoagulant and anti-inflammatory potential. Chondroitin sulfate inhibits the formation of periodontal pathogen biofilms (Ratri et al. 2017) and supports joint and bone health, offering anti-inflammatory effects and protection against cartilage damage (Martel-Pelletier et al. 2015).

Flavonoid

Flavonoids in *S. hermanii* have antioxidant benefits, inhibiting activities like peroxidase and xanthine oxidase (Akerina and Sangaji 2019). Marliza et al. (2022) added that flavonoids in marine animals reduce apoptosis, promoting anticancer properties by inducing programmed cell death. Flavonoids in *S. hermanii* are proven to trigger apoptosis, inhibiting cancer growth (Windari et al. 2019; Prameswari et al. 2020; Marliza et al. 2022).

Table 1. Table of bioactive compounds and their benefits in *Stichopus hermanii*

Main bioactive compounds	Benefits	References
Protein	This species' protein is extremely healthy for the body	(Prameswari et al. 2020; Safithri et al. 2022; Taurina and Andrie 2022)
	The golden sea cucumber has 86% protein, which the pepsin enzyme readily dissolves	(Rasyid 2018)
	The golden sea cucumber is regarded as a marine creature that is high in sulfated glycosaminoglycans, low in lipids, and high in protein It is also well recognized for being used as medication and for being highly successful in curing a variety of illnesses. It can support antioxidant, antiviral, and anti-inflammatory functions	(De Fretes et al. 2020)
Saponin	Act as a high-protein food source, prevent blood clotting, prevent arthritis, hasten wound healing, strengthen the immune system, fight weariness, and prevent cancer	(Oktaviani et al. 2018; Pringgenies et al. 2018; Yatmasari et al. 2021; Rusmini et al. 2023)
	Saponins, which are categorized as holothurins and were first found in sea cucumbers, are known for a wide range of physiological functions. Saponins in <i>Stichopus hermanii</i> are found in the skin, flesh, and tubular Cuvierian organs. These elevated levels of saponins function as antibacterial agents and a defense mechanism against predators. Holotoxins, which are found in pure sea cucumber extract, have effects comparable to those of antimycin at dosages of 6.25-25 µg/mL	(Nurwidodo et al. 2018; Rusmini et al. 2023)
	Golden sea cucumbers' saponins have a high antioxidant concentration and promote cell regeneration. Moreover, saponins have antimicrobial properties Antioxidants that have been shown to alleviate hyperglycemia and hyperlipidemia in test animals, such as rats. By dissolving cytoplasmic membranes and destroying cells, saponins function as antibacterial agents. Compounds like riboflavin, flavonoids, saponins, tannins, and omega-3 fatty acids are responsible for <i>S. hermanii</i> 's antioxidant properties Saponins are a primary component of the antimicrobial properties in <i>S. hermanii</i>	(Pringgenies et al. 2018) (Cushnie et al. 2014; Irfan et al. 2014) (Safithri et al. 2020b)
Triterpenoid	Triterpenoids with antimicrobial properties	(Pringgenies 2013)
	Triterpenoids found in a variety of marine creatures have antibacterial, antifungal, and anticancer effects that are beneficial to the body	(Cushnie et al. 2014; Irfan et al. 2014) (Akerina and Sangaji 2019)
	It can lower levels of Triacylglycerol (TAG), Low-Density Lipoprotein (LDL), and blood cholesterol	(Zhafira 2016)
	Triterpenoids improve antioxidant properties in serum and plasma, lowering oxidative stress, inflammation, and DNA damage	(Han and Bakovic 2015)
	Triterpenoids are tested by dissolving extracts in 0.5 mL chloroform, then adding 2 mL H ₂ SO ₄ and 0.5 mL acetic anhydride	(Anggraeni et al. 2014)

