

From the sea to aquafeed: A perspective overview

Eroldogan, Tufan; Glencross, Brett; Novoveska, Lucie; Gaudencio, Susana; Rinkevich, Buki; Varese, Giovanna; Carvalho, Maria; Tasdemir, Deniz; Safarik, Ivo; Nielsen, Søren Laurentius; Rebours, Céline; Lada, Lukic; Robbens, Johan; Strode, Evita; Haznedaroglu, Berat; Kotta, Jonne; Evliyaoglu, Ece; Olivera, Juliana; Girão, Mariana; Vasquez, Marlen; Cabarkapa, Ivana; Rakita, Sladana; Klun, Katja; Rotter, Ana

Published in:
Reviews in Aquaculture

DOI:
[10.1111/raq.12740](https://doi.org/10.1111/raq.12740)

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Eroldogan, T., Glencross, B., Novoveska, L., Gaudencio, S., Rinkevich, B., Varese, G., Carvalho, M., Tasdemir, D., Safarik, I., Nielsen, S. L., Rebours, C., Lada, L., Robbens, J., Strode, E., Haznedaroglu, B., Kotta, J., Evliyaoglu, E., Olivera, J., Girão, M., ... Rotter, A. (2022). From the sea to aquafeed: A perspective overview. *Reviews in Aquaculture, Early View*, 1-30. <https://doi.org/10.1111/raq.12740>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain.
- You may freely distribute the URL identifying the publication in the public portal.

Take down policy

If you believe that this document breaches copyright please contact rucforsk@kb.dk providing details, and we will remove access to the work immediately and investigate your claim.

REVIEW

From the sea to aquafeed: A perspective overview

Orhan Tufan Eroldoğan^{1,2}  | Brett Glencross^{3,4} | Lucie Novoveska⁵ |
 Susana P. Gaudêncio^{6,7} | Buki Rinkevich⁸ | Giovanna Cristina Varese⁹ |
 Maria de Fátima Carvalho^{10,11} | Deniz Tasdemir^{12,13} | Ivo Safarik^{14,15} |
 Søren Laurentius Nielsen^{16,17}  | Céline Rebours¹⁸ | Lukić Bilela Lada¹⁹ |
 Johan Robbens²⁰ | Evita Strode²¹ | Berat Z. Haznedaroğlu²² | Jonne Kotta²³ |
 Ece Evliyaoglu¹ | Juliana Oliveira^{6,7} | Mariana Girão¹⁰ | Marlen I. Vasquez^{24,25} |
 Ivana Čabarkapa²⁶ | Slađana Rakita²⁶ | Katja Klun²⁷ | Ana Rotter²⁷ 

Correspondence

Orhan Tufan Eroldoğan, Faculty of Fisheries,
 Department of Aquaculture, Cukurova
 University, 01330 Adana, Turkey.
 Email: mtufan@cu.edu.tr

Funding information

ACTINODEEPSEA project and FCT-Fundação para a Ciência e a Tecnologia, Grant/Award Numbers: PTDC/BIA-MIC/31045/2017, UIDB/04423/2020, UIDP/04423/2020; Climate Change Mitigation and Adaptation" call I "Ecosystem resilience increased" project "Impacts of invasive alien species and climate change on marine ecosystems in Estonia; Erasmus+ Development of master curricula in ecological monitoring and aquatic bioassessment for Western Balkans, Grant/Award Number: ECOBIAS_609967-EPP-1-2019-1-RS-EPPKA2-CBHE-JP; GA; ERDF 1.1.1.2. post-doctoral project, Grant/Award Number: 1.1.1.2/VIAA/3/19/465; European Union Agency for Network and Information Security, Grant/Award Number: 817806; FCT-Fundação para a Ciência e a Tecnologia, Grant/Award Numbers: LA/P/0140/2020, PTDC/EEI-EEE/0415/2021, PTDC/QUI-QUI/119116/2010, UIDP/04378/2020; Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant/Award Number: 451-03-68/2022-14/200222; Research Council of Norway and Møreforsking AS, Grant/Award Numbers: 312947, 319577; Research Unit of Cukurova University, Grant/Award Number: FBA-2020-13387;

Abstract

Aquaculture has been one of the fastest-growing food production systems sectors for over three decades. With its growth, the demand for alternative, cheaper and high-quality feed ingredients is also increasing. Innovation investments on providing new functional feed alternatives have yielded several viable alternative raw materials. Considering all the current feed ingredients, their circular adaption in the aquafeed manufacturing industry is clearly of the utmost importance to achieve sustainable aquaculture in the near future. The use of terrestrial plant materials and animal by-products predominantly used in aquafeed ingredients puts a heavily reliance on terrestrial agroecosystems, which also has its own sustainability concerns. Therefore, the aquafeed industry needs to progress with functional and sustainable alternative raw materials for feed that must be more resilient and consistent, considering a circular perspective. In this review, we assess the current trends in using various marine organisms, ranging from microorganisms (including fungi, thraustochytrids, microalgae and bacteria) to macroalgae and macroinvertebrates as viable biological feed resources. This review focuses on the trend of circular use of resources and the development of new value chains. In this, we present a perspective of promoting novel circular economy value chains that promote the re-use of biological resources as valuable feed ingredients. Thus, we highlight some potentially important marine-derived resources that deserve further investigations for improving or addressing circular aquaculture.

KEYWORDS

alternative protein, aquafeed, circular aquaculture, fatty acid, lipids, single cell protein

For affiliation refer to page 19

This is an open access article under the terms of the [Creative Commons Attribution](https://creativecommons.org/licenses/by/4.0/) License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited.

© 2022 The Authors. *Reviews in Aquaculture* published by John Wiley & Sons Australia, Ltd.

Slovenian Research Agency and European Regional Development Fund, Grant/Award Numbers: 7032, internal ref. 8MED20_4.1_SP_001, P4-0432

1 | INTRODUCTION

The predicted increase in the world population, combined with enhanced well-being and life quality demands, will require a significant increase in food production and a reduction in food waste. Overpopulation, climate change, ethical production and responsible consumption of food and health are each intricately intertwined; higher population growth requires more food production, which generally generates more waste and emissions and produces greater vulnerability to climate-related and human health impacts if we are not adjusting our lifestyle. To meet the Sustainable Developmental Goals (SDGs) and the main initiatives for the protection and restoration of marine environment, new production concepts are required to address this growing demand and provide sufficient quantities of high-quality food in the future.^{1,2} Aquaculture is currently one of the fastest-growing food-producing industries in the world. According to newly released SOFIA 2022, by 2050, aquaculture production is projected to reach 140 million tonnes under business-as-usual scenarios, compared with 2030 (previously projected to 109 million tonnes) as a result of technological improvements.¹ However, that growth is dependent on sustainable supplies of protein feedstuff to feed aquaculture animals.³ Proteins and lipids are fundamental macronutrients in aquaculture.⁴ Traditionally, feeds were reliant on the use of marine ingredient resources (proteins and oils, mainly from fisheries—Aquafeed v1.0). However, recognition of the constraints to the supply of those resources led to significant progress in the development of alternative feed resources for aquaculture mainly deriving from terrestrial-animal or plant-based sources (Aquafeed v2.0).⁵ More recently, the efforts are focused on developing of circular and regenerative ingredient resources (Aquafeed v3.0) that valorise by-products from other sectors or even remediate nutrient discharges, for example, macroalgal and microbial protein sources.^{6–8}

Aquaculture heavily relies on marine-derived resources such as fish meal (FM) and fish oil (FO). These are strategic ingredients in aquafeed as their supply is cannot match the demand.^{6,9} Although considerable progress has been made in replacing them, many cultured species have identified various challenges.^{6,10–12} Numerous feedstuffs have been intensively tested and adopted to remove or substantially reduce FM and FO inclusion in aquafeed without affecting the growth and health of the cultured fish. For instance, to reduce the use of wild catch fish as feed in salmon aquaculture, aquafeed manufacturers substitute the fishmeal with soy protein to reduce the marine origin of ingredients to approximately 30%¹³ and soy protein has become an important ingredient, replacing up to half of the fishmeal used in aquaculture.¹⁴ Plant-based feed is considered to have a lower environmental impact than fishmeal-based feed.¹⁵ However, the soy production for fish feed ingredients is recognised to cause significant ecosystem losses,¹⁶ increased degradations of the vulnerable habitat.¹⁷

The global use of proteins and oils, of terrestrial origin, for livestock, including aquatic animals, significantly contributes to the negative impact of livestock production on the environment and climate change.¹¹ Additionally, increasing pressure on freshwater resources for the production of terrestrial feed ingredients is an additional drawback to the use of many alternative feedstuffs in aquaculture, as most available alternative feed resources are also fed to terrestrial animal production systems such as pigs and poultry, thereby accentuating pressure on the resources supply to the feed-food-chain.¹² Aquaculture competes for crop resources with livestock, the energy industry and direct human consumption, raising concerns about the impact of aquatic farming on global food resilience, albeit representing only a small fraction of resources compared to other animal food production systems.¹⁸ Hence, there is still a need to find appropriate, economic and sustainable protein and lipid sources to underpin the increasing demands for aquafeed based on sustainably sourced ingredients.

In addition to macro-nutrients, many feed ingredients contain certain bioactive compounds (natural products including secondary metabolites) that influence the growth and the overall health of animals.^{19,20} Such nutrients often act in a preventative or responsive manner to animal health issues and have colloquially been termed nutraceuticals. In an animal production system, where medicinal antibiotics are increasingly subject to regulations, nutraceuticals have been eagerly embraced as a 'natural' way to address animal health issues. The variety of bioactive compounds that have purported nutraceutical benefits is growing and frequently seen as the 'point-of-difference' among the range of feed ingredients used. Ingredients such as yeasts are known for their β -glucan as a prebiotic and nucleotide content and their protein value.⁷ On the other hand, probiotics, that is, live microorganisms providing health benefits in aquacultural settings are gaining increasing attention. Probiotics do not only stimulate the immune system of the cultured fish and ameliorate the effects of stress, but also improve the growth and feed conversion, thereby reducing the use of FM to support a more sustainable aquaculture.^{21,22}

The European Union considers blue bioeconomy as any economic activity associated with the use of renewable aquatic biological resources to make products.²³ This involves all activities that are involved in growing, extraction, processing and transformation of raw materials.²³ The contribution of aquaculture to blue bioeconomy is fully embedded into Aquafeed v3.0, either by selecting novel feed resources from aquatic organisms, or by valorising by-catch or discards from fisheries and aquaculture that accumulate during capture and processing. Indeed, around 130 million tonnes of fish waste are produced each year by fisheries and aquaculture and its disposal is connected to economic losses and environmental impact.²⁴ However, their valorisation represents an opportunity to increase production, while enhancing sustainability.²⁵ Moreover, these high-potential new value chains can create additional jobs, thus contributing to economic



prosperity. The valorisation of discards can be done through biorefinery, a process that collects, valorises and reutilises biomass for the production of value-added bio-based products and processes through additional value chains.²⁶ Such circularity of bioresources, minimises and repurposes waste and can lead to stress-resilient fisheries and aquaculture.²⁷ This way, circular aquaculture drives sustainability.²⁸ Considering the sustainable production of the abovementioned nutrients and certain bioactive compound, circular aquaculture has clear relevance to sustainability. Indeed, it aims to produce biological resources, facilitating conversion of these resources and waste streams into value added products, such as feed, food, biobased products and compounds. However, it is important to keep in mind that, when developing alternative/circular feed and aquaculture strategies, evaluation of these should be assessed through environmental, economic, social, legislative, technical and business criteria.²⁸ Such assessment is necessary to evaluate the new products in relation to existing products and concepts and provides producers with relevant data and evaluation that can finalise the development of novel circular strategies.

This review, therefore, aims to establish a broad overview and provide a preliminary analysis of some of the potential marine resources that can be applied to the sustainable nutrient demand challenge by embracing the circular aquaculture bio-economy framework. In this regard, we examine a wide range of potential organisms and their use in novel aquafeeds, their potential mode of use and benefits, not only as alternative nutrient sources, but also as promoters of growth and health. We also offer a novel view on the circular aquaculture potential, and assess its two levels: the direct one, through valorisation of waste and the indirect one, through integrated multitrophic aquaculture (IMTA), emerging as a sustainable and circular alternative to traditional monoculture of aquatic species.

2 | MICROORGANISMS AS SINGLE-CELL INGREDIENTS

Microorganisms such as microalgae, yeasts, bacterial and fungal-like proteins, represent sustainable and renewable protein-enriched ingredients of single-cell ingredients (SCI) with a wide array of use in the aquaculture sector. These organisms can environmentally utilise nutrients derived from different waste streams and other industrial by-products and turn-over time is short and therefore shows high productivity.⁸ Thus, this microbial-based feedstock can be produced more sustainably and circularly. On one hand, such broad class of SCI can be dried and/or processed and used as a source of protein (SCP), lipids and specific nutritional components in aquaculture feed, or to enhance the survival and immune response and, on the other hand, when microorganisms remain viable, they can be used as probiotics.^{7,29,30}

2.1 | Microalgae resources

An increased awareness of circular bio-economy affected the intensive utilisation of microalgae as alternative feed source for sustainable

aquaculture. Microalgal resources are considered sustainable sources of nutrient and high-value-added compounds such as phycobiliproteins/phycoobilins, fatty acids, carotenoids and antioxidants.^{31,32} Microalgal production provides the base for circular aquaculture industry by cultivating on non-arable land, minimising water demand, recovering and converting nutrients into high-quality feed ingredients.³³ Along with these beneficial effects, microalgae cultivation offers the possibility of CO₂-uptake (i.e. 1 tonne of microalgae corresponds to 1.47 tonnes CO₂) and is of interest to advance the objective of a circular bio-economy.³⁴ Integrating algal production system into aquaculture industry also underpin several UN Sustainable Development goals (SDG), specifically no. SDG1, SDG2, SDG12 and SDG14, which considers no poverty, zero hunger, reasonable consumption and production and life below water, respectively. This concept of bio-economy reveals major opportunities for microalgae to take a part in reducing environmental footprint, water pollution and deleterious ecological effects, but creating renewable and healthy diets for the aquaculture and people in the end, thus providing eco-friendly value chain.³³ In this part of the review, we will mainly focus on microalgal resources as essential nutrients, pigments and antioxidants, along with their biocircular effects in aquafeed.

Microalgae are currently being researched for their usefulness in remediating nutrients in organic waste, and a source of different nutrients, that is, fatty acids, amino acids, vitamins and carotenoids in feed. Despite the high nutrient content of essential polyunsaturated fatty acids (PUFAs) and amino acids in many species of microalgae (i.e. genera *Nannochloropsis*, *Dunaliella*, *Chlorella*), the data on the substitution of FM or FO with microalgal biomass suggests that there is an upper limit to how large a fraction of the fish feed can be composed of microalgal biomass derivatives. The recent review by Shah et al.³⁵ Glencross et al.⁸ summarises recent studies on applications of microalgae biomass as feed for aquaculture. The effect of microalgae varies among microalgae species, type of aquaculture species and % of FM replaced and/or % dietary inclusion level. All studies where microalgae replaced less than 30% of the fish meal demonstrated either positive impact or there were no effects observed. The benefits of including microalgae in the diet of aquaculture species were increased growth and survival rate, improved pigmentation, enhanced immunological response and overall health of the organisms.^{35–37} Besides protein content, new microalgal resources have attracted much attention due to their long-chain polyunsaturated fatty acids content. It was possible to achieve eicosapentaenoic acid (EPA, 20:5n – 3) yields of up to 133 mg/L of culture under optimum conditions (21.5–23.0°C and pH 7.6) for the diatom *Phaeodactylum tricorutum*. In this case, EPA constituted 30%–40% of the total fatty acid.³⁸ Similarly, the marine *Nannochloropsis* sp., contains a large quantity of EPA and under optimum conditions EPA production can be maximised, reaching 0.1–0.4 µg cell⁻¹.³⁹ Other examples for a heterotrophic marine microalga, *Cryptocodinium cohnii* was identified as a good producer of docosahexaenoic acid (DHA, 22:6n – 3). This strain can accumulate lipids in more than 20% of its biomass dry weight, with DHA representing 30% of the total lipids content.⁴⁰



There are several marine microorganisms capable of producing arachidonic acid (ARA, 20:4n – 6). The cyanobacterium *Phormidium pseudopristleyi* can produce between 24% and 32% of ARA of the total fatty acids.⁴¹ Besides the reported cyanobacterium, Su et al.⁴² described that unicellular red alga, *Porphyridium purpureum* showed significant ARA production under stress conditions, reaching up to 36% of the total fatty acids. *Cylindrotheca gryllotalpa* is another marine microalga that presents the ability to produce essential metabolites, such as fatty acids like ARA. Similarly, *C. closterium* produced significant amounts of ARA when it was first grown in a photobioreactor at 20°C. It was then suddenly stressed by decreasing the temperature at the stationary growth phase. In this way, the alga could produce 502 mg of ARA per 100 g of biomass.⁴³ The production of ARA was also reported in a comparison study of microalgae where *Chlorella vulgaris*, *Haematococcus pluvialis* and *Isochrysis galbana* were identified as ARA producers. In this case, these strains could produce 12 mg of ARA, 292 mg and 69 mg (100 g⁻¹ of biomass), respectively.⁴⁴

The algae, *Isochrysis galbana* can produce 9.0% of linoleic acid (LA, 18:2n – 6) and 10.9% alpha-linolenic acid (ALA, 18:3n – 3) in total fatty acids, which correspond to 2245 mg (100 g⁻¹ wet weight) and 2557 mg (100 g⁻¹ wet weight), respectively.⁴⁵ In another study, the lipid content and fatty acid profiles were analysed in 10 microalgae species, where *Chlorella vulgaris*, a freshwater microalga, produced 7.44% of LA and 22.17% of ALA, showing in this study the highest levels of linoleic and linolenic acids, followed by the marine specie *Tetraselmis chuii* that could produce 6.2% of LA and 17.67% of ALA.⁴⁶ On the other hand, oleic acid was produced in low quantity (0.2%–1.3%) by *Crinoidea* sp.⁴⁷ *Nocardioides* isolate MSL-01^T produced 4.3% of linoleic acid.⁴⁸ Four actinobacteria strains, belonging to *Salinispora* genus, were capable of producing stearic acid. *S. tropica* (3.7%), *S. vitiensis* (3.2%), *S. mooreana* (2.1) and *S. fenicalii* (2.9%) managed to produce stearic acid.⁴⁹ Different microorganisms were identified as fatty acid producers, in a study performed by Ratledge,⁵⁰ *Candida diddensiae*, *Cryptococcus albidus*, *C. curvatus*, *Lipomyces starkeyi*, *Rhodotorula glutinis*, *Rhodospiridium toruloides*, *Waltomyces lipofer* and *Yarrowia lipolytica* producing steric acid ranged from 1% to 15%. The same strains also produced different percentages of oleic acid between 28% to 66%. Furthermore, *C. diddensiae*, *C. albidus*, *C. curvatus*, *L. starkeyi*, *R. glutinis*, *W. lipofer* and *Y. lipolytica* produced between 3% and 51% of linoleic/linoleic acid.⁵⁰

Pigments are another important microalgae-generated compound class. The most important pigments extracted from microalgae for use in aquaculture are no doubt astaxanthin and β-carotene. Astaxanthin is a red pigment of huge commercial interest as a food and flesh colourant, such as a fish feed additive. It is especially important to give the flesh of farmed Atlantic salmon (*Salmo salar*) and rainbow trout (*Oncorhynchus mykiss*) its desired colour by consumers.⁵¹ Wild catch of salmon and rainbow trout has this colour from their natural diet, the pink pigment originally deriving from the microalgal base of the feed chain. Astaxanthin is the only pigment that can be incorporated into fish flesh.⁵² It may be obtained from various sources, including chemical synthesis, but the increasing demand for astaxanthin is making biological sources for this pigment increasingly important, the

most important microalgal sources being *Haematococcus pluvialis*, *Chlorella zofingiensis* and *Chlorococcum* spp.⁵³ In addition to its role as a flesh colourant, astaxanthin may serve as a vitamin A precursor in some fish.⁵⁴ This is especially important in fish unable to absorb β-carotene, which is the most important precursor for vitamin A in fish and in other organisms. β-carotene is found in high concentrations in many species of microalgae, especially in species of the Chlorophyte *Dunaliella*.⁵⁵

Many microalgal pigments and phycobiliproteins have also been shown to have antioxidant properties. These include β-carotene and astaxanthin.⁵⁶ Other microalgal pigments and phenolic substances from microalgae have been shown to have antioxidant properties.^{57,58} The most important microalgal species in terms of substances with anti-oxidant properties are *Tetraselmis suecica*, *Botryococcus braunii*, *Neochloris oleoabundans*, *Chlorella vulgaris*, *Phaeodactylum tricoratum* and *Isochrysis* spp.⁵⁷ Various antioxidant properties are thus widespread across various taxa of microalgae. Besides carotenoids, microalgae contain other types of powerful antioxidants including polyphenols (e.g. phenols and flavonoids), sterols, vitamins (e.g. vitamin A and E) and other compounds (e.g. butylated hydroxyanisole and butylated hydroxytoluene). The antioxidant power of compounds produced by microalgae is well documented and, in some cases superior to that of plants or fruits.⁵⁹

Besides providing essential nutritional requirements, the research focus on novel aquaculture feed can be widened to include additional benefits and innovations, specifically additional nutraceutical value, disease prevention and improved sustainability and circular economy. As described above, microalgae are rich in protein and valuable oils, pigments and antioxidants; however, microalgal biomass contains other beneficial compounds such as vitamins and a variety of bioactive compounds. These bioactive compounds are central to innovative aquaculture research because of their immune-stimulating properties and even anti-parasitic effects. For example, the immune response of freshwater prawn *Macrobrachium rosenbergii* increased after replacing 8% of fishmeal with *Chlorella vulgaris*. The positive immune response was demonstrated by higher total haemocyte count and phenol oxidase activity, which enhanced the resistance of prawns to *Aeromonas hydrophila* infection.⁶⁰ Similarly, consumption of chlorophyte *Dunaliella salina* enhanced the immune response (superoxide dismutase and catalase) in shrimp *Penaeus monodon* making the shrimp more resistant to white spot syndrome.⁶¹

2.2 | Fungi and thraustochytrids

2.2.1 | Fungi (filamentous and yeast) as a source of antimicrobial compounds for aquaculture

Fungal biomass has increasingly been regarded as a potential feed source given its nutritional content including protein, essential amino acids, PUFAs, fibres, minerals and vitamins.⁶² The utilisation of fungi as an alternative protein source in feed is not new concept. In most cases, data refers to fungi of terrestrial origin, which, however, from a



nutritional point of view, do not present significant differences compared to those of marine origin. This is partly due to the fact that there is a consolidated tradition in using of fungi as effective biorefineries to valorise agricultural by-products, while there are still few applications in aquaculture. The increasing availability of fungal strains of marine origin, and the development of new production chains in the blue bio-economy will soon fill this gap.

Numerous papers report the efficacy of by-products of mushroom production as an FM replacer.^{63,64} Fungal biomasses or their derivatives have been used as prebiotics, with beneficial effects demonstrated in several fish and shrimp species.^{65,66} Dadi et al.⁶⁷ reported that the cell-free supernatants of two marine fungi endophytes can be used as feed supplements to protect shrimps (*P. vannamei*) against hepatopancreatic necrosis disease caused by *Vibrio* spp. Moreover, several publications recently demonstrated that marine fungi are a source of antimicrobial compounds for use in aquaculture against fish pathogens. Fungi from sponges have been screened for the production of antimicrobial compounds active against different fish pathogens, that is, *Lactococcus garvieae*, *Vibrio anguillarum*, *Vibrio harveyi*, *Yersinia ruckeri* and *Vagococcus salmoninarum*.^{68–71} Since bacterial pathogens are a serious threat in aquaculture and the antimicrobial resistance in cultured aquatic animals is at concerning levels,⁷² there is an increasing need for new tools and approaches to manage aquaculture sustainably. New antimicrobial agents from marine fungi have received considerable attention to overcome difficulties and limitations related to widespread multidrug-resistant bacteria. Hence, further research is needed on the lead compounds generated by these fungal strains that have the potential for use as feed additives as an alternative to antibiotics.

