Benefits of Functional Foods from Marine Biota: A Systematic Review

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Abstract. In making food product choices, consumers usually prefer food products presented by industries to have functional values. This study aimed to analyze international research publications on marine product-based functional foods to determine their benefits. PRISMA was used to collect data using keyword searches in different databases such as Scopus, Science Direct, Google Scholar, Indonesian Scientific Journal Database, and Indonesian Publication Index. The result showed marine-based biota primarily functions to prevent and treat degenerative diseases such as high blood pressure, hyperglycemia, hyperlipidemia, hypertension, diabetes, rheumatism, cancer, cytotoxicity, high cholesterol problems, cardiovascular diseases, inflammation and Blackfoot. However, the focus of most Indonesian research is on the potential use of these foods as supplements.

Keywords: Functional foods, Systematic literature review, Marine biota.

1 Introduction

The term 'functional foods' was introduced in Japan in 1980 to denote 'foods for specified health uses' (FOSHU). However, this term has not been used by governments and scientific communities in recent times, for example, due to the lack of consensus at the international level, it was not used in a regulation issued by the Food and Drug Control Agency in 2016 concerning the supervision of claims on processed food labels and advertisements. This regulation supersedes the one issued by the agency in 2005 regarding basic food monitoring functional provisions and another issued in 2011 on foods with other functional claims like the ability to decrease risks of diseases. Moreover, the Codex Guidelines for Use of Nutrition and Health Claims (CAC/GL 23-1997 Rev. 2013) revealed no new work has been approved on functional foods since the beginning of 2001 except when it is discussed under health claims. There has been an increase in the research to expand the sources of ingredients for functional foods especially by shifting from the ones made from vegetables or plants which are considered conventional to the ones from marine products and fishes categorized as modern. The studies are focused more on the probiotic functions from different types of content and raw materials based on assessment guidelines. These guidelines show the number and benefits to the health need to be proven with valid and consistent conclusive clinical trial results to determine efficacy. This should include identification of

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strains, the quantities, and duration of usage recommended by the manufacturer, health benefits produced as well as possible side effects. The probiotics need to be approved by the authorized agency, both from the country of origin and the government of Indonesia. The strategy employed in marketing functional food products is expected to indicate the genus, species, and strain of probiotics on the label. The main objective was to analyze the performance of functional foods research in national and global contexts as reflected in the publications from 2003 to 2019. Moreover, the specific objectives were to identify the benefits of the functional food from marine biota and review the topics of research publications on these foods.

2 Research Method

2.1. Criteria for Publication Selection

Publications on functional foods, especially with the use of marine biota as raw material between 2003-2019, were collected from different databases including Scopus, Google Scholar, Garuda, Indonesian Scientific Journal, and Indonesian Publication Index. A spreadsheet was used for data analysis while the search strings used for data retrieval include 'functional foods and marine' and 'functional foods and biota'.

2.2. Search Methods for Identification of Studies

A systematic literature review with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) was used as the research protocol and the publications collected include case studies from research and journal articles with focus on functional foods, marine commodity, biota, and benefits while non-English articles, news, books, and chapters of books were excluded [1]–[3].

2.3. Data Selection

The publications on functional foods found in Scopus, Google Scholar, and Science Direct were 1524, 94,600, and 5443 respectively and after further refinement using 'marine biota' and 'raw materials' as the searching keywords, 437 articles were retrieved. Moreover, due to the selection of only full-text articles discussing the benefits of marine-derived functional foods, 65 articles were obtained from 40 journals and 2 proceedings. The steps taken for the PRISMA systematic literature review (SLR) are shown in the following table.

Table 1. SLR steps in PRISMA guidelines

No	Process Stages	Objectives	Products or Actions
1.	Identify research questions	Transform the problems related to technology management of marine biota-derived functional foods into research questions	Research questions: What are the benefits of functional food from marine biota and the emphases of Indonesian and international researchers on these foods?

