








Review

# The Use of Invasive Algae Species as a Source of Secondary Metabolites and Biological Activities: Spain as Case-Study

Antia G. Pereira <sup>1,2</sup> , Maria Fraga-Corral <sup>1,2</sup> , Paula Garcia-Oliveira <sup>1,2</sup> , Catarina Lourenço-Lopes <sup>1</sup> ,  
Maria Carpena <sup>1</sup> , Miguel A. Prieto <sup>1,2,\*</sup>  and Jesus Simal-Gandara <sup>1,\*</sup> 

- <sup>1</sup> Nutrition and Bromatology Group, Department of Analytical and Food Chemistry, Faculty of Food Science and Technology, University of Vigo, Ourense Campus, E32004 Ourense, Spain; antia.gonzalez.pereira@uvigo.es (A.G.P.); maria.fraga.corral@hotmail.es (M.F.-C.); paula.garcia.oliveira@uvigo.es (P.G.-O.); c.lopez@uvigo.es (C.L.-L.); maria.carpena.rodriguez@uvigo.es (M.C.)
- <sup>2</sup> Centro de Investigação de Montanha (CIMO), Instituto Politécnico de Bragança, Campus de Santa Apolonia, 5300-253 Bragança, Portugal
- \* Correspondence: mprieto@uvigo.es (M.A.P.); jsimal@uvigo.es (J.S.-G.)

**Abstract:** In the recent decades, algae have proven to be a source of different bioactive compounds with biological activities, which has increased the potential application of these organisms in food, cosmetic, pharmaceutical, animal feed, and other industrial sectors. On the other hand, there is a growing interest in developing effective strategies for control and/or eradication of invasive algae since they have a negative impact on marine ecosystems and in the economy of the affected zones. However, the application of control measures is usually time and resource-consuming and not profitable. Considering this context, the valorization of invasive algae species as a source of bioactive compounds for industrial applications could be a suitable strategy to reduce their population, obtaining both environmental and economic benefits. To carry out this practice, it is necessary to evaluate the chemical and the nutritional composition of the algae as well as the most efficient methods of extracting the compounds of interest. In the case of northwest Spain, five algae species are considered invasive: *Asparagopsis armata*, *Codium fragile*, *Gracilaria vermiculophylla*, *Sargassum muticum*, and *Grateulopia turuturu*. This review presents a brief description of their main bioactive compounds, biological activities, and extraction systems employed for their recovery. In addition, evidence of their beneficial properties and the possibility of use them as supplement in diets of aquaculture animals was collected to illustrate one of their possible applications.

**Keywords:** seaweeds; aquaculture feed; invasive macroalgae species; biological activity; metabolites



**Citation:** Pereira, A.G.; Fraga-Corral, M.; Garcia-Oliveira, P.; Lourenço-Lopes, C.; Carpena, M.; Prieto, M.A.; Simal-Gandara, J. The Use of Invasive Algae Species as a Source of Secondary Metabolites and Biological Activities: Spain as Case-Study. *Mar. Drugs* **2021**, *19*, 178. <https://doi.org/10.3390/md19040178>

Academic Editor: Marisa Silva

Received: 28 February 2021

Accepted: 22 March 2021

Published: 24 March 2021

**Publisher's Note:** MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



**Copyright:** © 2021 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

Invasive alien species (IAS), also known as exotic or non-native species, are plants or animals that have been introduced, intentionally or not, into regions where it is not usual to find them [1,2]. This situation often leads to negative consequences for the new host ecosystem, generally related to the community biodiversity reduction, changes in the abundance of the species and in the population's configuration across the habitats, as well as trophic displacements that can trigger other cascade effects [3]. Spanish law 42/2007, of 13 December, on Natural Heritage and Biodiversity, defines IAS as “species that are introduced and established in an ecosystem or natural habitat, which are an agent of change and a threat to native biological diversity, either by their invasive behavior, or by the risk of genetic contamination”. IAS usually present high growth and reproduction rates, the ability to prosper in different environments, the capacity to use several food sources, and the ability to tolerate a wide range of environmental conditions. All these factors, along with the lack of natural predators, make these organisms more difficult to control and allow them to succeed in colonizing new ecosystems [3,4]. In addition, these species may feed on natural species or may carry pathogens for native organisms and even

humans [5]. The invasion of non-native species also entails economic cost, which have been estimated at \$1.4 trillion in the last decade [6].

