Jurnal Akuakultur Indonesia
Review Article
ISSN: 1412-5269
EISSN: 2354-6700
Vol. 25 No. 2, July 2026
DOI: 10.19027/jai.25.2.260-272

Mini-review: Utilization of *Sargassum* and its role in the non-specific immune resistance of fish and shrimp against bacterial infections

Pemanfaatan *Sargassum* dan peranannya dalam ketahanan imun non spesifik ikan dan udang terhadap infeksi bakteri

Kanisius Ogy Syaputra Bere[1*], Muiza Nugrahaini[1], Muhamad Firdaus[2], Yunita Maimunah[3]

[1]Graduate Student of Aquaculture, Faculty of Fisheries and Marine Science, Brawijaya University, Malang 65145, Indonesia
[2]Department of Fisheries and Marine Resources Management, Faculty of Fisheries and Marine Science, Brawijaya University, Malang 65145, Indonesia
[3]Aquaculture Department, Faculty of Fisheries and Marine Science, Brawijaya University, Malang 65145, Indonesia
*Corresponding author: ogybere@gmail.com

(Received July 21, 2025; Revised November 6, 2025; Accepted March 5, 2026)

ABSTRACT

Bacterial infections are a major problem in fish farming, causing significant economic losses. Excessive use of antibiotics can lead to the risk of resistance and environmental pollution, making the use of safe and environmentally friendly natural antimicrobials crucial. *Sargassum*, a type of brown macroalgae, has the potential to act as a natural immunostimulant that can enhance fish's non-specific immune resistance to bacterial infections. Various species *Sargassum*, including *S. kjellmanianum*, *S. muticum*, *S. polycystum*, *S. ilicifolium*, and *S. vulgaris*, have been explored as a bioactive source through methods such as ethanol extraction, solvent fractionation, sequential extraction, phytochemical screening, and probiotic fermentation. In compound identification, phenolics, flavonoids, terpenoids, saponins, sulfated polysaccharides, and fucoidan have been found to be the dominant components. Administration through feed or seaweed supplements has been shown to increase immune gene expression (*IL-1β*, *IL-8*, *TNF-α*, *IGF-1*, *LGBP*, peroxinectin, prophenoloxidase, TLR, penaeid), leukocyte count, lysozyme activity, total complement, NBT, bactericidal activity, growth performance, and resistance to bacterial stress or challenge (*Aeromonas hydrophila*, *Vibrio harveyi*, *Vibrio parahaemolyticus*) in target species such as rainbow trout (*Oncorhynchus mykiss*), Asian seabass (*Lates calcarifer*), oscar fish (*Astronotus ocellatus*), common carp (*Cyprinus carpio*), yellow catfish (*Pelteobagrus fulvidraco*), and black tiger shrimp (*Penaeus monodon*). These findings indicate that *Sargassum* has great potential as a crucial feed immunostimulant to support the health and growth of fish and shrimp.

Keywords: aquaculture, bacterial infections, innate immunity, *Sargassum*

ABSTRAK

Infeksi bakteri merupakan salah satu masalah utama dalam budidaya ikan yang dapat menyebabkan kerugian ekonomi yang signifikan. Pemakaian antibiotik secara berlebihan dapat memicu risiko resistensi dan pencemaran lingkungan, sehingga kebutuhan akan penggunaan antimikroba alami yang aman dan ramah lingkungan menjadi sangat penting. *Sargassum*, jenis makroalga cokelat, memiliki potensi sebagai imunostimulan alami yang dapat meningkatkan ketahanan imun non-spesifik ikan terhadap infeksi bakteri. Berbagai spesies *Sargassum*, termasuk *S. kjellmanianum, S. muticum*, *S. polycystum*, *S. ilicifolium*, dan *S. vulgare*, telah dieksplorasi sebagai sumber bioaktif melalui metode seperti ekstraksi etanol, fraksinasi pelarut, ekstraksi berurutan, skrining fitokimia, dan fermentasi probiotik. Dalam identifikasi senyawa, telah ditemukan bahwa fenolik, flavonoid, terpenoid, saponin, polisakarida tersulfatisasi, dan fucoidan merupakan komponen-komponen yang dominan. Pemberian melalui pakan atau suplemen rumput laut terbukti meningkatkan ekspresi gen imun (*IL-1β*, *IL-8*, *TNF-α*, *IGF-1*, *LGBP*, *peroxinectin*, *prophenoloxidase*, *TLR*, *penaeidin*), jumlah leukosit, aktivitas lisozim, komplemen total, *NBT*, aktivitas bakterisidal, performa pertumbuhan, dan ketahanan terhadap stres atau tantangan bakteri (*Aeromonas hydrophila*, *Vibrio harveyi*, *Vibrio parahaemolyticus*) pada spesies target seperti rainbow trout (*Oncorhynchus mykiss*), Asian seabass (*Lates calcarifer*), oscar fish (*Astronotus ocellatus*), common carp (*Cyprinus carpio*), yellow catfish (*Pelteobagrus fulvidraco*), dan Black tiger shrimp (*Penaeus monodon*). Temuan tersebut mengungkapkan bahwa *Sargassum* berpotensi besar sebagai imunostimulan pakan yang krusial untuk menunjang kesehatan dan pertumbuhan ikan maupun udang.

Kata kunci: akuakultur, imun non-spesifik, infeksi bakteri, *Sargassum*

INTRODUCTION

It is common for intensive aquaculture to face several problems. These include infections caused by pathogens like bacteria, fungi, and viruses. These infections pose a major challenge in intensive aquaculture practices (Irshath *et al.,* 2023; Mahardika *et al.,* 2020; Mugimba *et al.,* 2021). The outbreak of such disease epidemics in aquaculture settings occurs mainly due to a disturbance of the balance that exists among environmental factors, aquatic microorganisms, and the fish hosts (Deng *et al.,* 2023; Linayati *et al.,* 2024). Moreover, higher stocking rates in intensive aquaculture practices also pose another contributory factor. These conditions often trigger stressful reactions in fish, which in turn causes immune function impairment in fish (Muahiddah & Isnansetyo, 2023; Yarahmadi *et al.,* 2016).

The use of antibiotics is a common approach in managing bacterial infections in fish farming (Legrand *et al.,* 2020). However, the continuous use of antibiotics without regulation and even using improper doses has shown an ability to encourage the emergence of bacteria resistant to the drugs (Bernika, 2023; Peng *et al.,* 2024; Prasaja *et al.,* 2024; Yuan *et al.,* 2023). Apart from the problem of antibiotic resistance, the residues of the antibiotics themselves pose serious risks to the health of the consumers (Ebtasaria & Aini, 2024; Hakimah *et al.,* 2021). In order to mitigate the negative impact that occurs through the use of antibiotics, it is necessary to use natural compounds as immunostimulants as an alternative strategy (Gruber *et al.,* 2025; Thépot *et al.,* 2021).

An immunostimulant can be defined as a substance or chemicals that can enhance the immune system of fish both specific and non-specific immunity. The use of natural immunostimulants, such as those found in macroalgae extract, is acknowledged as a useful strategy to boost the non-specific immune system of fish without causing any problems linked with antimicrobial resistance or residue formation. The former two factors are usually observed when antibiotics are used for a prolonged period of time (Doan *et al.,* 2023; Thépot *et al.,* 2021). Seaweed belonging to the genus *Sargassum* has been acknowledged as one of the most successful natural immunostimulants (Melchor-Martínez *et al.,* 2025; Siddik *et al.,* 2023; Wazzan, 2016). There are many bioactive substances, like sulfated polysaccharides, polyphenols, and terpenoids, present in the seaweed, which can help boost the immune responses in fish and shrimp (Khanzadeh *et al.,* 2025; Kim *et al.,* 2022).