Collagen	<p>Tyrosinase activity in melanogenesis can be inhibited by collagen, which also possesses antioxidant qualities. Another source of collagen is sea cucumbers. Collagen is abundant in <i>S. hermanii</i>.</p> <p>Golden sea cucumbers' omega-3 and glycosaminoglycans also promote healing by raising collagen levels.</p> <p>Collagen content in <i>S. hermanii</i> can reach 70% of the total protein in the body. The amino acids, chondroitin, and glucosamine in <i>S. hermanii</i> include the most collagen.</p> <p>The tissues that support teeth benefit from this extracellular collagen.</p> <p>Reducing the duration of illness recovery.</p>	<p>(Safithri et al. 2018)</p> <p>(Shahrulazua et al. 2013; Sari and Wahjuningsih 2017; Siahaan 2017a)</p> <p>(Damaiyanti et al. 2019)</p> <p>(Siahaan et al. 2017b)</p> <p>(Pringgenies et al. 2018)</p> <p>(Ratri et al. 2017)</p> <p>(Shahrulazua et al. 2013).</p>
GAGs	<p>There are a lot of Glycosaminoglycans (GAGs) in <i>S. hermanii</i>.</p> <p><i>S. hermanii</i>'s GAGs have anti-inflammatory, anticoagulant, and wound-healing qualities, among other health advantages. By preserving skin suppleness and hydration and promoting cell renewal, GAGs improve skin health. Moreover, they may be able to restore cartilage and connective tissues, which would be helpful in the treatment of illnesses of the joints and osteoarthritis.</p> <p>Heparin sulfate and chondroitin sulfate are examples of GAGs. Golden sea cucumbers contain heparin sulfate, a complex polysaccharide with anticoagulant and anti-inflammatory properties that is involved in many biological processes. The development of periodontal pathogen biofilms is inhibited by chondroitin sulfate.</p> <p>Promotes bone and joint health by providing anti-inflammatory benefits and defense against cartilage degradation.</p>	<p>(Sari et al. 2012; Damaiyanti et al. 2019; De Fretes et al. 2020)</p> <p>(Rusmini et al. 2023)</p> <p>(Ratri et al. 2017)</p> <p>(Martel-Pelletier et al. 2015)</p>
Flavonoid	<p>Possess antioxidant properties via blocking enzymes such as xanthine oxidase and peroxidase.</p> <p>Reduce apoptosis to induce planned cell death, which will promote anticancer qualities. It has been demonstrated that flavonoids in <i>S. hermanii</i> cause apoptosis, which stops the growth of cancer.</p>	<p>(Akerina and Sangaji 2019)</p> <p>(Prameswari et al. 2020; Windari et al. 2019; Marliza et al. 2022)</p>
Mineral	<p>The golden sea cucumber <i>Simplisia</i> had zinc (Zn) levels of 9.32 mg/kg, according to testing conducted by the Pontianak Standardization and Industrial Research Institute. Zinc influences bacterial activity and is essential for optimal cell growth, DNA polymerase synthesis, and wound healing.</p> <p><i>S. hermanii</i> also contains other minerals, such as silicon and calcium, which aid in the synthesis of its structural materials.</p>	<p>(Sari et al. 2020)</p> <p>(Floren et al. 2023)</p>
Glutathione	<p>Glycine, glutamate, and cysteine are amino acids found in <i>S. hermanii</i> that are precursors to glutathione, the body's main antioxidant.</p> <p>Glutathione prevents cancer by lowering oxidative activity.</p> <p>By giving free radicals electrons, you can stop cell damage.</p> <p>With the aid of glutathione peroxidase, it transfers electrons to hydrogen peroxide (H₂O₂) and superoxide (O₂^{-*}), creating H₂O.</p>	<p>(Espinosa-Diez et al. 2015)</p> <p>(Wardhani 2019)</p> <p>(Cahyati et al. 2018)</p> <p>(Safithri et al. 2022)</p>
Alkaloid	<p><i>S. hermanii</i>'s alkaloid content gives it antibacterial qualities.</p> <p>Alkaloids are secondary chemicals with nitrogen atoms in their structure that are produced from amino acids. Alkaloids from <i>S. hermanii</i> can suppress both Gram-positive and gram-negative bacteria, although they can be harmful if taken in excess.</p> <p>They help treat diabetes by stimulating the hypothalamus, which lowers blood sugar, gluconeogenesis, and insulin needs.</p>	<p>(Cushnie et al. 2014; Irfan et al. 2014; Zhafira 2016; Susanto et al. 2018; Rahmadani 2023)</p> <p>(Tamara et al. 2015)</p> <p>(Rasouli et al. 2020)</p>
Methanol	<p>Bioactive substances such as alkaloids, saponins, and triterpenoids are present in the methanol extract of <i>S. hermanii</i>, promoting strong antioxidant activity.</p> <p>By generating molecules with pharmacological effects, such as those that treat pain, arthritis, AIDS, and cancer, these bioactive compounds have an impact on organisms. Additionally, they improve antioxidant activity, anti-inflammatory, anti-diabetic, anti-obesity, and anti-aging properties.</p>	<p>(Zhafira 2016)</p> <p>(Pringgenies 2019)</p>
Hyaluronic Acid	<p>Other beneficial components of <i>S. hermanii</i> include hyaluronic acid.</p> <p>Also contains chondroitin sulfate, heparinsulfate, and dermatan sulfate which can help activate and bind GFs, especially FGF-2. In order to create healthy collagen, <i>S. hermanii</i> also contains unsaturated fatty acids, which are the primary agents in regulating fibroblast proliferation, collagen production, and the inflammatory process in wound healing. Another benefit of having unsaturated fatty acids is that they strengthen connective tissue and reduce the creation of scars.</p>	<p>(Sari et al. 2012; Prameswari et al. 2020)</p> <p>(Sari et al. 2012)</p>

Mineral

S. hermanii contains various minerals. Testing by the Pontianak Standardization and Industrial Research Institute identified zinc (Zn) levels at 9.32 mg/kg in golden sea cucumber *Simplisia*. Zinc is crucial for normal cell growth, DNA polymerase production, and wound healing, influencing bacterial activity (Sari et al. 2020). Other minerals like calcium and silicon are also present in *S. hermanii*, contributing to its structural mineral formation (Floren et al. 2023).

Glutathione

S. hermanii contains amino acids like glycine and glutamate, precursors to glutathione, a primary antioxidant in the body composed of glycine, cysteine, and glutamate (Espinosa-Diez et al. 2015). Glutathione reduces oxidative activity, preventing cancer (Wardhani 2019) by donating electrons to free radicals, thus preventing cell damage (Cahyati et al. 2018). It transfers electrons to superoxide (O₂^{-*}) and hydrogen peroxide (H₂O₂), forming H₂O with the help of glutathione peroxidase (Safithri et al. 2022).

Alkaloid

S. hermanii has antibacterial properties due to its alkaloid content (Cushnie et al. 2014; Irfan et al. 2014; Zhafira 2016; Susanto et al. 2018; Rahmadani 2023). Alkaloids are secondary compounds derived from amino acids, categorized by nitrogen atoms in their structure. Despite their toxicity when improperly consumed, alkaloids from *S. hermanii* can inhibit both Gram-positive and gram-negative bacteria (Tamara et al. 2015). They stimulate the hypothalamus, reducing gluconeogenesis, blood sugar, and insulin requirements, beneficial for diabetes treatment (Rasouli et al. 2020).

Methanol

The methanol extract of *S. hermanii* contains bioactive compounds like alkaloids, saponins, and triterpenoids, supporting high antioxidant activity (Zhafira 2016). These bioactive compounds influence organisms by producing chemicals with pharmacological effects, such as treating cancer, AIDS, arthritis, and pain. They also offer health benefits, enhancing antioxidant function, anti-obesity, anti-diabetes, anti-inflammatory, and anti-aging activities (Pringgenies 2019).

Hyaluronic acid

S. hermanii has various other good ingredients, such as hyaluronic acid (Sari et al. 2012; Prameswari et al. 2020). Apart from hyaluronic acid, *S. hermanii* also contains chondroitin sulfate, heparinsulfate, and dermatan sulfate which can help activate and bind Growth Factors (GFs), especially Fibroblast Growth Factor-2 (FGF-2). *S. hermanii* also contains unsaturated fatty acids which are the main agents in controlling the inflammatory process in wound healing, regulating fibroblast proliferation and collagen synthesis to produce healthy collagen. Another advantage of the presence of unsaturated fatty acids is that it minimizes scar formation and increases connective tissue strength (Sari et al. 2012).

THERAPEUTIC POTENTIAL OF GOLDEN SEA CUCUMBER

Golden sea cucumber has numerous therapeutic potentials. Therapeutic pertains to the treatment of diseases or the healing of patients. The golden sea cucumber can be used as a medicinal ingredient for various diseases. It possesses high-value-added compounds that are functional as biomedical materials and derivatives. Its use as a natural medicine is supported by the significant benefits and potential of the organism as an alternative to chemical drugs, which often have high side effects (Adam et al. 2022a). Its therapeutic properties include fatty acids, vitamins, amino acids, glycosaminoglycans, keratin, glucosamine, triterpene glycosides, carotenoids, peptides, chondroitin, cell growth factors, mucopolysaccharides, glycosides, lectins, minerals, omega-3 and 6, and collagen. Research shows that the golden sea cucumber can regenerate tissues, relieve pain, and act as an antimicrobial, fungicide, antioxidant, and anticancer agent (Utami and Yudho 2022).