Among marine IAS declared in Europe, around 20–40% are macroalgae (seaweeds) [7], a term that refers to several species of multicellular and macroscopic marine algae, including different types of Chlorophyta (green), Phaeophyta (brown), and Rhodophyta (red) macroalgae. Non-native seaweeds are particularly prone to become invasive due to their high reproductive rates, the production of toxic metabolites, and their perennial status that makes them more competitive than native species [1]. Several species periodically become a major problem, causing red tides, fouling nets, clogging waterways, and changing nutrient regimes in areas near to fisheries, aquaculture systems, and desalination facilities [1,4]. In the last years, the presence of invasive macroalgae in the northwestern marine areas of Spain has become a common problem due to growing globalization, climate change, aquaculture, fisheries, and marine tourism [8]. However, their proliferation could also offer new opportunities since the recovery of the algal biomass and their novel applications in different economic sectors could increase their added value. Obtaining natural compounds with biological properties of interest for both the food and the pharmaceutical industries is one of these possible applications. The aim of the present work is to summarize the existing knowledge about the bioactive compounds of the principal invasive species affecting the Galician coasts (northwest Spain).

## 2. Possible Exploitation of the Invasive Species

The exploitation of macroalgae is a growing industry with several applications, including human food and animal feed, biorefinery, fertilizers, production of phycocolloids, and obtaining compounds with biological properties [6,9]. Several applications are briefly discussed below.

### 2.1. Food Industry

Macroalgae have been consumed since ancient times in many countries around the world, mainly in the Asian regions. Nevertheless, their consumption has increased in the last decades in western countries, which has been attributed to the high nutritional values of macroalgae and their health benefits [10,11]. Some of the most consumed macroalgae are nori or purple laver (*Porphyra* spp.), kombu (*Laminaria japonica*), wakame (*Undaria pinnatifida*), Hiziki (*Hizikia fusiforme*), or Irish moss (*Chondrus crispus*), which can be consumed in different food formats (salads, soups, snacks, pasta, etc.) [11,12]. Still, most of them are considered an innovative niche product. Macroalgae are also widely used in the food industry to produce phycocolloids (polysaccharides of high molecular weight composed mostly of simple sugars), mainly alginates, agars, and carrageenans, which are frequently used as thickeners, stabilizers, as well as for probiotics encapsulation, gels, and water-soluble films formation [6,13]. Furthermore, diverse molecules present in algae have been shown to exert several bioactivities, such as antioxidant, anti-inflammatory, antimicrobial, and antiviral effects. These bioactive compounds (mainly proteins, polyunsaturated fatty acids, carotenoids, vitamins, and minerals) may play important roles in functional foods (e.g., dairy products, desserts, pastas, oil derivatives, or supplements) with favorable outcomes on human health [14]. Other applications of algae in the food industry include their use as colorant agents and the extraction of valuable oils (such as eicosapentaenoic acid, docosahexaenoic acid, and arachidonic acid) [15].

### 2.2. Biofuel

The development of algal biofuels (“third-generation biofuels”) has been considered an option to reduce the use of petroleum-based fuels and avoid competition between food and energy production for arable soil, since macroalgae grow in water. These organisms do not contain lignin, thus they are good substrates for biogas production in anaerobic digesters, while fermentable carbohydrates are fit for bioethanol production. Although the production of bioenergy from macroalgae is not economically feasible nowadays, several

measures have been proposed to achieve a rational production cost in the future [16]. On the other hand, microalgae are considered a more suitable source to produce biodiesel due to the greater ease of controlling the life cycle and increasing the reproduction rate [17]. Microalgae biomass can be used for electricity generation or biofuel production after the lipid extraction. It has shown 80% of the average energy content of petroleum. The lipid content is highly dependent on the microalgae species and the cultivation conditions, thus not all species will be profitable, and choosing appropriate microalga strain is crucial [18]. Some microalgae used to produce biofuel are *Chlorella* spp., *Dunaliella salina*, *Haematococcus pluvialis*, *Spirulina platensis*, *Porphyridium cruentum*, *Microcystis aeruginosa*, and *Scenedesmus obliquus* [19].