Fungal bioactive molecules display various biological properties, such as antioxidant, anti-cancer, anti-microbial and immunostimulation; indeed, they can activate the innate immune system in either of two ways, by direct stimulation of the immune cells and by improving the growth of intestinal microbiota.⁶⁶ The intestinal tracts of animals host a wide diversity of microbiota, which form a complicated gut microbiome with numerous roles in physiological processes, including, but not limited to, the inhibition of pathogenic bacteria and maturation of the immune system and metabolism.^{73,74} Fungal ingredients can stimulate growth and enhance immune responses and defence mechanisms against pathogenic microbes and abiotic stressors. Fungal polysaccharides and crude polysaccharides mainly produced from processing waste from mushrooms intended for human consumption act as prebiotic substances and are deemed as a nutritional component for regulating growth and health conditions.⁶⁵ Such immune enhancers can improve the health of aquatic animals, including sea cucumbers, by modifying the host intestinal microbiota structure.^{75–79}

Recent papers highlight the environmental sustainability of mycoproteins with respect to animal- or plant-based proteins as demonstrated by life cycle assessment analysis.^{80,81} The benefit of mycoprotein production for sustainable feed production lies in their capability to grow in bioreactors with high metabolic rates using different by-products such as C and N sources.^{81–84} Fungal biomasses rich in proteins, can be produced both in submerged^{68–72} and in solid-

state fermentation^{85,86} of agro-industrial residues according to circularity assessment criteria that have been outlined in the introduction. This approach has two important advantages: (i) it reduces the production costs; (ii) valorises processing by-products otherwise treated as waste. To date, most of the works refer to the conversion of agricultural by-products. Still, recent studies have demonstrated the feasibility of converting fish processing wastewater into feed ingredients through the submerged cultivation of filamentous fungi.^{87,88} The studies revealed the adaptability provided by the integration of fungal cultivation to fish processing industries, and demonstrated a range of economic and environmental advantages (significant chemical oxygen demand [COD], total solids and nitrogen decrease). Fungi produce a wide range of enzymes that enable them to biotransform various substrates into biomasses rich in proteins and in additional bioactive molecules (e.g. essential amino acids, *n* – 3 long-chain [LC PUFAs] and polysaccharides with immunostimulant activity). Moreover, they perform better in reducing COD levels compared to unicellular microorganisms (e.g. bacteria and microalgae) that typically entail costly biomass recovery processes.⁸⁷ Therefore, mycoproteins obtained through a circular economy approach have increasingly been studied as an alternative ingredient for animal feed production.

Furthermore, fungi could shortly be used to limit the environmental effects of aquaculture (i.e. nutrient and effluent build-ups and release of antibiotics). Recently, some marine fungi isolated from salmon farming areas in the south of Chile have been reported to degrade antibiotics such as oxytetracycline that are routinely administered in the diet, both in the freshwater smolt phase and in marine farms.⁸⁹ These vast quantities of antibiotics cause severe detrimental effects to the environment where they are disseminated and remain active for months, thus favouring the development of antimicrobial resistance.⁹⁰ It is essential that the aquaculture industry incorporates biotechnological innovations to mitigate its negative environment impact. For example, existing chemical and physical strategies to degrade organic pollutants from the fish farming industry are costly and produce waste that needs to be quenched after treatment, thus unlikely to be realistically implemented in aquaculture facilities.⁹¹ Moreover, potential alternatives could be based on microorganisms or enzymes able to degrade harmful organic pollutants efficiently. Using bio-based approaches to tackle environmental issues associated with aquaculture represents a sustainable, green and cost-efficient strategy that should be strongly considered. Mycoremediation approaches have proven to be effective for treating contaminated water with antibiotics^{92,93} and hopefully, they will also be applied in circular aquaculture in the near future.

2.2.2 | Thraustochytrids

Thraustochytrids are heterotrophic eukaryotic protists, with a wide geographic distribution from polar regions to the tropics, ubiquitously distributed in all shallow and deep waters habitats as saprophytes, detritivores, parasites, pathogens (including edible invertebrates⁹⁴) and bacterivores.^{94–106} For more than four decades, the research on



Thraustochytrids focused on the producing of valuable nutrition sources. Yet recently, more research efforts revealed the importance of these unicellular organisms in circular economies.^{33,107} Just an example is the employment of waste Thraustochytrids biomass following lipid extraction as an efficient adsorbent for triphenylmethane dye in aquaculture.¹⁰⁸

Within the Thraustochytrids, the genus *Schizochytrium* is the most commonly used in aquaculture.¹⁰⁹ Several *Schizochytrium* products containing high DHA concentrations have been developed commercially. Further, the dried *Schizochytrium* product is highly effective when included in the diets of channel catfish, *Ictalurus punctatus*,¹¹⁰ and Asian seabass, *Lates calcarifer*¹¹¹ and has been employed as a replacement for FO in the diets of various species.^{112,113} The global research community attention has shifted to Thraustochytrids only in the last two decades, primarily due to their high lipid contents, particularly EPA and DHA. Consequently, the research on mass cultivation of Thraustochytrids targeting the potential production of valuable bioactive compounds (such as $n - 3$ LC PUFAs, DHA, squalene, carotenoids and more) has been attracting significant scientific and commercial interest.^{114,115} With their high levels of saturated fatty acids, the Thraustochytrids have been further explored in industrial biotechnology as source materials for biofuels and lipid biofactories,¹¹⁶ supplying numerous nutraceuticals, food additives, squalene, carotenoids and other products of economic significance^{115,117,118} and contribute to the essentials of marine biotechnology.¹¹⁹

Since dietary DHA is an essential nutrient for optimal growth and development of many fish species, Thraustochytrids have been considered a novel alternative source of $n - 3$ LC PUFAs. *Thraustochytrium striatum* can produce a high content of DHA, ranging from 5.18 to 83.63 mg g⁻¹ biomass, when monosaccharides, like glucose, D-fructose, D-xylose, among others, are used as carbon sources.¹²⁰ Moreover, the thraustochytrid *Schizochytrium limacinum*, isolated from the coastal seawater in the west of Pacific Ocean, produced DHA content between 36.9% and 37.6%, at a temperature of 16–30°C and salinity at 0.9%–3.6%.¹²¹ Until recently, most of the DHA supply for aquafeed originated from FO obtained from wild harvested fish. As an alternative strategy, the literature has reported three avenues for using this group of unicellular eukaryotic organisms as aquaculture feed. The first avenue is the direct use of Thraustochytrids (spray dried or freeze dried) and their derived oils for aquafeeds.^{98,122} An increasing number of species have been fed such Thraustochytrids, including invertebrates such as shrimp and molluscs (geoduck clam, abalone) and a wide range of fish, including Nile tilapia, rainbow trout (*Oncorhynchus mykiss*) and Atlantic salmon (*Salmo salar*).^{113,123–126} The second avenue deals with replacing yeasts and algal cells supplemented with rotifers and *Artemia* nauplii, which are employed as larval fish feed in marine aquaculture.¹²⁷ A third feeding avenue deals with newly formulated fishmeal formulations that include thraustochytrid-derived oil (not the cells with the other materials included), an approach already extensively worked-out with various fish species, including salmon parr, channel catfish (*Ictalurus punctatus*), Atlantic salmon post-smolt, giant grouper (*Epinephelus lanceolatus*) and longfin yellowtail (*Seriola rivoliana*).⁹⁸

2.3 | Marine bacteria as a source of ingredients for aquaculture feeds and probiotics

In aquaculture, SCP sources, such as bacteria, have been gathering interest as they represent an effective approach to managing production expenses, not only by maintaining feed performance, but also by benefiting the health of aquaculture fish.²⁹ Besides vitamins, phospholipids and other functional compounds, bacteria can produce high values of crude protein, essential amino acids and bioactive secondary metabolites. A wide range of inexpensive and waste-based feedstocks that various microorganisms can utilise—methane, methanol, synthetic gas, H₂, CO₂ and sugars—as carbon and energy source to grow and enhance biomass production has also inspired deeper exploration of bacteria as SCP.^{127–129} Bacterial SCP-based products can be used as effective growth promoters,^{130–135} as an alternative protein source with no adverse effects, to replace FM,^{136–140} or even as a boost to improve immune response and survival,^{133,140,141} with applicability across a wide range of aquaculture relevant species such as salmonids and shrimps.

Bacteria can be useful at different levels in aquaculture systems: they can feed different taxonomic groups of zooplankton used as live food to larvae in aquaculture hatcheries, or directly included in the diet of various groups of organisms, such as fish, bivalves and crustaceans. In the early stages of production, larvae of aquaculture organisms require essential nutrients such as $n - 3$ long-chain PUFAs (such as EPA and DHA), so live food organisms, as such as rotifers, nematodes or *Artemia*, must be enriched prior to larval feeding, using, for instance, marine bacteria or marine bacteria-sourced products.¹⁴² As an example, marine cyanobacterium *Synechococcus elongatus* is used as food for *Artemia franciscana*.¹⁴³ Other examples can be mentioned, as the use of heterotrophic marine bacteria to improve the survival, population growth and nauplii production of the copepod *Apocyclops dengizicus*, using a low-cost waste-based diet¹⁴⁴; and the incorporation of the marine bacterium *Rhodovulum sulfidophilum* in the rotifer *Brachionus rotundiformis* diet to increase protein and fatty-acids yields.¹⁴⁵ Marine bacteria can moreover be relevant in digestibility, another major milestone in aquaculture feed. Several *Bacillus* strains isolated from marine sediments produced beneficial enzymes such as proteases, carbohydrases and lipases.¹⁴⁶

Apart from the beneficial role that marine bacteria-sourced products can have on aquaculture diets, marine bacteria can also be a key to improve animal health within aquaculture systems. In addition to traditional nutrients, quality functional food must contain components able to add immune or physiological gains.¹⁴⁷ In this regard, live microorganisms with probiotic effects can positively affect the host performance by improving food degradation, enhancing their nutritional value or upgrading the quality of the environmental parameters¹⁴⁸ and are currently gaining increasing attention by the research sector and the aquaculture industry. Some successful examples of the applications of bacteria as probiotics in aquaculture with antimicrobial activity against several microorganisms responsible for diseases in economically important aquaculture fish species are reported (i) the marine sponge symbiont *Pseudovibrio denitrificans*, effectively used to



control pathogenic *Vibrio* sp. in aquaculture shrimps¹⁴⁹; (ii) marine-derived Actinobacteria of the family Bifidobacteriaceae, which produced bacteriocins¹⁵⁰; (iii) marine *Phaeobacter* sp. strain, isolated from a mollusc, with protective effect against shellfish and fish pathogens¹⁵¹; (iv) *Methylococcus capsulatus* that prevented the development of enteritis in salmon when incorporated in the diet as SCP¹⁴⁰; (v) marine-derived *Bacillus* and *Aeromonas* strains, isolated from *Artemia* cultures that protect *Artemia* against different pathogens¹⁵²; (vi) several marine-derived *Streptomyces* strains, recovered from sediment samples, which when used as food supplement decreased mortality in nauplii and adult *Artemia* cultures¹⁵³; and (vii) various deep-sea bacteria associated with the haemolymph of marine bivalves that proved to be important to bivalve protection, conferring a health benefit to the host.¹⁵⁴

An emerging and very logical trend is the use of fish gut-associated microbiota in aquaculture. As the gut microbiota is crucial for health and plays an essential role in the growth, reproductive performance, digestion and mucosal tolerance of the fish,¹⁵⁵ it offers versatile and multifaceted support for sustainable aquaculture. The first layer uses indigenous gut microbiota as probiotics, that is, as living microbial food additives. Most commercial probiotics originate from terrestrial organisms or products (e.g., milk, cheese).^{21,156} Growing evidence indicates that the indigenous microflora, particularly bacteria, of the fish digestive tract (also called as host associated or intrinsic bacteria) confer greater probiotic effect and higher performance.¹⁵⁷ The finfish alone have provided many beneficial lactic acid bacteria (LAB) belonging to genera of, for example, *Lactococcus*, *Lactobacillus*, *Leuconostoc* and *Carnobacterium* with well-known probiotic effects.¹⁵⁵ LAB and other host-associated probiotics (HAP) adapt easily to the colonic environment. They are more beneficial to the host on specific parameters, including growth performance, nutrient digestibility, immune system response and better persistence in the host gut after removal of the probiotic.¹⁵⁸ A recent study compared the efficacy of HAP *Enterococcus faecium* derived from the intestine of adult Caspian roach and the commercial probiotic strain (*Pediococcus acidilactici*). Indigenous *E. faecium* was more effective in promoting growth, feeding efficiency, secretion of digestive enzymes and enhancing the mucosal and systemic immune systems than the commercial probiotic in roach fingerlings. Commercial probiotics suppressed some immune parameters such as lysozyme or complement activity, indicating potential antagonistic effects on the native roach microbiota.¹⁵⁶ These results suggest that bacteria derived from the gut environment of the fish host are more suitable sources of probiotics for the aquaculture sector. Besides Gram-positive host-associated bacteria, several members of Gram-negative bacterial genera, such as *Vibrio*, *Pseudomonas* or *Roseobacter* have also been proposed as probiotics.^{21,159} Additionally, many probiotics also have antimicrobial activities on other microbial populations. They produce ribosomal peptides (such as bacteriocins, as mentioned above), siderophores, quorum quenching compounds or hydrogen peroxide, thus preventing the growth of opportunistic pathogens.¹⁶⁰ Some LAB obtained from fish guts have been shown to inhibit the growth of fish pathogens, for example, *Aeromonas salmonicida*, *Vibrio anguillarum*, *V. harveyi* and *V.*

splendidus, thereby decreasing the incidence of fish diseases and increasing larval survival.^{21,160,161} Fish gut-associated microorganisms may also provide long-chain PUFAs. Several EPA-producing *Vibrio* or *Shewanella* strains have been isolated and characterised from various freshwater fish species.^{162,163} Hence, the microbiota of marine fish with all types of microbial components (bacteria, fungi and yeast) should be studied more intensively to untap their full potential for feed and other multiple health beneficial effects on cultured fish.

Overall, marine microorganisms represent an untapped and realistic potential for their use in a circular aquaculture setup. They can be used in bioremediation to improve aquaculture water quality, as converters of waste and as underexploited alternatives to land-based nutrient resources. However, alternative ingredients must meet environmental sustainability and economic viability criteria.¹⁶⁴ Hence, to guarantee the sustainability of circular use of microorganisms in aquaculture, more effort is needed to optimise the processes and reduce costs of growing, handling, processing and extraction processes.¹⁶⁵

3 | MACROORGANISMS AS AQUACULTURE FEEDS

3.1 | Macroalgae

Macroalgae as aquafeed were recently reviewed by Moreira et al.¹⁶⁶ Besides their nutritional value (mostly protein source), seaweeds contain several compounds and secondary metabolites that could benefit farmed fish. In particular, various seaweed extracts exhibit properties that indicate they could be used as prophylactic and/or therapeutic agents in aquaculture.¹⁶⁷

In recent years, several investigations were made to evaluate the potential of seaweed as a source of fish feed protein. With current technology, producing protein for fish feed using seaweed biomass is neither economical nor environmentally sustainable without key technical innovations to overcome several existing bottlenecks (available volume of seaweed biomass, protein content and biomass conservation technology).¹⁶⁸⁻¹⁷⁰ Nonetheless, in some countries, such as Norway, the seaweed industry, the technology suppliers and food and feed manufacturers are showing strong interest in participating or supporting the needed step to increase the seaweed volume produced locally.¹⁷¹ Furthermore, the fermentation process was recognised for improving the nutritional quality of plant protein sources.¹⁷² It has been recently explored to improve the nutrient efficiency and nutritional quality of the seaweed proteins.

Further, all groups of seaweeds exhibit significant antimicrobial properties against many infectious agents of fish and shrimp. Still, the genera exhibiting a broader range of antibacterial properties are *Asparagopsis* spp. (red seaweed) and *Sargassum* spp. (brown seaweed).¹⁶⁷ This bioactivity can, however, be affected by many factors. The extraction method is one of the most important steps to consider when extracting these compounds: organic solvents appear more efficient. When the antimicrobial properties are studied in vivo, the seaweed extracts are either incorporated directly into the feeds (dry or



live) or added into the water in which the fish and shrimp are reared. Incorporating the extracts into the feeds appears to be an effective delivery method for preventing and treating different infectious diseases. To the best of our knowledge, there have been no complete studies reported on the pharmacodynamics and pharmacokinetics of seaweed extracts in fish or shrimp. Besides antimicrobial activity, seaweeds also demonstrate anti-inflammatory activities and immune modulation properties in fish.^{173,174} Another issue that has not been examined yet is the increased technology readiness level to use these bioactive extracts on a commercial scale. Hence, further research is needed to assess the full potential of seaweed ingredients in aquafeed.

3.2 | Invertebrates

Many commercially important fish species, produced in aquaculture, are unable to grow if fed exclusively with formulated inert feed during their early developmental stages. However, there have been some encouraging results on sing of fish meals with species of fish that were considered to demand live feed exclusively.^{175,176} Nonetheless, many finfish larvae still rely on live feed for the first few weeks of their life. This type of production demands trained personnel and infrastructure investments to maintain hatcheries or optimise the supply chains to guarantee the steadiness of live feed provision when obtained from external producers.

The two main reasons for fish depending on live feed are (i) small size of larval mouths, and underdevelopment of their gut at the time of the first feeding. This necessitates feeding on the live feed, supplying exoenzymes to the fish and helping to digest the prey.¹⁷⁵ (ii) Additionally, moving prey attracts the fish more than inert particles.¹⁷⁷ This is of the utmost importance to some altricial fish larvae that may need to feed within short time spans after hatching due to the rapid depletion of their energy reserves, which may occur within a few hours for some species.¹⁷⁸

Most hatcheries are using brine shrimps (*Artemia* spp.) as live feed due to the easy use of these organisms. However, many of these hatcheries suffer from high mortality among the first developmental stages of the fish larvae despite using these live feeds. This is due to the unfavourable biochemical composition of *Artemia*, requiring their enrichment before using them as first feeds.^{179,180} In addition, the size of *Artemia* is too large for early feeding in many fish larvae with very small mouths. Furthermore, *Artemia* is harvested in the wild (in salt lakes) and its availability is subject to variation due to climatic factors and other parameters, leading to varying or, even worse, increasing prices of this feed item.¹⁸¹ Together with *Artemia*, rotifers have great potential for live feed in aquaculture, particularly marine hatcheries. The two main species used are *Brachionus plicatilis* and *B. rotundiformis*. Rotifers are parthenogenetic, reproducing at high rates and achieving high densities in cultures.¹⁸² The availability of rotifers as live prey has contributed to successful hatchery production of several marine finfish and crustacean species.¹⁸² However, just as for *Artemia*, the biochemical composition of rotifers is poor, and they need enrichment to be used as live feed.

Copepods are not often used in aquaculture, even though it is well accepted that they are valuable feed sources for fish larvae. Compared to *Artemia* or rotifers, their favourable biochemical composition indicates that they should become more frequently used in the future,^{183,184} which will also significantly raise the number of fish species that can be successfully produced in aquaculture. Both cultured and wild-harvested copepods possess biochemical characteristics that make them attractive as live prey in fish larvae rearing.¹⁷⁸ Compared to both *Artemia* and rotifers, copepods have a higher content of PUFAs and they especially have more favourable content of the two important PUFAs, DHA and EPA represent two highly bioactive and physiologically important fatty acids within the $n - 3$ series.¹⁸³ Their DHA/EPA, ratios and DHA + EPA/total fatty acids, ratios are closer to those needed by fish than those of alternative feed organisms, which make them more easily digestible for fish larvae and with a higher nutritional value for fish than either rotifers and *Artemia*.¹⁸³ Copepods also have higher contents of essential amino acids than both rotifers and *Artemia*.¹⁸³ Further, copepods experience a slower gut passage in fish larvae than alternative live feed items, leading to a complete digestion and more efficient nutrient uptake in the fish larvae.¹⁸⁵ It has been argued that this is due to a higher digestive enzyme content in copepods, used by the fish larvae as exoenzymes.¹⁸⁶ Copepods are part of the natural fish feed present in aquaculture ponds, and good results from sustainable intensive cultures have been achieved.^{184,187} Copepods are used at a semi-intensive scale in some form of aquaculture,^{188,189} and several attempts have been made to scale up copepod production and use to a full, intensive, industrial-scale.^{183,190} More than 60 species of copepods have been cultivated in the laboratory, but the copepod industry is still not fully developed due to a certain lack of knowledge dissemination of large-scale cultivation of copepods, especially regarding recent developments in the field.^{191,192} This lack of dissemination of knowledge has led to a situation, where copepod cultivation is generally perceived as overly complicated within the aquaculture industry. One of the factors limiting the use of copepods in industrial-scale aquaculture is that large-scale production of copepods also necessitates a large-scale production of microalgae as feed for the copepods,¹⁹³ which is expensive. New results indicate that some species of copepods are in fact capable of synthesising essential $n - 3$ PUFAs such as DHA, EPA and ALA on their own, something that has previously been assumed only to take place in lower organisms, such as microalgae.¹⁹⁴ This means that these species of copepods can be fed low-quality feed such as baker's yeast and do not need to be fed with microalgae.¹⁹⁵ This will contribute greatly to making the production of copepods for aquaculture easier, cheaper and biocircular. It is easier and cheaper as baker's yeast can be acquired from outside the aquaculture industry, with no need for an integrated production of the feed, as is the case with microalgae. It will also contribute to a more circular bioeconomy in the aquaculture sector, as baker's yeast is a waste product from bread and beer production, so the utilisation of baker's yeast in aquaculture production will serve as an example of a waste product from one sector being a resource for another sector. Hence, future investigations are needed to optimise and promote the use of copepods as an aquaculture feed.

The use of meal rendered from macroinvertebrates as a potential alternative to marine-origin FM have been reported as a promising approach.^{196,197} Different worms have been particularly studied as potential sources of live feeds for marine fish larvae as a potential food source for aquaculture hatcheries.¹⁹⁸ Macroinvertebrates, especially amphipods are a significant part of benthic communities¹⁹⁹ and an important food for many fish and invertebrate species as natural live prey in aquaculture feed. Amphipods are usually rich in proteins, representing the main biochemical class of organic compounds, approximately 40% of dry weight.²⁰⁰ Many crustacean species can be cultivated in laboratory cultures. Still, there is a dearth of research on the potential of marine gammarids as a novel aquatic crop to be produced in commercial-scale feed systems²⁰¹ and missing knowledge about the use of live organisms as feed-grade ingredients that can be sustainably produced.²⁰² Overall, marine amphipods have shown advantages and disadvantages with their use as natural live aquaculture feed. For example, lipid content in marine amphipods was more suitable for aquaculture than freshwater species.¹⁹⁶ Caprellid amphipods have been identified as possible candidates for exploitation as a live aquaculture feed.¹⁹⁸ They can be either field collected, or cultured. Indeed, laboratory culturing methods have been successfully performed.²⁰³ The *Monoporeia affinis* which is highly abundant in the Baltic Sea, is tolerant to low oxygen concentrations and certain chemicals.^{204–206} Such tolerant species could be suitable for cultivating as aquafeed. However, *M. affinis* females give birth to only 20–80 juveniles, which happens only once during 2–4 years.^{204,206} Although this species can live in laboratory cultures and give birth to the next generation, the quality of most eggs is not satisfactory (Strode E. pers. obs., unpublished results). Moreover, pilot research showed that protein concentration decreased in *M. affinis* with longer cultivation time. *M. affinis* usually live in deep water sediments (>20 m) with decreased oxygen concentration. Hypoxia could lead to physiological changes in organisms, such as increased ventilation frequency, decreased protein synthesis, further retarded individual and population growth and increased mortalities.^{207,208} In general, amphipods have adequate nutritional values for applications in aquaculture, but cultivation processes lead to low survival rates or species reproduction.²⁰¹ Overall, the optimal cultivation conditions for these organisms are still not defined and more research efforts should be put to optimise the cultivation techniques, taking into consideration the available knowledge on organism ecology, biology, feeding and reproduction becomes important.