In a similar manner, according to Noyanti *et al.* (2023), there are many secondary metabolites, like alkaloids, saponins, and steroids, present in the *Sargassum* seaweed. In addition to this, Al-Mur & Alsiary (2025) have found that seaweed possesses many biological activities, such as antibacterial, anticancer, anti-inflammatory, and antioxidant activities. It should be noted that despite the proven efficacy of *Sargassum* in various i*n vitro* and in vivo experiments, some challenges remain associated with studies investigating the use of immunological markers longitudinally in intensive farming systems in tropical conditions. In particular, these challenges involve the optimal dose of bioactive agents and the duration of their administration, as well as the effect of these components on fish immune response signaling pathways. Hence, an integrated study methodology must be developed that will allow for applying *Sargassum* as an immunostimulant effectively, measurably, and adaptively in the environment and, as a consequence, to replace antibiotics as a fish pathogen therapy. The aim of this mini-review is to conduct a systematic review concerning the use of various types of *Sargassum* as immunostimulants in aquaculture.

METHODS

The present study involves conducting a literature review that is a compilation of scholarly articles indexed through the use of databases such as Scopus, Web of Science, PubMed, and Google Scholar, between the years 2015 and 2025. The main aim of this review will be to evaluate the possibility of using different varieties of the *Sargassum* seaweed as feed immunostimulants for fish and shrimp with a particular focus on their ability to promote growth and enhance the immune response. These data will be collected through the use of methods such as ethanol extraction, solvent fractionation, sequential extraction, phytochemical screening, or probiotic fermentation with major active substances including phenolics, flavonoids, terpenoids, saponins, sulfated polysaccharides, and fucoidan. The target organisms include rainbow trout (*Oncorhynchus mykiss*), Asian seabass (*Lates calcarifer*), oscar fish (*Astronotus ocellatus*), common carp (*Cyprinus carpio*), yellow catfish (*Pelteobagrus fulvidraco*), and black tiger shrimp (*Penaeus monodon*) while the analyzed variables will include immune gene expression, number of leukocytes, lysozyme activity, total complement, NBT, bactericidal activity, growth performance, and tolerance to stress or pathogen challenge by *Aeromonas hydrophila*, *Vibrio harveyi*, and *Vibrio parahaemolyticus*.

Non-specific immune parameters in evaluating the effectiveness of immunostimulants

Generally, fish have an immune system made up of two major immune systems, namely the non-specific (innate) immune system and the specific (adaptive) immune system, which work together in defending against diseases (Hopo *et al.,* 2024; Mokhtar *et al.,* 2023; Muahiddah & Diamahesa, 2022). The non-specific immune system acts as the first immune defense system comprising phagocytic cells such as neutrophils and macrophages, soluble lysozyme, and complement proteins, while the specific immune system consists of T-cells and antibodies from B-cells (Dezfuli *et al.,* 2023; Jones & Cain, 2023; Mokhtar *et al.,* 2023). The evaluation of the immunity status in fish is usually done based on various physiological factors, some of which include the total leukocytes count, the differential leukocytes profile such as lymphocytes, neutrophils, monocytes, and phagocytic index (Do-Huu *et al.,* 2023; Singh *et al.,* 2024; Yu *et al.,* 2025). The presence of an increase in the number of leukocytes, especially neutrophils and monocytes, signifies that there are pathogens or immunostimulants in the fish (Alarape *et al.,* 2024; Witeska *et al.,* 2023).

Aside from using blood indicators, molecular indicators, which include pro-inflammatory cytokines like Tumor Necrosis Factor alpha (TNF-α) expression, are also employed to determine the activation of the immune system (Kong *et al.,* 2021; Mufidah *et al.,* 2022; Sakai *et al.,* 2021). TNF-α is an essential protein involved in the regulation of inflammatory responses and activates immune cells (Kong *et al.,* 2021; Liyanage *et al.,* 2020). The increase in the levels of the pro-inflammatory protein can therefore serve as an indication that the immune system has been activated due to infections like those caused by *Aeromonas hydrophila*.

Bioprospecting of *Sargassum* as a Source of Bioactive Compounds

The genus *Sargassum*, consisting of brown macroalgae belonging to the order Phaeophyceae, has a worldwide distribution range, including the coastlines of Indonesia (Forestin *et al.,* 2024; Ghazali *et al.,* 2024). *Sargassum* is a seaweed which contains a variety of bioactive components, including polysaccharides (e.g., alginate, laminarin), phenols, flavonoids, and other bioactive pigments that possess various biological properties (Table 1), among which are antibacterial and immunostimulating activities (Datu *et al.,* 2024; Sedjati *et al.,* 2024; Widyaswari *et al.,* 2024). *Sargassum* has traditionally been used as raw material in the food and pharmaceutical industries, and recently, it received much interest in the field of aquaculture due to its ability to provide bioactive compounds naturally (Catarino *et al.,* 2023; Melchor-Martínez *et al.,* 2025; Zaidan *et al.,* 2019). Bioprospection of *Sargassum* implies the discovery, identification, and characterization of different bioactive compounds contained in *Sargassum* species, especially those capable of stimulating immunity in cultured organisms, for example, fish (Gora *et al.,* 2018; Khanzadeh *et al.,* 2024).

More than 300 species of *Sargassum* exist worldwide, and among them are those that have been noted to possess economic value and great bioactivity. These species include *Sargassum polycystum*, *Sargassum* crassifolium, *Sargassum* fusiforme, *Sargassum ilicifolium*, and *Sargassum* sp. (Álvarez-Canali *et al.,* 2024; Puspita *et al.,* 2020; Yip *et al.,* 2020). Within Southeast Asia and specifically in Indonesia, extensive growth of *Sargassum* is evident in coastal areas despite the fact that *Sargassum* has been considered a vastly unexploited biological entity within the region (Litaay *et al.,* 2022; Sutrisno *et al.,* 2024; Widyaswari *et al.,* 2024). They are harvested mainly from the wild but some countries are already making efforts towards domestication. The wide species variety makes them suitable to be used as sources of natural immunostimulants owing to the diverse nature of their bioactive components (García-Pozza *et al.,* 2020; Widyaswari *et al.,* 2024)

Immunostimulatory Effects of *Sargassum* in Aquaculture

Immunostimulants are natural or synthetic compounds that enhance the immune response of organisms against pathogens by stimulating the innate and/or adaptive immune systems (Aly *et al.,* 2024; Jain *et al.,* 2022; Kamaliah *et al.,* 2025; Vijayaram *et al.,* 2022). In aquaculture practices, immunostimulants have been widely employed to enhance disease resistance in fish and serve as alternatives to antibiotics, which are known to contribute to the emergence of resistant strains and harmful residues in fish products (Nafiqoh *et al.,* 2021; Pelic *et al.,* 2024). One of the most commonly used groups of immunostimulants is polysaccharides, particularly β-glucans, which are structural components of the cell walls of fungi, yeast, and certain algae (Ching *et al.,* 2021; Khanjani *et al.,* 2022; Lee *et al.,* 2018; Muahiddah & Isnansetyo, 2023; Rodrigues *et al.,* 2020).