No	Process Stages	Objectives	Products or Actions
2.	Develop a systematic review research protocol	Provide guidance to conduct the systematic reviews	Adopt PRISMA steps
3.	Determine the databases to be searched	Provide search area restrictions for relevant research – Ini sama dng no. 4	Search Google Scholar, Scopus, Science Direct, Indonesian Scientific Journal, and Garuda databases
4.	Provide search area restrictions for relevance	Collect research articles relevant to the research questions	Table 2
5.	Choose relevant research articles	Determine the criteria for appropriate research literature	Inclusion criteria: Case studies and research publications with a focus on functional foods, marine commodity, marine biota, and benefits of functional foods Exclusion criteria: Non-English publications
6.	Extract data from individual studies	Find important results	Research publications
7.	Synthesize results with the narrative method	Synthesize results with meta-analysis or narrative techniques (meta-synthesis)	Discussion of results
8.	Present the results	Produce the results of the study	Paper

3 Result and Discussion

3.1. Data Collection and Analysis

The 65 articles selected from the 42 journals and 2 proceedings using the stated criteria are shown in Table 2 and 10 of these journals are Indonesian marked with an asterisk. It is important to reveal that most of these articles were found published in journals in the fields of food technology and marine biota.

3.2. Sources of Functional Foods from Marine Biota

Marine products-based functional foods are commonly produced from sources such as shrimps, fishes, seaweed or algae. However, research has been conducted in Indonesia from sources such as abalone (Heliotis, sp.), seagrasses, and sea cucumbers.

3.2.1. Research on Functional Foods from Marine Biota and their Benefits

Numerous studies have shown foods produced from marine biota have nutritional values and antioxidants with potential beneficial effects on human health. It was reported that chitosan lowers body weight, controls hyperlipidemia, and prevents Blackfoot disease while green algae Ulva sp [4]. contains high carbohydrates, minerals, and protein with low fat [5]. Polyphenols are bioactive compounds found in marine algae with potential antihyperlipidemic, antihyperglycemic, and anti-inflammatory effects. Moreover, the modulation of these risk factors using bioactive polyphenols may represent a useful strategy for disease prevention and management. Phlorotannin found in marine brown algae can also be used to prevent and treat diabetes types 2 and cardiovascular diseases (Murray et al., 2018). Ecklonia caca extract from edible brown algae also has benefits on the blood lipid profile by reducing total and LDL cholesterols [6]. Furthermore, bioactive compounds from Echium oil are alternative natural ingredients to be applied in functional foods to reduce the risk factors of cardiovascular disease [7]. Njinkoue (2016) studied two fish species, Pseudotolithus typus, and Pseudotolithus elongatus, from Cameroonian coasts and found no similarities in the chemical composition of the two species but they are both good sources of proteins [8]. The most abundant trace elements are zinc and iron in the edible parts and bones while the natrium/kalium ratio values and ω3 fatty acids contents show the ability of the fishes to prevent cardiovascular diseases when consumed.

The low cytotoxicity and anticarcinogenic effects of the soluble dietary fiber fractions of κ-carrageenan from marine red algae Kappaphycus alvarezii on HCT116 show it can be used an alternative approach to metastatic human colon cancer therapy and also highlights its importance as a food supplement. Moreover, those with low molecular weight could be an ideal functional food ingredient and supplement contributing to the efficacy of a variety of health-supporting benefits [9]. Furthermore, Perinereis Aibuhitensis Peptide (PAP), as a natural marine bioactive substance, inhibited proliferation and induced apoptosis of human lung cancer H1299 cells. PAP is likely to be exploited as the functional food or adjuvant to be used for the prevention or treatment of human non-small cell lung cancer [10]. In addition, bioactive peptides, COS, SPs, phlorotannin, and carotenoids pigments including fucoxanthin and astaxanthin from marine foods and their by-products can also be used indirectly as functional ingredients to reduce cancer formation in human [11].