Among Cnidaria, a few scyphozoan pelagic jellyfish species could be exploited for developing aquafeed supplements due to their high content of proteins, phenols, essential $n - 3$ long-chain PUFAs (EPA and DHA), essential $\omega - 6$ fatty acids as linoleic acid, essential minerals (Na, Mg, K and Ca) and trace elements (Fe, Zn, Cu, Mn and Se), as reported for the Mediterranean pelagic jellyfish, a mauve stinger *Pelagia noctiluca*.²⁰⁹ Some others, such as *Aurelia aurita* and *Chrysaora pacifica*, with also peculiar metal profiles, have already shown to support the growth and survival of farmed lobster *Ibacus novemdentatus* phyllosomas.²¹⁰

Among macroinvertebrates, amphipods constitute a significant part of benthic communities¹⁹⁹ as an important feed for many fish and invertebrate species and are utilised as natural live prey in aquaculture feed. Amphipods are often rich in proteins (estimated at 40% of their dry weight) and contain less than 10% of carbohydrates and lipids.²⁰⁰ They also show well-balanced fatty acid composition, with high levels of favourable PUFAs such as DHA and EPA. Although many crustacean species can be cultivated under laboratory conditions, sustainable technologies are still lacking to enable a commercial scale production of such a novel aquatic crop²⁰¹ and manufacturing a feed-grade ingredient out of amphipods.²⁰² Marine amphipods may have more suitable lipid content than their freshwater counterparts.¹⁹⁶ Amphipods are already reported as valuable feed for farmed and exploited populations of fish. *Melita palmata* may be attractive as a food resource for aquaculture mainly due to its high phospholipid and $\omega - 3$ PUFA levels. Similarly, *Microdeutopus gryllotalpa* and *Monocorophium acherusicum* have high lipid and DHA concentrations. These two amphipods' size is notably smaller (<0.5 cm) than other amphipods species, meaning a higher number of specimens are necessary to obtain the proper amount of biomass for fish feeding.²⁰⁰ The Caprellid amphipods have also been identified as a possible candidate for exploitation as a live aquaculture feed.¹⁹⁸ Some amphipod species such as *Corophium volutator*, *Gammarus locusta* and *Monoporeia affinis* have been extensively used in bioassays.^{203–206} As they often tolerate a wide range of environmental conditions, including oxygen concentration and chemicals and have high productivity, they may be good candidates for aquafeed species. Among these species *M. affinis* is known to have high lipid levels.²¹¹ However, some cultivation trials with *M. affinis* showed a low reproduction success and a declined protein concentration along with cultivation time. Here, hypoxia could have profound physiological changes in organisms, such as increased ventilation frequency, oxygen affinity to decreased protein synthesis, and further retarded individual and population growth and increased mortalities.^{207,208} Similarly, many other gammarid amphipods have shown rewarding nutritional value for applications in aquaculture, but poor cultivation performance under laboratory conditions.^{201,206}

Mollusc meat is another promising source of essential nutrients for shrimps and also possesses excellent chemo-attractant properties for fish.²¹² Importantly, farming and harvesting mussel species can be a promising internal measure for eutrophication control in many estuarine ecosystems and regional seas.²¹³ In the Baltic Sea, due to low salinity, mussels are small and making it difficult to process them into a meal. To overcome this limitation, black soldier fly larvae were first fed a paste made of blue mussels, spiking the larvae with $\omega - 3$ fatty acids from mussels. The larvae were then dried and turned into a meal, rich in protein but also valuable fatty acids.

The sea urchin *Diadema setosum* has been reported as alternative fish food for the African cichlid fish, *Oreochromis niloticus* during growth,²¹⁴ but also a chemoattractant for juveniles of barramundi, *Lates calcarifer* which makes this echinoderm species a potential candidate for aquafeed.²¹⁵ Free-living nematodes have a great potential for use as live food in the early stages of life of several species in marine aquaculture. Still, data on cultivating of marine nematode



species suitable for fish/shrimps aquafeed are scarce. Thus, nematodes of the genus *Panagrellus* have long been used in larviculture of a numerous fish²¹⁶ and shrimp species^{217,218} as well as a liquid culture of free-living nematodes *Panagrolaimus* sp.²¹⁹ While freshwater oligochaetes were widely used, cultured as a supplement or fish/crustacean food,²²⁰ only a few species of marine oligochaetes have been introduced for cultured purposes. Maheswarudu and Vineetha²²¹ described a protocol for culturing the littoral oligochaete *Pontodrilus bermudensis* in sand vermibed enriched with various organic amendments for use as a supplementary diet for maturation and spawning of broodstock of penaeid prawns (*Fenneropenaeus indicus*, *P. monodon*, *P. semisulcatus*) and portunid mud crab *Scylla tranquebarica*.

In the last decade, several studies have focused on polychaetes of the family Nereididae and their potential applications in aquafeed: (i) as an alternative feed source that could replace FM and FO or used as a dietary supplement in artificial fish diets^{222,223}; (ii) as a stimulator of gonad development and prawn/ shrimp spawning, due to particular lipid content²²⁴; (iii) as chemoattractants for many species of fish and shrimp through increasing food palatability (mostly due to glutamic acid, arginine and glycine content)^{222,225}; (iv) as a source of glycosaminoglycans (GAGs) for supplement in farmed cartilaginous fish²²⁵; and (v) as a bioremediator in integrated multitrophic aquaculture system (IMTA).²²⁶ Besides *Hediste diversicolor* (= *Nereis diversicolor*), an excellent biopotential was reported for *Sabella spallanzanii* through a gross protein content of almost 55% of dry matter, which is significantly higher than that of the bivalve *Mytilus galloprovincialis* (8%), the anemone *Anemonia viridis* (11%) and the lobster *Nephrops norvegicus* (19%–20%), essential amino acid composition and a low ω -3 and ω -6 fatty acids ratio (1.7),²²⁵ but also its bioremediation role in an IMTA, with the macroalga *Chaetomorpha linum*.²¹⁶

Among the invertebrates mentioned above, non-indigenous species (NIS) can also be considered under certain conditions as natural resource in aquaculture nutrition regarding their protein content. To date, the dispersal of NIS by human activities, such as aquaculture, shipping and creation of artificial canals, is redefining the biogeography of the oceans and seas.²²⁷ The consequences of the introduction of NIS span from detrimental environmental effects to a complete reorganisation of ecosystems, threats to human health and severe impacts on human wellbeing and different economies such as tourism and fishing.^{228–231} The latter might have substantial social, economic and cultural consequences.^{232,233} The Global Assessment Report on Biodiversity and Ecosystem Services, prepared by the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES)²³⁴ identified NIS as one of the five top direct drivers of biodiversity loss, pointing to one of the most significant threats for humanity in the next decade.²³⁴

The significantly negative consequences of NIS on marine ecosystems and relevant industries triggered the establishment of novel NIS mitigation strategies that are defined as 8R—Recognise, Reduce, Replace, Reuse, Recycle, Recover/Restore, Remove and Regulate²³⁵ and the Regulation (EU) No. 1143/2014 on the prevention and management of the introduction and spread of NIS. This Regulation sets

out rules to prevent, minimise and mitigate the adverse impact on the biodiversity of the introduction and spread of NIS both intentional and unintentional, within the Union. The management measures consider lethal or non-lethal physical, chemical or biological actions aimed at restricting, restricting or controlling a population of NIS. Although eradicating of marine NIS is unfeasible, this regulation allows the commercial use of already established NIS as a part of management measures directed toward their elimination, control or prevention of their spread, if there is a justifiable reason for it. In such a context, the exploitation of NIS as a food for fish may become an important contributor to circularity and sustainable aquaculture systems. Although NIS may contribute to highly nutritious and valuable organic aquaculture feed, they primarily represent an unexploited natural protein resource in aquaculture nutrition. Besides the published evidence there are many other local or regional initiatives to exploit the potential of NIS in fish feed, such as round goby *Neogobius melanostomus* in the Baltic Sea region.

Another potential candidate of NIS to exploit for aquafeed is the veined rapa whelk (*Rapana venosa*) which have invaded the Indo-Pacific region to Black, Red and Adriatic Seas, the south-eastern coasts of South America. *R. venosa* has a high protein level (72%) and rewarding amino acid composition. Despite that its nutritional profile may greatly vary depending on the environmental conditions and season, the species has relatively constant nutritional value throughout the year.²³⁶ Edible tissues of the whelk contain high levels of ω -3 fatty acids, especially EPA and DHA.²³⁷ Hemocyanin and its functional units isolated from veined rapa whelk exhibited antimicrobial activity, antiviral activity and phenol oxidase activity.²³⁶ Since veined rapa whelk is widely spread throughout the world waters and has beneficial nutritional value, it could be a good protein source in aquafeed.

The zebra mussel (*Dreissena polymorpha*) could also serve as an alternative feed supplement for fish. To date, there is no evidence of the use of zebra mussels in aquafeed. On the other hand, zebra mussels were documented to be a palatable feed ingredient for chicken.²³⁸ The literature suggests that zebra mussels have a protein content of up to 70%.²³⁹ In contrast, according to McLaughlan et al.,²³⁸ zebra mussels contain lower protein and energy levels because mussel meal consists of meat and shell. The shell contains a small amount of protein, which is scleroprotein, while flesh has considerable protein content. For zebra mussels to be utilised as a sustainable and long-term feedstuff for fish, flesh should be secluded from the shells economically.

Starfish (*Asterias rubens*) is a natural predator of mussels and if occurring at high densities they may deplete natural and commercially grown mussels. The species is native to the northern Atlantic Ocean but was recently introduced to the Black Sea.²⁴⁰ Starfish are another underutilised natural source of protein and collagen. Hence, they have a huge potential to be successfully valorised into aquafeed. It was estimated that 10,000 tons of starfish catch can turn into approximately 2500 tons of starfish meal. Starfish meal has high nutritional value as it may contain up to 70% proteins, which surpasses the protein content of seaweed and mussels.²⁴¹ The quality of protein fraction in starfish meal is comparable to FM.²⁴² It was documented that



the protein-containing liquid part of starfish should be collected and drained rapidly to obtain a high protein level in the starfish meal. Furthermore, starfish meal is interestingly characterised by a better amino acid profile than other plant alternatives. The biochemical composition of starfish is variable and depends significantly on the season, environmental factors, size and freshness.²⁴² According to Sørensen and Nørgaard,²⁴² starfish meal has comparable fat content to FM but higher ash and calcium content. Numerous chemical components with antimicrobial, antifungal or antiviral activities found in starfish meal make this alternative feed ingredient suitable for general animal nutrition.²⁴²

Overall, the growth conditions for these NIS are still not defined and more research efforts to increase knowledge on ecology, biology, feeding and reproduction. The collection methods should be optimised and mitigation measures developed to control their invasions should at the same time to make use of their collected biomass in aquafeed.

4 | MARINE SIDE STREAMS (FROM INDUSTRY/DISCARD): A CIRCULAR AQUACULTURE PERSPECTIVE

In recent years, a shift in the global bio-economy is becoming apparent with a transition from linear models (produce-use-dispose as waste) to the development of the circular models (produce-use-value side streams in other industries). Regarding alternative aquaculture sources, two circularity levels have emerged: (i) indirect and (ii) direct. Concerning the 'indirect' circularity level, aquaculture generates significant amounts of waste, these become investigated as potential sustainable sources of biomolecules in various industries, such as cosmetics, pharmaceuticals, food packaging, energy, aquaculture or cattle feed ingredients.^{243,244} Indeed, alternative use as feed for several fishery by-products is obvious. Since the fisheries discard ban and landing obligation in the frame of the Common Fisheries Policy (https://ec.europa.eu/oceans-and-fisheries/fisheries/rules/discarding-fisheries_en), undersized fish need to be landed, however, they cannot be used for human food.²⁴⁵ The same goes for side streams from the fish processing industry. Producing fish silage is an excellent way to valorise these byproducts as feed in aquaculture and agriculture, particularly relevant for countries with small-scale fisheries. Nutritional quality depends on the freshness and composition of the raw material.²⁴⁶ Alternatively, enzymatic hydrolysis and microbial conversion could also be used to valorise such sidestreams for FM and other applications.²⁴⁷ Regarding second circularity levels—'direct', the concept of integrated multi-trophic aquaculture and the acronym IMTA was proposed almost two decades ago,²⁴⁸ making a revolutionary contribution to aquaculture sustainability. This combined cultivation of fed species (finfish or shrimps) with extractive species, which utilise the inorganic (e.g. seaweeds) and organic (e.g. suspension-and/or deposit-feeders) nutrients from fed aquaculture for their growth, showed a more sustainable solution than monoculture. Created as a bio-mitigation strategy that aims to reduce the adverse

effects of aquafarming pollutants (i.e. depletion of oxygen in water, algal blooms and dead zones) on the marine ecosystem, through the co-cultivation of complementary species, IMTA also finds the best practices for 'by-products' reuse. As a new generation of aquaculture, IMTA provides engineering systems for environmental sustainability, economic stability and diversification of commercial production, as well as societal acceptability due to better management practices.²⁴⁹ Conceived from the beginning as 'a concept, not a formula', IMTA implies a multidisciplinary approach and dynamic system that is subject to change in response to local/global challenges (environmental, climatic, social, political, etc.), as well as new scientific knowledge.²⁵⁰ To significantly improve bio-mitigation efficiency and economic farm production, designing the best locally suited IMTA (and marine IMTA, i.e. MIMTA) demands creating a comprehensive database of individual-based sub-models for IMTA candidate organisms as recently suggested.²⁵¹

Thus, besides the need for aquafeed, marine macroinvertebrates may contribute to water quality close to aquafarms, in integrated mariculture composed of filter/deposit-feeding animals such as sponges and echinoderms.²⁵² For the sea cucumber *Holothuria tubulosa* as one of the most commercially exploited echinoderms, the ability of organic waste consumption from fish farms was recently described, making it a strong candidate for the potential development of IMTA in the Mediterranean region.^{253,254} Marine sponges are sessile filter feeders that can act as biofilters and bioremediators²⁵⁵ as already demonstrated for *Hymeniacidon perlevis*, capable of bioremediating bacterial pollution in the intensive aquaculture water system of turbot *Scophthalmus maximus*²⁵⁶ or in co-culture with mussel *Mytilus galloprovincialis*.²⁵⁷ In addition, their ability to survive in eutrophic conditions supports their potential role as a 'biofilter' in MIMTA, while the resistance of the sponge-associated microbial communities to opportunistic infections even in polluted water suggests the bioactive compound synthesis, as demonstrated by *Gelliodes obtuse*.²⁵⁸

Most sponges use dissolved organic matter (DOM; 0.2–0.7 μm ²⁵⁹) in their organic diet, which is not bioavailable to most other heterotrophic organisms. In contrast, particulate organic matter (POM) represents a minor proportion of their total organic intake. Their ability to turn a DOM into a POM through a pathway called 'the sponge loop', in which resources stored in the DOM efficiently return to the benthic food chain,²⁶⁰ making them an important participant in IMTA. The preferred sponge candidates for mariculture applications and IMTA are those with beneficial bioactive compounds, such as the common Mediterranean demosponges, *Chondrosia reniformis*, due to its collagen-rich cortex with great biomedical potential,²⁶¹ *Sarcotragus spinosulus*²⁶² and *Aplysina aerophoba*, a gold-mine of various biomaterials with biomimetic and pharmacologic potential.²⁶³ Moreover, Giangrade et al.²⁶⁴ recently listed a set of macrobenthic filter-feeding invertebrates, such as sabellid polychaetes, sponges and mussels, coupled with macroalgae, which act as bioremediators in inshore marine fish farms. Further challenges of this complex, innovative MIMTA necessitate serious valorisation of the biomass obtained as value-added by-products.²⁶⁴ The cultivation of polychaetes on waste products from finfish and crustacean aquaculture, using their

coprophagous feeding behaviour, represents a promising practice example in the waste handling challenges of the aquaculture industry. A few studies have highlighted the importance of intensive farming of polychaete *Hediste diversicolor* (= *Nereis diversicolor*), rich in PUFAs, cultivated on waste streams from freshwater aquaculture with great sturgeon, *Huso huso*²⁶⁵ and marine finfish aquaculture with European bass, *Dicentrarchus labrax* and gilthead sea bream, *Sparus aurata*, wastes.²⁶⁶ Moreover, the cultivation of *Hediste diversicolor* on salmon smolt waste, converted by polychaetes to high valuable compounds as protein and lipids, should be considered as an alternative aquafeed source with excellent potential in sustainable aquaculture production.²⁶⁷

5 | ADDED VALUE ACTIVITIES FOR NOVEL AQUAFEED

Besides the direct contribution to circularity in aquaculture, the use of novel aquafeeds from the marine environment offers additional benefits to the cultured species. They are important to highlight when evaluating the circularity criteria to incentivise researchers, producers and consumers about secondary added values of proposing Aquaculture v3.0 products.

At least 22 bacterial genera have been reported in the literature as pathogenic to fish, including Gram-positive bacteria *Mycobacterium*, *Streptococcus*, *Lactococcus*, *Aerococcus*, *Renibacterium*, *Nocardia*, *Clostridium* and *Enterobacterium*²⁶⁸ and gram-negative bacteria *Vibrio*, *Allivibrio*, *Moritella*, *Photobacterium*, *Aeromonas*, *Edwardsiella*, *Pseudomonas*, *Flavobacterium*, *Tenacibaculum*, *Piscirickettsia*, *Heptabacter*, *Francisella*, *Chlamydia* and *Yersinia*. Hence, despite the global increase in the aquaculture sector, it still faces numerous challenges connected to the frequent use of antibiotics, their persistence in the environment and the spread of antimicrobial resistance.^{269,270}

For many years, traditional antibiotics used in human medicine such as oxytetracycline and amoxicillin, have also been used to treat fish diseases in the aquaculture industry. However, antibiotic-resistant bacteria associated with fish diseases are increasing, mainly due to the absence of safer and more effective use of antibiotics. It is becoming necessary to search for alternative compounds to mitigate this problem. Using natural products from marine organisms can be a possible alternative for inspiring veterinary drug discovery for prevent and treat fish infectious diseases. Marine natural products are formed by natural selection through the high selectivity and efficient interaction with cellular targets, tailored to avoid resistance.²⁷¹⁻²⁷⁵ Natural products isolated from marine-derived micro and macroorganisms with biological activity against the pathogenic bacteria associated with fish diseases have been comprehensively reviewed and are summarised in Table 1, these natural products are suggested for drug lead development of antibiotics for fish treatment. In detail, *Laurencia johnstonii*, a marine alga, produces several bioactive compounds, including laurinterol, which has an antimycobacterial effect against *Mycobacterium fortuitum*.²⁷² Nodosol, a natural product produced by the marine angiosperm *Cymodocea nodosa*, showed strong activity against *M. fortuitum*. Nodosol has a simple meroterpenoid structure, and this characteristic makes it a

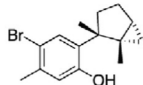
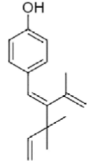
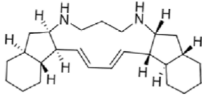
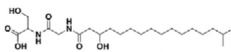
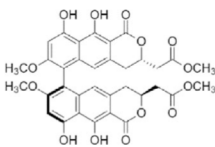
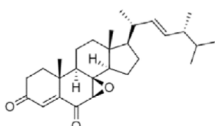
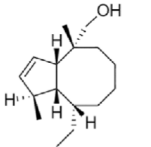
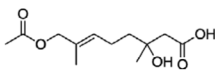
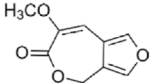
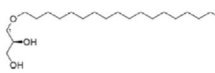
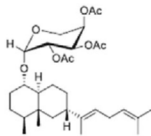
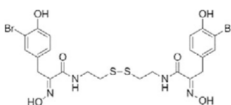
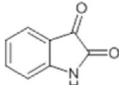
feasible target for its chemical modification and synthesis, which can optimise of its antibacterial activity.²⁷⁶ Furthermore, *Mycobacterium marinum* was inhibited by (–)-papaumine, isolated from the crude organic extract of the marine sponge *Haliclona* sp. 10.²⁷⁷

The pathogens that cause streptococcosis disease can be tackled with several marine natural products. Bacteria from the genus *Algibacter*, isolated from the Barents Sea, produced lipid 430, with activity against *Streptococcus agalactiae*.²⁷⁸ *S. agalactiae* was also inhibited by rhamnolipids produced by the Arctic marine bacterium *Pseudomonas fluorescens*.²⁷⁹ *S. iniae* and *S. parauberis* were both suppressed by viriditoxin, a natural product isolated from the jellyfish (*Nemopilema nomurai*)-derived fungus *Paecilomyces variotii*. Interestingly, viriditoxin was 10 times more potent against these drug-resistant fish pathogens than oxytetracycline (a traditionally used antibiotic in aquaculture).²⁸⁰ Rhizome crude extracts obtained from *Juncus maritimus*, an extremophile plant, showed potent activity against *S. dysgalactiae*, another pathogenic bacterium responsible for streptococcosis disease in fish.²⁸¹ Besides *Streptococcus* sp., *Aerococcus viridans* and *Lactococcus garvieae* are also fish pathogenic bacteria that cause streptococcosis disease. Several extracts from Caribbean gorgonian corals inhibited *A. viridans*. However, the overall studies suggested that the inhibition of bacterial growth is not the primary ecological function of secondary metabolites of gorgonian corals.²⁸² Moreover, two antimicrobial peptides (AMP), *arasin-likeSp* and *GRPSp*, were obtained from the mud crab, *Scylla paramamosain*. These AMPs showed antibacterial activity against *A. viridans*, suggesting their involvement in the immune responses of this mud crab and possible future use to combat these bacteria.²⁸³ *Lactococcus garvieae* was efficiently inhibited by an ethyl acetate extract obtained from a marine sponge associated with marine fungus *Aspergillus iizukae*.⁶⁹ *Arthrobacter davidanieli*, a non-pathogenic actinobacterium, is used and licensed in Canada as an effective live vaccine against *Renibacterium salmoninarum*.²⁸⁴ To date, no marine natural products have been reported for *R. salmoninarum*, *Clostridium botulinum* and *Enterobacterium catenabacterium* inhibition. Nevertheless, natural compounds are considered potent inhibitors against *C. botulinum*, such as nitrophenyl psoralen, a small natural product extracted from Indian plants.²⁸⁵