The supplementation of β-glucans in fish diets has been shown to improve phagocytic activity, leukocyte proliferation, and the production of key immune molecules such as lysozyme and pro-inflammatory cytokines (Hadiuzzaman *et al.,* 2022; Purbomartono *et al.,* 2024; Rodrigues *et al.,* 2020; Saha *et al.,* 2023; Siwicki *et al.,* 2015). These immune responses are triggered through the recognition of β-glucans by pattern recognition receptors (PRRs) on macrophages or other immune cells, leading to intracellular signaling pathways and the upregulation of immune-related genes such as TNF-α and IL-1β (Han *et al.,* 2020; Petit *et al.,* 2019). Moreover, β-glucans exhibit immunomodulatory effects that can contribute to the enhancement of long-term specific immune responses (Hadiuzzaman *et al.,* 2022; Purbomartono *et al.,* 2024).

Numerous studies have demonstrated that *Sargassum* extracts can enhance hematological parameters in fish, including increased hematocrit and leukocyte differentials, as well as stimulate phagocytic activity an essential component of the non-specific immune response (Yudiati *et al.,* 2022; Yuliana *et al.,* 2021). Enhancing the phagocytic activity of immune cells, including macrophages and neutrophils, contributes to increased resistance in fish against bacterial infections, particularly those caused by opportunistic pathogens such as *Aeromonas hydrophila* (Gazali *et al.,* 2024; Sönmez *et al.,* 2021). This phenomenon is corroborated by multiple investigations (Table 2). An analysis of the collected data indicates that the immunostimulating properties of *Sargassum polycystum* have been confirmed in two aquatic organisms. Thus, in rainbow trout (Oncorhynchus mykiss), an extract of *S. polycystum* demonstrated the ability to increase transcriptional expression of several genes of inflammatory cytokines, namely IL-1β and IL-8. This effect led to higher survival rates after infections caused by *Aeromonas hydrophila* (Sönmez *et al.,* 2021). At the same time, in black tiger shrimp (Penaeus monodon), an extract of *S. polycystum* was found to enhance transcriptional expression of important immune genes, including LGBP (lipopolysaccharide and β-1,3-glucan binding protein), peroxinectin, prophenoloxidase, toll-like receptors, and penaeidin. These effects were involved in the nonspecific immune response against infections with *Vibrio parahaemolyticus* (Chin *et al.,* 2024). Therefore, these results indicate a broad spectrum of immunostimulating effects in aquatic animals.

Moreover, *S. ilicifolium* has been found to possess strong immunomodulatory effects as shown by upregulation of TNF-α, IL-1β, and IGF-1 genes and increased survival rate after being challenged with *Vibrio* sp. in Asian seabass (Lates calcarifer) (Khanzadeh *et al.,* 2025). Other studies also revealed that *S. ilicifolium* supplementation for oscar fish (Astronotus ocellatus) resulted in the elevation of immune factors like the number of leukocytes, lysozyme activity, total complement, NBT activity, and bactericidal activity along with growth enhancement (Khanzadeh *et al.,* 2024). Such findings highlight the effectiveness of *S. ilicifolium* as an immune booster in terms of both gene expression and physiological aspects. Likewise, *Sargassum* linearifolium supplementation for Asian seabass (Lates calcarifer) yielded promising results in terms of immune stimulation, resistance against *Vibrio harveyi*, and growth performance (Siddik *et al.,* 2025).

It has been demonstrated that *Sargassum vulgare* significantly increases the levels of a variety of hematological and immunological biomarkers among common carp (*Cyprinus carpio*) by boosting their hematocrit, hemoglobin, HDL, total protein, globulin, lysozyme activity, and complement activation. This demonstrates the extensive range of benefits offered by *S. vulgare* for improving the well-being and nonspecific immunity of fish (Sabzi *et al.,* 2023). On the other hand, *Sargassum kjellmanianum* has shown significant potential as an additive for yellow catfish (Pelteobagrus fulvidraco) through improved growth, immune response, antioxidant capacity, and resistance to ammonia toxicity (Hu *et al.,* 2024). Although the effect on pathogens is not included in this study, it can be reasonably assumed that *S. kjellmanianum* may offer both protective and adaptive properties.

There are certain active components of *Sargassum*, namely sargachromanol and fucoidan, which exhibit significant anti-inflammatory properties. They help regulate the production of inflammatory cytokines like TNF-α and IL-1β, which have an important role in immune responses to various pathogens and stressors (Chang *et al.,* 2023; Jayawardena *et al.,* 2020; Liyanage *et al.,* 2023; Park *et al.,* 2024). Moreover, the extracts of *Sargassum* have been reported to be effective against various pathogenic bacteria, such as *Vibrio* spp. (Datu *et al.,* 2024; Lambert *et al.,* 2024; Senggagau & Bond, 2023), and *Aeromonas hydrophila* (Ali *et al.,* 2016; Waruwu *et al.,* 2024). The suppression is either due to its antibacterial properties or improved immunity of the hosts. Thus, incorporating *Sargassum* into the fish diet as an immunostimulant could prove quite beneficial for their disease resistance in a sustainable manner.

It can be noted from Table 1 that there are differences in the profiles of the bioactive compounds present in the *Sargassum* genus. These differences are associated with the specific characteristics of the species in question, the method used to extract them, and even the solvent used to do so. It is therefore possible that the differences in bioactive composition between various species of *Sargassum* could affect its performance as an immunostimulator in aquaculture, since each compound performs a different role in stimulating the immune system. Sulfated polysaccharides present in *Sargassum* spp. (Rushdi *et al.,* 2020) are known to interact with pattern recognition receptors (PRRs) and trigger innate immunity as a result of these interactions. Moreover, high levels of total phenolics and flavonoids found in *S. muticum* (Bouzenad *et al.,* 2024) and *S. polycystum* (Sobuj *et al.,* 2024) can help protect immune cells from oxidative stress caused by inflammation due to pathogens. Furthermore, the presence of multiple other bioactive compounds such as alkaloids, terpenoids, and saponins may also help to increase phagocytosis and the formation of immune mediator compounds in fish.

However, it should be noted that at present the obtained results do not have sufficient ability to link the level of bioactive compounds in each *Sargassum* type with the immune responses found in aquatic animals. Therefore, in order to reveal the most effective *Sargassum* species and to find out the exact dosage required for its application in practice, it is essential to carry out full-scale studies including phytochemical analysis and in

Table 1. Bioactive compounds in various *Sargassum* species.

No.	*Sargassum* Species	Extraction Method & Solvent	Dominant Bioactive Compounds	Reference
1.	*Sargassum kjellmanianum*	Solvent fractionation (n-hexane, dichloromethane, n-butanol)	(+)-Kjellmanianone, *Sargassumlactam*, sulfated polysaccharides (SKP1–3)	(Rushdi *et al.,* 2020)
2.	*Sargassum muticum*	Sequential extraction (methanol, ethyl acetate, n-butanol)	Vanillin, Chrysin, total phenolics: 235.67 ± 1.13 µg GAE/mg	(Bouzenad *et al.,* 2024)
3.	*Sargassum polycystum*	Extraction using 100%, 70%, 50% methanol; FTIR and DPPH analyses	Total phenolics: 80.13 mg GAE/g, total flavonoids: 38.33 mg QE/g, terpenoids, saponins	(Sobuj *et al.,* 2024)
4.	*Sargassum polycystum*	Qualitative phytochemical screening (Harborne method)	Flavonoids, alkaloids, phenolics, tannins	(Sarika *et al.*2024)
5.	*Sargassum polycystum*	Ethanol extraction; spectrophotometric determination of total phenolics and flavonoids	Flavonoids, phenol hydroquinone, tannins, saponins	(Widyaswari *et al.,* 2024)
6.	*Sargassum ilicifolium*	Ethanol extraction; DPPH and IC50 antioxidant activity assay	Flavonoids, phenol hydroquinone, tannins, steroids	(Widyaswari *et al.,* 2024)

vivo tests of the immune-stimulating properties of the studied compounds under aquaculture conditions. In this regard, the diversity of bioactive compounds among different species of *Sargassum* has considerable prospects for developing ecological immunostimulants for aquaculture. However, a consistent scientific approach is necessary to apply them properly.