Wound healing and antifungal properties

Several researchers have found that golden sea cucumber is effective in wound healing, with 13.48% of sea cucumber researchers focusing on this hidden benefit (Mulawarmanti et al. 2019). When combined with extracts of snakehead fish, stingless bee honey, green betel leaf, and clove oil, it can enhance wound healing speed due to its strong adhesion effect (Lestari et al. 2023). In angiogenesis, golden sea cucumber increases the expression of Vascular Endothelial Growth Factor (VEGF) in wound healing (Soesilawati et al. 2019). The wound healing process can be observed through the increase in lymphocytes in ulcers (Arundina et al. 2015). Golden sea cucumber contains glycosaminoglycans and omega-3, which can accelerate wound healing of physiological disturbances or pain in soft mouth tissues (Sari and Wahjuningsih 2017). Extracts of golden sea cucumber containing hyaluronic acid combined with calcium carbonate from blood clam shells stimulate the healing process of tooth extraction complications and periodontal diseases (Sari et al. 2017). Extracts used as raw materials for wound healing drugs must undergo specific standardization such as organoleptic, water and ethanol content, phytochemical screening, protein content, and non-specific standardization (Rusmini et al. 2023). Standardization is done according to applicable Indonesian National Standards (SNI) to ensure reproducibility and maintain the quality of wound healing drugs (Taurina and Andrie 2022). Golden sea cucumber has also been extensively studied for its antifungal and anti-inflammatory properties, which are implemented in treating inflammatory diseases such as *Candida vaginitis* (Yudo et al. 2022). Variegatuside D and E have shown significant inhibition against *C. albicans*, *C. parapsilosis*, *C. neoformans*, *C. tropicalis*, *C. pseudotropicalis*, and *Nannizzia gypsea* (Carodoso et al. 2020). The antifungal properties of golden sea cucumber are due to its body wall and coelomic fluid, which inhibit the growth of *C. albicans*, *Aspergillus*

brasiliensis, *A. flavus*, *A. niger*, and *A. fumigatus* (Adipour et al. 2014).

Hipertrigliseridemia and hiperkholesterolemia

Hypercholesterolemia is a condition of the body that experiences too high an increase in cholesterol levels in the blood. This cholesterol has the potential to increase the risk of heart attack or stroke due to narrowing of blood vessels from the accumulation of fat. The body needs cholesterol as a constituent of healthy cells, Vitamin D producer, and produces various hormones. Cholesterol is produced by the liver and comes from food. However, if the cholesterol level is too high hypercholesterolemia is the term for elevated levels of total cholesterol, LDL cholesterol, and triglycerides in the blood, which exceed normal limits (Angelina et al. 2022).

Blood triglyceride levels exceeding normal limits can trigger coronary artery disease and cardiovascular disease. One bioactive compound in sea cucumbers is steroids, which function as aphrodisiacs and sex reversals (Meydia et al. 2016). Golden sea cucumber extract can reduce triglyceride levels in hyperlipidemic test rats, proving its potential as a supportive treatment for hypertriglyceridemia (Angelina et al. 2022). According to Hartono and Mukono (2020), the antioxidants in golden sea cucumber can lower cholesterol levels, which are a cause of hypercholesterolemia. This cholesterol reduction also lowers the potential for cardiovascular diseases and other life-threatening conditions.

Diabetes

Diabetes is a chronic disease characterized by high blood sugar levels. Glucose is the main source of energy for human cells. However, in people with diabetes, the glucose cannot be used by the body. Blood sugar (glucose) levels are controlled by the hormone insulin produced by the pancreas. However, in diabetics, the pancreas is unable to produce insulin according to the body's needs. Without insulin, the body's cells cannot absorb and process glucose into energy (Mariyanti 2017). Golden sea cucumber extract can treat diabetes (Fajarwati 2017; Setianingsih et al. 2021). *S. hermanii* powder used in Hyperbaric Oxygen (HBO) therapy acts as an antioxidant and antibacterial agent. Tests on 20 male Wistar rats treated with HBO therapy and *S. hermanii* powder showed a reduction in blood sugar levels, indicating its potential in treating diabetes mellitus characterized by hyperglycemia (Darojati et al. 2017). Golden sea cucumber powder has been shown to increase osteoprotegerin expression in diabetes mellitus with periodontitis (Aziza et al. 2016). Diabetes mellitus can cause metabolic disorders due to increased lipolysis, known as hyperlipidemia. The EPA-DHA, saponin, and flavonoid content in golden sea cucumber can act as anti-hyperlipidemic agents (Setianingsih et al. 2020). In addition to diabetes mellitus, golden sea cucumber can inhibit free radical oxidant activity and protect muscles in diabetic patients by activating Glut-4 and IL-6 proteins (Purwanto et al. 2019).

Bone and tooth regeneration

Research indicates that golden sea cucumber has strong potential in bone and tooth regeneration (Hlaing and Compston 2014; Hienz et al. 2015; Sheikh et al. 2017; Ho-Shui-Ling et al. 2018; Jalaluddin et al. 2018; Kruger 2019; Liu et al. 2019; Sari and Kurniawan 2019; Djais et al. 2020; Battafarano et al. 2021). Golden sea cucumber contains rich bioactive components (Fawzya et al. 2020). These bioactive components are beneficial as biocompatible materials in bone grafting, restoring adhesion, filling bone effects, and regenerating bone (Adam et al. 2022b). Golden sea cucumber bone graft can be used as a regenerative bone therapy and an effort to regenerate periodontitis (Adam et al. 2023b). Untreated periodontitis can lead to tooth loss (Adam et al. 2021). Through its content, including flavonoids, heparan sulfate, chondroitin sulfate, collagen, and hyaluronic acid, golden sea cucumber can prevent orthodontic relapse by increasing osteogenesis of the periodontal ligament in cases of orthodontic relapse or unwanted tooth movement (Sangian et al. 2024).