### 2.3. Therapeutic and Cosmetic Products

The use of macroalgae for therapeutic purposes has a long history, but the search for biologically active substances from these organisms is quite recent. Numerous studies have demonstrated the biological properties of macroalgae extracts and compounds, including antioxidant, anti-inflammatory [20], antithrombotic, anticoagulant and coagulant [21], antimicrobial [22], and anticancer [23]. In addition, macroalgae have been demonstrated to exert biological properties applicable to cosmetic products, such as photo-protection, anti-aging, or anti-cellulite (Table 1). Considering this range of activities, macroalgae extracts and compounds have been considered for different pharmacologic and cosmetic products [24]. Regarding cosmetics, brown and red seaweeds are usually employed. The interest of these species lies in their content in cosmeceuticals ingredients, such as phlorotannins, polysaccharides, and carotenoid pigments [25]. These compounds are incorporated into cosmetics due to their bioactivities, their capacity to improve organoleptic properties, and their capacity to stabilize and preserve the products [26].

**Table 1.** Properties and applications of extracts and compounds isolated from algae in the cosmetic field.

Treatment	Specie	Compound	Result	Ref.
Skin aging	<i>Alaria esculenta</i>	Extract	Decline the amount of progerin in aged fibroblasts at the lowest tested concentration (not for younger cells)	[27]
	<i>Phaeodactylum tricornutum</i>	Ethanol extract	Protecting the skin from the adverse effects of UV exposure; preventing and/or delaying the appearance of skin aging effects	[28]
	<i>Hizikia fusiformis</i>	Fucosterol	Inhibit metalloproteinase-1 expression	[29]
	<i>Ecklonia stolonifera</i>	Phlorotannins	Inhibit metalloproteinase-1 expression	[30]
Sunscreen	<i>Halidrys siliquosa</i>	Phlorotannins	UV-filter activity	[31]
	<i>Brown seaweeds</i>	Phlorotannins	Protective effect against photo-oxidative stress	[32]
	<i>Corallina pilulifera</i>	Phenolic compounds	Anti-photoaging activity and inhibition of matrix metalloproteinase	[33]
	<i>Sargassum</i> spp.	Fucoanthin	Protective effect on UV-B induced cell damage	[34]
	<i>Sargassum confusum</i>	Fucoidan	Suppress photo-oxidative stress and skin barrier perturbation in UVB-induced human keratinocytes	[35]
	<i>Macrocystis pyrifera</i> , <i>Porphyra columbina</i>	Acetone extracts	In vivo UVB-photoprotective activity	[36]
Moisturizer	<i>Fucus vesiculosus</i>	Fucoidan	Inhibition of hyaluronidase enzyme	[37]
	<i>Laminaria japonica</i>	5% water:propylene glycol (50:50) extracts	Hydration with the alga extract increased by 14.44% compared with a placebo	[38]
	<i>Rhizoclonium hieroglyphicum</i>	Polysaccharides and amino acids	Similar moisturizing effects to hyaluronic acid and glycerin	[39]
Whitening	<i>Nannochloropsis oculata</i>	Zeaxanthin	Antityrosinase activity	[40]
	<i>Laminaria japonica</i>	Fucoanthin	Antityrosinase activity	[41]
	<i>Arthrospira platensis</i>	Ethanol extract	Antityrosinase activity	[42]
Hair care	<i>Chlorella</i> spp.	Intact microalga cells	Soften and make flexible both skin and hair	[43]
	<i>Ecklonia cava</i>	Dioxinodehydroeckol	Promote hair growth	[44]

#### 2.4. Fertilizer and Animal Feed

Currently, the negative environmental impacts of synthetic fertilizers have been identified. Thus, the use of organic fertilizers, including macroalgae, has been proposed as a suitable alternative to reduce the impact on the environment [45,46]. In fact, macroalgae have been used since ancient times as fertilizers, and several beneficial effects have been described, such as enhancement of crops growth and yield, increased resistance against abiotic and biotic stresses, or nutrient intake [46–48]. The biostimulant effects of macroalgae have been attributed to diverse biological compounds such as plant hormones, phlorotannins, and oligosaccharides [48].