Recently, the steroid 7 β ,8 β -epoxy-(22E,24R)-24-methylcholesta-4,22-diene-3,6-dione, isolated from the deep sea-derived fungus, *Aspergillus penicillioides* showed antimicrobial activity against *Vibrio anguillarum*.²⁸⁶ The strain *Vibrio parahaemolyticus* was inhibited by a guaiane sesquiterpene derivative, guai-2-en-10 α -methanol, isolated from the abundant green seaweed *Ulva fasciata*.²⁸⁷ Furthermore, a new monoterpene, penicimonoterpene(+), was isolated and identified from the marine-derived endophytic fungus *Penicillium chrysogenum*. From this compound, derivatives with antimicrobial potential were synthesised. Five penicimonoterpene derivatives presented strong inhibition against *V. anguillarum* and *V. parahaemolyticus*.²⁸⁸ Moreover, from the crude extract of a sponge-derived fungus, *Penicillium* sp. LS54, a novel seven-membered lactone derivative, penicillilactone A, exhibited inhibition activity against *V. harveyi*.²⁸⁹ In addition, a lipidic compound, batyl alcohol, isolated from the Colombian Caribbean Sea soft coral *Eunicea* sp. and a terpenoid, fuscocside *E. peracetate*, isolated from *E. fusca* showed biofilm inhibition

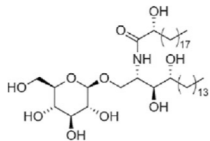
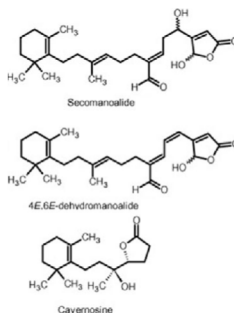
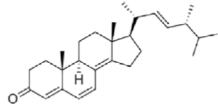
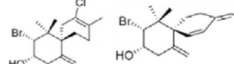
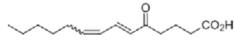
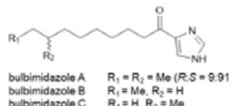
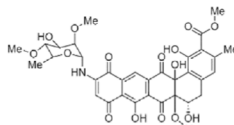


TABLE 1 Fish pathogenic bacteria, associated diseases and marine natural products with antimicrobial activity against the corresponding bacteria pathogen

Bacteria type	Pathogenic bacteria	Disease	Antimicrobial natural product name/ natural product source	Chemical structure	References
gram+	<i>Mycobacterium fortuitum</i>	Mycobacteriosis	Laurinterol <i>Laurencia johnstonii</i> (red alga)		272
			Nodosol <i>Cymodocea nodosa</i> (seagrass)		276
	<i>Mycobacterium marinum</i>		(-)-papuamine <i>Haliclona</i> sp. (sponge)		277
	<i>Streptococcus agalactiae</i>	Streptococcosis	Lipid 430 <i>Algibacter</i> sp. (bacteria)		278
	<i>Streptococcus iniae</i>		Viriditoxin <i>Paecilomyces variotii</i> (fungus)		280
	<i>Streptococcus parauberis</i>				
	<i>Aerococcus viridans</i>		Peptides arasin-likeSp and GRPsp <i>Scylla paramamosain</i> (crab)	NA	283
gram-	<i>Vibrio anguillarum</i>	Vibriosis	7 β ,8 β -epoxy-(22E,24R)- 24-methylcholesta-4,22-diene- 3,6-dione <i>Aspergillus penicilloides</i> (fungus)		286
			Guai-2-en-10 α -methanol <i>Ulva fasciata</i> (green alga)		287
	<i>Vibrio parahaemolyticus</i>		Penicimonoterpene-derivatives <i>Penicillium chrysogenum</i> (fungus)		288
	<i>Vibrio harveyi</i>		Penicillilactone A <i>Penicillium</i> sp. LS54 (bacteria)		289
		Batyl alcohol ^a <i>Eunicea</i> sp. (soft coral)		290	
		Fuscoside E peracetate ^a <i>Eunicea fusca</i> (soft coral)		290	
	<i>Vibrio vulnificus</i>		Psammaplina A <i>Poecillastra</i> sp., <i>Jaspis</i> sp. and <i>Poecillastra wondoensis</i> (sponges)		293
			Sulphated polysaccharides <i>Spirulina platensis</i> (microalga)	NA	294
	<i>Aeromonas salmonicida</i>	Aeromoniasis/ furunculosis	Isatin <i>Alteromonas</i> sp. (bacteria)		295

(Continues)

TABLE 1 (Continued)

Bacteria type	Pathogenic bacteria	Disease	Antimicrobial natural product name/ natural product source	Chemical structure	References
			Cerebroside <i>Axinella donnani</i> (sponge)		296
	<i>A. salmonicida</i> and <i>A. hydrophila</i>		Combination of secomanoalide, dehydromanoalide and cavernosine <i>Fasciospongia cavernosa</i> (sponge)		296
	<i>Edwardsiella tarda</i>	Edwardsiellosis	Ergosta-4,6,8(14),22-tetraene-3-one <i>Aspergillus penicillioides</i> SD-311 (fungus)		286
	<i>Pseudomonas anguilliseptica</i>	Pseudomoniasis	Chamigrene-derived sesquiterpenes <i>Laurencia chondrioides</i> (seaweed)		298
	<i>Tenacibaculum maritimum</i>	Flavobacteriosis	(6E,8Z)-5-oxo-6,8-tetradecadienoic acid <i>Micrococcus</i> sp. C5-9 (actinobacteria)		301
			Bulbimidazoles A-C <i>Microbulbifer</i> sp. (bacteria)		302
	<i>Chlamydia</i> sp.	Infection with Intracellular Bacteria	Naphthacene glycoside SF2446A2 <i>Streptomyces</i> sp. strain RV15 (actinobacteria)		303

Abbreviation: NA, not available in the cited reference.

^aAntibiofilm activity.

against *V. harveyi*.²⁹⁰ Antibiofilm natural products hold great promise as effective agents to overcome bacterial resistance to antibiotics, which makes them suitable resources for future controlling agents of aquatic pathogens.^{291,292} Psammaplins A, a natural product isolated from the marine sponges *Poecillastra* sp., *Jaspis* sp. and *Psammaplysilla* sp., exerted a strong inhibitory activity against *V. vulnificus*.²⁹³ Moreover, sulphated polysaccharide, isolated from *Spirulina platensis*, exhibited potent antibacterial activity against *V. vulnificus*. In fact, *Spirulina* is one of the most commercialised microalgae, due to its bioactive properties and nutritional value.²⁹⁴ Isatin is a biologically active secondary metabolite produced by *Alteromonas* sp., a synthetically modified isatin derivative was reported to have potent inhibitory activity against *A. salmonicida*, responsible for aeromoniasis and furunculosis disease.²⁹⁵

Several marine natural products have been isolated and identified against *A. sobria*, *A. hydrophila* and *A. salmonicida*. The most promising

antimicrobial activity against *A. salmonicida* was exhibited by the metabolite cerebroside, produced by the sponge *Axinella donnani*. Additionally, when combined, three metabolites, secomanoalide, dehydromanoalide and cavernosine, isolated from the sponge *Fasciospongia cavernosa*, had a synergistic antimicrobial effect against *A. salmonicida* and *A. hydrophila*.²⁹⁶ Furthermore, a novel natural protein, siganus oramin L-amino acid oxidase, isolated from the serum of the rabbitfish *Siganus oramin*, showed antibacterial activity against the fish pathogenic bacteria *A. sobria*. Although this protein was isolated from a marine organism, the protein was produced using the yeast eukaryotic expression system, by genetic engineering tools. The recombinant crude protein showed strong antimicrobial activity against *A. sobria*.²⁹⁷

The natural product ergosta-4,6,8(14),22-tetraene-3-one obtained from deep sea-derived fungi *Aspergillus penicillioides* showed strong inhibitory activity against the pathogenic bacteria *Edwardsiella tarda*.²⁸⁶ The fungus *Penicillium canescens*, isolated from the marine

sponge *Cacospongia* sp., collected from the Aegean Sea Coast of Turkey, revealed activity against *Yersinia ruckeri*, however, the bioactive compounds were not isolated nor identified.⁶⁹ Two chamigrene derived sesquiterpenoids isolated from the red seaweed *Laurencia chondrioides*, demonstrated antimicrobial bioactivity against *Pseudomonas anguilliseptica*.²⁹⁸ Furthermore, studies described the antibacterial capacity of the crude extracts of two marine sponges, *Neopetrosia exigua* and *Iotrochota birotulata* against *P. fluorescens*.²⁹⁹ Actinobacteria *Streptomyces* sp. (described as phylotype 44) associated with the bryozoan *Membranipora membranacea*, collected from the Baltic Sea, also revealed activity against *P. fluorescens*.³⁰⁰

Marine-derived actinobacteria from the genus *Micrococcus*, isolated from the stony coral *Cataphylia* sp., produced two new unsaturated keto fatty acids, (6E,8Z)-5-oxo-6,8-tetradecadienoic acid and (6E,8E)-5-oxo-6,8-tetradecadienoic acid (Table 1) that were effective in inhibiting the pathogenic bacteria *Tenacibaculum maritimum*.³⁰¹ In addition, three new alkanoyl imidazoles, bulbimidazoles A-C, isolated from the gammaproteobacterium *Microbulbifer* sp., demonstrated antimicrobial activity against *T. maritimum*. *Microbulbifer* sp. was also isolated from a stony coral belonging to *Tubastraea* genus.³⁰²

There are several reports of microorganisms capable of inhibiting *Piscirickettsia salmonis*. A live vaccine using the actinobacteria species *Arthrobacter davidanieli*, is used under field conditions in Chile. This live vaccine led to a significant reduction in the incidence of these pathogenic bacteria in coho salmon.³⁰² Moreover, the inhibitory activity of naphthacene glycoside SF2446A2 was reported against *Chlamydia* pathogenic bacteria (*C. trachomatis* considered a 'traditional' *Chlamydia* bacteria), a natural product isolated from *Streptomyces* sp. symbiont of the marine sponge *Dysidea tupa*, collected off Croatia.³⁰³ All the above-mentioned antimicrobial compounds can be suggested as leads developing and producing of aquaculture drugs or for prebiotics and probiotics applications for disease control.

It needs to be stated that secondary metabolites produced by microorganisms are particularly promising, as their production can be scaled-up through optimisation of fermentation conditions and/or heterologous expression of the secondary metabolites producing genes by recombinant microbes.²⁷⁵ Microorganisms are a sustainable and renewable resource that can be industrially cultured, rather than harvested from nature, facilitating future industrial compound scaling-up and circumventing raw material supply. Using microorganisms to improve aquaculture specie's health and wellbeing and in turn using aquaculture waste as carbon source for producing antimicrobial natural products or other biobased products for aquaculture purposes and needs are examples of circular bioeconomy approaches that can be developed.

6 | RISK ASSESSMENT OF THE USE OF POTENTIAL MARINE ORGANISMS FROM SEA-TO-AQUAFEED

Like all ingredients, any novel ingredients derived from marine origin also present the potential for introducing a range of risks. Managing these risks requires adopting a series of risk assessment strategies for

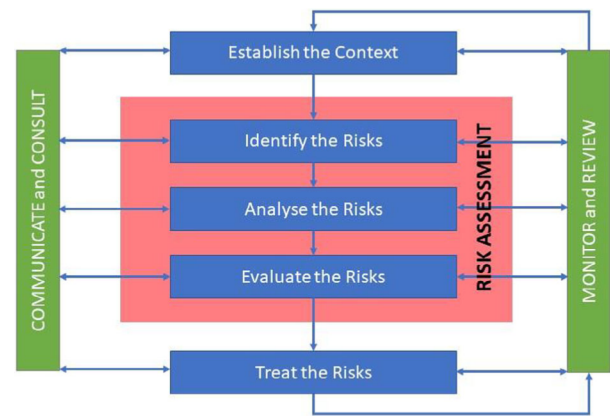


FIGURE 1 A standard risk analysis pathway map adapted from Colombo and Turchini⁸

which there are a systematic series of policies, procedures and practices can be applied.⁹ Risk assessment on scientific-based processes is generally represented as four stages: (i) hazard identification, (ii) hazard characterisation, (iii) exposure assessment and finally (iv) risk characterisation. From this process, it can be noted that fundamental to the risk analysis process is the communication of the issues, and establishment of the risk context, followed by the identification, analysis, evaluation, treatment, monitoring and review of the identified risks (Figure 1). Based on this series of approaches, the risk can be more clearly considered and assumptions and uncertainties about those risks can be evaluated in Codex Alimentarius Commission (CAC, <http://www.fao.org/fao-who-codexalimentarius/home/it/>). For further details on each stage of this risk assessment process.⁹

6.1 | Logistical risks

Applying any ingredient to feed brings with it a suite of production, safety and logistical risks. In feed production, different elements are associated with those risks that need to be considered. Feed production is a manufacturing process, there are always risks associated with producing a product to the required specifications. The ability to formulate and produce feed based on data of any specific batch of ingredients and have the final composition of the combination of various ingredients meet the planned expectations have varying degrees of probability subject to the number of ingredients used, the confidence around safety and performance the parameters being assessed and the fidelity of any analytical method used. Additionally, in this process of combining raw materials, there is also potential for those raw materials to bring in contaminants and pathogens.

Other critical logistical risks include the supply and price of the ingredients being considered. It is important to note that most feed production facilities have limited capacity for the number of (bulk) ingredients they can use. Because of this, there is a preference to use ingredients that can be reliably obtained at large volumes and consistent supply. The ability to obtain ingredients on such a basis





FIGURE 2 Standard technology readiness levels as defined by the European Commission.

significantly decreases the risk associated with the reliable production of feeds. However, this does not preclude the use of low volume and/or novel ingredients. Still, there is a critical need to scale through various technology readiness levels (TRLs in Figure 2) to meet this requirement and reduce logistical risk when introducing new ingredients. In addition, the logistical risks are accompanied by the price. Various economic factors influence the price of any ingredient and its utility in the feed sector. While it may be possible to produce an ingredient from arguably anything, this does not necessarily mean it can be done in the most cost-competitive manner. The cost efficiency includes a range of considerations: the cost of production, the qualities the ingredient contributes (e.g. compositional, sensory and structure) and the perceived value of the product by the buyer, the willingness to pay and the fact that the price will be consistently iterated to respond to market forces and competition. Therefore, the risk associated with cost viability may also change over time.

6.2 | Biological risks

Regarding biological risks, the primary ones likely to be encountered in the application of different marine ingredients include issues with the variability in nutrient supply, the potential for the presence of contaminants and the presence of anti-nutritional factors.⁹ Several groups of ANF have a potentially harmful compound and it is thus important to have sufficient information about the presence of ANFs in new aquafeed sources. These ANFs should be reduced or removed using appropriate physical or chemical methods.³⁰⁴⁻³⁰⁶ This way the biological risk to animal health, welfare, growth performance and safety of the final product is guaranteed.³⁰⁷ The ability to ascribe values to various compositional parameters and the variability in their nutritional effects is critical to determine the nutritional value of any ingredient. As such this process must commence with a characterisation of the ingredient (e.g. what is it and what is its composition) followed by an assessment

of its palatability and digestibility.^{308,309} Once an ingredient has been characterised and its palatability and digestibility constraints defined, its appropriate application in a diet formulation can be considered in any subsequent growth study. When any of these foundational steps are omitted, there can be a critical feed failure due to poor intake and/or incorrect nutrient supply, both of which can be effectively managed if known prior. Problems with variability in nutrient supply can be managed through the processes of characterisation of the ingredient followed by both palatability and digestibility assessment.^{308,309} However, in practice, the palatability and digestibility of each batch of ingredients are seldom appropriately assessed, although it is common practice in the feed industry to undertake the characterisation step of the ingredient for each batch based on an assessment of the composition, usually using modern near-infrared spectroscopy (NIR) techniques.³¹⁰ In contrast, it is more common to apply 'trade knowledge' to the palatability information requirement, and 'book values' or database values (e.g. <https://www.iaffd.com/>) to the digestibility information requirement. However, there is increasing capability being shown by the industry to adapt NIR to predict nutrient digestibility in both feeds and ingredients.^{311,312}

Contaminants present a significant risk in using of marine ingredients as many persistent pollutants accumulate in marine ecosystems from terrestrial run-offs. Various contaminants are known to exist but usually, there are either certain heavy metals or persistent organic pollutants (POPs). For a comprehensive review of the various potential contaminants affecting aquafeeds see Glencross et al.⁹ Notably, feed ingredients can also be contaminated during the production and processing stages. However, such contamination of an ingredient presents a significant risk to the animal to which it is being fed, and to the ultimate consumer of that animal that was fed. Most management of contaminant risk of feed ingredients is undertaken by maximum residue levels (MRLs) for each contaminant in the material of concern and monitoring materials considered risky. Globally, this is regulated by the United Nations (UN) through the World Health Organization

(WHO) and the Food and Agriculture Organisation (FAO) through the CAC. Additionally, most developed economies worldwide also have governmental authorities regulating this process (e.g. European Food Safety Authority).

7 | BOTTLENECKS AND OPPORTUNITIES OF SEA-TO-AQUAFEED

There is an increasing need to invest in research and development that will provide effective alternatives and new supply chains to replace FM and FO. However, before any successful and scalable market introduction of novel feed formulations, several challenges need to be addressed by the industry to achieve sustainable and responsible practices. Collaboration and investment: The blue growth initiative, proposed in 2013 by FAO, aims to build resilience of coastal communities, and restore the productive potential of the ocean by promoting the sustainable management of aquatic

resources.³¹³ To improve and boost the development of a sustainable aquaculture, there is a need for international and transdisciplinary research and innovation collaborations. These collaborations are supported through investment by national and international funding agencies to transfer the developed technologies to the industry.^{314,315} The European Union provides many strategies and funding mechanisms that can boost and stimulate innovations within marine biotechnology and improve the aquaculture sector. A detailed presentation of the EU's strategy and funding opportunities for marine biotechnology is presented in the review by Rotter et al.¹¹⁹ To promote the development and commercialisation of novel aquafeeds, a cross-sectorial and transnational collaboration is needed to create more efficient and financially supported networks along the new value and supply chains of seafood and aquaculture sectors.^{316,317} These involve research and develop experts to cover the lower TRLs and develop/test the efficiency of extraction/small scale production of novel aquafeeds, as well as representatives from the industry (e.g., commercial farms) for testing novel aquafeeds in an operational

	Potential organisms	Nutritional content †	Scientific Knowledge	Bio-circularity	Practical application	Feasibility /Cost
Micro-organisms	<i>Microalgae Resources</i>	+	+	+	+	-
	<i>Fungi and Thraustochytrids</i>	+	+	+	-	-
	<i>Marine bacteria</i>	+	+	+	-	-
Macro-organisms	<i>Macroalgae</i>	+	+	+	+	-
	<i>Invertebrates</i>	+	+	+	-	-
	Marine side streams	+	+	+	+	+

FIGURE 3 A qualitative assessment of potential organisms considered circular aquaculture along with nutritional content, scientific knowledge, practical application (large-scale production and commercially applicable in aquafeed) and feasibility/cost of production. Positive (+) represents an alternative protein source with high potential while negative (–) represents that has still need some development according to allocated criteria. †Nutritional content of the potential organisms was subjective and reported based on a comparison with FM in Figure S1.

environment. Importantly, as the prototyping of novel aquafeeds advances through the technology readiness, other expertise is necessary, such as legal, market research supply chain and potential customer feedback/market acceptance.

7.1 | Sustainability

Research on the sustainability of alternative feed production should be tackled on four levels: (i) supply sustainability, (ii) environmental sustainability, (iii) economic sustainability and (iv) social sustainability. Supply chains must be examined to determine the network of entities and activities from primary alternative feed providers to feed producers, suppliers, distributors and finally to final users—aquafeed marketers and fish farmers.^{317,318} Strengths and weaknesses of each link have to be identified to propose management and mitigation strategies.³¹⁷ Environmental sustainability is essential as aquaculture is markedly impacted by climate change effects,³¹⁹ especially water shortage, and resource declines that impact the use of terrestrial feed ingredients.³²⁰ Moreover, alternative feedstuffs are needed to counterbalance the unsustainable feed ingredients. Although some alternative feedstuffs hold a great promise to maintain the environmental sustainability of aquaculture, they still need to consider the release of waste by the fed organisms, the resultant nutrient loading in surrounding waters as a result of uneaten feed, bad feeding strategies or poor feed quality.³²¹ Economic sustainability is needed that links innovation, market trends, consumer demand and consumer acceptance balanced with cost calculations.³¹³

Finally, social responsibility involves the responsibility from all stakeholders involved in the industry for application of good practices. These include the sharing of resources, knowledge, education, promoting the health and environmental benefits (especially as a result of a circular approach). It is important, however, to highlight the need of assessment of circularity through environmental, economic, social, legislative, technical and business criteria²⁸ and provide indicators to monitor the implementation and success of implemented novel aquafeeds as contributors to sustainable bioeconomy practices.³²² These can produce indicators and impacts that can be used by all stakeholders, including the policy makers and the final consumers, to make decisions on further supporting the development and implementation of these circular practices.

7.2 | Legal requirements

As one of the fastest growing industries within global food production sectors, an increasing attention to legal requirements especially in developing new technologies and applications has been placed on the aquaculture sector. In the early 1990s, the United Nations provided The Convention on Biological Diversity, which represented a framework for countries to structure regulations and legislation on the access, use, exchange and benefit of genetic resources. Access and benefit sharing (ABS) is a legal framework for regulating access and use of genetic resources that controlled by the provider, as well as

sharing benefits resulting from research and commercial use of the provider.³²³ Three other international agreements also frame national legislations on exchanging aquaculture genetic material: Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from Their Utilisation to the Convention on Biological Diversity, Agreement on trade-related aspects of intellectual property rights and, United Nations Convention on the Law of the Sea. A recent study demonstrated the low levels of awareness and application of some of these regulatory frameworks in the blue biotechnology sector and consequently, proposed a series of recommendations to close the breach at the European, national and organisational levels.³²⁴ Recent reviews^{323,325} also show that those international agreements are insufficient for sustainable aquaculture, where the aim is to provide nature conservation, food and health security. Finally, they have examined the ABS of aquaculture genetic resources, emphasising that most aquaculture products are provided by developing countries (mostly from Asia) that use over 580 species. It is suggested that international and national ABS legislations on aquaculture genetic resources should be restructured and tailor-made (species-specific, geographically specific) after an in-depth analysis of the global status of ABS within the aquaculture industry. In the European Union, the pursue to find novel feed ingredients to build new sustainable food systems and the creation of alternative sustainable businesses and jobs is strategically included in the guidelines to build a more sustainable and competitive aquaculture by the year 2030.³¹⁶ In the context of circular aquaculture, there is hence an increasing need to reinforce the dialogue between the policy makers and aquaculture specialists. This can, for example, incentivise a broader adoption of circular fish feed in countries that still do not legally authorise the adoption of alternative proteins for the aquaculture industry.³¹⁶

8 | FINAL REMARKS AND FUTURE PERSPECTIVES

As in other industries, aquaculture is transitioning from linear to circular models, involving the valorisation of a wide range of resources from the marine environment. These biological resources can be used as whole (either as a live feed or their biomass) or through the valorisation of their bioactive compounds, including as effective alternative feedstuffs. However, more research is needed to understand the production of bioactive compounds in organisms and their impact on target aquaculture species. It is also important to bear in mind that the greatest challenges to alternative protein sources derived from the marine sources in aquafeed include varied protein content (Figure S1), scientific knowledge, practical application in the industry, feasibility along with the biocircularity of these resources (Figure 3). Given these challenges, like all alternative ingredients, some of these potential organisms have critical scalability and cost points at where they compete. Thus, more effort should be put into transitioning to innovative aquaculture approaches using the same producer organisms that can economically complement the traditional fish sources for FM and FO as a



source of additional advantages. Putting further efforts into better understanding these micro and macro organisms, namely their contribution as value-added products and their capacity to improve animal performance, nutrient availability, food palatability and digestibility, could be part of the route to successfully integrating them as vital resources in aquaculture feeds. Broader systems and sustainability values of various resources should be investigated in addition to the nutritional benefits associated with the consumption of marine organisms. An example is provided by the use of macroalgae and bacteria that are also effective at treating wastewater generated by aquaculture production, hence providing a win-win service for the aquaculture industry. As many of these alternative feed resources are still under development but critically needed in the growing aquaculture sector, now is the right time for additional investment into collaborations that will drive the development of market-ready products with validated value to entire supply chains. In addition, close collaborations need to be maintained with the local, national and international legislation to design novel waste management strategies, invest in necessary infrastructures and raise awareness among the end users of products that have been developed respecting the circularity design principles.