Various *Sargassum* species used as dietary supplements in fish feed have been proven to enhance immune responses and resistance to bacterial infections, primarily due to their abundance of natural bioactive compounds. One of the key components, sulfated polysaccharides such as fucoidan, has been shown to activate the expression of critical immune-related genes, including *IL-1β* and *TNF-α*, thereby strengthening the innate immune response in fish (Khanzadeh *et al.,* 2025). Moreover, according to Chin *et al.* (2024), the fucoidan presence in brown algae can activate the signaling pathway of toll-like receptors (TLRs), which plays an important role in recognizing pathogens and activating immune response promptly. The phenolic components of *Sargassum* have strong antioxidant properties that prevent immune cells from oxidative damage, which usually occurs under bacteria invasion (Hu *et al.,* 2024; Rajivgandhi *et al.,* 2021; Sedjati *et al.,* 2017). The prevention of oxidative damage plays a significant role in sustaining the viability

Table 2. Dietary application of *Sargassum* species as immunostimulants in fish and shrimp.

No.	*Sargassum* Species	Administration Methods and Immunomodulatory Effects in Fish and Shrimp	Aquaculture Target Species	Bacterial Challenge	Reference
1.	*S. polycystum*	Dietary supplementation with ethanol extract enhances *IL-1β* and *IL-8* gene expression and improves survival rate.	Rainbow trout (*Oncorhynchus mykiss*)	*Aeromonas hydrophila*	(Sönmez *et al.,* 2021)
2.	*S. ilicifolium*	Seaweed meal as a dietary supplement enhances *TNF-α*, *IL-1β*, and *IGF-1* gene expression and improves survival rate	Asian seabass (*Lates calcarifer*)	*Vibrio harveyi*	(Khanzadeh *et al.,* 2025)
3.	*S. linearifolium*	Probiotic-fermented seaweed administered via feed enhances immune responses, resistance to infection, and growth performance.	Barramundi (*Lates calcarifer*)	*Vibrio harveyi*	(Siddik *et al.,* 2025)
4.	*S. polycystum*	The extract supplemented in the diet upregulates genes related to *LGBP*, *peroxinectin*, *prophenoloxidase*, *TLR*, and *penaeidin*.	Black tiger shrimp (*Penaeus monodon*)	*Vibrio parahaemolyticus*	(Chin *et al.,* 2024)
5.	*S. ilicifolium*	Fucoidan extract administered via feed enhances immune parameters (leukocyte count, lysozyme activity, total complement, NBT, bactericidal activity) as well as growth performance	Oscar fish (*Astronotus ocellatus*)	*Aeromonas hydrophila*	(Khanzadeh *et al.,* 2024)
6.	*S. vulgare*	Seaweed extract as a dietary supplement enhances hematocrit, hemoglobin, HDL, total protein, globulin, lysozyme activity, and complement system activity	Common carp (*Cyprinus carpio*)	–	(Sabzi *et al.,* 2023)
7.	*S. kjellmanianum*	Incorporation of seaweed meal into the diet improves growth performance, immune responses, antioxidant status, and resistance to ammonia stress.	Yellow catfish (*Pelteobagrus fulvidraco*)	–	(Hu *et al.,* 2024)

and functioning of macrophages and neutrophils, the two major immune cells of fish (Sönmez *et al.,* 2021). Additionally, *S. ilicifolium* and *S. horneri* extracts increase hemocyte numbers and activate various immune-related gene expression, such as prophenoloxidase, SOD, penaeidin3a, lysozyme, α2-macroglobulin, and peroxinectin, in whiteleg shrimp (Litopenaeus vannamei) (Lee *et al.,* 2020; Pourazad *et al.,* 2024).

Based on the data (Table 2), it can be concluded that various *Sargassum* species demonstrate significant potential in enhancing the immune system and survival of aquaculture organisms exposed to pathogens, with diverse mechanisms depending on the species and the immunological parameters assessed. The authors posit that the diversity in immunostimulatory effects is not solely related to the *Sargassum* species utilized but is also influenced by the cultured organism species and the type of challenging pathogen. For instance, the use of *S. polycystum* in rainbow trout (*Oncorhynchus mykiss*) and black tiger shrimp (*Penaeus monodon*) has been shown to upregulate immune-related genes such as *IL-1β*, *IL-8*, and other non-specific defense genes, contributing to enhanced resistance against bacterial infections including *Aeromonas hydrophila* and *Vibrio parahaemolyticus* (Chin *et al.,* 2024; Sönmez *et al.,* 2021). Meanwhile, *S. ilicifolium* has been reported to improve humoral and cellular immune parameters, including leukocyte counts, lysozyme activity, and the expression of *TNF-α* and *IGF-1* genes in grouper and oscar fish, which is relevant in strengthening the fish immune system against *harveyi* and *A. hydrophila* infections (Khanzadeh *et al.,* 2024, 2025).

However, the authors point out that the above-mentioned results prove *Sargassum*'s ability to enhance innate and adaptive immunity in various types of marine life organisms like fish and shrimp via increased phagocytosis, increased production of the effector molecules of immunity, and controlled expression of genes involved in resistance to pathogens. However, further studies considering dose-response relations, optimal delivery systems, and continuous assessment of immune system parameters should be performed to increase the efficiency o f u sing *Sargassum* in aquaculture as an immunostimulatory feed additive. Furthermore, it should be mentioned that according to the authors, in addition to its ability to stimulate immunity, feeding with *Sargassum* may positively affect other aspects like growth performance and antioxidant condition. This conclusion can be drawn from several cases when *S. kjellmanianum* was fed to yellow catfish and *S. vulgare* was added to the common carp diet (Hu *et al.,* 2024; Sabzi *et al.,* 2023).

Safety and Efficacy of *Sargassum* Extracts

Additionally, the results have shown that, within certain levels of concentrations, the extract is safe in terms of lack of toxic reactions or deaths among tested fish species (Azuwarita *et al.,* 2021; Negara *et al.,* 2021; Pratiwy *et al.,* 2018). Moreover, acute toxicity experiments conducted using different freshwater fishes including the African catfish (*Clarias gariepinus*), Nile tilapia (*Oreochromis niloticus*), and golden pompano (Trachinotus blochii) have shown that extracts of the tested *Sargassum* species do not cause significant changes to physiological parameters like breathing rate, hematocrit index, and survival among other aspects, only if they are at certain concentration levels Ghazali *et al.,* 2024. In general, all these findings prove that the use of *Sargassum* species is appropriate and safe to be used in aquaculture practices Muahiddah & Isnansetyo, 2023; Setiyowati *et al.,* 2022; Yuliana *et al.,* 2021.