Regarding animal feed, macroalgae have been employed for this purpose since ancient times as feed but also as nutritious supplements [49]. Several studies have evaluated the positive effects of macroalgae-enriched food, both for terrestrial animals [50] and specially in aquaculture animals [51–54].

### 3. Main Invasive Species of Northwest Spain and Their Bioactive Compounds

According to the Spanish Catalogue of IAS of Algae [55], there are 14 species of invasive seaweeds in Spain which can be divided into: (i) red species: *Acrothamnion preissii*, *Asparagopsis armata*, *Asparagopsis taxiformis*, *Grateloupia turuturu*, *Lophocladia lallemandii*, and *Womersleyella setacea*; (ii) brown species: *Gracilaria vermiculophylla*, *Sargassum muticum*, *Styopodium schimper*, and *Undaria pinnatifida*; and (iii) green species: *Caulerpa taxifolia*, *Codium fragile*, and *Caulerpa racemosa*. In addition, there are also invasive diatoms, such as the *Didymosphenia geminata*, also known as rock snot or didymo (Table 2). However, it should be noted that this catalogue is a dynamic instrument subjected to continuous changes and updating. Most of these invasive species are originally from the Indo-Pacific Ocean (Western Australia, New Zealand, and Japan), and it is thought that they have been introduced into the Spanish coasts through the Suez Canal. Maritime traffic, ballast water, fishing nets, trade of oysters, aquaculture, and fouling are considered the main routes of dispersion [8,56–58].

**Table 2.** Invasive algae species in Spain: taxonomy, origin, geographical distribution, and principal uses.

Specie	Taxonomy	Native Distribution	Distribution in Spain	Other Regions in Which They Are Invasive	Principal Uses
Red species					
<i>Acrothamnion preissii</i>	Phylum: <i>Rhodophyta</i> Class: <i>Florideophyceae</i> Order: <i>Ceramiales</i> Family: <i>Ceramiales</i>	Western Australia	All Spain	Temperate coastlines on the Pacific coast of North America and western coasts of Europe	- Unknown
<i>Asparagopsis armata</i>	Phylum: <i>Rhodophyta</i> Class: <i>Florideophyceae</i> Order: <i>Bonnemaisoniales</i> Family: <i>Bonnemaisoniaceae</i>	Indo-Pacific Ocean	All Spain	Mediterranean, Portugal, and Ireland	- Pharmaceutical potential as antibiotic
<i>Asparagopsis taxiformis</i>	Phylum: <i>Rhodophyta</i> Class: <i>Rhodophyceae</i> Order: <i>Nemaliales</i> Family: <i>Bonnemaisoniaceae</i>	Australia and New Zealand	Except Canarias	Portugal	- Human consumption - Antifungal
<i>Grateloupia turuturu</i>	Phylum: <i>Rhodophyta</i> Class: <i>Florideophyceae</i> Order: <i>Halymeniales</i> Family: <i>Halymeniaceae</i>	Pacific Ocean	All Spain	North America, Europe, and Oceania	- Human consumption - Fertilizer
<i>Lophocladia lallemandii</i>	Phylum: <i>Rhodophyta</i> Class: <i>Florideophyceae</i> Order: <i>Ceramiales</i> Family: <i>Rhodomelaceae</i>	Indo-Pacific Ocean	All Spain	Mediterranean	- Unknown
<i>Womersleyella setacea</i>	Phylum: <i>Rhodophyta</i> Class: <i>Rhodophyceae</i> Order: <i>Ceramiales</i> Family: <i>Rhodomelaceae</i>	Indo-Pacific Ocean	All Spain	Mediterranean	- Unknown

Table 2. Cont.