Traditionally, sea cucumber processing is done by manual cleaning and preservation techniques in the form of drying or smoking (Herliany et al. 2016). Sea cucumbers have traditionally been used as medicine by eating them directly in the form of food. Medicinal processed foods come in the form of steamed dishes and soups with traditional kitchen spices such as turmeric, ginger, and pepper. Another traditional processing involves kneading it into a paste as a wound ointment (Hanifaturahmah et al. 2024). This is in contrast to modern processes such as bioactive extraction which are more diverse and functional. Bioactive extraction is processed in aqueous solution to preserve collagen, saponins and fatty acids. The use of tools also tends to be more modern, more hygienic and guaranteed.

Currently, research on the therapeutic efficacy of golden sea cucumber is still limited due to the lack of literature on clinical trials. The literature found is still in the in vitro or in vivo stage. In chemical tests, it is difficult to determine the standardization of raw materials because the composition of the tested golden sea cucumber bioactive compounds is highly dependent on habitat, season, and diet. In addition, due to the small number of participants in studies using human samples, the statistical significance of the conclusions was not tested. Further research and development is recommended to identify new compounds that may not have been previously identified. This can also be done by analyzing the molecular structure of the active ingredients to determine their specific effects on the human body. Research may include metabolomics techniques to study potential contributing metabolites. Various extraction models equipped with up-to-date information and tools can be used to produce highly pure bioactive compounds and conduct large-scale, multidimensional clinical studies. Interaction studies with other drugs can be conducted to investigate various reactions and discover new drugs. To facilitate research, optimizing sea cucumber cultivation using genetic

engineering is one way to increase high-quality biomass so that it can provide meaningful data for research.

CONCLUSION

Golden sea cucumber (*S. hermanii*) contains many bioactive compounds that provide various therapeutic benefits. The chemical profiles, namely protein, saponin, triterpenoid, collagen, GAGs, flavonoid, mineral, glutathione, alkaloid, methanol, and hyaluronat acid. This species also have great potential as therapeutic agents, such as wound healing, antifungal properties, hipertrigliseridemia, hypercholesterolemia, diabetes, bone and tooth regeneration. With this compound content, golden sea cucumbers can serve as a basis for developing innovative and sustainable biomedical products. Utilizing these compounds for health could lead to improvements in regenerative therapies, diabetes management, and protection from infection. Apart from its promising health benefits, processing golden sea cucumbers can improve the welfare of coastal communities through industrial cultivation and biotechnology. Therefore, conservation measures for this species must continue to be carried out so that it remains sustainable in nature and can be used wisely by humans.