AUTHOR CONTRIBUTIONS

Orhan Tufan Eroldogan: Conceptualization; data curation; formal analysis; project administration; validation; visualization; writing – original draft; writing – review and editing. **Brett Glencross:** Conceptualization; resources; validation; visualization; writing – original draft; writing – review and editing. **Lucie Novoveska:** Conceptualization; data curation; methodology; writing – original draft; writing – review and editing. **Susana P. Gaudêncio:** Conceptualization; data curation; visualization; writing – original draft; writing – review and editing. **Buki Rinkevich:** Data curation; project administration; visualization; writing – original draft; writing – review and editing. **Giovanna Cristina Varese:** Conceptualization; data curation; visualization; writing – original draft; writing – review and editing. **Fátima Carvalho:** Conceptualization; data curation; project administration; visualization; writing – original draft; writing – review and editing. **Deniz Tasdemir:** Conceptualization; funding acquisition; visualization; writing – original draft; writing – review and editing. **Ivo Safarik:** Data curation; visualization; writing – original draft; writing – review and editing. **Søren Laurentius Nielsen:** Conceptualization; formal analysis; visualization; writing – original draft; writing – review and editing. **Celine Rebours:** Conceptualization; visualization; writing – original draft; writing – review and editing. **Lada Lukić Bilela:** Conceptualization; resources; writing – original draft; writing – review and editing. **Johan Robbens:** Conceptualization; resources; visualization; writing – original draft; writing – review and editing. **Evita Strode:** Formal analysis; investigation; methodology; visualization; writing – original draft. **Berat Haznedaroglu:** Methodology; writing – original draft; writing – review and editing. **Jonne Kotta:** Investigation; methodology; writing – original draft. **Ece Evliyaoglu:** Data curation; formal analysis; writing – review and editing. **Juliana Oliveira:** Investigation; visualization; writing – original draft. **Mariana Girão:** Data curation; software; visualization; writing – original draft. **Marlen Vazquez:** Data curation; writing – original draft; writing – review and editing. **Ivana Cabarkapa:**

Investigation; methodology; writing – original draft; writing – review and editing. **Sladjana Rakita:** Data curation; methodology; visualization; writing – original draft; writing – review and editing. **Katja Klun:** Conceptualization; data curation; visualization; writing – original draft; writing – review and editing. **Ana Rotter:** Conceptualization; data curation; writing – original draft; writing – review and editing.

AFFILIATIONS

¹Faculty of Fisheries, Department of Aquaculture, Cukurova University, Adana, Turkey

²Biotechnology Research and Application Center, Cukurova University, Adana, Turkey

³Institute of Aquaculture, University of Stirling, Stirling, UK

⁴IFFO - The Marine Ingredients Organisation Unit C, London, UK

⁵Scottish Association for Marine Science, Oban, UK

⁶UCIBIO-Applied Molecular Biosciences Unit, Chemistry Department, Blue Biotechnology and Biomedicine Lab, NOVA School of Science and Technology, NOVA University of Lisbon, Caparica, Portugal

⁷Associate Laboratory i4HB – Institute for Health and Bioeconomy, NOVA School of Science and Technology, NOVA University Lisbon, Caparica, Portugal

⁸Israel Oceanography and Limnological Research, National Institute of Oceanography, Haifa, Israel

⁹Department of Life Sciences and Systems Biology, University of Torino, Torino, Italy

¹⁰CIIMAR, Interdisciplinary Centre of Marine and Environmental Research of the University of Porto, Terminal de Cruzeiros do Porto de Leixões, Avenida General Norton de Matos, Matosinhos, Portugal

¹¹ICBAS, Institute of Biomedical Sciences Abel Salazar, University of Porto, Porto, Portugal

¹²GEOMAR Centre for Marine Biotechnology (GEOMAR-Biotech), Research Unit Marine Natural Products Chemistry, GEOMAR Helmholtz Centre for Ocean Research Kiel, Kiel, Germany

¹³Faculty of Mathematics and Natural Sciences, Kiel University, Kiel, Germany

¹⁴Department of Nanobiotechnology, Biology Centre, ISBB, CAS, Ceske Budejovice, Czech Republic

¹⁵Regional Centre of Advanced Technologies and Materials, Czech Advanced Technology and Research Institute, Palacky University, Olomouc, Czech Republic

¹⁶Department of Science and Environment, Roskilde University, Roskilde, Denmark

¹⁷Ocean Institute, Copenhagen, Denmark

¹⁸Møreforskning AS, Ålesund, Norway

¹⁹Department of Biology, Faculty of Science, University of Sarajevo, Sarajevo, Bosnia and Herzegovina

²⁰Flanders Research Institute for Agriculture, Fisheries and Food, Ostend, Belgium

²¹Latvian Institute of Aquatic Ecology, Agency of Daugavpils University, Riga, Latvia

²²Institute of Environmental Sciences, Bogazici University, Istanbul, Turkey

²³Estonian Marine Institute, University of Tartu Tallinn, Tallinn, Estonia



²⁴Department of Chemical Engineering, Cyprus University of Technology, Limassol, Cyprus

²⁵Department of Science and Technology, European University of Technology, Limassol, Cyprus

²⁶Institute of Food Technology, University of Novi Sad, Novi Sad, Serbia

²⁷Marine Biology Station Piran, National Institute of Biology, Piran, Slovenia

ACKNOWLEDGEMENTS

This publication is based upon work from COST Action CA18238 (Ocean4Biotech), supported by COST (European Cooperation in Science and Technology) program, which provided open access support. Also, Orhan Tufan Eroldoğan gratefully acknowledges the Research Unit of Cukurova University for their financial support to achieve this review (Project no. FBA-2020-13387). Susana P. Gaudêncio and Juliana Oliveira would like to thank national funds from FCT–Fundação para a Ciência e a Tecnologia, IP, in the scope of the project UIDP/04378/2020 of the Research Unit on Applied Molecular Biosciences–UCIBIO and the project LA/P/0140/2020 of the Associate Laboratory Institute for Health and Bioeconomy–i4HB finishing the research and the project Laboratory Institute for Health and Bioeconomy–i4HB, and also the projects OceanTreasures–PTDC/QUI-QUI/119116/2010 and DIGIAqua–PTDC/EEI-EEE/0415/2021. Evita Strode received financial grant from the ERDF 1.1.1.2 post-doctoral project (1.1.1.2/VIAA/3/19/465). Ana Rotter and Katja Klun gratefully acknowledges the funding provided by the Slovenian Research Agency (Research core funding P4-0432). Ana Rotter also acknowledges the Interreg MED Programme, cofinanced by the European Regional Development Fund (Project No. 7032, internal ref. 8MED20_4.1_SP_001)–B-Blue project for financing this work. Céline Rebours gratefully acknowledges the Research Council of Norway and Møreforsking AS for their financial support to achieve this review within the SAFER-IMTA (Project no. 319577) and the SeaGreen (Project no. 312947) projects. Maria de Fátima Carvalho wishes to acknowledge the funding from ACTINODEEPSEA project (project no. PTDC/BIA-MIC/31045/2017) co-financed by COMPETE 2020, Portugal 2020, European Regional Development Fund (ERDF) and FCT and Strategic Funding UIDB/04423/2020 and UIDP/04423/2020 through national funds provided by FCT and ERDF. Lukić Bilela Lada: the publication is part of a project that has received funding from the Erasmus+ Development of master curricula in ecological monitoring and aquatic bioassessment for Western Balkans HEIs/ECOBIAAS (Project no. ECOBIAS_609967-EPP-1-2019-1-RS-EPPKA2-CBHE-JP; GA.2019-1991/001-001). Deniz Tasdemir acknowledges funding from European Union (Horizon 2020 Research and Innovation Programme) to achieve this review within the project SUMMER (Grant Agreement 817806). Jonne Kotta acknowledge financial support from the EEA grant ‘Climate Change Mitigation and Adaptation’ call I ‘Ecosystem resilience increased’ project ‘Impacts of invasive alien species and climate change on marine ecosystems in Estonia’. Slađana Rakita and Ivana Čabarkapa acknowledge the funding from the Ministry of Education, Science and

Technological Development of the Republic of Serbia (Grant number: 451-03-68/2022-14/200222).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest on this article.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Orhan Tufan Eroldoğan  <https://orcid.org/0000-0001-6978-7524>

Søren Laurentius Nielsen  <https://orcid.org/0000-0003-4309-5153>

Ana Rotter  <https://orcid.org/0000-0002-6879-0980>

REFERENCES

1. FAO (Food and Agriculture Organization). *The State of World Fisheries and Aquaculture 2022. Towards Blue Transformation*. FAO; 2022. doi:10.4060/cc0461en
2. Hua K, Cobcroft JM, Cole A, et al. The future of aquatic protein: implications for protein sources in aquaculture diets. *One Earth*. 2019;1(3):316–329.
3. Suarez JA, Tudela C, Davis D, et al. Replacement of fish meal by a novel non-GM variety of soybean meal in cobia, *Rachycentron canadum*: ingredient nutrient digestibility and growth performance. *Aquaculture*. 2013;416–417:328–333. doi:10.1016/j.aquaculture.2013.09.049
4. Schweiggert-Weisz U, Eisner P, Bader-Mittermaier S, Osen R. Food proteins from plants and fungi. *Curr Opin Food Sci*. 2020;32:156–162. doi:10.1016/j.cofs.2020.08.003
5. Gatlin DM III, Barrows FT, Brown P, et al. Expanding the utilization of sustainable plant products in aquafeeds: a review. *Aquacult Res*. 2007;38(6):551–579. doi:10.1111/j.1365-2109.2007.01704.x
6. Turchini GM, Trushenski JT, Glencross BD. Thoughts for the future of aquaculture nutrition: realigning perspectives to reflect contemporary issues related to judicious use of marine resources in aquafeeds. *N Am J Aquac*. 2019a;81(1):13–39. doi:10.1002/naaq.10067
7. Glencross BD, Huyben D, Schrama JW. The application of single-cell ingredients in aquaculture feeds—a review. *Fishes*. 2020a;3:22. doi:10.3390/fishes5030022
8. Colombo SM, Turchini GM. Aquafeed 3.0: creating a more resilient aquaculture industry with a circular bioeconomy framework. *Rev Aquac*. 2021;13(3):1156–1158. doi:10.1111/raq.12567
9. Glencross BD, Baily J, Berntssen MH, Hardy R, MacKenzie S, Tocher DR. Risk assessment of the use of alternative animal and plant raw material resources in aquaculture feeds. *Rev Aquac*. 2020b; 12(2):703–758. doi:10.1111/raq.12347
10. Turchini GM, Torstensen BE, Ng WK. Fish oil replacement in finfish nutrition. *Rev Aquac*. 2009;1(1):10–57. doi:10.1111/j.1753-5131.2008.01001
11. Gibbs HK, Rausch L, Munger J, et al. Brazil's soy moratorium. *Science*. 2015;347(6220):377–378. doi:10.1126/science.aaa0181
12. Pahlow M, van Oel PR, Mekonnen MM, Hoekstra AY. Increasing pressure on freshwater resources due to terrestrial feed ingredients for aquaculture production. *Sci Total Environ*. 2015;536:847–857. doi:10.1016/j.scitotenv.2015.07.124
13. Ytrestøyl T, Aas TS, Åsgård T. Utilisation of feed resources in production of Atlantic salmon (*Salmo salar*) in Norway. *Aquaculture*. 2015;448:365–374. doi:10.1016/j.aquaculture.2015.06.023

14. Peisker M. Manufacturing of soy protein concentrate for animal nutrition. In: Brufau J, ed. *Feed Manufacturing in the Mediterranean Region. Improving Safety: From Feed to Food*. CIHEAM; 2001: 103-107.
15. Samuel-Fitwi B, Meyer S, Reckmann K, Schroeder JP, Schulz C. Aspiring for environmentally conscious aquafeed: comparative LCA of aquafeed manufacturing using different protein sources. *J Clean Prod*. 2013;52:52225-52233. doi:10.1016/j.jclepro.2013.02.031
16. Raucci GS, Moreira CS, Alves PA, et al. Greenhouse gas assessment of Brazilian soybean production: a case study of Mato Grosso state. *J Clean Prod*. 2015;96:418-425.
17. Carvalho WD, Mustin K, Hilário RR, Vasconcelos IM, Eilers V, Fearnside PM. Deforestation control in the Brazilian Amazon: a conservation struggle being lost as agreements and regulations are subverted and bypassed. *Perspect Ecol Conserv*. 2019;17(3):122-130. doi:10.1016/j.pecon.2019.06.002
18. Troell M, Naylor RL, Metian M, et al. Does aquaculture add resilience to the global food system? *Proc Natl Acad Sci USA*. 2014; 111(37):13257-13263. doi:10.1073/PNAS.1404067111
19. Benkendorff K. Aquaculture and the production of pharmaceuticals and nutraceuticals. In: Burnell G, Allan G, eds. *New Technologies in Aquaculture*. Woodhead Publishing; 2009:866-891.
20. Yaakob Z, Ali E, Zainal A, Mohamad M, Takriff MS. An overview: biomolecules from microalgae for animal feed and aquaculture. *J Biol Res (Thessaloniki)*. 2014;21(1):1-10.
21. Zorriehzahra MJ, Delshad ST, Adel M, et al. Probiotics as beneficial microbes in aquaculture: an update on their multiple modes of action: a review. *Vet Q*. 2016;36(4):228-241. doi:10.1080/01652176.2016.1172132
22. Nayak SK. Probiotics and immunity: a fish perspective. *Fish Shellfish Immunol*. 2010;29:2-14. doi:10.1016/j.fsi.2010.02.017
23. European Commission. *European Market Observatory for Fisheries and Aquaculture Products (EUMOFA), Blue Bioeconomy, Situation report and perspectives*. Publications Office of the European Union; 2018. doi:10.2771/053734
24. Ghosh PR, Fawcett D, Sharma SB, Poinern GE. Progress towards sustainable utilisation and Management of Food Wastes in the global economy. *Int J Food Sci*. 2016;2016:3563478. doi:10.1155/2016/3563478
25. Malcorps W, Newton RW, Sprague M, Glencross BD, Little DC. Nutritional characterisation of European aquaculture processing by-products to facilitate strategic utilisation. *Front Sustain Food Syst*. 2021;5:720595. doi:10.3389/fsufs.2021.720595
26. Leong HY, Chang CK, Khoo KS, et al. Waste biorefinery towards a sustainable circular bioeconomy: a solution to global issues. *Biotechnol Biofuels*. 2021;14:87. doi:10.1186/s13068-021-01939-5
27. Lakra WS, Krishnani KK. Circular bioeconomy for stress-resilient fisheries and aquaculture. In: Varjani S, Pandey A, Bhaskar T, Mohan SV, Tsang DCW, eds. *Biomass, Biofuels, Biochemicals: Circular Bioeconomy: Technologies for Biofuels and Biochemicals*. Elsevier; 2022:481-516.
28. Alamerew YA, Kambanou ML, Sakao T, Brissaud D. A multi-criteria evaluation method of product-level circularity strategies. *Sustainability*. 2020;12:5129. doi:10.3390/su12125129
29. Jones SW, Karpol A, Friedman S, Maru BT, Tracy BP. Recent advances in single cell protein use as a feed ingredient in aquaculture. *Curr Opin Biotechnol*. 2020;61:189-197. doi:10.1016/j.copbio.2019.12.026
30. Gamboa-Delgado J, Márquez-Reyes JM. Potential of microbial-derived nutrients for aquaculture development. *Rev Aquac*. 2018; 10(1):224-246. doi:10.1111/raq.12157
31. Velea S, Oancea F, Fischer F. Heterotrophic and mixotrophic microalgae cultivation. In: Gozalez-Fernandez C, Munoz R, eds. *Microalgae-based Biofuels and Bioproductions from Feedstock Cultivation to End-products*. 1st ed. Elsevier; 2017:45-58.
32. Oliveira CYB, Oliveira CDL, Prasad R, et al. A multidisciplinary review of *Tetrademus obliquus*: a microalga suitable for large-scale biomass production and emerging environmental applications. *Rev Aquac*. 2021;13(3):1594-1618. doi:10.1111/raq.12536
33. Yarnold J, Karan H, Oey M, Hankamer B. Microalgal aquafeeds as part of a circular bioeconomy. *Trends Plant Sci*. 2019;24(10):959-970. doi:10.1016/j.tplants.2019.06.005
34. Mohan SV, Modestra JA, Amulya K, Butti SK, Velvizhi G. A circular bioeconomy with biobased products from CO₂ sequestration. *Trends Biotechnol*. 2016;34(6):506-519. doi:10.1016/j.tibtech.2016.02.012
35. Shah MR, Lutz GA, Alam A, et al. Microalgae in Aquafeeds for a sustainable aquaculture industry. *J Appl Phycol*. 2018;30(1):197-213. doi:10.1007/s10811-017-1234-z
36. Jiang M, Zhao HH, Zai SW, Shepherd B, Wen H, Deng DF. A defatted microalgae meal (*Haematococcus pluvialis*) as a partial protein source to replace fishmeal for feeding juvenile yellow perch *Perca flavescens*. *J Appl Phycol*. 2019;31(2):1197-1205. doi:10.1007/s10811-018-1610-3
37. Tibbetts SM, Mann J, Dumas A. Apparent digestibility of nutrients, energy, essential amino acids and fatty acids of juvenile Atlantic salmon (*Salmo salar* L.) diets containing whole-cell or cell-ruptured *Chlorella vulgaris* meals at five dietary inclusion levels. *Aquaculture*. 2017;481:25-39. doi:10.1016/j.aquaculture.2017.08.018
38. Yongmanitchai W, Ward OP. Screening of algae for potential alternative sources of Eicosapentaenoic acid. *Phytochemistry*. 1991;30: 2963-2967. doi:10.1016/S0031-9422(00)98231-1
39. Sukeinik A, Wahnoun R. Biochemical quality of marine unicellular algae with special emphasis on lipid composition. I. *Isochrysis galbana*. *Aquaculture*. 1991;97(1):61-72. doi:10.1016/0044-8486(91)90279-G
40. De Swaaf ME, Sijtsma L, Pronk JT. High-cell-density fed-batch cultivation of the docosahexaenoic acid producing marine alga *Cryptocodinium cohnii*. *Biotechnol Bioeng*. 2003;81:666-672. doi:10.1002/bit.10513
41. Pushparaj B, Buccioni A, Paperi R, et al. Fatty acid composition of Antarctic cyanobacteria. *Phycologia*. 2008;47(4):430-434.
42. Su G, Jiao K, Chang J, et al. Enhancing total fatty acids and arachidonic acid production by the red microalgae *Porphyridium purpureum*. *Bioresour Bioprocess*. 2016;3(1):1-9. doi:10.1186/s40643-016-0110-z
43. Almeyda MD, Scodelaro Bilbao PG, Popovich CA, Constenla D, Leonardi PI. Enhancement of polyunsaturated fatty acid production under low-temperature stress in *Cylindrotheca closterium*. *J Appl Psychol*. 2020;32(2):989-1001. doi:10.1007/s10811-020-02047-x
44. Batista AP, Gouveia L, Bandarra NM, Franco JM, Raymundo A. Comparison of microalgal biomass profiles as novel functional ingredient for food products. *Algal Res*. 2013;2(2):164-173. doi:10.1016/j.algal.2013.01.004
45. Bonfanti C, Cardoso C, Afonso C, et al. Potential of microalga *Isochrysis galbana*: bioactivity and bioaccessibility. *Algal Res*. 2018;29: 242-248. doi:10.1016/j.algal.2017.11.035
46. Ohse S, Derner RB, Ozório RÁ, Corrêa RG, Furlong EB, Cunha PCR. Lipid content and fatty acid profiles in ten species of microalgae. *Ideia*. 2015;33(1):93-101.
47. Takagi T, Kaneniwa M, Itabashi Y. Fatty acids in Crinoidea and Ophiuroidea: occurrence of all-cis-6, 9, 12, 15, 18, 21-tetracosahexaenoic acid. *Lipids*. 1986;21(7):430-433. doi:10.1007/BF02536398
48. Dastager SG, Lee JC, Pandey A, Kim CJ. *Nocardioides mesophilus* sp. nov., isolated from soil. *Int J Syst Evol*. 2010;60(10):2288-2292. doi:10.1099/ijs.0.019059-0
49. Román-Ponce B, Millán-Aguiñaga N, Guillen-Matus D, et al. Six novel species of the obligate marine actinobacterium *Salinispora*, *Salinispora cortesiana* sp. nov., *Salinispora fenicalii* sp. nov., *Salinispora goodfellowii* sp. nov., *Salinispora mooreana* sp. nov., *Salinispora*