3.2.2. Research on the Benefits of Functional Foods from Marine Algae

Marine bioactive substances exhibit significant anti-hyperlipidemic effects and also have a variety of biological activities by possessing the ability to lower blood pressure, serve as anti-tumor, and regulate immunity (Wang et al., 2018). Another research by Koo et al. (2019) showed fucoxanthin (FX) and Phaeodactylum extract (PE), which are marine carotenoids found in macroalgae and microalgae, have the potential to be commercial functional foods. Moreover, PE and FX dose-dependently have the ability to decrease lipid contents in adipocytes without cytotoxicity while PE exerts anti-obesity effects by inhibiting adipocytic lipogenesis to induce fat mass reduction and decrease FX powder. Crowley (2018) also revealed functional food ingredients play a role in systemic and brain health as well as in healthy aging [12]. Given the significant impact of gut microbiota on health, this marine multi-mineral blend could be a promising digestive-health promoting functional food ingredient. The research conducted by Sasaki et al. (2018) showed pearl oyster shell proteins has the ability to become the new raw materials for the production of functional foods against hypertension [13]. A purified extract derived from Cyclina sinensis or the WPMGF peptide has the potential to be used in antihypertensive functional foods while showed marine microalga Tisochrysis lutea is a promising source to control. Moreover, Marine molluscs represent a relatively untapped source of natural functional food ingredients with potential antidiabetic effects [8], [14], [15]. Another research showed marine cryophytes produced by algae have the ability to reduce serum cholesterol and be a good alternative for the ecologically sustainable and profitable production of health-promoting lipids [16]. Protein hydrolysate of stripe trevally fish (Selaroides leptolepis) produced by enzymatical hydrolysis using local protease also had great potential for antihypertensive effects [14]. In another study, the phlorotannin of a marine brown seaweed Ecklonia cava was found to have an ACE inhibitory activity applicable in the production of functional foods to lower blood pressure [17].

3.2.3. Research on other Marine Sources as Raw Materials for Functional Foods

Indonesian marine fishery had a production volume of 6.6 tons with a value of Rp184 trillion (US$12 million) and this includes seaweed cultivation with a production volume of 9.7 tons and a value of Rp 211.890.494.716 [18]. Seaweed is usually consumed as processed foods and drinks while its benefit as a functional food is generally not known to the consumers. This means most research works conducted in the Indonesian food industry have always focused on the production of a variety of foods for public consumption.

According to Murata M. and Nakazoe J., the dietary intake of marine algae is approximately 1/5 higher than what was observed in fish [19]. However, in recent times, the increase in the incidence of adult diseases in Japan has been associated with diabetes, hypertension, hyperlipidemia, etc. which can be reduced by the ability of Undaria pinnatifida (Wakame) to decrease the concentration of serum and liver triacylglycerol. Seaweeds as a sustainable functional food working as a complementary and alternative anti-obesity and anti-chronic metabolic therapy, especially with diabetes, heart disease, hypertension, hyperlipidemia, and cancer [20]. However, Bajpai (2017) revealed the use of these natural therapies as synthetic drugs to combat these ailing conditions has effects on the livers and kidneys at high doses or prolonged use [21].

The function of antioxidant was explained in the study of Fernando et al. (2018) with the isolation of squalene indicated to have prominent antioxidant and anti-inflammatory activity and Caulerpa racemosa is an edible green alga which was observed to be possessing nutraceutical and bioactive properties enabling it to be used as a functional food ingredient [22]. Moreover, Pinteus et al. (2017) showed Sargassum muticum is a brown seaweed with strong potential mainly due to its antioxidant and protective properties which are evidenced by the inhibition of hydrogen peroxide production and Caspase-9 activity [23]. Kolsi et al. (2017) also revealed Seagrass (Cymodocea nodosa) possesses high antioxidant and antihypertensive ability which is concentration-dependent [24].