Specie	Taxonomy	Native Distribution	Distribution in Spain	Other Regions in Which They Are Invasive	Principal Uses
Brown species					
<i>Gracilaria vermiculophylla</i>	Phylum: <i>Rhodophyta</i> Class: <i>Florideophyceae</i> Orden: <i>Gracilariales</i> Family: <i>Gracilariaceae</i>	North-east Pacific	All Spain	Europe and North America	- Animal feed - Biofuels - Fertilizer - Human consumption
<i>Sargassum muticum</i>	Phylum: <i>Ochrophyta</i> Class: <i>Phaeophyceae</i> Order: <i>Fucales</i> Family: <i>Sargassaceae</i>	Indo-Pacific Ocean	All Spain	Pacific Coast of North America, North Sea, Portugal, and the Mediterranean	- Animal feed - Food additive - Pesticide
<i>Styopodium schimperi</i>	Phylum: <i>Ochrophyta</i> Class: <i>Phaeophyceae</i> Order: <i>Dictyotales</i> Family: <i>Dictyotaceae</i>	Indo-Pacific Ocean and Red Sea	All Spain	Africa and Southwest Asia	- Unknown
<i>Undaria pinnatifida</i>	Phylum: <i>Heterokontophyta</i> Class: <i>Phaeophyceae</i> Order: <i>Laminariales</i> Family: <i>Alariaceae</i>	Asia	All Spain	Europe	- Human consumption - Animal feed
Green species					
<i>Caulerpa taxifolia</i>	Phylum: <i>Chlorophyta</i> Class: <i>Bryopsidiphyceae</i> Orden: <i>Bryopsidales</i> Family: <i>Caulerpaeae</i>	Tropical area	All Spain	Mediterranean, California, and southern Australia	- Laboratory use
<i>Codium fragile</i>	Phylum: <i>Chlorophyta</i> Class: <i>Chlorophyceae</i> Orden: <i>Codiales</i> Family: <i>Codiaceae</i>	North of the Pacific Ocean and coast of Japan	All Spain	Widespread in the Mediterranean	- Human consumption
<i>Caulerpa racemosa</i>	Phylum: <i>Chlorophyta</i> Class: <i>Bryopsidiphyceae</i> Orden: <i>Bryopsidales</i> Family: <i>Caulerpaeae</i>	Tropical areas	Except Canarias	Mediterranean: from Spain to Turkey	- Human consumption
Diatoms					
<i>Didymosphenia geminata</i>	Phylum: <i>Ochrophyta</i> Class: <i>Bacillariophyceae</i> Orden: <i>Cymbellales</i> Family: <i>Gomphonemataceae</i>	Boreal and alpine regions of North America and Northern Europe	All Spain	New Zealand and Patagonia, South America	- Ornamental

The use of some algae (e.g., *Caulerpa racemosa*) as ornamental species in aquariums has also contributed to their proliferation [59,60]. Among these species, only five are considered invasive (\*) or potentially invasive (\*\*) in Galicia (northwest Spain): *Asparagopsis armata*\*\*, *Codium fragile* subs. *tomentosoides*\*, *Grateloupia turuturu*\*\*, *Sargassum muticum*\*, and *Gracilaria vermiculophylla*\*. Galician waters also feature the presence of two other exotic invasive species, though they do not appear in the regulation of Real Decreto (RD) 1628/201; these are *Gymnodinium catenatum* and *Bonamia ostreae* [61].

