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Review article

Medicinal and health benefit effects of functional sea cucumbers

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ABSTRACT

Sea cucumbers have long been used as food and traditional medicine in Asian countries with *Stichopus hermanni*, *Thelenota ananas, Thelenota anax, Holothuria fuccogilva,* and *Actinopyga mauritiana* as most highly-valued species. These organisms are potential source of high value-added compounds with therapeutic properties such as triterpene glycosides, carotenoids, bioactive peptides, vitamins, minerals, fatty acids, collagens, gelatins, chondroitin sulfates, amino acids. In the recent years, health benefit effects of sea cucumbers have been validated through scientific research and have shown medicinal value such as wound healing, neuroprotective, antitumor, anticoagulant, antimicrobial, and antioxidant. These functional materials lead to potential development in various foods and biomedicine industries. In this review, we have presented a general view of major medicinal and health benefit effects of functional sea cucumbers from Asia region. The structural significance and the potential application of sea cucumber-derived functional materials as well as their nutritional value are also discussed.

1. Introduction

The increasing number of scientific papers published in the last few decades correlating functional materials derived from natural resources and some chronic diseases has shown the extraordinary possibilities of functional foods and nutraceuticals as well as biomedicine products to support, or even to improve, our health beyond the provision of basic nutritional requirements.[1,2] As a consequence, consumer's interest in the relationship between health, diseases prevention, and well-being has grown substantially worldwide. The sources of functional foods, nutraceuticals and biomedicine products are exist in many reservoirs and may be found in terrestrial and marine environments. Terrestrial resources such as fruits, vegetables, cereals, probiotics, and mushrooms; however, is by far more explored than the marine resources.[2] Even though the majority of those products in the marketplace are of terrestrial origin, marine organisms-based products are gaining attention due to their unique features, which are not found in terrestrial-based resources.[3]

Among marine organisms, sea cucumber is an interesting natural source of novel functional materials with biological activities that could be used in food as well as biomecicine industries. Sea cucumbers are soft bodied marine invertebrate from the class Holothuroidea. Sea cucumbers have a leathery skin and an elongated body containing a single branched gonad. These organisms constitute 1716 species, with the greatest biodiversity being in the Asia Pacific region. Sea cucumber is also known as "*teripang* or *trepang*" in Indonesian; "*beche-de-mer*", a French term that means marine food product, and "*balate*" in Chamorro. Sea cucumbers are organisms that live in complex environments submitted to extreme conditions, therefore, they must adapt to the new environmental conditions to survive, and produce secondary biologically active metabolites which cannot be found in other organisms. According to the Ming dynasty report (1368–1644 BC), the sea cucumber harbored the same medicinal properties as the herb ginseng, therefore, it also called as "haishen" which means "ocean ginseng".[4] Indonesia is well known as mega biodiversity country located in the center of Coral Triangle (the earth's storehouse of biological diversity), and also one of the largest sovereign nation in the worlds. It has been reported that Indonesia is the oldest and major sea cucumber exporter in the world.[5] Approximately, 350 sea cucumber species from Indonesian waters have been recorded with more than half were collected from the depth of more than 3000 m. Of the 350 sea cucumber species, at least 26 with economic value have

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been reported, these economic value sea cucumbers which bring benefits to fishers for centuries were called as trepan or teripang in Indonesia.[6] Not only, Indonesia, Malaysia and Philippines are also an important exporter of the sea cucumber and their products.[7] Globally, The Southeast Asia represents the global market hotspots for sea cucumbers trade due to their known mega biodiversity. Many of sea cucumber is gathered for human consumption and some are cultivated in aquaculture systems.

Hence, the objectives of this article are first to present the results obtained of a detailed bibliographical search about the composition of sea cucumbers from tropical regions especially Asia and secondly, to discuss their biological activities and possibilities as new sources of functional ingredients. The information provided on the various species of sea cucumbers does not refer in many cases to the same constituents since it has been taken from different research papers with different objectives. However, we believe the information provided can be useful to many research groups considering a huge interest in the search for nutritional and medicinal value of sea cucumbers.

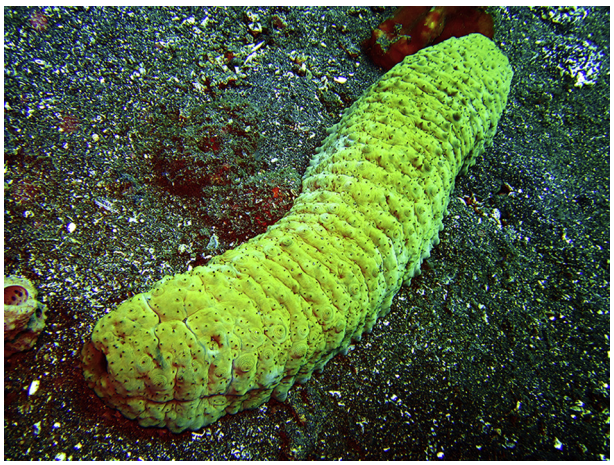

Fig. 1. *Stichopus hermanni* from Lembeh strait, Indonesia.