REFERENCES

- Adam M, Achmad H, Nasir M, Putri SW. 2022a. Stimulation of osteoblast and osteocalcin in the bone regeneration by giving bonegraft golden sea cucumber. *J Intl Dent Med Res* 3 (23): 1722.
- Adam M, Achmad H, Tanumihardja M, Oktawati S, Ramadhan SR J, Masyta N. 2023a. The effectiveness of deproteinized golden sea cucumber (*Stichopus hermanii*) combination of deproteinized bovine bone xenograft in stimulating the formation of Bmp-2 and Opg in the process of bone tissue regeneration. *J Intl Den Med Res* 16 (1): 117-123.
- Adam M, Achmad H, Tanumihardja M. 2022b. The benefits of golden sea cucumber (*Stichopus hermanni*) as an alternative antimicrobial material in oral health. *J Intl Dent Med Res* 12 (62): 1949.
- Adam M, Achmad H, Tanumihardja. 2023b. The effectiveness of deproteinized golden sea cucumber (*Stichopus hermanii*) combination of deproteinized bovine bone xenograft in stimulating. *J Intl Dent Med Res* 03 (20): 2077.
- Adam M, Thahir H, Supiaty HA, Putri SW. 2021. The potential of golden sea cucumber (*Stichopus hermanii*) in the regeneration of periodontal tissues: A literature review. *Ann Rom Soc Cell Biol* 25 (6): 4407-4418.
- Adipour N, Aliasgarian S, Nabipour I, Kazemi S, Yousefzadi M. 2014. Antifungal activity of body wall and coelomic fluid from the sea cucumber (*Stichopus hermanii*) against pathogenic fungi. *Iranian Journal of Fisheries Sciences*. 13(2): 468–477.
- Akerina FO, Sangaji J. 2019. Analisis fitokimia dan toksisitas serta aktivitas antioksidan beberapa jenis teripang di Desa Kakara, Halmahera Utara. *Agrikan: Jurnal Agribisnis Perikanan* 12 (2): 188-196. DOI: 10.29239/j.agrikan.12.2.188-196. [Indonesian]
- Angelina N, Mukono IS, Fatimah N, Zakaria S, Rochmanti M. 2022. Efek pemberian ekstrak teripang emas terhadap kadar trigliserida tikus Wistar (*Rattus norvegicus*) hiperlipidemia. *Jurnal Medika Udayana* 11(5): 39-44. [Indonesian]
- Anggraeni ON, Fasya AG, Hanapi A. 2014. Uji aktivitas antioksidan fraksi etil asetat, kloroform, petroleum eter, dan N-heksana hasil hidrolisis ekstrak metanol mikroalga *Chlorella* sp. *Alchemy: J Chem* 3 (2): 173-188. DOI: 10.18860/al.v0i1.2911. [Indonesian]
- Arundina I, Soesilawati P, Damaiyanti, DW, Maharani D. 2015. The effects of golden sea cucumber extract (*Stichopus hermanii*) on the number of lymphocytes during the healing process of traumatic ulcer on wistar rat's oral mucous. *Dent J: Majalah Kedokteran Gigi* 48 (2): 100-103. DOI: 10.20473/j.djmk.v48.i2.p100-103.
- Aziza LS, Parisihni K, Mulawarmanti D. 2016. The effect of golden sea cucumber (*Stichopus hermanii*) and hyperbaric oxygen therapy to the expression of osteoprotegerin in diabetes mellitus induce by *Porphyromonas gingivalis* bacteria. *Denta J* 10 (2): 165-174. DOI: 10.30649/denta.v10i1.40.
- Baker-Médard M, Ohl KN. 2019. Sea cucumber management strategies: Challenges and opportunities in a developing country context. *Environ Conserv* 46 (4): 267-277. DOI: 10.1017/S0376892919000183.
- Battafarano G, Rossi M, De Martino V. 2021. Strategies for bone regeneration: From graft to tissue engineering. *Intl J Mol Sci* 22 (3): 1128. DOI: 10.3390/ijms22031128.
- Bordbar S, Anwar F, Saari N. 2011. High-value components and bioactives from sea cucumbers for functional foods—a review. *Mar Drugs* 9 (10): 1761-1805. DOI: 10.3390/md9101761.
- Brown KT, Southgate PC, Hewavitharane CA, Lal MM. 2022. Saving the sea cucumbers: Using population genomic tools to inform fishery and conservation management of the Fijian sandfish *Holothuria (Metriatyla) scabra*. *Plos One* 17 (9): e0274245. DOI: 10.1371/journal.pone.0274245.
- Cahyati M, Rahmawati PAA, Kusuma N, Adam SA. 2018. Pemanfaatan antioksidan (glutathione) teripang emas laut (golden Stichopus variegatus) berbasis nanoteknologi dalam apoptosis sel skuamosa kanker mulut. *E-Prodenta J Dent* 2 (2): 149-154. DOI: 10.21776/ub.eprodenta.2018.002.02.2. [Indonesian]
- Cankaya IIT, Somuncuoglu EI. 2021. Potential and prophylactic use of plants containing saponin-type compounds as antibiofilm agents against respiratory tract infections. *Evid Based Complement Alternat Med* 2021: 6814215. DOI: 10.1155/2021/6814215.
- Carodoso J, Nakayama DG, Sousa E, Pinto E. 2020. Marine-derived compounds and prospects for their antifungal application. *Molecules* 25: 5856. DOI: 10.3390/molecules25245856.
- Cushnie TPT, Cushnie B, Lamb AJ. 2014. Review-Alkaloids: An overview of their antibac-terial, antibiotic-enhancing and antivirulence activities. *Intl J Antimicrob Agents* 44 (5): 377-386. DOI: 10.1016/j.ijantimicag.2014.06.001.
- Damaiyanti D, Soesilawati P, Arundina I, Sari R. 2019. Effectiveness of gold sea cucumber (*Stichopus hermanii*) extracts in accelerating the healing process of oral traumatic ulcer in rats. *Padjadjaran J Dent* 31 (3): 208-214. DOI: 10.24198/pjd.vol31no3.22555.
- Darojati RR, Rizka Y, Revianti S. 2017. Effect of hyperbaric oxygen therapy combined with golden sea cucumber (*Stichopus hermanii*) powder to the level of blood glucose diabetic Wistar rat induced *Porphyromonas gingivalis*. *Denta: Jurnal Kedokteran Gigi* 11 (2): 18-28. DOI: 10.30649/denta.v11i2.94.
- De Fretes CC, Kakisina P, Rumahlatu D. 2020. Concentration of heavy metal Hg, Au, and Fe in sediments, water, and tissue damage of golden sea cucumber *Stichopus hermanni* (Semper, 1868) (Holothuroidea; Stichopodidae) in Kayeli Bay, Indonesia. *Acta Aquat Turc* 16 (1): 113-123. DOI: 10.22392/actaquat.603602.
- Djais AI, Achmad H, Dewiayu D, Sukmana BI, Huldani. 2020. Effect of combination of demineralization freeze dentin matrix *Moringa oleifera* osteoprotegerin (opg) and receptor activator of nuclear factor kappa ligand (rankl) as a marker of bone remodeling. *Syst Rev Pharm* 11 (6): 771-779.
- Escobar-Sánchez ML, Sánchez- Sánchez L, Sandoval-Ramírez J. 2015. Steroidal saponins and cell death in cancer. In: Ntuli TM (eds). *Cell Death - Autophagy, Apoptosis and Necrosis*. InTechOpen, London. DOI: 10.5772/61438.
- Espinosa-Diez C, Miguel V, Mennerich D, Kietzmann T, Sánchez-Pérez S, Cadanas S, Lamas S. 2015. Antioxidant responses and cellular adjusmant to oxidative stress. *Redox Biol* 6: 183-197. DOI: 10.1016/j.redox.2015.07.008.
- Fajarwati Y. 2017. Aktivitas Penghambatan Malondialdehida (MDA) secara In Vitro dan Toksisitas Ekstrak Metanol *Stichopus hermanii* dan *Spirulina platensis*. [Skripsi]. Institut Pertanian Bogor, Bogor. [Indonesian]
- Fawzya YN, Putra NA, Witarto AB, Patantis G. 2020. Golden sea cucumber: Identification and the antioxidant activity of its collagen hydrolysates. *Squalen Bull Mar Fish Postharvest Biotechnol* 15: 119-129. DOI: 10.15578/squalen.v15i3.511.
- Floren A, Hayashizaki KI, Tuntiprapas P, Prathep A. 2023. Modeling of the elements Ca²⁺, Mg²⁺ and Si in the Sediments and the body walls of