Besides their safety, extracts of the *Sargassum* species have been found effective against the pathogenic bacteria of *Aeromonas hydrophila* which is responsible for the disease of MAS in freshwater fish as noted by Waruwu *et al.* (2024). The bioactive compounds contained in this species of brown algae, such as fucoidan, phenolics, and flavonoids, are expected to exhibit their antimicrobial effects by causing bacteria cell membrane disruption, protein synthesis inhibition, and oxidative stress in bacteria cells (Noyanti *et al.,* 2023; Sidauruk *et al.,* 2021). The antimicrobial properties make *Sargassum* useful not only as a prophylactic agent that enhances the immunity of fish but also as an ecological and sustainable means of combating pathogens. It offers a viable alternative to antibiotics, which have been associated with antibiotic resistance and the development of unwanted byproducts.

CONCLUSION

There appears to be substantial evidence that the genus *Sargassum* can be used effectively as a natural immunostimulant for aquaculture because of its capability of increasing nonspecific immune response and improving resistance against bacterial pathogens in fish and shrimp. The effects are mainly attributed to a variety of bioactive components in *Sargassum* such as sulfated polysaccharides, phenolics, and flavonoids, which play a vital role in modulating several immune parameters such as the number of leukocytes, phagocytosis, lysozyme levels, as well as gene expression of IL-1β and TNF-α. Additionally, the use of *Sargassum* is associated with improved growth indices and antioxidation properties, hence giving the substance two roles in aquaculture as an additive with health-improving and growth-promoting capabilities. However, it is crucial to conduct extensive research on dose-response characteristics, methods of administration, and sustained immuno-modulation in intensive aquaculture settings. The use of *Sargassum* as an immunostimulant in aquaculture systems is expected to provide environmentally friendly practices and a viable alternative to antibiotic treatments.

ACKNOWLEDGMENT

On behalf of the authors, we like to express our heartfelt gratitude to Lembaga Pengelola Dana Pendidikan (LPDP), Republic of Indonesia Ministry of Finance, for providing funds through the LPDP scholarship program, which has made an immense contribution toward preparing this manuscript.

REFERENCES

Al-Mur, BA, Alsiary WA. 2025. Bioactivities related to pigments content of *Sargassum* sp. Collected from Jeddah coast, Saudi Arabia, Red Sea. Egyptian Journal of Aquatic Research 51: 181–188.

Alarape SA, Adeoye DD, Amusa AO, Adeyemo OK. 2024. Haematological parameters and biochemical indices of African catfish (*Clarias gariepinus*) exposed to glyphosate-based herbicide (Force up®) for 96 hours. Frontiers in Toxicology 6: 1–16.

Ali SS, Shaaban MT, Abomohra AEF, El-Safity K. 2016. Macroalgal activity against multiple drug resistant *Aeromonas hydrophila*: A novel treatment study towards enhancement of fish growth performance. Microbial Pathogenesis 101: 89–95.

Álvarez-Canali D, Sansón M, Sangil C, Tronholm A. 2024. Multigene phylogenetics of *Sargassum* (*Phaeophyceae*) revealed low molecular diversity in contrast to high morphological variability in the NE Atlantic Ocean. Journal of Phycology 60: 1–29.

Aly SM, ElBanna NI, Elatta MA, Hegazy M, Fathi M. 2024. Effects of natural and synthetic immunostimulants on growth, feed utilization, immune status, and disease resistance against vibriosis in sea bream (*Sparus aurata*). Aquaculture International 32: 2739–2756.

Azuwarita M, Wulandari R, Zahra A. 2021. Pengaruh ekstrak *Sargassum* sp. terhadap aktivitas fagositosis ikan kakap putih (*Lates calcarifer*) yang diinfeksi bakteri *Vibrio alginolyticus*. Intek Akuakultur 5: 27–39.

Bernika VA. 2023. Resistensi Bakteri *Vibrio* spp. terhadap Antibiotik Oksitetrasiklin, Eritromisin, Dan Ciprofloksasin [Thesis]. Bandar Lampung (ID): Universitas Lampung.

Bouzenad N, Ammouchi N, Chaib N, Messaoudi M, Bousabaa W, Bensouici C, Sawicka B, Atanassova M, Ahmad SF, Zahnit W. 2024. Exploring bioactive components and assessing antioxidant and antibacterial activities in five seaweed extracts from the Northeastern Coast of Algeria. Marine Drugs 22: 273.

Catarino MD, Silva-Reis R, Chouh A, Silva S, Braga SS, Silva AMS, Cardoso SM. 2023. Applications of antioxidant secondary metabolites of *Sargassum* spp. Marine Drugs 21: 172.

Chang S, Chen X, Chen Y, You L, Hileuskaya K. 2023. UV/H_2O_2-Degraded polysaccharides from *Sargassum fusiforme*: Purification, structural properties, and anti-inflammatory activity. Marine Drugs 21: 561.

Chin YK, Haifa-Haryani WO, Nazarudin MF, Ahmad MI, Azzam-Sayuti M, Mohamad A, Ida-Muryany MY, Karim M, Salleh A, Amal MNA, Norhariani MN, Ina-Salwany MY. 2024. The synergistic *Lactobacillus plantarum* L20 and *Sargassum polycystum* -added diet for improvement of Black tiger shrimp, *Penaeus monodon* 's growth, immune responses, bacterial profiles, and resistance against *Vibrio parahaemolyticus* associated Acute hepato. Aquaculture Reports 34: 1–22

Ching JJ, Shuib AS, Abdul NN, Taufek MN. 2021. Immunomodulatory activity of β-glucans in fish: Relationship between β-glucan administration parameters and immune response induced. Aquaculture Research 52: 1824–1845.

Datu SS, Angraeni, Fatwasari F, Jarir DV, Sabilah AA. 2024. Antibacterial screening of *Sargassum* sp. extract opposing *Vibrio*

Parahaemolyticus bacteria. MSJ : Majority Science Journal 2: 288–295.

Deng Y, Feng L, Ruan Y. 2023. Editorial: Environment-microbe-host interactions in aquaculture ecosystems. Frontiers in Marine Science 10: 8–10.

Dezfuli BS, Lorenzoni M, Carosi A, Bosi LG, Giampaolo. 2023. Teleost innate immunity, an intricate game between immune cells and parasites of fish organs: who wins, who loses. Frontiers in Immunology 14: 1250835.

Doan HV, Prakash P, Hoseinifar SH, Ringø E, El-Haroun E, Faggio C, Olsen RE, Tran HQ, Stejskal V, Abdel-Latif HMR, Dawood MAO. 2023. Marine-derived products as functional feed additives in aquaculture: A review. Aquaculture Reports 31: 1–8.

Do-Huu H, Nguyen HTN, Vo HT. 2023. Effects of dietary Mannan Oligosaccharides on growth, nonspecific immunity and tolerance to salinity stress and *Streptococcus* iniae challenge in golden pompano, *Trachinotus ovatus*. Aquaculture Nutrition 2023: 1–15.

Ebtasaria M, Aini AN. 2024. Studi kandungan residu antibiotik kloramfenikol pada produk pangan olahan madu, udang, dan ikan di Sulawesi dan Maluku. Euroditio 5: 1–17. (In Indonesian).

Forestin KV, Dewi EN, Widowati I. 2024. Analysis of sustainability status and management of brown seaweed *Sargassum* sp. in the waters of Ujung Kulon Conservation area. Asian Journal of Current Research 9: 25–38.

García-Poza S, Leandro A, Cotas C, Cotas J, Marques JC, Pereira L, Gonçalves AMM. 2020. The evolution road of seaweed aquaculture: Cultivation technologies and the industry 4.0. International Journal of Environmental Research and Public Health 17: 6528.