2. Chemical composition of various sea cucumbers

Functional ingredients from sea cucumbers have become an increasingly interesting way to develop new foods as well as biomedicine products. Sea cucumbers are a source of high value-added compounds with health benefit effects to be used as functional ingredients. Bioactive peptides, vitamins, minerals, fatty acids, saponins, carotenoids, collagens, gelatins, chondroitin sulfates, amino acids, fatty acids and other bioactive compounds are example of such sea cucumber derived functional ingredients that can be added at different stages of the food and biomedisine production process.[8] The sea cucumber species (*Stichopus hermanni*, *Thelenota ananas, Thelenota anax, Holothuria fuscogilva, Holothuria leucospilota, Holothuria atra, Holothuria scabra* and *Actinopyga mauritiana)* described in this article has been selected considering edible species, medicinal effects, and low toxicity. The aforementioned selected varieties are some of high-value sea cucumbers in Asia. Assuming that any new functional ingredient obtained from sea cucumbers could be used for further development of new products in food and pharmaceuticals industries. Another important factor is their nutritional value and potential as new sources of functional ingredients.

2.1. *S. hermanni (local name in Indonesia: gamat emas, gamat kacang, taikongkong)*

Sea cucumber *S. hermanni* (curryfish, golden sea cucumbers) belongs to the genus Stichopus; these species were formerly known as *Stichopus variegatus*. In Indonesia and Malaysia, sea cucumber *S. hermanni* (Fig. 1) has long been used for the preparation of traditional medicinal products like gamat water and gamat oil.[9] These species are gaining much recognition among consumers, medical and biomedical researchers due to their potential health benefits. In Asian region communities, *S. hermanni* have been exploited for medicinal purposes; however such applications needs to be proven on a scientific basis using some clinical models.

As shown in Table 1, *S. hermanni* contains high amount of protein (47.00% ± 0.36%) and low percentage of lipid (0.80% ± 0.02%). This sea cucumber contain significant amount of sulfated glycosaminoglycan. Glycosaminoglycan are long, unbranched polysaccharides composed of repeating disaccharide units consisting of alternating uronic acids (D-glucuronic acid or L-iduronic acid) and amino sugars (D-galactosamine or D-glucosamine) Glycosaminoglycan are divided into non-sulfated and sulfated glycosaminoglycan. Sulfated glycosaminoglycan extracted from *S. hermanni* possess various chemico-biological functions.[10] Compared to other parts such as internal organs and coelomic fluid; integument body wall of *S. hermanni* contain highest glycosaminoglycan, both sulfated and non-sulfated. Further, sulfated glycosamioglican from integument has been demonstrated to accelerate wound healing process in rats.[11] More than 60% of wound heal area in rats was observed after daily treatment with sulfated glycosaminoglycan (20 μL of 1 μg/mL) for 12 days. The healing activity of sulfated glycosaminoglycan was mediated through acceleration of wound contraction in wound healing phase I. In addition, 40% of *Stichopus hermanii* extract were able increase the number of lymphocytes during the healing process of traumatic ulcer on Wistar rat's oral mucous.[12] Most recently, Arundina et al. (2016) extracted *S. hermanni* from Kalimantan, Indonesia and demonstrated their growth stimulating effects in mesenchymal stem cells.[13] Mesenchymal stem cells are self-renewing cells that have the capacity to differentiate into adipocytes, chondrocytes, myocytes, and osteoblast. Following treatment with *S. hermanni* extract and osteogenic induction medium for 4 weeks, mesenchymal stem cells were differentiated into osteoblast. Collectively, it can be assumed that sea cucumber *S. hermanni* is able to accelerate wound healing process. Further, these sea cucumber species can be used to prepare lotion or a topical ointment for wound healing management.

Neuroprotection may defined as mechanisms and strategies used in order to protect neuronal cells against injury, apoptosis, dysfunction and or degeneration in the central nervous system (CNS).[3] In the CNS, there are two classes of cells, including neuron, and glia (microglia, astrocytes and the related Schwann cells and oligodendrocytes). Astrocytes plays an important structures that provide housekeeping functions necessary to maintain neuronal function, actively shape synaptic function, and act as neural precursors in adult neurogenic regions. In addition, astrocytes also preserve the host integrity following injury. Recently, Patar et al. (2012) prepared water extract of *S. hermanni* from Malaysia and showed their growth promoting effect to promote proliferation of spinal astrocytes.[14] In pathological cases like spinal cord injury, proliferating reactive astrocytes are proven essential for early regeneration process, provide neuroprotective effects and preserve motor function after acute injury. Further, it was demonstrated by GC-MS results that 37% of the total *S. hermanni* water extracts were comprised of amino acids (37%) followed by hydrocarbon (21%), ester compounds (16%), the orther remaining compounds consisted of phenols, alcohol groups and unidentified compounds. The 2-carbamoyl-3-methylquinoaxaline was found to be the most abundant compounds in *S. hermanni* extracts.[15] Interestingly,

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