- sea cucumbers in the tropical seagrass meadows. *Diversity* 15 (2): 146. DOI: 10.3390/d15020146.
- Han N, Bakovic M. 2015. Biologically active triterpenoids and their cardioprotective and anti-inflammatory effects. *J Bioanal Biomed* 12: S12. DOI: 10.4172/1948-593X.S12-005.
- Hanifaturahmah F, Ratih DH, Usatun H, Mala N. 2024. Karakteristik kimia dan aktivitas antioksidan teripang (*Holothuria* sp.) segar dan olahan secara tradisional di Papua Barat. *Indones J Aquat Prod Technol* 22 (3): 309-318. DOI: 10.17844/jphpi.v27i4.51323. [Indonesian]
- Hartati R, Widianingsih, Umi F. 2015. Re-deskripsi teripang *Stichopus hermanii* dari Kepulauan Karimunjawa melalui analisa morfologi, anatomi. *Jurnal Kelautan Tropis* 18 (2): 70-75. DOI: 10.14710/jkt.v18i2.517. [Indonesian]
- Hartono F, Mukono IS. 2020. Effects of golden sea cucumber (*Stichopus hermanii*) ethanol extracts on cholesterol levels of hypercholesterolemic rats. *Indian J Public Health Res Dev* 11 (5): 650-654.
- Herliany NE, Nofridiansyah E, Sasongko B. 2016. Studi pengolahan teripang kering. *Jurnal Enggano* 1 (2): 11-19. DOI: 10.31186/jenggano.1.2.11-19.
- Hienz SA, Paliwal S, Ivanovski S. 2015. Cells B, Homeostasis mechanisms of bone resorption in periodontitis. *J Immunology Res* 2015: 1-10. DOI: 10.1155/2015/615486.
- Hlaing TT, Compston JE. 2014. Biochemical markers of bone turnover—uses and limitations Bone formation. *Ann Clin Biochem* 51 (2): 189-202. DOI: doi: 10.1177/0004563213515190.
- Ho-Shui-Ling A, Bolander J, Rustom LE, Johnson AW, Luyten FP, Picart C. 2018. Bone regeneration strategies: Engineered scaffolds, bioactive molecules and stem cells current stage and future perspectives. *Biomaterials* 180: 143-162. DOI: 10.1016/j.biomaterials.2018.07.017.
- Hossain A, Dave D, Shahidi F. 2022. Antioxidant potential of sea cucumbers and their beneficial effects on human health. *Mar Drugs* 20 (8): 521. DOI: 10.3390/md20080521.
- Irfan M, Ahmed S, Sharma M. 2014. Antimicrobial activity of terpenoids from *Sphaeranthus indicus*. *L. Asian J Plant Sci Res* 4 (1): 1-6.
- Jalaluddin M, Mahesh J, Mahesh R, Jayanti I, Faizuddin M, Kripal K. 2018. Effectiveness of platelet rich plasma and bonegraft in the treatment of intrabony defects: A clinicoradiographic study. *Open Dent J* 12 (1): 133-154. DOI: 10.2174/1874210601812010133.
- Kruger T. 2019. Advances in biomaterials for oral-maxillofacial bone regeneration. *Adv Healthcare Mater* 8 (3): rbae078.
- Lestari A, Andrie M, Taurina W. 2023. Uji stabilitas sifat fisik salep kombinasi ekstrak ikan gabus, teripang emas menggunakan HPMC. *Med Sains Jurnal Ilmiah Kefarmasian* 8 (2): 777-788. DOI: 10.37874/ms.v8i2.757. [Indonesian]
- Liu J, Ruan J, Weir MD, Ren K, Schneider A, Wang P., Oates TW, Chang X, Xu HHK 2019. Periodontal bone- ligament-cementum regeneration via scaffolds and stem cells. *Cells* 8 (6): 537. DOI: 10.3390/cells8060537.
- Ma B, Liu Y, Pan W, Li Z, Ren C, Hu C, Luo P. 2022. Integrative application of transcriptomics and metabolomics provides insights into unsynchronized growth in sea cucumber (*Stichopus monotuberculatus*). *Intl J Mol Sci* 23 (24): 15478. DOI: 10.3390/ijms232415478.
- Mariyanti S. 2017. Kandungan Kimia dan Aktivitas Penghambatan Alfa-glukosidase secara In Vitro dari Ekstrak Metanol *Stichopus hermanii* dan *Spirulina platensis*. [Skripsi]. Institut Pertanian Bogor, Bogor. [Indonesian]
- Marks DB, Marks AD, Smith CM. 2014. Biokimia Kedokteran Dasar: Sebuah Pendekatan Klinis. EGC, Jakarta. [Indonesian]
- Marliza H, Nurliyasman N, Hariyani R, Lestari V. 2022. Pre-eliminatory studi aktivitas sitotoksik biota laut Pantai Sekilak Batam terhadap larva udang (*Artemia salina* Leach). *Jurnal Katalisator* 7 (1): 115-124. DOI: 10.62769/katalisator.v7i1.960. [Indonesian]
- Martel J, Farrán A, Montell E, Vergés, J, Pelletier J. 2015. Discrepancies in composition and biological effects of different formulations of chondroitin sulfate. *Molecules* 20: 4277-4289. DOI: 10.3390/molecules20034277.
- Meydia M, Suwandi R, Suptijah P. 2016. Isolation of compounds of steroids teripang gamat (*Stichopus variegatus*) with various types of solvents. *Jurnal Pengolahan Hasil Perikanan Indonesia* 19 (3): 363-369. DOI: 10.17844/jphpi.v19i3.14548.
- Mnif SM, Chamkha, Marc Labat, Sayadi S. 2011. Simultaneous hydrocarbon biodegradation and biosurfactant production by oilfield-selected bacteria. *J Appl Microbiol* 111 (3): 525-536. DOI: 10.1111/j.1365-2672.2011.05071.x.