Gazali M, Effendi I, Husni A, Nurjanah N, Wahyuni S, Kurniawan R. (2024). *Sargassum* sp. extract improve hematological profile of tilapia fish (*Oreochromis niloticus*). F1000Research 12: 1–20.

Ghazali M, Bella P, Saraswati A. 2024. Diversity of *Sargassum* spp on Lendang Luar Beach, West Nusa Tenggara. Jurnal Biologi Tropis 24: 203–209.

Gora AH, Sahu NP, Sahoo S, Rehman S, Dar SA, Ahmad I, Agarwal D. 2018. Effect of dietary *Sargassum* wightii and its fucoidan-rich extract on growth, immunity, disease resistance and antimicrobial peptide gene expression in Labeo rohita. International Aquatic Research 10: 115–131.

Gruber C, Ocelova V, Kesselring JC, Wein S. 2025. Phytogenic feed additives as a sustainable alternative to antibiotics: Enhancing Growth and disease resistance in Nile tilapia (*Oreochromis niloticus*). Animals 15: 380.

Hadiuzzaman M, Moniruzzaman M, Shahjahan M, Bai SC, Min, T, Hossain Z. 2022. β-Glucan: Mode of action and its uses in fish immunomodulation. Frontiers in Marine Science 9: 1–15.

Hakimah N, Pawestri W, Suseno DN, Anjarsari SW. 2021. Deteksi Residu Oksitetrasiklin pada Ikan Lele yang Dipasarkan di Kota Yogyakarta. Jurnal Veteriner 22: 499–507.

Han B, Baruah K, Cox E, Vanrompay D, Bossier P. 2020. Structure-functional activity relationship of β-Glucans from the perspective of immunomodulation: A Mini-Review. Frontiers in Immunology 11: 658.

Hopo MG, Mabrok M, Abu-Elala N, Yu Y. 2024. Navigating fish immunity: Focus on mucosal immunity and the evolving landscape of mucosal vaccines. Biology 13: 1–29.

Hu P, Shi Q, Wen Z, Wang J, Qin C. 2024. Potential effects of *Sargassum kjellmanianum* as a dietary supplement on the growth performance, immunity response, antioxidant status, and ammonia resistance of yellow catfish (*Pelteobagrus fulvidraco*). Aquaculture Reports 36: 102–181.

Irshath AA, Rajan AP, Vimal S, Prabhakaran VS, Ganesan R. 2023. Bacterial pathogenesis in various fish diseases: Recent advances and specific challenges in vaccine development. Vaccines 11: 1–14.

Jain P, Darji P, Thakur BS, Jain A, Jain PK, Khare B. 2022. Immunostimulants: Concepts, types and functions prince. Asian Journal of Dental and Health Sciences Open 2: 26–24.

Jayawardena TU, Asanka Sanjeewa KK, Nagahawatta DP, Lee HG, Lu YA, Vaas APJP, Abeytunga DTU, Nanayakkara CM, Lee DS, Jeon YJ. 2020. Anti-inflammatory effects of sulfated polysaccharide from *Sargassum* swartzii in macrophages via blocking tlr/nf-kb signal transduction. Marine Drugs 18: 601.

Jones EM, Cain KD. 2023. An Introduction to relevant immunology principles with respect to oral vaccines in aquaculture. Microorganisms 11: 2917.

Kamaliah SN, Yuhana M, Widanarni W, Setiawati M, Afiff U. 2025. Growth, immune responses, and resistance of vannamei shrimp fed with Lactobacillus paracasei probiotic and paraprobiotic and infected with *Vibrio parahaemolyticus*. Jurnal Akuakultur Indonesia 24: 199–210.

Kela E. 2022. Significance of immunostimulants in aquaculture: A Review. Aquaculture & Fisheries 6: 1–4.

Khanjani MH, Sharifinia M, Ghaedi G. 2022. Β-Glucan As a Promising Food Additive and Immunostimulant in Aquaculture Industry. Annals of Animal Science 22: 817–827.

Khanzadeh M, Hoseinifar SH, Zargari A, Tabibi H, Van DH, Rabetimarghezar N. 2024. Fucoidan derived from *Sargassum ilicifolium* affects growth and hemato-immunological parameters and antioxidant defense in Oscar (*Astronotus ocellatus*). Frontiers in Marine Science 11: 1–16.

Khanzadeh M, Hoseinifar SH, Zargari A, Van DH. 2025. Effects of dietary supplements *Sargassum ilicifolium* and *Spirulina* platensis on growth parameters, immunity and gene expression in juvenile Asian seabass (*Lates calcarifer*). Journal of Agriculture and Food Research 19: 101–129.

Kim S, Choi SK, Van S, Kim ST, Kang YH, Park SR. 2022. Geographic differentiation of morphological characteristics in the brown seaweed *Sargassum thunbergii* along the Korean Coast: A response to local environmental conditions. Journal of Marine Science and Engineering 10: 1–10.

Kong L, Qian K, Wu S, Li B, Guo Z, Yin X, Huang Y, Ye J, Tu X, Fu S. 2021. Functional characterization of TNF-α in pufferfish (*Takifugu obscurus*) in immune response and apoptosis against *Aeromonas hydrophila*. Journal of Fish Diseases 44: 1343–1353.

Lambert P, Radouani F, Ahmed MS, Roos C, Lebrini M. 2024. Extract from *Sargassum fluitans* III: A Promisin Valuable resource of Anti-bacterial metabolites. Advances in Biochemistry and Biotechnology 9: 10118.

Lee JH, Kim JW, Kang YJ, Ko DW, Kim JM, Choi SH, Park KH. 2018. Effects of β-1,3-glucan on innate immunity responses and mortality induced by *Vibrio harveyi*, hemorrhagic septicemia virus, or Miamiensis avidus in the olive flounder Paralichthys olivaceus. Aquaculture International 26: 743–756.

Lee PT, Quan THT, Huang HT, Nan FH, Lee MC. 2020. *Sargassum horneri* extracts stimulate innate immunity, enhance growth performance, and upregulate immune genes in the white shrimp *Litopenaeus vannamei*. Fish and Shellfish Immunology 102: 276–285.

Legrand TPRA, Catalano SR, Wos-Oxley ML, Wynne JW, Weyrich LS, Oxley APA. 2020. Antibiotic-induced alterations and repopulation dynamics of yellowtail kingfish microbiota. Animal Microbiome 2: 1–21

Linayati L, Mardiana TY, Syakirin MB, Madusari BD, Purnama CA. 2024. Upaya pencegahan penyakit ikan di Desa Silirejo, Kecamatan Tirto Kabupaten Pekalongan. Jurnal Pengabdian Kepada Masyarakat Radisi 04: 71–77. (In Indonesian).

Litaay C, Arfah H, Pattipeilohy F. 2022. The potential of seaweed resources on the coastal of Ambon Island as food ingredient. Jurnal Pengolahan Hasil Perikanan Indonesia 2: 405–417.

Liyanage NM, Lee HG, Nagahawatta DP, Jayawardhana HHACK, Song KM, Choi YS, Jeon YJ, Kang MC. 2023. Fucoidan from *Sargassum autumnale* inhibits potential inflammatory responses via NF-κB and MAPK Pathway Suppression in Lipopolysaccharide-Induced RAW 264.7 Macrophages. Marine Drugs 21: 374.