- oceanensis* sp. nov. and *Salinispora vitiensis* sp. nov. and emended description of the genus *Salinispora*. *Int J Syst Evol*. 2020;70(8):4668-4682. doi:10.1099/ijsem.0.004330
50. Ratledge C. Microbial oils: an introductory overview of current status and future prospects. *Ocl*. 2013;20(6):D602. doi:10.1051/oc/2013029
 51. Lorenz RT, Cysewski GR. Commercial potential for *Haematococcus microalgae* as a natural source of astaxanthin. *Trends Biotechnol*. 2000;18(4):160-167. doi:10.1016/s0167-7799(00)01433-5
 52. Becker W. Microalgae for aquaculture—the nutritional value of microalgae for aquaculture. In: Richmond A, ed. *Handbook of Microalgal Culture: Biotechnology and Applied Phycology*. Blackwell Publishing Ltd; 2004a:380-390.
 53. Ambati RR, Phang SM, Ravi S, Aswathanarayana RG. Astaxanthin: sources, extraction, stability, biological activities and its commercial applications—a review. *Mar Drugs*. 2014;12(1):128-152. doi:10.3390/md12010128
 54. Torrissen OJ, Christiansen R. Requirements for carotenoids in fish diets. *J Appl Ichthyol*. 1995;11(3-4):225-230. doi:10.1111/j.1439-0426.1995.tb00022.x
 55. Becker W. Microalgae in human and animal nutrition. In: Richmond A, ed. *Handbook of Microalgal Culture: Biotechnology and Applied Phycology*. Blackwell Publishing Ltd.; 2004b:312-351.
 56. Rammuni MN, Ariyadasa TU, Nimarshana PHV, Attalage RA. Comparative assessment on the extraction of carotenoids from microalgal sources: Astaxanthin from *H. pluvialis* and beta-carotene from *D. salina*. *Food Chem*. 2019;277:128-134. doi:10.1016/j.foodchem.2018.10.066
 57. Goiris K, Muylaert K, Fraeye I, Foubert I, De Brabanter J, De Cooman L. Antioxidant potential of microalgae in relation to their phenolic and carotenoid content. *J Appl Phycol*. 2012;24(6):1477-1486. doi:10.1007/s10811-012-9804-6
 58. Guedes AC, Amaro HM, Malcata FX. Microalgae as sources of carotenoids. *Mar Drugs*. 2011;9(4):625-644. doi:10.3390/md9040625
 59. Sansone C, Brunet C. Promises and challenges of microalgal antioxidant production. *Antioxidants*. 2019;8(7):199. doi:10.3390/antiox8070199
 60. Maliwat GC, Velasquez S, Robil JL, et al. Growth and immune response of giant freshwater prawn *Macrobrachium rosenbergii* (De man) postlarvae fed diets containing *Chlorella vulgaris* (Beijerinck). *Aquacult Res*. 2017;48(4):1666-1676. doi:10.1111/are.13004
 61. Madhumathi M, Rengasamy R. Antioxidant status of *Penaeus monodon* fed with *Dunaliella salina* supplemented diet and resistance against WSSV. *Int J Eng Sci Technol*. 2011;3(10):7249-7259.
 62. Finnigan T, Needham L, Abbott C, et al. Mycoprotein: a healthy new protein with a low environmental impact. In: Nadathur SR, ed. *Sustainable Protein Sources*. Academic Press; 2017:305-325.
 63. Katya K, Yun Y, Park G, Lee JY, Yoo G, Bai SC. Evaluation of the efficacy of fermented by-product of mushroom, *Pleurotus ostreatus*, as a fish meal replacer in juvenile Amur catfish, *Silurus asotus*: effects on growth, serological characteristics and immune responses. *Asian-Australas J Anim Sci*. 2014;27(10):1478-1486. doi:10.5713/ajas.2014.14038
 64. Srichanun M, Nganwisuthiphan T, Wanlem S, Rakkamon T. Effects of different mushroom by-product types and levels on growth performance and survival rate in dietary of Nile tilapia (*Oreochromis niloticus*). *Int J Agric Technol*. 2017;13(7.1):1093-1101.
 65. Sarlin PJ, Philip R. Marine yeasts as feed supplement for Indian white prawn *Fenneropenaeus indicus*: screening and testing the efficacy. *Int J Curr Microbiol App Sci*. 2016;5(1):55-70. doi:10.20546/ijcmas.2016.501.005
 66. Mohan K, Ravichandran S, Muralisankar T, et al. Potential uses of fungal polysaccharides as immunostimulants in fish and shrimp aquaculture: a review. *Aquaculture*. 2019;500:250-263. doi:10.1016/j.aquaculture.2018.10.023
 67. NCT D, Yatip P, Krataitong K, et al. Culture medium from a marine endophytic fungus protects shrimp against acute hepatopancreatic necrosis disease (AHPND). *Aquaculture*. 2022;547:737528. doi:10.1016/j.aquaculture.2021.737528
 68. Altunok M, Ozkaya FC, Engin S, Tanrikul TT, Aydinlik S, Ulukaya E. In vitro antibacterial activity of sponge-associated fungi against bacterial aquaculture pathogens. *Fresen Environ Bull*. 2015;24(6A):2158-2166.
 69. Özkaya FC, Peker Z, Camas M, Camas AS, Altunok M. Marine fungi against aquaculture pathogens and induction of the activity via co-culture. *Clean-Soil Air Water*. 2017;45(8):1700238. doi:10.1002/clen.201700238
 70. Xu P, Ding L, Wei J, et al. New aquatic pathogen inhibitor produced by the marine fungus *aspergillus* sp. LS116. *Aquaculture*. 2020;520:734670. doi:10.1016/j.aquaculture.2019.734670
 71. Wang W, Li Q, Lai Q, Lin Y, Zhang Q. Chen j. screening of anti-vibrio activity of marine fungal methanolic fractions to control vibriosis in white shrimp (*Litopenaeus vannamei*). *Aqua Res*. 2021;52(11):5517-5526. doi:10.1111/are.15425
 72. Schar D, Zhao C, Wang Y, Larsson DG, Gilbert M, Van Boeckel TP. Twenty-year trends in antimicrobial resistance from aquaculture and fisheries in Asia. *Nat Commun*. 2021;12(1):1-10. doi:10.1038/s41467-021-25655-8
 73. Ma N, Guo P, Zhang J, et al. Nutrients mediate intestinal bacteria-mucosal immune crosstalk. *Front Immunol*. 2018;9:5. doi:10.3389/fimmu.2018.00005
 74. Pagliari D, Saviano A, Newton EE, et al. Gut microbiota-immune system crosstalk and pancreatic disorders. *J Mediat Inflamm*. 2018;2018:1-13. doi:10.1155/2018/7946431
 75. Udayangani RMC, Dananjaya SHS, Nikapitiya C, Heo GJ, Lee J, Zoysa MD. Metagenomics analysis of gut microbiota and immune modulation in zebrafish (*Danio rerio*) fed chitosan silver nanocomposites. *Fish Shellfish Immunol*. 2017;66:173-184. doi:10.1016/j.fsi.2017.05.018
 76. Yang C, Chen S, Lu C, Chen S, Lai K, Liao W. Effect of mushroom beta glucan (MBG) on immune and haemocyte response in Pacific white shrimp (*Litopenaeus vannamei*). *J Aquac Res Dev*. 2014a;5(6):1-5. doi:10.4172/2155-9546.1000275
 77. Yang F, Nie Q, Chen C. Effects of yeast cell wall polysaccharides on growth performance, immune and anti-stress ability of *Carassius auratus gibelio*. *China Feed*. 2014b;7:017.
 78. Song X, Feng Z, Tan J, Wang Z, Zhu W. Dietary administration of *Pleurotus ostreatus* polysaccharides (POPS) modulates the non-specific immune response and gut microbiota diversity of *Apostichopus japonicus*. *Aquaculture Reports*. 2021;19:100578. doi:10.1016/j.aqrep.2020.100578
 79. Derbyshire EJ, Delange J. Fungal protein—what is it and what is the health evidence? A systematic review focusing on mycoprotein. *Front Sustain Food Syst*. 2020;5:581682. doi:10.3389/fsufs.2021.581682
 80. Mahboubi A, Ferreira JA, Taherzadeh MT, Lennartsson PR. Production of fungal biomass for feed, fatty acids, and glycerol by *Aspergillus oryzae* from fat-rich dairy substrates. *Fermentation*. 2017;3:48. doi:10.3390/fermentation3040048
 81. Souza Filho PF, Andersson D, Ferreira JA, Taherzadeh MJ. Mycoprotein: environmental impact and health aspects. *World J Microbiol Biotechnol*. 2019;35:147. doi:10.1007/s11274-019-2723-9
 82. Satari B, Karimi K. Mucoralean fungi for sustainable production of bioethanol and biologically active molecules. *Appl Microbiol Biotechnol*. 2018;102:1097-1117. doi:10.1007/s00253-017-8691-9
 83. Roustani N, Ferreira JA, Taherzadeh MJ. Production of L-carnitine-enriched edible filamentous fungal biomass through submerged

- cultivation. *Bioengineered*. 2021;12(1):358-368. doi:10.3389/fmars.2020.00178
84. Ahlborn J, Stephan A, Meckel T, Maheshwari G, Rühl M, Zorn H. Upcycling of food industry side streams by basidiomycetes for production of a vegan protein source. *Int J Recycl Org Waste Agric*. 2019;8(Suppl 1):447-455. doi:10.1007/s40093-019-00317-4
 85. Awasthi MK, Ferreira JA, Sirohi R, et al. A critical review on the development stage of biorefinery systems towards the management of apple processing-derived waste. *Renew Sustain Energy Rev*. 2021; 143:110972. doi:10.1016/j.rser.2021.110972
 86. Lopez-Linares JC, García-Cubero MT, Coca M, Lucas S. A biorefinery approach for the valorization of spent coffee grounds to produce antioxidant compounds and biobutanol. *Biomass Bioenergy*. 2021; 147:106026.
 87. Sar T, Ozturk M, Taherzadeh MJ, Ferreira JA. New insights on protein recovery from olive oil mill wastewater through bioconversion with edible filamentous fungi. *Processes*. 2020;8:1210. doi:10.3390/pr8101210
 88. Sar T, Ferreira JA, Taherzadeh MJ. Conversion of fish processing wastewater into fish feed ingredients through submerged cultivation of *Aspergillus oryzae*. *SMAB*. 2021;1:100-110. doi:10.1007/s43393-020-00009-5
 89. Ahumada-Rudolph R, Novoa V, Becerra J, Cespedes C, Cabrera-Pardo JR. Mycoremediation of oxytetracycline by marine fungi mycelium isolated from salmon farming areas in the south of Chile. *Food Chem Toxicol*. 2021;152:112198. doi:10.1016/j.fct.2021.112198
 90. Reverter M, Sarter S, Caruso D, et al. Aquaculture at the crossroads of global warming and antimicrobial resistance. *Nat Commun*. 2020; 11(1):1870. doi:10.1038/s41467-020-15735-6
 91. Cha J, Carlson KH. Biodegradation of veterinary antibiotics in lagoon waters. *Process Saf Environ Protect*. 2019;127:306-313. doi:10.1016/j.psep.2019.04.009
 92. Sharma B, Dangi AK, Shukla P. Contemporary enzyme based technologies for bioremediation: a review. *J Environ Manage*. 2018; 210(15):10-22. doi:10.1016/j.jenvman.2017.12.075
 93. Akhtara N, Mannan MAU. Mycoremediation: expunging environmental pollutants. *Biotechnol Rep*. 2020;26:e00452. doi:10.1016/j.btre.2020.e00452
 94. Mass PAY, Kleinschuster SJ, Dykstra MJ, Smolowitz R, Parent J. Molecular characterization of QPX (quahog parasite unknown), a pathogen of *Mercenaria mercenaria*. *J Shellfish Res*. 1999;18: 561-567.
 95. Porter D. Phylum Labyrinthulomycota. In: Margulis L, Corliss JO, Melkonian M, Chapman DJ, eds. *Handbook of Protoctista*. Jones and Bartlett; 1990:388-398.
 96. Raghukumar S. Bacterivory: a novel dual role for thraustochytrids in the sea. *Mar Biol*. 1992;113:165-169.
 97. Chang KJL, Nichols CM, Blackburn SI, Dunstan GA, Koutoulis A, Nichols PD. Comparison of thraustochytrids *Aurantiochytrium* sp., *Schizochytrium* sp., *Thraustochytrium* sp., and *Ulkenia* sp. for production of biodiesel, long-chain omega-3 oils, and exopolysaccharide. *Marine Biotechnol*. 2014;16(4):396-411.
 98. Marchan LF, Chang KJL, Nichols PD, Mitchell WJ, Polglase JL, Gutierrez T. Taxonomy, ecology and biotechnological applications of thraustochytrids: a review. *Biotechnol Adv*. 2018;36:26-46. doi:10.1016/j.biotechadv.2017.09.003
 99. Naganuma T, Takasugi H, Kimura H. Abundance of thraustochytrids in coastal plankton. *Mar Ecol Prog Ser*. 1998;162:105-110. doi:10.3354/meps162105
 100. Liu Y, Singh P, Liang Y, et al. Abundance and molecular diversity of thraustochytrids in coastal waters of southern China. *FEMS Microbiol Ecol*. 2017;93(6):1-9. doi:10.1093/femsec/fix070
 101. Rinkevich B. Cell cultures from marine invertebrates: obstacles, new approaches and recent improvements. *J Biotechnol*. 1999;70:133-153. doi:10.1016/S0168-1656(99)00067-X
 102. Rabinowitz C, Douek J, Weisz E, Shabtay A, Rinkevich B. Isolation and characterization of four novel thraustochytrid strains from a colonial tunicate. *Indian J Mar Sci*. 2006;35:341-350.
 103. Grasele JJ, Pomponi SA, Rinkevich B, Grima J. Efforts to develop a cultured sponge cell line: revisiting an intractable problem. *In Vitro Cell Dev Biol Anim*. 2012;48:12-20. doi:10.1007/s11626-011-9469-5
 104. Qarri A, Rinkevich Y, Rinkevich B. Employing marine invertebrate cell cultures media for isolation and cultivation of thraustochytrids. *Bot Mar*. 2021;64(6):447-454. doi:10.1515/bot-2021-0035
 105. Mo C, Rinkevich B. A simple, reliable and fast protocol for thraustochytrids DNA extraction. *Marine Biotechnol*. 2001;3:100-102. doi:10.1007/s101260000069
 106. Mo C, Douek J, Rinkevich B. Development of a PCR strategy for thraustochytrids identification based on 18S-rDNA sequence. *J Mar Biol*. 2002;140:883-889. doi:10.1007/s00227-002-0778-9
 107. Gupta A, Barrow CJ, Puri M. Multiproduct biorefinery from marine thraustochytrids towards a circular bioeconomy. *Trends Biotechnol*. 2022;40(4):448-462. doi:10.1016/j.tibtech.2021.09.003
 108. Baldikova E, Mullerova S, Prochazkova J, et al. Use of waste *Japono-chytrium* sp. biomass after lipid extraction as an efficient adsorbent for triphenylmethane dye applied in aquaculture. *Biomass Conv Bioref*. 2019;9:479-488. doi:10.1007/s13399-018-0362-2
 109. FAO (Food and Agriculture Organization). 2017. Genetic resources for microorganisms of current and potential use in aquaculture. Thematic Background Study No. 2, 43 p. <http://www.fao.org/cofi/46054-0758de68f3799088c2c9633d04d81a313.pdf>
 110. Li MH, Robinson EH, Tucker CS, Manning BB, Khoo L. Effects of dried algae *Schizochytrium* sp., a rich source of docosahexaenoic acid, on growth, fatty acid composition, and sensory quality of channel catfish *Ictalurus punctatus*. *Aquaculture*. 2009;292:232-236. doi:10.1016/j.aquaculture.2009.04.033
 111. Glencross B, Rutherford N. A determination of the quantitative requirements for docosahexaenoic acid for juvenile barramundi (*Lates calcarifer*). *Aquacult Nutr*. 2011;17(2):e536-e548.
 112. Van Hoestenbergh S, Fransman C-A, Luyten T, et al. Schizochytrium as a replacement for fish oil in a fishmeal free diet for jade perch, *Scortum barcoo* (McCulloch & Waite). *Aquacult Res*. 2014;47: 1747-1760. doi:10.1111/are.12631
 113. Sprague M, Walton J, Campbell P, Strachan F, Dick JR, Bell JG. Replacement of fish oil with a DHA-rich algal meal derived from *Schizochytrium* sp. on the fatty acid and persistent organic pollutant levels in diets and flesh of Atlantic salmon (*Salmo salar*, L.) post-smolts. *Food Chem*. 2015;185:413-421. doi:10.1016/j.foodchem.2015.03.150
 114. Raghukumar S. Ecology of the marine protists, the Labyrinthulomycetes (Thraustochytrids and Labyrinthulids). *Eur J Protistol*. 2002; 38(2):127-145. doi:10.1078/0932-4739-00832
 115. Gupta A, Barrow CJ, Puri M. Omega-3 biotechnology: Thraustochytrids as a novel source of omega-3 oils. *Biotechnol Adv*. 2012;30: 1733-1745. doi:10.1016/j.biotechadv.2012.02.014
 116. Soheidein MNA, Wan WAAQI, Ilham Z, Babadi AA, Hui-Yin Y, Siew-Moi P. Vital parameters for biomass, lipid, and carotenoid production of thraustochytrids. *J Appl Phycol*. 2020;32:1003-1016. doi:10.1007/s10811-019-01970-y
 117. Singh P, Liu Y, Li L, Wang G. Ecological dynamics and biotechnological implications of Thraustochytrids from marine habitats. *Appl Microbiol Biotechnol*. 2014;98:5789-5805. doi:10.1007/s00253-014-5780-x
 118. Aasen IM, Ertesvåg H, Heggset TMB, et al. Thraustochytrids as production organisms for docosahexaenoic acid (DHA), squalene, and carotenoids. *Appl Microbiol Biotechnol*. 2016;100:4309-4321. doi:10.1007/s00253-016-7498-4
 119. Rotter A, Barbier M, Bertoni F, et al. The essentials of marine biotechnology. *Front Mar Sci*. 2021;8:158. doi:10.3389/fmars.2021.629629



120. Burja AM, Radianingtyas H, Windust A, Barrow CJ. Isolation and characterization of polyunsaturated fatty acid producing *Thraustochytrium* species: screening of strains and optimization of omega-3 production. *Appl Microbiol Biotechnol.* 2006;72(6):1161-1169. doi:10.1007/s00253-006-0419-1
121. Zhu L, Zhang X, Ji L, Song X, Kuang C. Changes of lipid content and fatty acid composition of *Schizochytrium limacinum* in response to different temperatures and salinities. *Process Biochem.* 2007;42(2):210-214. doi:10.1016/j.procbio.2006.08.002
122. Chang KJ, Parrish CC, Simon CJ, Revill AT, Nichols PD. Feeding whole thraustochytrid biomass to cultured Atlantic Salmon (*Salmo salar*) fingerlings: culture performance and fatty acid incorporation. *J Mar Sci Eng.* 2020;8(3):207. doi:10.3390/jmse8030207
123. Miller MR, Nichols PD, Carter CG., replacement of fish oil with thraustochytrid *Schizochytrium* sp. L oil in Atlantic salmon parr (*Salmo salar* L) diets. *Comp Biochem Physiol Part A Mol Integr Physiol.* 2007;148:382-392. doi:10.1016/j.cbpa.2007.05.018
124. Sarker PK, Kapuscinski AR, Lanois AJ, Livesey ED, Bernhard KP, Coley ML. Towards sustainable aquafeeds: complete substitution of fish oil with marine microalgae *Schizochytrium* sp. improves growth and fatty acid deposition in juvenile Nile tilapia (*Oreochromis niloticus*). *PLoS One.* 2016;11:e0156684. doi:10.1371/journal.pone.0156684
125. Allen KM, Habte-Tsion HM, Thompson KR, Filer K, Tidwell JH, Kumar V. Freshwater microalgae (*Schizochytrium* sp.) as a substitute to fish oil for shrimp feed. *Sci Rep.* 2019;9:6178. doi:10.1038/s41598-019-41020-8
126. Yamasaki T, Aki T, Mori Y, et al. Nutritional enrichment of larval fish feed with thraustochytrid producing polyunsaturated fatty acids and xanthophylls. *J Biosci Bioeng.* 2007;104(3):200-206. doi:10.1263/jbb.104.200
127. Nasser A, Rasoul-Amini S, Morowvat M, Ghasemi Y. Single cell protein: production and process. *Am J Food Technol.* 2011;6(2):103-116. doi:10.3923/ajft.2011.103.116
128. Ritala A, Häkkinen ST, Toivari M, Wiebe MG. Single cell protein—state-of-the-art, industrial landscape and patents 2001–2016. *Front Microbiol.* 2017;8:2009. doi:10.3389/fmicb.2017.02009
129. Aas TS, Grisdale-Helland B, Terjesen BF, Helland SJ. Improved growth and nutrient utilisation in Atlantic salmon (*Salmo salar*) fed diets containing a bacterial protein meal. *Aquaculture.* 2006;259(1-4):365-376. doi:10.1016/j.aquaculture.2006.05.032
130. Glencross B, Irvin S, Arnold S, Blyth D, Bourne N, Preston N. Effective use of microbial biomass products to facilitate the complete replacement of fishery resources in diets for the black tiger shrimp, *Penaeus monodon*. *Aquaculture.* 2014;431:12-19. doi:10.1016/j.aquaculture.2014.02.033
131. Glencross B, Arnold S, Irvin S. Bioactive factors in microbial biomass have the capacity to offset reductions in the level of protein in the diet of black tiger shrimp, *Penaeus monodon*. *Aquaculture.* 2015a;446:74-79. doi:10.1016/j.aquaculture.2015.04.007
132. Arnold S, Smullen R, Briggs M, West M, Glencross B. The combined effect of feed frequency and ration size of diets with and without microbial biomass on the growth and feed conversion of juvenile *Penaeus monodon*. *Aquacult Nutr.* 2016;22(6):1340-1347. doi:10.1111/anu.12338
133. Chumpol S, Kantachote D, Nitoda T, Kanzaki H. Administration of purple nonsulfur bacteria as single cell protein by mixing with shrimp feed to enhance growth, immune response and survival in white shrimp (*Litopenaeus vannamei*) cultivation. *Aquaculture.* 2018;489:85-95. doi:10.1016/j.aquaculture.2018.02.009
134. Wang J, Chen L, Xu J, et al. C1 gas protein: a potential protein substitute for advancing aquaculture sustainability. *Rev Aquac.* 2022. doi:10.1111/raq.12707
135. Øverland M, Tauson AH, Shearer K, Skrede A. Evaluation of methane-utilising bacteria products as feed ingredients for monogastric animals. *Arch Anim Nutr.* 2010;64(3):171-189. doi:10.1080/17450391003691534
136. Dantas JE, Valle B, Brito C, Calazans N, Peixoto S, Soares R. Partial replacement of fishmeal with biofloc meal in the diet of postlarvae of the Pacific white shrimp *Litopenaeus vannamei*. *Aquacult Nutr.* 2016;22(2):335-342. doi:10.1111/anu.12249
137. Tlustý M, Rhyne A, Szczebak JT, et al. A transdisciplinary approach to the initial validation of a single cell protein as an alternative protein source for use in aquafeeds. *Peer J.* 2017;5:e3170.
138. Hamidoghli A, Yun H, Won S, Kim S, Farris NW, Bai SC. Evaluation of a single-cell protein as a dietary fish meal substitute for whiteleg shrimp *Litopenaeus vannamei*. *Fish Sci.* 2019;85(1):147-155. doi:10.1007/s12562-018-1275-5
139. Hardy RW, Patro B, Pujol-Baxley C, Marx CJ, Feinberg L. Partial replacement of soybean meal with *Methylobacterium extorquens* single-cell protein in feeds for rainbow trout (*Oncorhynchus mykiss* Walbaum). *Aquacult Res.* 2018;49(6):2218-2224. doi:10.1111/are.13678
140. Romarheim OH, Øverland M, Mydland LT, Skrede A, Landsverk T. Bacteria grown on natural gas prevent soybean meal-induced enteritis in Atlantic salmon. *J Nutr.* 2011;141(1):124-130. doi:10.3945/jn.110.128900
141. Sellars MJ, Rao M, Polymeris N, et al. Feed containing Novacq improves resilience of black tiger shrimp, *Penaeus monodon*, to gill-associated virus-induced mortality. *J World Aquac Soc.* 2015;46(3):328-336. doi:10.1111/jwas.12190
142. Ayub F, Seychelles L, Strauch O, Wittke M, Ehlers RU. Monoxenic liquid culture with *Escherichia coli* of the free-living nematode *Panagrolaimus* sp.(strain NFS 24-5), a potential live food candidate for marine fish and shrimp larvae. *Appl Microbiol Biotechnol.* 2013;97(18):8049-8055. doi:10.1007/s00253-013-5061-0
143. Sánchez-Saavedra M, Paniagua-Chávez C. Potential of refrigerated marine cyanobacterium *Synechococcus elongatus* used as food for *Artemia franciscana*. *Lat Am J Aquat Res.* 2017;45(5):937-947. doi:10.3856/vol45-issue5-fulltext-9
144. Isa NFM, Loo PL, Sabaratnam V. Waste-grown heterotrophic microorganisms improve the production of *Apocyclops dengizicus*. *Aquaculture.* 2020;528:735566. doi:10.1016/j.aquaculture.2020.735566
145. Loo P, Vikineswary S, Chong V. Nutritional value and production of three species of purple non-Sulphur bacteria grown in palm oil mill effluent and their application in rotifer culture. *Aquacult Nutr.* 2013;19(6):895-907. doi:10.1111/anu.12035
146. Ochoa-Solano JL, Olmos-Soto J. The functional property of bacillus for shrimp feeds. *Food Microbiol.* 2006;23(6):519-525. doi:10.1016/j.fm.2005.10.004
147. Soto JO, de Jesús Paniagua-Michel J, Lopez L, Ochoa L. Functional feeds in aquaculture. In: Kim SK, ed. *Springer handbook of marine biotechnology*. Springer; 2015:1303-1319.
148. Verschuere L, Rombaut G, Sorgeloos P, Verstraete W. Probiotic bacteria as biological control agents in aquaculture. *Microbiol Mol Biol Rev.* 2000;64(4):655-671. doi:10.1128/MMBR.64.4.655-671.2000
149. Domínguez-Borbor C, Ardiles V, Bermeo M, et al. The marine symbiont *Pseudovibrio denitrificans*, is effective to control pathogenic vibrio spp. in shrimp aquaculture. *Aquaculture.* 2019;508:127-136. doi:10.1016/j.aquaculture.2019.04.077
150. Rather IA, Galope R, Bajpai VK, Lim J, Paek WK, Park YH. Diversity of marine bacteria and their bacteriocins: applications in aquaculture. *Rev Fish Sci Aquac.* 2017;25(4):257-269. doi:10.1080/23308249.2017.1282417
151. Prado S, Barja JL, Luzardo A, Dubert J, Blanco J. Encapsulation of live marine bacteria for use in aquaculture facilities and process evaluation using response surface methodology. *Appl Microbiol Biotechnol.* 2020;104(5):1993-2006. doi:10.1007/s00253-019-10332-0