Furthermore, marine plants are utilized as a healthy food item for human consumption. For example, Paiva et al. (2017) reported the ACE-inhibition and antioxidant properties of Fucus spiralis protein hydrolysate - ultrafiltrate (FSPH-UF) which are used to prevent and treat hypertension and/or oxidative stress-related diseases may be due to the bioactive peptides and polyphenols released during the enzymatic hydrolysis [17]. Shannon et al. (2016) also found the benefits of fucoxanthin in marine brown algae, Fucus vesiculosus, to include anti-diabetic, anti-obesity, anti-cancer, and antioxidant [11].

In another research, Sanger et al. (2018) reported three seaweeds, Gracilaria salicornia, Turbinaria decurens, and Halimeda macroloba of North Sulawesi, have can be used as a functional food and also serve as a source of natural pigments and antioxidant compounds [25]. Lee et al. (2017) also detected the anti-inflammatory effects of Distromium decumbens (DDE) of Marine algae using enzyme-linked immunosorbent assays. It was discovered that DDE reduced the expression of IL-6 and IL-8 stimulated by Pseudomonas Aeruginosa Lipopolysaccharide (PA-LPS) in nasal polyp-derived fibroblasts (NPDFs) and also significantly attenuated PA-LPS-induced migration of differentiated HL-60 cells. This means DDE potentially inhibited inflammation through the ERK1/2, Akt, and NF-κB signaling pathways in NPDFs [26].

Suleria et al. (2017) further revealed the use of abalone (Haliotis sp.) as a traditional functional food for consumption provides health benefits [27]. For instance, blacklip abalone extract was discovered to have anti-inflammatory activity in vitro and this requires further investigation into the bioactive constituents to discover its potential use as therapeutics. Wali, Adil Farooq et al. (2019) showed some marine sponge species Fish, Ircinia fasciculate, molluscs, echinoderms, crustaceans, Penicillium chrysogenum, and several algae potentially have anti-inflammatory, antitumor, and immunosuppressant ability [28]. In another study conducted by Thanh-Sang Vo, and Se-Kwon Kim (2013) on the use of fucoidans as a natural bioactive ingredient, it was found that it has anti-coagulant, anti-virus, anti-inflammatory, anti-allergic, anti-oxidant, anti-obesity, anti-tumor, and gastric protection abilities, as well as defense against hyperoxaluria [29]. Park H.-K. et al. (2013) also mentioned laminarin from luminaria digitate of marine brown algae has potential with anticancer effects on the human colon [30]. Ridhowati, Sherly, et al. (2018) researched the anticancer and antioxidant activities of Sea Cucumber (Stichopus variegatus) in vitro against colon, breast, T47D, and normal cancer cells. In addition, its enzyme-extract fraction could be further developed as a complementary cancer remedy [31]. Ratih, Pangestuti and Dedy Kurnianto (2017) reported Green Seaweeds possess the potential to be anticancer, antioxidant, antihyperlipidemic, as well as anticoagulant while the research conducted by Pangestuti, Ratih, Se-Kwon Kim (2011) on phlorotannin, alginates, fucoidan, sargaquinoic acid, and carotenoids from marine algae showed they also possess the great potency to be neuroprotection agents applied as part of the nutraceuticals and functional foods [7], [18].

In another study by Pangestuti, Ratih, and Singgih Wibowo (2013), marine brown algae were discovered to be a source of structurally diverse bioactive compounds mainly due to the presence of chlorophyll and carotenoid respectively known for antioxidant and anticancer and anti-obesity properties, respectively. Ridhowati, Sherly, et. al. (2014) also researched the potential of sea cucumber, especially with regards to the prevention of cancer, and the strategies to develop it as functional food using enzymatic hydrolysis in an in vivo study. Moreover, Sri Harti, Agnes, et al. (2010) revealed Chito-oligosakarida (COS) from wasted shrimp shell is a source of natural prebiotic functional food with the ability to reduce cholesterol level in symbiotic and ox gall media by 0.3%. The synergistic and symbiotic effect in vivo further showed a decrease in the HDL and LDL cholesterol levels of the tested animals. It is, therefore, possible to apply COS biopreparation and prebiotics in yogurt functional foods .