Liyanage TD, Nikapitiya C, Lee J, De Zoysa M. 2020. Potential immune regulatory role of miR-146a upon *Aeromonas hydrophila* and *Edwardsiella piscicida* infections in zebrafish. Brazilian Journal of Microbiology 51: 931–937.

Mahardika K, Mastuti I, Roza D, Syahidah D, Astuti WW, Ismi S. 2020. Pemantauan insidensi penyakit pada ikan di pembenihan dan keramba jaring apung di Bali Utara. 15: 89–102. (In Indonesian).

Melchor-Martínez EM, Reyes AG, Peña-Rodríguez A, Delgado-Cortez IG, Flores-Contreras EA. 2025. Utilization of brown algae and pre-treatment strategies as a source of bioactive nutrients for aquaculture species. Journal of Applied Phycology 37: 221–246.

Mokhtar DM, Zaccone G, Alesci A, Kuciel M, Hussein MT, Sayed RKA. 2023. Main components of fish immunity: An overview of the fish immune system. Fishes 8: 113–125.

Muahiddah N, Diamahesa WA. 2022. Pengaruh imunostimulan dari bahan-bahan alami pada ikan dalam meningkatkan imun non-spesifik untuk melawan penyakit (Review). Jurnal

Perikanan Air Tawar 3: 37–44. (In Indonesian).

Muahiddah N, Dwiyanti S. 2024. Potensi *Sargassum* sebagai imunostimulan pada bidang akuakultur (Review). Ganec Swara 18: 540–553.

muahiddah n, isnansetyo a. 2023. Pemberian fucoidan secara oral dari hasil ekstraksi *Sargassum* sp. untuk menanggulangi motile *Aeromonas* septicemia pada ikan lele (*Clarias sp.*). Jurnal Riset Akuakultur 18: 197–220. (In Indonesian).

Mufidah T, Sukenda, Widanarni, Darusman HS, Lusiastuti AM. 2022. Analysis of the pathogenesis of *Aeromonas Hydrophila* in the African catfish, *Clarias gariepinus* and involvement of the Tnf-A in response to the infection. Indonesian Aquaculture Journal 17: 73–85.

Mugimba KK, Byarugaba DK, Mutoloki S, Evensen O, Munang'Andu HM. 2021. Challenges and solutions to viral diseases of finfish in marine aquaculture. Pathogens 10: 1–21.

Nafiqoh N, Andriyanto S, Novita H, Sugiani D, Taukhid T. 2021. Kombinasi sirih dan kipahit sebagai imunostimulan terhadap penyakit *Streptococcosis* pada ikan nila (*Oreochromis niloticus*). Jurnal Riset Akuakultur 16: 1–39. (In Indonesian).

Negara BFSP, Sohn JH, Kim JS, Choi JS. 2021. Effects of phlorotannins on organisms: Focus on the safety, toxicity, and availability of phlorotannins. Foods 10: 1–19.

Noyanti R, Sofiana MSJ, Warsidah W. 2023. Analisis kandungan nutrisi, mineral esensial dan uji fitokimia *Sargassum* sp. asal perairan Pulau Temajo, Kabupaten Mempawah. Jurnal Laut Khatulistiwa 6: 60–85. (In Indonesian).

Park Y, Cao L, Baek S, Jeong S, Yun HJ, Kim MB, Lee SG. 2024. The role of sargahydroquinoic acid and sargachromenol in the anti-inflammatory effect of *Sargassum yezoense*. Marine Drugs 22: 1–16.

Pelic DL, Radosavljevic V, Pelic M, Balos MZ, Puvaca N, Jug-Dujakovic J, Gavrillovic A. 2024. Antibiotic residues in cultured fish: Implications for food safety and regulatory concerns. Fishes 9: 1–23.

Peng C, Moniroth S, Khy P, Chea S, Thanh C, Heng O, Sarter S, Cheng S, Caruso D. 2024. Antibiotic resistance profiles of sentinel bacteria isolated from aquaculture in Cambodia. National Library of Medicine 22: 1033–1043.

Petit J, Bailey EC, Wheeler RT, Oliveira CAFD, Forlenza M, Wiegertjes GF. 2019. Studies into β-glucan recognition in fish suggests a key role for the C-Type lectin pathway. Frontiers in Immunology 10: 225-237

Pourazad M, Bagheri D, Sotoudeh E, Ghasemi A. 2024. Effects of dietary sulfated polysaccharides extracted from brown macroalgae *Sargassum ilicifolium* on growth indices, antioxidant status, and immune genes expression in white shrimp (*Litopenaeus vannamei*). Aquaculture Reports 39: 102-387.

Prasaja AG, Wulandari E, Tyas T, Anggaeni K, Sukmawinata E. 2024. *Escherichia coli* penghasil Extended-spectrum *β-Lactamases* yang diisolasi pada peternakan broiler-ikan terintegrasi. ACTA Veterinaria Indonesiana 12: 25–31. (In Indonesian).

Pratiwy FM, Kohbara J, Susanto AB. 2018. Effectiveness of *Sargassum* meal as feed additive on growth performance of Nile tilapia, *Oreochromis niloticus*. Aquaculture Science 66: 25–31.

Purbomartono C, Prihandoko A, Mulia DS, Wakhudin, Widjarnako B. 2024. Respon imun non-spesifik ikan tawes (Barbonymus gonionotus) melalui suplementasi β-glucan dan efektivitasnya terhadap ikan mas (*Cyprinus carpio*). Jurnal Riset Sains Dan Teknologi 8: 183–194. (In Indonesian).

Puspita M, Setyawidati NAR, Stiger-Pouvreau V, Vandanjon L, Widowati I, Radjasa OK, Bedoux G, Bourgougnon N. 2020. Indonesian *Sargassum* species bioprospecting: potential applications of bioactive compounds and challenge for sustainable development. In Advances in Botanical Research 95: 1–19.

Rajivgandhi GN, Kanisha CC, Ramachandran G, Manoharan N, Mothana RA, Siddiqui NA, Al-Rehaily AJ, Ullah R, Almarfadi OM. (2021). Phytochemical screening and anti-oxidant activity of *Sargassum wightii* enhances the anti-bacterial activity against *Pseudomonas aeruginosa*. Saudi Journal of Biological Sciences 28: 1763–1769.

Rodrigues MV, Zanuzzo FS, Koch JFA, de Oliveira CAF, Sima P, Vetvicka V. 2020. Development of fish immunity and the role of β-Glucan in immune responses. Molecules 25: 1–33.

Rushdi MI, Abdel-Rahman IAM, Saber H, Attia EZ, Abdelraheem WM, Madkour HA, Hassan HM, Elmaidomy AH, Abdelmohsen UR. 2020. Pharmacological and natural products diversity of the brown algae genus *Sargassum*. RSC Advances 10: 24951–24972.

Sabzi E, Mohammadiazarm H, Salati AP. 2023. Synergistic effects of *Sargassum vulgare* extract and lipid levels on growth performance, blood biochemical indices, immunological competence, and antioxidant capacity in juvenile common carp (*Cyprinus carpio*). Aquaculture Reports 33: 101–829.

Saha TK, Mariom, Rahman T, Moniruzzaman M, Min T, Hossain Z. 2023. Immuno-physiological effects of dietary reishi mushroom powder as a source of beta-glucan on Rohu, *Labeo rohita* challenged with *Aeromonas veronii*. Scientific Reports 13: 14652.

Sakai M, Hikima J, Kono T. 2021. Fish cytokines: current research and applications. Fisheries Science 87: 1–9.