- Mondol MAM, Shin H J, Rahman MA, Islam MT. 2017. Sea cucumber glycosides: Chemical structures, producing species and important biological properties. *Mar Drugs* 15 (10): 317. DOI: 10.3390/md15100317.
- Monika R, Pringgenies D, Setyati WA. 2021. Potensi ekstrak *Stichopus hermanii*, Semper 1868 (Holothuroidea: Stichopodidae) sebagai penghasil senyawa antibakteri terhadap *Streptococcus mutans* Clarke, 1924 (Bacilli : Streptococcaceae). *Jurnal Penelitian Kelautan* 10 (3): 421-427. DOI: 10.14710/jmr.v10i3.31097. [Indonesian]
- Mulawarmanti D, Parisihni K, Widyastuti. 2019. The effect of *Sticopos hermanii*-hyperbaric oxygen therapy to inflammatory response of diabetic periodontitis. *IOP Conf Ser: Earth Environ Sci* 217: 012060. DOI: 10.1088/1755-1315/217/1/012060.
- Mulawarmanti D, Widyastuti KP, Wardani G. 2022. Formulation and physical stability test evaluations of golden sea cucumber extract gel (*Stichopus hermanii*) as anti periodontitis using variations in base concentration. *Intl J Pharm Bio Med Sci* 2 (08): 295-301. DOI: 10.47191/ijpbms/v2-i8-06.
- Nurwidodo, Rahardjanto A, Husamah H, Mas'odi, Hidayatullah MS. 2018. Buku Panduan Mudahnya Budidaya Teripang (Terintegrasi dengan Rumput Laut). Kota Tua, Malang. [Indonesian]
- Oh GW, Ko SC, Lee DH. 2017. Biological activities and biomedical potential of sea cucumber (*Stichopus japonicus*): A review. *Fish Aquatic Sci* 20: 28. DOI: 10.1186/s41240-017-0071-y.
- Oktaviani PD, Wahjuningsih E, Andriani D. 2018. Efektivitas suplementasi teripang emas (*Stichopus hermanii*) dalam mencegah terjadinya oral candidiasis pada tikus wistar. *DENTA Jurnal Kedokteran Gigi* 12 (1): 9-15. DOI: 10.30649/denta.v12i1.155. [Indonesian]
- Pangkey H, Lantu S, Manuand L, Mokolensang J. 2012. Prospect of sea cucumber culture in Indonesia as potential food sources. *J Coast Dev* 15 (2): 114-124.
- Pilus NSM, Muhamad A, Shahidan MA, Yusof NYM. 2022. Potential of epidermal growth factor-like peptide from the sea cucumber *Stichopus horrens* to increase the growth of human cells: In silico molecular docking approach. *Mar Drugs* 20 (10): 596. DOI: 10.3390/md20100596.
- Prameswari N, Brahmanta A, Revianti S. 2020. The effect of *Stichopus hermanii* to TLR-4 in mediating periodontal ligament remodeling during orthodontic relapse. *Syst Rev Pharm* 11 (3): 667-673.
- Prawitasari DS, Safitri I, Notopuro H. 2019. Effects of golden sea cucumber extract (*Stichopus hermanii*) on fasting blood glucose, plasma insulin, and mda level of male rats (*Rattus norvegicus*) induced with streptozotocin. *Fol Med Indones* 55 (2): 107-111. DOI: 10.20473/fmi.v55i2.24586.
- Pringgenies D, Rudiyaniti S, Yudiati E. 2018. Exploration of sea cucumbers *Stichopus hermanii* from Karimunjawa Islands as production of marine biological resources. *IOP Conf Ser: Earth Environ Sci* 116 (1): 12039. DOI: 10.1088/1755-1315/116/1/012039.
- Pringgenies D. 2013. antibacterial activity of sea cucumbers harvested from Karimunjawa. *Squalen Bull Mar Fish Postharvest Biotechnol* 8: 87-94. DOI: 10.15578/SQUALEN.V8I2.90.
- Pringgenies D. 2019. Explorations of symbiotic microbe from sea cucumber gut as an anti-multi-drug resistant microbe agent for utilization in hand. *AACL Bioflux* 12 (3): 737.
- Purwanto B, Wiyasihati SI, Masyitha PA, Wigati KW, Irwadi I. 2019. Golden sea cucumber extract revives glucose transporter-4 and interleukin-6 protein level in diabetic mouse muscle. *Vet World* 2 (8): 57-77. DOI: 10.14202/vetworld.2019.684-688.
- Rahmadani R. 2023. Solid lipid nanoparticle formulation and antihyperglycemic activity test of sea cucumber (*Stichopus hermanii*). *Indones J Multidiscipl Sci* 3 (1): 40-48. DOI: 10.55324/ijoms.v3i1.677.
- Rasouli H, Yarani R, Pociot F, Popović-Djordjević J. 2020. Anti-diabetic potential of plant alkaloids: Revisiting current findings and future perspectives. *Pharmacol Res* 155: 104723. DOI: 10.1016/j.phrs.2020.104723.
- Rasyid A. 2018. Mengungkap Potensi Teripang dari Indonesia. Deepublish, Yogyakarta. [Indonesian]
- Ratri DL, Mulawarmanti D, Widyastuti . 2017. Study of hyperbaric oxygen therapy and gold sea cucumber (*Stichopus hermanii*) 3% for collagen density of rat's with diabetes mellitus induced by porphyromonas gingivalis bacteri. *Denta* 11 (2): 73-82. DOI: 10.30649/denta.v11i2.100.