Custódio L. et al. (2015) reported that Cystoseira tamariscifolia, Cystoseira nodicaulis (Sargassaceae) had the highest antiradical activity and are important sources of nutraceutical compounds with the ability to improve cognitive functions. The nutrient composition of G. gracilis was also discussed in this study and the seaweed species were suggested to have the potential to be used as raw material or an ingredient in preparing healthy foods for human beings (Rasyid, Abdullah, et al. 2019). Erniati, et al. (2016) showed seaweeds are required to be free from heavy metal and other pollutants and contain bioactive components and high nutrients to be developed into the functional food product. This means good cultivation and postharvest handling standard have to be applied in its cultivation and the processing should be carefully handled to avoid damaging the bioactive components.

According to Susanto, E. and A. S. Fahmi (2012), the functional properties of fish protein have been widely used in various food products. For instance, the bioactive peptide compounds are applied to reduce pathogenic bacteria and increase the shelf life of food products. In addition, the antibacterial contained in the peptides is used to prevent the growth of Clostridium botulinum bacteria spores in cheese products. Three green seaweed research articles were discovered to be discussing antioxidants, alkaloids, tannins, phenol hydroquinone, flavonoids, phycocyanin, steroids, terpenoids, and triterpenoids. Eight articles on red seaweed discussed proximate, dietary fiber, minerals, fatty acids, amino acids, iodine, carrageenan (fikokoloid), natural antioxidants, and pigments. Five brown seaweed research articles also discussed antioxidants, fucoxanthin, total lipids, carotenoids bioactive compounds, and fucoidans while sea cucumbers were studied in eight publications and the content include anticancer, cytotoxic component, antioxidant activities, triterpene glycosides, carotenoids, bioactive peptides, vitamins, minerals, fatty acids, amino acids, collagens, gelatins, and chondroitin sulfates. Moreover, three articles that examined crabs showed small ones contain chitooligosaccharides (COS) which is a source of natural probiotics.

Furthermore, Mendis, Eresha and Se-Kwon Kim (2011) reported the prospect of developing seaweed as a functional food based on the strong scientific evidence of biochemical compounds such as peptides, amino acids, polysaccharides, phytochemicals, lipids and minerals with numerous benefits to the consumers' health. The results also showed both micro and macro algae have great potential to be used as ingredients and are, however, required to be cultivated and harvested using sustainable and environmentally friendly means. Moreover, continuous improvement in scientific technology was discovered to enable complete characterization of polyphenols and phlorotannin in macroalgae contents and also allow a better understanding of the health-enhancing effects of each of the phlorotannins and those working synchronously. This further helps to determine the effect of macroalgae polyphenols in the body and the reflection of the required health outcomes which are expected to be made clearer through several studies being conducted on humans. Experimental studies showed phlorotannins from marine macroalgae have many positive effects related to health. Moreover, Ecklonia cava has been discovered to show great potential as a source of bioactive marine polyphenols as evidenced by the anti-hyperglycemia and anti-hyperlipidemia effects in the completed trials on human populations. However, other macroalgae species should not be ignored and other research works should be conducted to understand their true potentials.

4 Conclusion

Several international studies have been conducted on the benefits of functional foods made from marine biota to prevent and treat several degenerative diseases using their blood pressure lowering, anti-hyperglycemia, anti-hyperlipidemia, anti-hypertension, anti-diabetic, anti-rheumatic, anti-cancer, cytotoxic, serum cholesterol reduction, cardiovascular disease risk factors reduction, anti-inflammatory, immunosuppressant, probiotic ingredients, symbiotic substances, and infectious diseases abilities. However, those conducted in Indonesia focused only on the benefits of functional foods from marine biota while their potential as functional food and supplements is still being studied. Policy and management are needed to support the research on the benefits of marine resources as a functional food. The quality of marine resources depends on the natural conditions of the sea weather and pollution. The sustainability and availability of marine raw materials depends on sea conditions and national Policies.