Sarika PV, Baboo RVC, Sirajudheen MK. 2024. Pharmacognostical, phytochemical investigation on *Lepidagathis keralensis* and *Sargassum polycystum*: An exploratory study 13: 118–129.

Sedjati S, Suryono, Santosa A, Supriyantini E, Ridlo A. 2017. Aktivitas antioksidan dan kandungan senyawa fenolik makroalga coklat *Sargassum* sp.. Jurnal Kelautan Tropis 20: 117–123. (In Indonesian).

Sedjati S, Trianto A, Jessica S, Larasati H, Haqqu AA. 2024. Metabolit *Sargassum* sp. sebagai agen antioksidan dan fotoprotektif radiasi ultraviolet. Jurnal Kelautan Tropis 27: 487–498. (In Indonesian).

Senggagau B, Bond MM. 2023. Application of gallic acid, rutin and quercetin from marine macroalgae *Sargassum* sp. to control *Vibrio parahaemolyticus*. E3S Web of Conferences 442: 1–9.

Setiyowati D, Aryono B, Zainuddin M, Puspita M, Andrean AR. 2022. Pemanfaatan *Sargassum* sp. secara enzimatik dalam pakan terhadap konsumsi pakan, efisiensi pemanfaatan pakan dan pertumbuhan ikan nila salin (*Oreochromis sp*.). Journal of Marine Research 11: 521–528. (In Indonesian).

Sidauruk SW, Ira SN, Diharmi A, Arif I. 2021. Aktivitas antibakteri ekstrak *Sargassum plagyophyllum* terhadap bakteri *Listeria monocytogenes* dan *Pseudomonas aeruginosa*. Jurnal Pengolahan Hasil Perikanan Indonesia 24: 27–37. (In Indonesian).

Siddik MAB, Francis DS, Islam SMM, Salini MJ, Fotedar R. 2025. Fermentation and fortification of *Sargassum linearifolium* with multi-strain probiotics improves mucosal barrier status, inflammatory response and resistance to *Vibrio harveyi* infection in barramundi *Lates calcarifer*. Aquaculture 595: 741–752.

Siddik MAB, Francis P, Rohani MF, Azam MS, Mock TS, Francis DS. 2023. Seaweed and seaweed-based functional metabolites as potential modulators of growth, immune and antioxidant responses, and gut microbiota in fish. Antioxidants 12: 2066.

Singh A, Singh R, Parganiha A, Tripathi MK. 2024. Annual rhythm in immune functions of blood leucocytes in an ophidian, Natrix piscator. Scientific Reports 14: 1–12.

Siwicki AK, Schulz P, Robak S, Kazuñ K, Kazuñ B, Głąbski E, Szczuciñska E. 2015. Influence of β-glucan Leiber®Beta-S on selected innate immunity parameters of European eel (*Anguilla anguilla*) in an intensive farming system. Central European Journal of Immunology 40: 5–10.

Sobuj MKA, Shemul MS, Islam MS, Islam MA, Mely SS, Ayon MH, Pranto SM, Alam MS, Bhuiyan MS, Rafiquzzaman SM. 2024. Qualitative and quantitative phytochemical analysis of brown seaweed *Sargassum polycystum* collected from Bangladesh with its antioxidant activity determination. Food Chemistry Advances 4: 100–115.

Sönmez AY, Bilen S, Taştan Y, Serag KJB, Toring CC, Romero JB, Kenanoğlu ON, Terzi E. 2021. Oral administration of *Sargassum polycystum* extracts stimulates immune response and increases survival against *Aeromonas hydrophila* infection in *Oncorhynchus mykiss*. Fish and Shellfish Immunology 117: 291–298.

Sutrisno D, Rifaie F, Rudiastut AW, Rahadiati A, Purwandani A, Rahman A, Pratama BB. 2024. A Systematic review of the scientific literature to identify challenges for the sustainable development of seaweed farming in Indonesia. Journal of Marine and Island Cultures 13: 136–159.

Thépot V, Campbell AH, Rimmer MA, Paul NA. 2021. Meta-analysis of the use of seaweeds and their extracts as immunostimulants for fish: a systematic review. Reviews in Aquaculture 13: 907–933.

Vijayaram S, Sun YZ, Zuorro A, Ghafarifarsani H, Doan VH, Hoseinifar SH. 2022. Bioactive immunostimulants as health-promoting feed additives in aquaculture: A review. In Fish and Shellfish Immunology 11: 294–308.

Waruwu E, Agung A, Putri A, Wiradana PA, Made I. 2024. *In vitro* evaluation of brown algae extract from S*argassum aquifolium* in inhibiting *Aeromonas hydrophila*, the causative agent of motile *aeromonas septicemia* (MAS). Journal of Aquaculture Science 9: 117–127.

Wazzan IMA. 2016. Fucoidan *Sargassum cristaefolium* Sebagai Immunostimulam pada Ikan Nila *Oreochromis niloticus* [Thesis]. Yogyakarta (ID): Universitas Gadjah Mada.

Widyaswari SG, Metusalach, Kasmiati, Amir N. 2024. Bioactive compounds and DPPH antioxidant activity of underutilized macroalgae (*Sargassum* spp.) from coastal water of Makassar, Indonesia. Biodiversitas 25: 162–168.

Witeska M, Kondera E, Bojarski B. 2023. Hematological and hematopoietic analysis in fish toxicology-A review. Animals 13: 1–12.

Wulandari DK, Junianto J. 2024. Kajian Literatur : Efektivitas berbagai meningkatkan sistem imunitas ikan. Jurnal Kolaboratif Sains 7: 1–11.

Yarahmadi P, Miandare HK, Fayaz S, Caipang CMA. 2016. Increased stocking density causes changes in expression of selected stress- and immune-related genes, humoral innate immune parameters and stress responses of rainbow trout (*Oncorhynchus mykiss*). Fish and Shellfish Immunology 1: 43–53.

Yip ZT, Quek RZB, Huang D. 2020. Historical biogeography of the widespread macroalga *Sargassum* (Fucales, Phaeophyceae). Journal of Phycology 56: 300–309.

Yu X, Yang Q, Jiang Y, Li Y, Wu Z. 2025. Enhanced early innate immunity and phagocytosis in grass carp (*Ctenopharyngodon idella*) induced by *Aeromonas hydrophila* fermentation broth during initial vaccine response. Aquaculture Reports 40: 102-110.

Yuan X, Lv Z, Zhang Z, Han Y, Liu Z, Zhang H. 2023. A review of antibiotics, antibiotic resistant bacteria, and resistance genes in aquaculture: Occurrence, contamination, and transmission. Toxics 11: 420.

Yudiati E, Djunaedi A, Azhar N, Alghazeer RO. 2022. Alginate from *Sargassum* sp. Improve the hematology performance and oxygen tolerance exposure of *Lates calcarifer*. Jurnal Kelautan Tropis 25: 439–447.

Yuliana A, Wulandari R, Zahra A. 2021. Pemberian ekstrak *Sargassum* sp. melalui pakan komersil terhadap nilai hematokrit dan diferensial leukosit pada ikan bawal bintang *Trachinotus blochii*. 5: 36–49.

Zaidan S, Abdillah S, Arfian N, Arozal W. 2019. Hypolipidemic effect of brown seaweed (*Sargassum crassifolium*) extract in vivo (Study of histopathology, mRNA expression, and immunohistochemistry (*IHC*) with *VCAM-1*, *ICAM-1*, and *MCP-1* parameters). ArXiv 3: 395–396.