152. Marques A, Thanh TH, Sorgeloos P, Bossier P. Use of microalgae and bacteria to enhance protection of gnotobiotic *Artemia* against different pathogens. *Aquaculture*. 2006;258(1-4):116-126. doi:10.1016/j.aquaculture.2006.04.021
153. Das S, Ward LR, Burke C. Screening of marine *Streptomyces* spp. for potential use as probiotics in aquaculture. *Aquaculture*. 2010;305(1-4):32-41. doi:10.1016/j.aquaculture.2010.04.001
154. Desriac F, Le Chevalier P, Brillet B, et al. Exploring the hologenome concept in marine bivalvia: haemolymph microbiota as a pertinent source of probiotics for aquaculture. *FEMS Microbiol Lett*. 2014;350(1):107-116. doi:10.1111/1574-6968.12308
155. Ringø E, Hoseinifar SH, Ghosh K, Doan HV, Beck BR, Song SK. Lactic acid bacteria in finfish—an update. *Front Microbiol*. 2018;9:1818. doi:10.3389/fmicb.2018.01818
156. Tarkhani R, Imani A, Hoseinifar SH, et al. Comparative study of host-associated and commercial probiotic effects on serum and mucosal immune parameters, intestinal microbiota, digestive enzymes activity and growth performance of roach (*Rutilus rutilus caspicus*) fingerlings. *Fish Shellfish Immunol*. 2020;98:661-669. doi:10.1016/j.fsi.2019.10.063
157. Niu KM, Kothari D, Lee WD, et al. Probiotic potential of the farmed olive flounder, *Paralichthys olivaceus*, autochthonous gut microbiota. *Probiotics Antimicrob*. 2021;13(4):1106-1118. doi:10.1007/s12602-021-09762-y
158. Lazado CC, Caipang CM, Estante EG. Prospects of host-associated microorganisms in fish and penaeids as probiotics with immunomodulatory functions. *Fish Shellfish Immunol*. 2015;45(1):2-12. doi:10.1016/j.fsi.2015.02.023
159. Borges N, Keller-Costa T, Sanches-Fernandes GMM, Louvado A, Gomes NCM, Costa R. Bacteriome structure, function, and probiotics in fish larviculture: the good, the bad, and the gaps. *Annu Rev Anim Biosci*. 2021;9:423-452. doi:10.1146/annurev-animal-062920-113114
160. Alonso S, Carmen Castro M, Berdasco M, de la Banda IG, Moreno-Ventas X, de Rojas AH. Isolation and partial characterization of lactic acid bacteria from the gut microbiota of marine fishes for potential application as probiotics in aquaculture. *Probiotics Antimicrob Proteins*. 2019;11(2):569-579. doi:10.1007/s12602-018-9439-2
161. Gatesoupe FJ. Lactic acid bacteria increase the resistance of turbot larvae, *Scophthalmus maximus*, against pathogenic vibrio. *Aquat Living Resour*. 1994;7(4):277-282. doi:10.1051/alr:1994030
162. Ringø E, Jostensen JP, Olsen RE. Production of eicosapentaenoic acid by freshwater vibrio. *Lipids*. 1992;27:564-566. doi:10.1007/BF02536141
163. Dailey FE, McGraw JE, Jensen BJ, et al. The microbiota of freshwater fish and freshwater niches contain omega-3 fatty acid-producing *Shewanella* species. *Appl Environ Microbiol*. 2015;82(1):218-231. doi:10.1128/AEM.02266-15
164. Nagappan S, Das P, AbdulQuadir M, et al. Potential of microalgae as a sustainable feed ingredient for aquaculture. *J Biotechnol*. 2021;341:1-20.
165. Ahmad A, Hassan SW, Banat F. An overview of microalgae biomass as a sustainable aquaculture feed ingredient: food security and circular economy. *Bioengineered*. 2022;13(4):9521-9547.
166. Moreira A, Cruz S, Marques R, Cartaxana P. The underexplored potential of green macroalgae in aquaculture. *Rev Aquac*. 2022;14(1):5-26. doi:10.1111/raq.12580
167. Vatsos IN, Rebours C. Seaweed extracts as antimicrobial agents in aquaculture. *J Appl Phycol*. 2015;27(5):2017-2035. doi:10.1007/s10811-014-0506-0
168. Philis G, Gracey EO, Gansel LC, Fet AM, Rebours C. Comparing the primary energy and phosphorus consumption of soybean and seaweed-based aquafeed proteins—a material and substance flow analysis. *J Clean Prod*. 2018;200:1142-1153. doi:10.1016/j.jclepro.2018.07.247
169. Emblemsvåg J, Kvadsheim NP, Halfdanarson J, et al. Strategic considerations for establishing a large-scale seaweed industry based on fish feed application: a Norwegian case study. *J Appl Phycol*. 2020;32(6):4159-4169. doi:10.1007/s10811-020-02234-w
170. Koesling M, Kvadsheim NP, Halfdanarson J, Emblemsvåg J, Rebours C. Environmental impacts of protein-production from farmed seaweed: comparison of possible scenarios in Norway. *J Clean Prod*. 2021;307:127301. doi:10.1016/j.jclepro.2021.127301
171. Stévant P, Rebours C. Landing facilities for processing of cultivated seaweed biomass: a Norwegian perspective with strategic considerations for the European seaweed industry. *J Appl Phycol*. 2021;33(5):3199-3214.
172. Dawood MA, Koshio S. Application of fermentation strategy in aquafeed for sustainable aquaculture. *Rev Aquac*. 2020;12(2):987-1002. doi:10.1111/raq.12368
173. Wan AH, Soler-Vila A, O'Keeffe D, Casburn P, Fitzgerald R, Johnson MP. The inclusion of *Palmaria palmata* macroalgae in Atlantic salmon (*Salmo salar*) diets: effects on growth, haematology, immunity and liver function. *J Appl Phycol*. 2016;28(5):3091-3100. doi:10.1007/s10811-016-0821-8
174. Ikeda-Ohtsubo W, López Nadal A, Zaccaria E, et al. Intestinal microbiota and immune modulation in zebrafish by fucoidan from *Okina mozuku* (*Cladosiphon okamuranus*). *Front Nutr*. 2020;6:7:1-12. doi:10.3389/fnut.2020.00067
175. Cahu C, Infante JZ. Substitution of live food by formulated diets in marine fish larvae. *Aquaculture*. 2001;200:161-180. doi:10.1016/S0044-8486(01)00699-8
176. FernandezDiaz C, Yufera M. Detecting growth in gilthead seabream, *Sparus aurata* L, larvae fed microcapsules. *Aquaculture*. 1997;153(1-2):93-102. doi:10.1016/S0044-8486(97)00017-3
177. Bruno E, Hojgaard JK, Hansen BW, Munk P, Stotttrup JG. Influence of swimming behavior of copepod nauplii on feeding of larval turbot (*Scophthalmus maximus*). *Aquac Int*. 2018;26:225-236. doi:10.1007/s10499-017-0199-x
178. Naess T, Germainhenry M, Naas KE. First feeding of Atlantic halibut (*Hippoglossus hippoglossus*) using different combinations of artemia and wild zooplankton. *Aquaculture*. 1995;130:235-250. doi:10.1016/0044-8486(94)00323-g
179. Rainuzzo JR, Reitan KI, Olsen Y. The significance of lipids at early stages of marine fish: a review. *Aquaculture*. 1997;155(1-4):103-115. doi:10.1016/S0044-8486(97)00121-x
180. Sargent JR, McEvoy LA, Bell JG. Requirements, presentation and sources of polyunsaturated fatty acids in marine fish larval feeds. *Aquaculture*. 1997;155(1-4):117-127. doi:10.1016/S0044-8486(97)00122-1
181. Sorgeloos P, Dhert P, Candrea P. Use of the brine shrimp, *Artemia* spp., in marine fish larviculture. *Aquaculture*. 2001;200(1-2):147-159. doi:10.1016/S0044-8486(01)00698-6
182. Dhert P, Rombaut G, Suantika G, Sorgeloos P. Advancement of rotifer culture and manipulation techniques in Europe. *Aquaculture*. 2001;200(1-2):129-146. doi:10.1016/S0044-8486(01)00697-4
183. Drillet G, Jorgensen NOG, Sorensen TF, Ramlov H, Hansen BW. Biochemical and technical observations supporting the use of copepods as live feed organisms in marine larviculture. *Aquacult Res*. 2006;37(8):756-772. doi:10.1111/j.1365-2109.2006.01489.x
184. Payne MF, Rippingale RJ, Cleary JJ. Cultured copepods as food for West Australian dhufish (*Glaucosoma hebraicum*) and pink snapper (*Pagrus auratus*) larvae. *Aquaculture*. 2001;194(1-2):137-150. doi:10.1016/S0044-8486(00)00513-5
185. Pedersen BH. The intestinal evacuation rates of larval herring (*Clupea harengus* L.) predating on wild plankton. *Dana*. 1984;3:21-30.
186. Munillamorán R, Stark JR, Barbour A. The role of exogenous enzymes in digestion in cultured turbot larvae (*Scophthalmus maximus* L.). *Aquaculture*. 1990;88(3-4):337-350. doi:10.1016/0044-8486(90)90159-k

187. Sun B, Fleegeer JW. Sustained mass culture of *Amphiascoides atopus* a marine harpacticoid copepod in a recirculating system. *Aquaculture*. 1995;136(3–4):313–321. doi:10.1016/0044-8486(95)01064-5
188. Lindley LC, Phelps RP. Production and collection of copepod Nauplii from brackish water ponds. *J Appl Aquac*. 2009;21(2):96–109. doi:10.1080/10454430902892867
189. Sorensen TF, Drillet G, Engell-Sorensen K, Hansen BW, Ramlov H. Production and biochemical composition of eggs from neritic calanoid copepods reared in large outdoor tanks (Limfjord, Denmark). *Aquaculture*. 2007;263(1–4):84–96. doi:10.1016/j.aquaculture.2006.12.001
190. Jepsen PM, BJORBAEK NS, Rayner TA, Vu MTT, Hansen BW. Recommended feeding regime and light climate in live feed cultures of the calanoid copepod *Acartia tonsa* Dana. *Aquac Int*. 2017;25(2):635–654. doi:10.1007/s10499-016-0063-4
191. Abate TG, Nielsen R, Nielsen M, Drillet G, Jepsen PM, Hansen BW. Economic feasibility of copepod production for commercial use: result from a prototype production facility. *Aquaculture*. 2015;436:72–79. doi:10.1016/j.aquaculture.2014.10.012
192. Drillet G, Lombard F. A first step towards improving copepod cultivation using modelling: the effects of density, crowding, cannibalism, tank design and strain selection on copepod egg production yields. *Aquacult Res*. 2015;46(7):1638–1647. doi:10.1111/are.12317
193. Sarkisian BL, Lemus JT, Apeitos A, Blaylock RB, Saillant EA. An intensive, large-scale batch culture system to produce the calanoid copepod. *Acartia Tonsa Aquaculture*. 2019;501:272–278. doi:10.1016/j.aquaculture.2018.11.042
194. Nielsen BLH, Greve HV, Hansen BW. Cultivation success and fatty acid composition of the tropical copepods *Apocyclops royi* and *Pseudodiaptomus annandalei* fed on monospecific diets with varying PUFA profiles. *Aquacult Res*. 2021;52(3):1127–1138. doi:10.1111/are.14970
195. Nielsen BLH, Greve HV, Rayner TA, Hansen BW. Biochemical adaptation by the tropical copepods *Apocyclops royi* and *Pseudodiaptomus annandalei* to a PUFA-poor brackish water habitat. *Mar Ecol Prog Ser*. 2020;655:77–89. doi:10.3354/meps13536
196. Baeza-Rojano E, García S, Garrido D, Guerra-García JM, Domingues P. Use of amphipods as alternative prey to culture cuttlefish (*Sepia officinalis*) hatchlings. *Aquaculture*. 2010;300:243–246. doi:10.1016/j.aquaculture.2009.12.029
197. Baeza-Rojano E, Hachero-Cruzado I, Guerra-García JM. Nutritional analysis of freshwater and marine amphipods from the strait of Gibraltar and potential aquaculture applications. *J Sea Res*. 2014;85:29–36. doi:10.1016/j.seares.2013.09.007
198. Awal S, Christie A, Nieuwesteeg D. Substrate selectivity and food preference of the Caprellid amphipod (*Caprella penantis*); evaluation of a possible aquaculture resource for marine hatcheries. *J Aquac Mar Biol*. 2016;4(1):00073. doi:10.15406/jamb.2016.04.00073
199. Tempestini A, Rysgaard S, Dufresne F. Species identification and connectivity of marine amphipods in Canada's three oceans. *PLoS One*. 2018;13:e0197174. doi:10.1371/journal.pone.0197174
200. Jiménez-Prada P, Hachero-Cruzado I, Giráldez I, et al. Crustacean amphipods from marsh ponds: a nutritious feed resource with potential for application in integrated multi-trophic aquaculture. *PeerJ*. 2018;6:e4194. doi:10.7717/peerj.4194
201. Alberts-Hubatsch H, Slater MJ, Beermann J. Effect of diet on growth, survival and fatty acid profile of marine amphipods: implications for utilisation as a feed ingredient for sustainable aquaculture. *Aquac Environ Interact*. 2019;11:481–491. doi:10.3354/aei00329
202. Olsen RL, Hasan MR. A limited supply of fishmeal: impact on future increases in global aquaculture production. *Trends Food Sci Technol*. 2012;27(2):120–128. doi:10.1016/j.tifs.2012.06.003
203. Podleśńska W, Dąbrowska H. Amphipods in estuarine and marine quality assessment—a review. *Oceanologia*. 2019;61(2):179–196. doi:10.1016/j.oceano.2018.09.002
204. Sundelin B, Rosa R, Wiklund AKE. Reproduction disorders in the benthic amphipod *Monoporeia affinis*: an effect of low food resources. *Aquat Biol*. 2008;2:179–190. doi:10.3354/ab00048
205. Strode E, Balode M. Toxic-resistance of Baltic amphipod species to heavy metals. *Crustaceana*. 2013;86(7–8):1007–1024. doi:10.1163/15685403-00003208
206. Strode E, Jansons M, Puriņa I, Balode M, Berezina N. Sediment quality assessment using survival and embryo malformation test in amphipod crustaceans: the Gulf of Riga, Baltic Sea as case study. *J Mar Syst*. 2017;172:93–103. doi:10.1016/j.jmarsys.2017.03.010
207. Gorokhova E, Löf M, Halldórsson HP, et al. Single and combined effects of hypoxia and contaminated sediments on the amphipod *Monoporeia affinis* in laboratory toxicity bioassays based on multiple biomarkers. *Aquat Toxicol*. 2010;99(2):263–274. doi:10.1016/j.aquatox.2010.05.005
208. Gorokhova E, Löf M, Reutgard M, Lindström M, Sundelin B. Exposure to contaminants exacerbates oxidative stress in amphipod *Monoporeia affinis* subjected to fluctuating hypoxia. *Aquat Toxicol*. 2013;127:46–53. doi:10.1016/j.aquatox.2012.01.022
209. Costa R, Capillo G, Albergamo A, et al. A multi-screening evaluation of the nutritional and nutraceutical potential of the Mediterranean jellyfish *Pelagia noctiluca*. *Mar Drugs*. 2019;17(3):172. doi:10.3390/md17030172
210. Wakabayashi K, Sato R, Hirai A, Ishii H, Akiba T, Tanaka Y. Predation by the phyllosoma larva of *Ibacus novemdentatus* on various kinds of venomous jellyfish. *Biol Bull*. 2012;222(1):1–5.
211. Lehtonen KK. Ecophysiology of the benthic amphipod *Monoporeia affinis* in an open-sea area of the northern Baltic Sea: seasonal variations in body composition, with bioenergetic considerations. *Mar Ecol Prog Ser*. 1996;143:87–98. doi:10.3354/meps143087
212. Hertrampf JW, Piedad-Pascual F. Mollusc products. *Handbook on Ingredients for Aquaculture Feeds*. Springer; 2000.
213. Kotta J, Futter M, Kaasik A, et al. Cleaning up seas using blue growth initiatives: mussel farming for eutrophication control in the Baltic Sea. *Sci Total Environ*. 2020;709:136144. doi:10.1016/j.scitotenv.2019.136144
214. Omolo SO. Sea urchin as an alternative feed for fish. *East Afr Agric for J*. 1991;57(2):121–130. doi:10.1080/00128325.1991.11663597
215. Isaeva O, Oahn L, Zharkov ML, Kasumyan AO. Taste Attractiveness Of Echinoderms For Predator Fish, Barramundi Lates calcarifer (Bloch, 1790). Book of Abstracts 7th International Conference on Fisheries and Aquaculture 2020 (ICFA 2020), Pitakotte, Sri Lanka, 39; 2020.
216. Kolesnik N, Simon MA, Marenkov O, Nesterenko OS. The cultivation of the nematodes *Panagrellus*, *Turbatrix* (*Anguillula*) and *Rhabditis* for using in fish feeding in fish feeding. *Ribogospodars'ka Nauka Ukraini*. 2019;3(49):16–31. doi:10.15407/fsu2019.02.016
217. Schleichtrien C, Ricci M, Focken U, Becker K. The suitability of the free-living nematode *Panagrellus redivivus* as live food for first-feeding fish larvae. *J Appl Ichthyol*. 2004;20(3):161–168. doi:10.1111/j.1439-0426.2004.00542.x
218. Focken U, Schleichtrien C, Von Wuthenau M, García-Ortega A, Puello-Cruz A, Becker K. *Panagrellus redivivus* mass produced on solid media as live food for *Litopenaeus vannamei* larvae. *Aquacult Res*. 2006;37(14):1429–1436. doi:10.1111/j.1365-2109.2006.01578.x
219. Honnens H, Ehlers RU. Liquid culture of *Panagrolaimus* sp. for use as food for marine aquaculture shrimp and fish species. *Nematology*. 2013;15(4):417–429. doi:10.1163/15685411-00002689
220. Brüggeman J. Nematodes as live food in larviculture—a review. *J World Aquac Soc*. 2012;43(6):739–763. doi:10.1111/j.1749-7345.2012.00608.x

221. Maheswarudu G, Vineetha A. Culture of the littoral oligochaete *Pontodrilus bermudensis* Beppard. *Bioprocess Technol.* 2013;97:142-155.
222. Leelatanawit R, Uwaisetwathana U, Khudet J, et al. Effects of polychaetes (*Perinereis nuntia*) on sperm performance of the domesticated black tiger shrimp (*Penaeus monodon*). *Aquaculture.* 2014;433:266-275. doi:10.1016/j.aquaculture.2014.06.034
223. Santos A, Granada L, Baptista T, et al. Effect of three diets on the growth and fatty acid profile of the common ragworm *Hediste diversicolor* (O.F. Müller, 1776). *Aquaculture.* 2016;465:37-42. doi:10.1016/j.aquaculture.2016.08.022
224. Bischoff A, Fink P, Waller U. The fatty acid composition of *Nereis diversicolor* cultured in an integrated recirculated system: possible implications for aquaculture. *Aquaculture.* 2009;296(3):271-276. doi:10.1016/j.aquaculture.2009.09.002
225. Stabili L, Sicuro B, Daprà F, et al. The biochemistry of *Sabella spallanzanii* (Annelida: Polychaeta): a potential resource for the fish feed industry. *J World Aquac Soc.* 2013;44(3):384-395. doi:10.1111/jwas.12038
226. Stabili L, Cecere E, Licciano M, Petrocelli A, Sicuro B, Giangrande A. Integrated multitrophic aquaculture by-products with added value: the polychaete *Sabella spallanzanii* and the seaweed *Chaetomorpha linum* as potential dietary ingredients. *Mar Drugs.* 2019;17(12):677. doi:10.3390/md17120677
227. Marchini A, Ferrario J, Sfriso A, Occhipinti-Ambrogi A. Current status and trends of biological invasions in the lagoon of Venice, a hot-spot of marine NIS introductions in the Mediterranean Sea. *Biol Invasions.* 2015;17:2943-2962. doi:10.1007/s10530-015-0922-3
228. Streftaris N, Zenetos A. Alien marine species in the Mediterranean—the 100 ‘Worst Invasives’ and their impact. *Mediterr Mar Sci.* 2006;7:87-118.
229. Marchini A, Cardecchia A. Alien amphipods in a sea of troubles: cryptogenic species, unresolved taxonomy and overlooked introductions. *Mar Biol.* 2017;164(4):1-14. doi:10.1007/s00227-017-3093-1
230. Katsanevakis S, Wallentinus I, Zenetos A, et al. Impacts of invasive alien marine species on ecosystem services and biodiversity: a pan-European review. *Aquat Invasions.* 2014;9(4):391-423. doi:10.3391/ai.2014.9.4.01
231. Ojaveer H, Kotta J, Outinen O, Einberg H, Zaiko A, Lehtiniemi M. Meta-analysis on the ecological impacts of widely spread non-indigenous species in the Baltic Sea. *Sci Total Environ.* 2021;786:147375.
232. Giakoumi S, Katsanevakis S, Albano PG, et al. Management priorities for marine invasive species. *Sci Total Environ.* 2019;688:976-982. doi:10.1016/j.scitotenv.2019.06.282
233. Renzi M, Cilenti L, Scirocco T, et al. Litter in alien species of possible commercial interest: the blue crab (*Callinectes sapidus* Rathbun, 1896) as case study. *Mar Pollut Bull.* 2020;157:111300. doi:10.1016/j.marpolbul.2020.111300
234. Brondizio ES, Settele J, Díaz S, Ngo HT, eds. *Global assessment report on biodiversity and ecosystem services of the intergovernmental science-policy platform on biodiversity and ecosystem services.* IPBES Secretariat; 2019:1148. doi:10.5281/zenodo.3831673
235. Rotter A, Klun K, Francé J, Mozetič P, Orlando-Bonaca M. Non-indigenous species in the Mediterranean Sea: turning from pest to source by developing the 8Rs model, a new paradigm in pollution mitigation. *Front Mar Sci.* 2020;7:178. doi:10.3389/fmars.2020.00178
236. Sahin T, Yilmaz S, Ergün S. A potential substitute to fish meal: the veined rapa whelk, *Rapana venosa*. *Int J Ocean Aquac.* 2018;2(3):1-8.
237. Luo F, Xing R, Wang X, Peng Q, Li P. Proximate composition, amino acid and fatty acid profiles of marine snail *Rapana venosa* meat, visceral mass and operculum. *J Sci Food Agric.* 2017;97(15):5361-5368. doi:10.1002/jsfa.8425
238. McLaughlan C, Rose P, Aldridge DC. Making the best of a pest: the potential for using invasive zebra mussel (*Dreissena polymorpha*) biomass as a supplement to commercial chicken feed. *Environ Manag.* 2014;54(5):1102-1109. doi:10.1007/s00267-014-0335-6
239. Secor CL, Mills EL, Harshbarger J, Kuntz HT, Gutenmann WH, Lisk DJ. Bioaccumulation of toxicants, element and nutrient composition, and soft tissue histology of zebra mussels (*Dreissena polymorpha*) from New York state waters. *Chemosphere.* 1993;26:1559-1575. doi:10.1016/0045-6535(93)90224-S
240. Karhan SÜ, Kalkan E, Yokeş MB. First record of the Atlantic starfish, *Asterias rubens* (Echinodermata: Asteroidea) from the Black Sea. *Mar Biodivers Rec.* 2008;1:1-2. doi:10.1017/S175526720700663X
241. Nørgaard JV, Petersen JK, Tørring DB, Jørgensen H, Lærke H. Chemical composition and standardized ileal digestibility of protein and amino acids from blue mussel starfish, and fish silage in pigs. *Anim Feed Sci Technol.* 2015;205:90-97. doi:10.1016/j.anifeeds.2015.04.005
242. Sørensen P, Nørgaard JV. Starfish (*Asterias rubens*) as feed ingredient for piglets. *Anim Feed Sci Technol.* 2016;211:181-188. doi:10.1016/j.anifeeds.2015.11.012
243. Rudovica V, Rotter A, Gaudêncio S, et al. Valorization of marine waste: exploitation of industrial by-products and beach wrack towards the production of high added-value products. *Front Mar Sci.* 2021;8:723333. doi:10.3389/fmars.2021.723333
244. Fraga-Corral M, Ronza P, Garcia-Oliveira P, et al. Aquaculture as a circular bio-economy model with Galicia as a study case: how to transform waste into revalorized by-products. *Trends Food Sci Technol.* 2022;119:23-35. doi:10.1016/j.tifs.2021.11.026
245. Catchpole TL, Ribeiro-Santos A, Mangi SC, Hedley C, Gray TS. The challenges of the landing obligation in EU fisheries. *Mar Policy.* 2017;82:76-86. doi:10.1016/j.marpol.2017.05.001
246. van't Land M, Vanderperren E, Raes K. The effect of raw material combination on the nutritional composition and stability of four types of autolyzed fish silage. *Anim Feed Sci Technol.* 2017;234:284-294. doi:10.1016/j.anifeeds.2017.10.009
247. Vázquez JA, Durán AI, Mendiña A, Nogueira M. Biotechnological valorization of food marine wastes: microbial productions on peptones obtained from aquaculture by-products. *Biomolecules.* 2020;10:1184. doi:10.3390/biom10081184
248. Chopin T, Robinson S, Sawhney M, et al. The AquaNet integrated multi-trophic aquaculture project: rationale of the project and development of kelp cultivation as the inorganic extractive component of the system. *Bull Aquacult Assoc Can.* 2004;104:11-18.
249. Chopin T, Cooper JA, Reid G, Cross S, Moore C. Open-water integrated multi-trophic aquaculture: environmental biomitigation and economic diversification of fed aquaculture by extractive aquaculture. *Rev Aquac.* 2012;4(4):209-220.
250. Chopin T, Tacon AG. Importance of seaweeds and extractive species in global aquaculture production. *Rev Fish Sci Aquac.* 2021;29(2):139-148.
251. Zhang J, Zhang S, Kitazawa D, et al. Bio-mitigation based on integrated multi-trophic aquaculture in temperate coastal waters: practice, assessment, and challenges. *Lat Am J Aquat Res.* 2019;47:212-223. doi:10.3856/vol47-issue2-fulltext-1
252. Gökalp M, Mes D, Nederlof M, Zhao H, Merijn de Goeij J, Osinga R. The potential roles of sponges in integrated mariculture. *Rev Aquac.* 2020;13:1-13. doi:10.1111/raq.12516
253. Tolon MT, Emiroglu D, Gunay D, Ozgul A. Sea cucumber (*Holothuria tubulosa* Gmelin, 1790) culture under marine fish net cages for potential use in integrated multi-trophic aquaculture (IMTA). *Indian J Mar Sci.* 2017;46(4):749-756.
254. Neofitou N, Lolas A, Ballios I, Skordas K, Tziantziou L, Vafidis D. Contribution of sea cucumber *Holothuria tubulosa* on organic load reduction from fish farming operation. *Aquaculture.* 2019;501:97-103. doi:10.1016/j.aquaculture.2018.10.071