References

[1] S. Azwar, "Metode Penelitian; Penelitian Sebagai Kegiatan Ilmiah," *Yogyakarta: Pustaka Belajar*, 1999.

[2] L. J. Moleong, "Metodologi Penelitian Kualitatif Edisi Revisi, Cetakan keduapuluh dua, Bandung: PT," *Remaja Rosdakarya Offset*, 2006.

[3] P. Sugiyono, "Metode Penelitian Kuantitatif, Kualitatif, dan R&D," *Metod. Penelit. Kuantitatif, Kualitatif, dan R&D. Bandung CV Alf.*, 2010.

[4] J.-K. Chen, C.-H. Yeh, L.-C. Wang, T.-H. Liou, C.-R. Shen, and C.-L. Liu, "Chitosan, the marine functional food, is a potent adsorbent of humic acid," *Mar. Drugs*, vol. 9, no. 12, pp. 2488–2498, 2011.

[5] T. H. Jatmiko, D. J. Prasetyo, C. D. Poeloengasih, and Y. Khasanah, "Nutritional Evaluation of Ulva sp. from Sepanjang Coast, Gunungkidul, Indonesia," in *IOP Conference Series: Earth and Environmental Science*, 2019, vol. 251, no. 1, p. 12011.

[6] E.-K. Choi *et al.*, "Clinical trial of the hypolipidemic effects of a brown alga Ecklonia cava extract in patients with hypercholesterolemia," *Int. J. Pharmacol.*, vol. 11, no. 7, pp. 798–805, 2015.

[7] T.-S. Vo and S.-K. Kim, "Fucoidans as a natural bioactive ingredient for functional foods," *J. Funct. Foods*, vol. 5, no. 1, pp. 16–27, 2013.

[8] J. M. Njinkoue *et al.*, "Proximate composition, mineral content and fatty acid profile of two marine fishes from Cameroonian coast: Pseudotolithus typus (Bleeker, 1863) and Pseudotolithus elongatus (Bowdich, 1825)," *NFS J.*, vol. 4, pp. 27–31, 2016.

[9] M. Raman and M. Doble, "κ-Carrageenan from marine red algae, Kappaphycus alvarezii–A functional food to prevent colon carcinogenesis," *J. Funct. Foods*, vol. 15, pp. 354–364, 2015.

[10] S. Jiang *et al.*, "Anti-proliferation activity of a decapeptide from perinereies aibuhitensis toward human lung cancer H1299 cells," *Mar. Drugs*, vol. 17, no. 2, p. 122, 2019.

[11] E. Shannon and N. Abu-Ghannam, "Optimisation of fucoxanthin extraction from Irish seaweeds by response surface methodology," *J. Appl. Phycol.*, vol. 29, no. 2, pp. 1027–1036, 2017.

[12] F. Shahidi and P. Ambigaipalan, "Novel functional food ingredients from marine sources," *Curr. Opin. Food Sci.*, vol. 2, pp. 123–129, 2015.

[13] C. Sasaki *et al.*, "Isolation and identification of an angiotensin I-converting enzyme inhibitory peptide from pearl oyster (Pinctada fucata) shell protein hydrolysate," *Process Biochem.*, vol. 77, pp. 137–142, 2019.

[14] F. Yu *et al.*, "Identification and molecular docking study of a novel angiotensin-I converting enzyme inhibitory peptide derived from enzymatic hydrolysates of Cyclina sinensis," *Mar. Drugs*, vol. 16, no. 11, p. 411, 2018.

[15] E. Bigagli *et al.*, "Preliminary data on the dietary safety, tolerability and effects on lipid metabolism of the marine microalga Tisochrysis lutea," *Algal Res.*, vol. 34, pp. 244–

249, 2018.

[16] E. Peltomaa, M. D. Johnson, and S. J. Taipale, “Marine cryptophytes are great sources of EPA and DHA,” *Mar. Drugs*, vol. 16, no. 1, p. 3, 2018.