- Rusmini R, Taurina W, Andrie M. 2023. Standardization of golden sea cucumber (*Stichopus hermannii*) extracts from Pelapis Island, Kayong Regency, West Kalimantan. *Biol Med Nat Prod Chem* 12 (2): 539-545. DOI: 10.14421/biomedich.2023.122.539-545.
- Safithri M, Setyaningsih I, Tarman K, Suptijah P, Yuhendri VM, Meydia. 2018. Potensi kolagen teripang emas sebagai inhibitor tirosinase. *Jurnal Pengolahan Hasil Perikanan Indonesia* 21 (2): 295-303. DOI: 10.17844/jphpi.v21i2.23085. [Indonesian]
- Safithri M, Tarman K, Setyaningsih I, Fajarwati Y, Dittama IYE. 2022. In vitro and in vivo malondialdehyde inhibition activities of *Stichopus hermannii* and *Spirulina platensis*. *Hayati J Biosci* 29 (6): 771-781. DOI: 10.4308/hjb.29.6.771-781.
- Safithri M, Tarman K, Setyaningsih I, Zhafira AG. 2020a. Peredaman radikal DPPH oleh ekstrak metanol *Spirulina platensis* dan teripang emas (*Stichopus hermannii*). *Jurnal Masyarakat Pengolahan Hasil Perikanan Indonesia* 23 (3): 513-522. DOI: 10.17844/jphpi.v23i3.32509. [Indonesian]
- Safithri M, Tarman K, Suptijah P, Sagita SN. 2020b. Karakteristik kolagen larut asam teripang gama (*Stichopus variegatus*). *Jurnal Pengolahan Hasil Perikanan Indonesia* 23 (1): 166-177. DOI: 10.17844/jphpi.v23i1.31063. [Indonesian]
- Sangian FV, Nasir M, Paramma ZI. 2024. The role of golden sea cucumber (*Stichopus hermannii*) in preventing orthodontic relapse. *Makassar Dent J* 13 (1): 127-130.
- Sari RP, Kurniawan H. 2019. Effectiveness of *Anadara granosa* shell-*Stichopus hermannii* granules at accelerating woven bone formation fourteen days after tooth extraction. *Dent Journal* 52 (4): 177-182. DOI: 10.20473/j.djmk.v52.i4.p177-182.
- Sari RP, Sudjarwo SA, Rahayu RP, Prananingrum W, Revianti, Kurniawan H, Bachmid AF. 2017. The effects of *Anadara granosa* shell-*Stichopus hermannii* on bFGF expressions and blood vessel counts in the bone defect healing process of Wistar rats. *Dent J* 50 (4): 194-198. DOI: 10.20473/j.djmk.v50.i4.p194-198.
- Sari RP, Wahjuningsih E. 2017. The effectiveness of golden sea cucumber ethanol extract on the expression of endoglin in the maturation phase of healing mice with traumatic ulcers. *Denta: Jurnal Kedokteran Gigi* 11 (1): 43-50. DOI: 10.30649/denta.v11i1.124.
- Sari RP, Isidora K, Rizal MB, Tjhoeng HD. 2012. Karakterisasi ekstrak teripang emas sebagai bahan topikal untuk pemulihan mukosa rongga mulut. ASEAN Plus TOKUSHIMA Joint Intl Conf 2012. [Indonesian]
- Setianingsih H, Putri FSS, Desi WPM, Yatnasari E. 2020. The effect of golden sea cucumber (*Stichopus hermannii*) extracts to serum LDL cholesterol level as a result of insulin resistance. *Indones J Med Sci Public Health* 1 (1): 7-12. DOI: 10.11594/ijmp.01.01.02.
- Setianingsih H, Wisnumarta SE, Tjandra SA. 2021. Repairing of renal tubules in diabetic rats (*Rattus norvegicus*) diabetes after administration of golden sea cucumber (*Stichopus hermannii*). *Pharmacogn J* 16 (2): 43-54. DOI: 10.5530/pj.2021.13.123.
- Setiyowati D, Ayub AF, Zulkifli M. 2016. Statistik Sumber Daya Laut Dan Pesisir. BPS, Jakarta. [Indonesian]
- Shahrulazua A, Samsudin A, Iskandar M, Amran A. 2013. The in-vitro effects of sea cucumber (*Stichopus* sp.1) extract on human osteoblast cell line. *Malays Orthopaedic J* 7: 41-48. DOI: 10.5704/MOJ.1303.015.
- Shan X, Zhou J, Ma T, Chai Q. 2011. *Lycium barbarum* polysaccharides reduce exercise-induced oxidative stress. *Intl J Mol Sci* 12 (2): 1081-1088. DOI: 10.3390/ijms12021081.
- Sheikh Z, Hamdan N, Ikeda Y. 2017. Natural graft tissues and synthetic biomaterials for periodontal and alveolar bone reconstructive applications; a review. *Biomed Res Intl* 21 (9): 41-54. DOI: 10.1186/s40824-017-0095-5.
- Siahaan EA, Pangestu R, Munandar H, Kim SK. 2017a. Review cosmeceuticals properties of sea cucumbers: Prospects and trends. *Cosmetics* 4: 26. DOI: 10.3390/cosmetics4030026.
- Siahaan, EA, Pangestuti, R. 2017b. Marine functional food and nutraceutical: Prospects and challenges. *Depik Jurnal Ilmu-Ilmu Perairan, Pesisir dan Perikanan* 6 (3): 273-281. DOI: 10.13170/depik.6.3.6874. [Indonesian]
- Soesilawati P, Ambarani EL, Oki AS. 2019. Increased Vascular Endothelial Growth Factor (VEGF) expression in Wistar rat oral mucosa traumatic ulcer due to golden sea cucumber (*Stichopus hermannii*) extract. *Acta Med Philipp* 53 (6): 482-485. DOI: 10.47895/amp.v53i6.667.
- Song H, Song C, Yan C, Yang J, Song S. 2024. Sea cucumber polysaccharide from *Stichopus japonicus* and its photocatalytic degradation product alleviate acute alcoholic liver injury in mice. *Foods* 13 (6): 963. DOI: 10.3390/foods13060963.
- Susanto H, Safithri M, Tarman K. 2018. Antibacterial activity of *Stichopus hermannii* and *Stichopus variegatus* methanol extract. *Curr Biochem* 5 (2): 1-11. DOI: 10.29244/cb.11.1.2.
- Tamara R, Linda R, Paulus BT. 2015. Daya hambat ekstrak teripang emas (*Stichopus hermannii*) terhadap bakteri *Enterococcus faecalis*. *Denta: Jurnal Kedokteran Gigi* 9 (1): 1-11. DOI: 10.30649/denta.v9i1.4. [Indonesian]
- Taurina W, Andrie M. 2022. Standardization of simplicia golden sea cucumber (*Stichopus hermannii*) from Pelapis Island, West Kalimantan Trad Med J 27 (2): 146-152. DOI: 10.22146/mot.74667.
- Telahigue K, Ghali R, Nouiri E, Labidi A, Hajji T. 2020. Antibacterial activities and bioactive compounds of the ethyl acetate extract of the sea cucumber *Holothuria forskali* from Tunisian coasts. *J Mar Biol Assoc U K* 100 (2): 229-237. DOI: 10.1017/S0025315420000016.
- Utami PD, Yudho RV. 2022. Antimalarial activity prediction analysis of *Stichopus hermannii* on Plasmodium falciparum Hexose Transporter (PfHT1). *Intl J Health Sci* 6 (10): 134-152. DOI: 10.53730/ijhs.v6nS10.13346.
- Wang J, Wang H. 2017. Oxidative stress in pancreatic beta cell regeneration. *Oxid Med Cell Longev* 2017: 1930261. DOI: 10.1155/2017/1930261.
- Wardhani. 2019. Pemanfaatan Ekstrak Teripang Emas Laut (*Stichopus hermannii*) berbasis Nanoteknologi dalam Perbaikan Sel Epitel Bukal Tikus Putih Strain Wistar Pasca Induksi Dimethylbenz 7, 12-Aanthracene (DMBA). [Doctoral Dissertation]. Universitas Brawijaya, Malang. [Indonesian]
- Wargasetia TL, Permana S, Widodo. 2018. The role of sea cucumber active compound and its derivative as an anti-cancer agent. *Curr Pharmacol Rep* 4: 27-32. DOI: 10.1007/s40495-018-0121-x.
- Windari HAS, Tarman K, Safithri M, Setyaningsih I. 2019. Antioxidant activity of *Spirulina platensis* and sea cucumber *Stichopus hermannii* in streptozotocin-induced diabetic rats. *Trop Life Sci Res* 30 (2): 119-129. DOI: 10.21315/tlsr2019.30.2.9.
- Yatnasari E, Setianingsih H, Riami. 2021. Potensi teripang emas (*Stichopus hermannii*) terhadap perubahan histopatologi hati pada tikus dengan induksi streptozotocin. *Surabaya Biomed J* 1 (1): 23-30. DOI: 10.30649/sbj.v1i1.6. [Indonesian]
- Yudo V, Notopuro H, Listiawan Y, Utomo B, Rejeki PS, Utami PD. 2022. Effects of golden sea cucumber extract (*Stichopus hermannii*) on hyphae, neutrophils and TNF- α in BALB/c mice inoculated with *C. albicans* intravaginally. *Pharmacogn J* 14 (4): 278-285. DOI: 10.5530/pj.2022.14.97.
- Zhafira AG. 2016. Aktivitas Antioksidan Ekstrak Metanol Teripang Emas (*Stichopus hermannii*) dan *Spirulina platensis* Menggunakan Metode DPPH. [Skripsi]. Institut Pertanian Bogor, Bogor. [Indonesian]