255. Milanese M, Chelossi E, Manconi R, Sarà M, Sidri M, Pronzato R. The marine sponge *Chondrilla nucula* Schmidt, 1862 as an elective candidate for bioremediation in integrated aquaculture. *Biomol Eng*. 2003;20:363-368. doi:10.1016/S1389-0344(03)00052-2
256. Zhang X, Zhang W, Xue L, Zhang B, Jin M, Fu W. Bioremediation of bacteria pollution using the marine sponge *Hymeniacidon perlevis* in the intensive mariculture water system of turbot *Scophthalmus maximus*. *Biotechnol Bioeng*. 2010;105(1):59-68. doi:10.1002/bit.22522
257. Longo C, Cardone F, Corriero G, Licciano M, Pierri C, Stabili L. The co-occurrence of the demosponge *Hymeniacidon perlevis* and the edible mussel *Mytilus galloprovincialis* as a new tool for bacterial load mitigation in aquaculture. *Environ Sci Pollut Res*. 2016;23:3736-3746.
258. Baquiran JIP, Conaco C. Sponge-microbe partnerships are stable under eutrophication pressure from mariculture. *Mar Pollut Bull*. 2018;136:125-134. doi:10.1016/j.marpolbul.2018.09.011
259. Benner R. Chemical composition and reactivity. In: Hansell D, Carlson C, eds. *Biogeochemistry of marine dissolved organic matter*. Academic Press Inc; 2002:59-90.
260. De Goeij JM, van Oevelen D, Vermeij MJA, et al. Surviving in a Marine Desert: the sponge loop retains resources within coral reefs. *Science*. 2013;342:108-110. doi:10.1126/science.1241981
261. Gökalp M, Wijgerde T, Sarà A, De Goeij JM, Osinga R. Development of an integrated Mariculture for the collagen-rich sponge *Chondrosia reniformis*. *Mar Drugs*. 2019;17(1):1-15. doi:10.3390/md17010029
262. Perez-Lopez P, Ledda FD, Bisio A, et al. Life cycle assessment of in situ mariculture in the Mediterranean Sea for the production of bioactive compounds from the sponge *Sarcotragus spinosulus*. *J Clean Prod*. 2017;142:4356-4368.
263. Binneweg B, Schubert M, Voronkina A, et al. Marine biomaterials: biomimetic and pharmacological potential of cultivated *Aplysina aerophoba* marine demosponge. *Mater Sci Eng C*. 2020;109:110566. doi:10.1016/j.msec.2019.110566
264. Giangrande A, Pierri C, Arduini D, et al. An innovative IMTA system: Polychaetes, sponges and macroalgae co-cultured in a southern Italian in-shore Mariculture plant (Ionian Sea). *J Mar Sci Eng*. 2020; 8(10):1-24. doi:10.3390/jmse8100733
265. Pajand ZO, Soltani M, Bahmani M, Kamali A. The role of polychaete *Nereis diversicolor* in bioremediation of wastewater and its growth performance and fatty acid composition in an integrated culture system with *Huso huso* (Linnaeus, 1758). *Aquacult Res*. 2017;48(10): 5271-5279. doi:10.1111/are.13340
266. Bischoff AA. *Solid Waste Reduction of Closed Recirculated Aquaculture Systems by Secondary Culture of Detritivorous Organisms*. Dissertation. Christian-Albrechts-Universität; 2007.
267. Wang H, Seekamp I, Malzahn A, et al. Growth and nutritional composition of the polychaete *Hediste diversicolor* (OF Müller, 1776) cultivated on waste from land-based salmon smolt aquaculture. *Aquaculture*. 2019;502:232-241. doi:10.1016/j.aquaculture.2018.12.047
268. Pridgeon JW, Phillip HK. Major bacterial diseases in aquaculture and their vaccine development. *CAB Rev Perspect Agric Vet Sci Nutr Nat Resour*. 2012;7(48):1-16. doi:10.1079/PAVSNNR20127048
269. Defoirdt T. Virulence mechanisms of bacterial aquaculture pathogens and antiviral therapy for aquaculture. *Rev Aquac*. 2014; 6(2):100-114. doi:10.1111/raq.12030
270. Preena PG, Swaminathan TR, Kumar VJR, Singh ISB. Antimicrobial resistance in aquaculture: a crisis for concern. *Biologia*. 2020;75: 1497-1517. doi:10.2478/s11756-020-00456-4
271. Bansemir A, Blume M, Schröder S, Lindequist U. Screening of cultivated seaweeds for antibacterial activity against fish pathogenic bacteria. *Aquaculture*. 2006;252(1):79-84. doi:10.1016/j.aquaculture.2005.11.051
272. García-Davis S, Leal-López K, Molina-Torres CA, et al. Antimycobacterial activity of laurinterol and aplysin from *Laurencia johnstonii*. *Mar Drugs*. 2020;18(6):1-9. doi:10.3390/md18060287
273. Jimenez PC, Wilke DV, Branco PC, et al. Enriching cancer pharmacology with drugs of marine origin. *Br J Pharmacol*. 2020;177(1):3-27. doi:10.1111/bph.14876
274. Barreca M, Spanò V, Montalbano A, et al. Marine anticancer agents: an overview with a particular focus on their chemical classes. *Mar Drugs*. 2020;18:619. doi:10.3390/md18120619
275. Shenouda ML, Ambilika M, Skellam E, Cox RJ. Heterologous expression of secondary metabolite genes in *Trichoderma reesei* for waste valorization. *J Fungi*. 2022;8:355. doi:10.3390/jof8040355
276. Kontiza I, Stavri M, Zloh M, Vagias C, Gibbons S, Roussis V. New metabolites with antibacterial activity from the marine angiosperm *Cymodocea Nodosa*. *Tetrahedron*. 2008;64(8):1696-1702. doi:10.1016/j.tet.2007.12.007
277. Barker LP, Lien BA, Brun OS, Schaak DD, McDonough KA, Chang LC. A mycobacterium Marinum zone of inhibition assay as a method for screening potential Antimycobacterial compounds from marine extracts. *Planta Med*. 2007;73(6):559-563. doi:10.1055/s-2007-981522
278. Schneider YKH, Hansen K, Isaksson J, Ullsten S, Hansen EH, Andersen JH. Anti-bacterial effect and cytotoxicity assessment of lipid 430 isolated from *Algibacter* sp. *Molecules*. 2019;24(21):1-15. doi:10.3390/molecules24213991
279. Kristoffersen V, Teppo R, Isaksson J, Andersen JH, Gerwick WH, Hansen E. Characterization of rhamnolipids produced by an Arctic marine bacterium from the *Pseudomonas fluorescence* group. *Mar Drugs*. 2018;16(163):1-19.
280. Noh TH, Sen L, Hong J, Lee JH, Moon HR, Jung JH. Antibacterial activities of Vviriditoxin congeners and synthetic analogues against fish pathogens. *Bioorg Med Chem Lett*. 2017;27(22):4970-4974. doi:10.1016/j.bmcl.2017.10.015
281. Sahli R, Rivière C, Neut C, et al. An ecological approach to discover new bioactive extracts and products: the case of extremophile plants. *J Pharm Pharmacol*. 2017;69(8):1041-1055. doi:10.1111/jphp.12728
282. Jensen PR, Harvell CD, Wirtz K, Fenical W. Antimicrobial activity of extracts of Caribbean gorgonian corals. *Mar Biol*. 1996;125(2):411-419. doi:10.1007/bf00346321
283. Imjongirak C, Amparyup P, Tassanakajon A. Two novel antimicrobial peptides, arasin-likeSp and GRPsp, from the mud crab *Scylla paramamosain*, exhibit the activity against some crustacean pathogenic bacteria. *Fish Shellfish Immunol*. 2011;30(2):706-712.
284. Salenius K, Siderakis C, MacKinnon AM, Griffiths SG. Use of *Arthrobacter davidanieli* as a live vaccine against *Renibacterium salmoninarum* and *Piscirickettsia salmonis* in salmonids. *Dev Biol*. 2005;121: 189-197. doi:10.1007/s00018-009-0138-8
285. Patel KB, Cai S, Adler M, Singh BK, Parmar VS, Singh BR. Natural compounds and their analogues as potent antidotes against the Most poisonous bacterial toxin. *Appl Environ Microbiol*. 2018;84: e01280-18.
286. Chi LP, Yang SQ, Li XM, Li XD, Wang BG, Li X. A new steroid with 7 β ,8 β -epoxidation from the Deep Sea-derived fungus *aspergillus penicillioides* SD-311. *J Asian Nat Prod Res*. 2020;23:1-8. doi:10.1080/10286020.2020.1791096
287. Chakraborty K, Lipton AP, Paulraj R, Chakraborty RD. *Guaiane sesquiterpenes* from seaweed *Ulva fasciata* eille and their antibacterial properties. *Eur J Med Chem*. 2010;45(6):2237-2244. doi:10.1016/j.ejmech.2010.01.065
288. Zhao JC, Li XM, Gloer JB, Wang BG. First total syntheses and antimicrobial evaluation of penicimonoterpene, a marine-derived monoterpene, and its various derivatives. *Mar Drugs*. 2014;12(6):3352-3370. doi:10.3390/md12063352
289. Liu Y, Ding L, Fang F, He S, Penicillilactone A. A novel antibacterial 7-membered lactone derivative from the sponge-associated fungus *Penicillium* sp. LS54. *Nat Prod Res*. 2019;33(17):2466-2470. doi:10.1080/14786419.2018.1452012



290. Díaz YM, Laverde GV, Gamba LR, et al. Biofilm inhibition activity of compounds isolated from two *Eunicea* species collected at the Caribbean Sea. *Rev Bras Farm.* 2015;25(6):605-611. doi:10.1016/j.bjp.2015.08.007
291. Bauermeister A, Pereira F, Grilo IR, et al. Intra-clade metabolomic profiling of MAR4 Streptomyces from the Macaronesia Atlantic region reveals a source of anti-biofilm metabolites. *Environ Microbiol.* 2019;21(3):1099-1112. doi:10.1111/1462-2920.14529
292. Pereira F, Almeida JR, Paulino M, et al. Antifouling Napyradiomycins from marine-derived Actinomycetes *Streptomyces aculeolatus*. *Mar Drugs.* 2020;18:63. doi:10.3390/md18010063
293. Lee BC, Lee A, Jung JE, Choi SH, Kim TS. In vitro and in vivo anti-vibrio *Vulnificus* activity of Psammaphin a, a natural marine compound. *Mol Med Rep.* 2016;14(3):2691-2696. doi:10.3892/mmr.2016.5522
294. Rajasekar P, Palanisamy S, Anjali R, et al. Isolation and structural characterization of sulfated polysaccharide from *Spirulina platensis* and its bioactive potential: in vitro antioxidant, antibacterial activity and zebrafish growth and reproductive performance. *Int J Biol Macromol.* 2019;141:809-821. doi:10.1016/j.ijbiomac.2019.09.024
295. Majik MS, Rodrigues C, Mascarenhas S, D'Souza L. Design and synthesis of marine natural product-based 1H-Indole-2,3-Dione scaffold as a new antifouling/antibacterial agent against fouling bacteria. *Bioorg Chem.* 2014;54:89-95. doi:10.1016/j.bioorg.2014.05.001
296. Majik MS, Shirodkar D, Rodrigues C, D'Souza L, Tilvi S. Evaluation of single and joint of metabolites isolated from marine sponges, *Fasciospongia cavernosa* and *Axinella donnani* on antimicrobial properties. *Bioorg Med Chem Lett.* 2014;24(13):2863-2866. doi:10.1016/j.bmcl.2014.04.097
297. Li R, Li A. Antibacterial efficacy of recombinant *Siganus oramin* L-amino acid oxidase expressed in *Pichia pastoris*. *Fish Shellfish Immunol.* 2014;41(2):356-361. doi:10.1016/j.fsi.2014.09.017
298. Bansemir A, Just N, Michalik M, Lindequist U, Lalk M. Extracts and Sesquiterpene derivatives from the red alga *Laurencia Chondrioides* with antibacterial activity against fish and human pathogenic bacteria. *Chem Biodivers.* 2004;1:463-467. doi:10.1002/cbdv.200490039
299. Beesoo R, Bhagooli R, Neergeen-bhujun VS, Li WW, Kagansky A, Bahorun T. Antibacterial and antibiotic potentiating activities of tropical marine sponge extracts. *Comp Biochem Physiol Part C Toxicol Pharmacol.* 2017;196:81-90. doi:10.1016/j.cbpc.2017.04.001
300. Heindl H, Thiel V, Wiese J, Imhoff JF. Bacterial isolates from the bryozoan *Membranipora Membranacea*: influence of culture media on isolation and antimicrobial activity. *Int Microbiol.* 2012;15:17-32. doi:10.2436/20.1501.01.155
301. Sharma AR, Harunari E, Oku N, Matsuura N, Trianto A, Igarashi Y. Two antibacterial and PPAR α/γ -agonistic unsaturated Keto fatty acids from a coral-associated Actinomycete of the genus *Micrococcus*. *J Org Chem.* 2020;16:297-304. doi:10.3762/bjoc.16.29
302. Karim MRU, Harunari E, Oku N, Akasaka K, Igarashi Y. Bulbimida-zoles A–C, antimicrobial and cytotoxic alkanoyl imidazoles from a marine gammaproteobacterium *Microbulbifer* species. *J Nat Prod.* 2020;83(4):1295-1299. doi:10.1021/acs.jnatprod.0c00082
303. Reimer A, Blohm A, Quack T, et al. Inhibitory activities of the marine Streptomyces-derived compound SF2446A2 against *Chlamydia trachomatis* and *Schistosoma mansoni*. *J Antibiot.* 2015;68:674-679. doi:10.1038/ja.2015.54
304. Petroski W, Minich DM. Is there such a thing as “anti-nutrients”? A narrative review of perceived problematic plant compounds. *Nutrients.* 2020;12(10):2929. doi:10.3390/nu12102929
305. Popova A, Mihaylova D. Antinutrients in plant-based foods: a review. *Open Biotechnol J.* 2019;13:68-76. doi:10.2174/1874070701913010068
306. Kumar Y, Basu S, Goswami D, Devi M, Shivhare US, Vishwakarma RK. Anti-nutritional compounds in pulses: implications and alleviation methods. *Legum Sci.* 2021;4:e111. doi:10.1002/leg3.111
307. Robiaina L, Pirhonen J, Mente E, Sánchez J, Goosen N. Fish diets in aquaponics. In: Goddek S, Joyce A, Kotzen B, Burnell GM, eds. *Aquaponics Food Production Systems*. Springer; 2019:333-352.
308. Glencross BD, Booth M, Allan GL. A feed is only as good as its ingredients—a review of ingredient evaluation strategies for aquaculture feeds. *Aquacult Nutr.* 2007;13(1):17-34. doi:10.1111/j.1365-2095.2007.00450.x
309. Glencross BD. A feed is still only as good as its ingredients: an update on the nutritional research strategies for the optimal evaluation of ingredients for aquaculture feeds. *Aquacult Nutr.* 2020;26(6):1871-1883. doi:10.1111/anu.13138
310. Jiang Z. Ingredient variation: its impact and management. In: van der Poel AFB, Vahl JL, Kwakkel RP, eds. *Advances in Nutritional Technology. Proceedings of the 1st World Feed Conference, 7-8 November, 2001*. Wageningen Pers; 2001:47-56.
311. Glencross B, Bourne N, Hawkins W, et al. Using near infrared reflectance spectroscopy (NIRS) to predict the protein and energy digestibility of lupin kernel meals when fed to rainbow trout, *Oncorhynchus mykiss*. *Aquac Nutr.* 2015b;21(1):54-62. doi:10.1111/anu.12137
312. Glencross B, Bourne N, Irvin S, Blyth D. Using near-infrared reflectance spectroscopy to predict the digestible protein and digestible energy values of diets when fed to barramundi, *Lates calcarifer*. *Aquac Nutr.* 2017;23(2):397-405. doi:10.1111/anu.12406
313. Barki D, Deleze-Black L. *Review of maritime transport*. United Nations Conference on Trade and Development (UNCTAD); 2016:105.
314. Rust M, Barrows FT, Hardy RW, Lazur AM, Naughten K, Silverstein JT. The future of aquafeeds NOAA/USDA alternative feeds initiative; 2011.
315. Ruiz-Salmón I, Margallo M, Laso J, et al. Addressing challenges and opportunities of the European seafood sector under a circular economy framework. *Curr Opin Environ Sci Health.* 2020;13:101-106. doi:10.1016/j.coesh.2020.01.004
316. Balsells S, Bardóc T, Chary K, et al. Policy recommendations for a more circular aquaculture, iFISHiENCi Horizon 2020; 2022. http://ifishenci.eu/wp-content/uploads/2022/03/-IfishciENCi_Policydoc_Jan-2022Final.pdf.
317. El-Sayed AFM, Dickson MW, El-Naggar GO. Value chain analysis of the aquaculture feed sector in Egypt. *Aquaculture.* 2015;437:92-101. doi:10.1016/j.aquaculture.2014.11.033
318. Seung CK, Kim DH. Examining supply chain for seafood industries using structural path analysis. *Sustainability.* 2020;12(5):2061. doi:10.3390/su12052061
319. Bindoff NL, Cheung WW, Kairo JG, et al. Changing ocean, marine ecosystems, and dependent communities. In: Pörtner HO, Roberts DC, Masson-Delmotte V, et al., eds. *IPCC Special Report on the Ocean and Cryosphere in a Changing Climate*. IPCC; 2019.
320. Ahmed N, Thompson S, Glaser M. Global aquaculture productivity, environmental sustainability, and climate change adaptability. *Environ Manag.* 2019;63(2):159-172. doi:10.1007/s00267-018-1117-3
321. Salin KR, Arome AG. Aquaculture and the environment: towards sustainability. In: Hai F, Visvanathan C, Boopathy R, eds. *Sustainable Aquaculture. Applied Environmental Science and Engineering for a Sustainable Future*. Springer; 2018:1-62.
322. Robert N, Giuntoli J, Araujo R, et al. Development of a bioeconomy monitoring framework for the European Union: an integrative and collaborative approach, new biotechnology. 2020;59:10-19. doi:10.1016/j.nbt.2020.06.001
323. Humphries F. Banking on a patent solution for sharing ex situ genetic resources from Antarctic waters. *Biodiversity, Genetic Resources and Intellectual Property: Developments in Access and*

Benefit Sharing. Griffith University Law School Research Paper. Routledge; 2018:59-94.

324. Schneider XT, Stroil BK, Tourapi C, et al. Responsible research and innovation framework, the Nagoya protocol and other European blue biotechnology strategies and regulations: gaps analysis and recommendations for increased knowledge in the marine biotechnology community. *Mar Drugs*. 2022;20(5):290. doi:[10.3390/md20050290](https://doi.org/10.3390/md20050290)
325. Humphries F, Benzie JAH, Lawson C, Morrison C. A review of access and benefit-sharing measures and literature in key aquaculture-producing countries. *Rev Aquac*. 2021;13(3):1531-1548. doi:[10.1111/raq.12532](https://doi.org/10.1111/raq.12532)

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Eroldoğan OT, Glencross B, Novoveska L, et al. From the sea to aquafeed: A perspective overview. *Rev Aquac*. 2022;1-30. doi:[10.1111/raq.12740](https://doi.org/10.1111/raq.12740)