[17] W. Wijesinghe, S.-C. Ko, and Y.-J. Jeon, “Effect of phlorotannins isolated from Ecklonia cava on angiotensin I-converting enzyme (ACE) inhibitory activity,” *Nutr. Res. Pract.*, vol. 5, no. 2, pp. 93–100, 2011.

[18] R. Pangestuti and D. Kurnianto, “Green Seaweeds-Derived Polysaccharides Ulvan: Occurrence, Medicinal Value and Potential Applications,” in *Seaweed Polysaccharides*, Elsevier, 2017, pp. 205–221.

[19] M. MURATA and J. Nakazoe, “Production and use of marine aIgae in Japan,” *Japan Agric. Res. Q. JARQ*, vol. 35, no. 4, pp. 281–290, 2001.

[20] S. Shah Alam and N. Mohamed Sayuti, “Applying the Theory of Planned Behavior (TPB) in halal food purchasing,” *Int. J. Commer. Manag.*, vol. 21, no. 1, pp. 8–20, 2011.

[21] V. K. Bajpai, “A review on trend of marine sources for the development of functional foods,” 2017.

[22] I. P. S. Fernando, K. K. A. Sanjeewa, K. W. Samarakoon, W. W. Lee, H. Kim, and Y. Jeon, “Squalene isolated from marine macroalgae Caulerpa racemosa and its potent antioxidant and anti‐inflammatory activities,” *J. Food Biochem.*, vol. 42, no. 5, p. e12628, 2018.

[23] S. Pinteus *et al.*, “An insight into Sargassum muticum cytoprotective mechanisms against oxidative stress on a human cell in vitro model,” *Mar. Drugs*, vol. 15, no. 11, p. 353, 2017.

[24] R. B. A. Kolsi, H. Ben Salah, S. A. Saidi, N. Allouche, H. Belghith, and K. Belghith, “Evaluation of nutritional value, characteristics, functional properties of Cymodocea nodosa and its benefits on health diseases,” *Lipids Health Dis.*, vol. 16, no. 1, p. 238, 2017.

[25] G. Sanger, B. E. Kaseger, L. K. Rarung, and L. Damongilala, “Potensi beberapa jenis rumput laut sebagai bahan pangan fungsional, sumber pigmen dan antioksidan alami,” *J. Pengolah. Has. Perikan. Indones.*, vol. 21, no. 2, pp. 208–218, 2018.

[26] D.-S. Lee *et al.*, “Anti-inhibitory potential of an ethanolic extract of Distromium decumbens on pro-inflammatory cytokine production in Pseudomonas aeruginosa lipopolysaccharide-stimulated nasal polyp-derived fibroblasts,” *Int. J. Mol. Med.*, vol. 40, no. 6, pp. 1950–1956, 2017.

[27] H. A. R. Suleria, R. Addepalli, P. Masci, G. Gobe, and S. A. Osborne, “In vitro anti-inflammatory activities of blacklip abalone (Haliotis rubra) in RAW 264.7 macrophages,” *Food Agric. Immunol.*, vol. 28, no. 4, pp. 711–724, 2017.

[28] A. F. Wali *et al.*, “Natural products against cancer: Review on phytochemicals from marine sources in preventing cancer,” *Saudi Pharm. J.*, 2019.

[29] E. Mendis and S.-K. Kim, “Present and future prospects of seaweeds in developing functional foods,” in *Advances in food and nutrition research*, vol. 64, Elsevier, 2011, pp. 1–15.

[30] H.-K. Park, I.-H. Kim, J. Kim, and T.-J. Nam, “Induction of apoptosis and the regulation of ErbB signaling by laminarin in HT-29 human colon cancer cells,” *Int. J. Mol. Med.*, vol. 32, no. 2, pp. 291–295, 2013.

[31] S. Ridhowati, F. R. Zakaria, D. Syah, and E. Chasanah, “Anticancer and Antioxidant Activities from Sea Cucumber (Stichopus variegatus) Flour Dried Vacuum Oven.,” *Pertanika J. Trop. Agric. Sci.*, vol. 41, no. 3, 2018.