For many years, non-native species of algae have been considered threats, thus a series of methods to eradicate them from non-endemic areas have been developed and optimized. However, the marine biomass, including invasive macroalgae, is currently the focus of several industries, such as pharmaceutical, food, cosmetic, and biotechnological industries, due their biological activities, e.g., antioxidant, antimicrobial, anti-inflammatory, anticancer. The aim of these industries is to revalorize invasive macroalgae as a source of extracts and compounds with industrial interest [8]. Although many studies have evaluated the biological properties of various extracts of *A. armata*, *C. fragile*, *G. turuturu*, *S. muticum*, and *G. vermiculophylla*, in some cases, the bioactive compounds responsible for this activity have not yet been identified. In the following paragraphs, the current knowledge about target compounds for industrial applications and the bioactive compounds identified in the

macroalgae species considered invasive in Galicia are compiled. They are also summarized in Table 3.

### 3.1. Polysaccharides

In the case of *A. armata*, the polysaccharides derived from sulfated galactans have shown strong antiviral effects against human immunodeficiency virus (HIV), inhibiting its reproduction [62]. A study confirmed the inhibition of herpes simplex virus type 1 by different extracts of numerous red algae, including *A. armata*. Although the authors did not identify the compounds involved in the activity, the good results of the water extract were attributed to water-soluble polysaccharides [63]. Mannitol has been also identified in the ethanolic extract of *A. armata*, in a concentration of 34.70 mg/100 g of dry macroalgae [64].

In the case of *C. fragile*, several bioactivities have been attributed to its sulfated polysaccharides (SPs). The administration of this type of compounds reduced the oxidative damage associated with diabetes mellitus and obesity in several animal models without any cytotoxic effect [65,66]. Recently, a study stated that SPs from *C. fragile* scavenge effectively freed radicals in vitro and suppressed the oxidative damage caused by H<sub>2</sub>O<sub>2</sub> in Vero cell cultures and in zebrafish [67]. It has also been reported that SPs from *C. fragile* increased the coagulation time of human blood in a dose-dependent manner according to the methods activated partial thromboplastin time (APTT) [68,69], thrombin time (TT), and prothrombin time (PT) [69]. SPs from *C. fragile* inhibited HeLa cells proliferation [70] by stimulating tumor necrosis factor (TNF)-related apoptosis-inducing ligand, a promising anticancer target [71].

**Table 3.** Main compounds and bioactive compounds reported for the invasive macroalgae in northwest Spain.






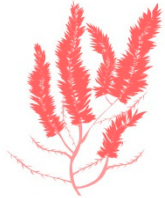




	Invasive Macroalgae				
Bioactive Compounds					
	<i>Asparagopsis armata</i>	<i>Codium fragile</i>	<i>Gracilaria vermiculophylla</i>	<i>Sargassum muticum</i>	<i>Gratelouia turuturu</i>
Polysaccharides	Sulphated galactan derivatives, Mannitol	Sulphated polysaccharides		Fucoidans, Alginate, Glucuronic acid, Mannuronic acid, Laminarin	
Lipids	Cholesterol, Cholesta-5,25-diene-3,24-diol, Palmitic acid, Stearic acid	Clerosterol	Cholesterol, 1-tetradecanol, 1-hexadecanol, 1-octadecanol, 1-eicosanol, 1-docosanol, Sterols, Monoacylglycerol	$\alpha$ -Linolenic acid	Phospholipids, Glycolipids, Eicosapentaenoic acid
Proteins			Mycrosporine-like aminoacids*		
Pigments		$\beta$ -carotene, Siphonaxanthin		Fucoxanthin	R-phycoerythrin
Vitamins		$\alpha$ , $\beta$ , $\gamma$ , $\delta$ -tocopherol, $\gamma$ -tocotrienol	$\alpha$ -tocopherol	$\alpha$ , $\gamma$ -tocopherol	$\alpha$ -tocopherol, Phytonadione (vitamin K1)

Table 3. Cont.

	Invasive Macroalgae				
Bioactive Compounds					
	<i>Asparagopsis armata</i>	<i>Codium fragile</i>	<i>Gracilaria vermiculophylla</i>	<i>Sargassum muticum</i>	<i>Grateloupia turuturu</i>
Phenolic compounds	Not specified	Flavonoids, tannins	Gallic acid, Protocatechuic acid, Gentisic acid, Hydroxybenzoic acid, vVnillic acid, Syringic acid	Hydroxybenzoic acid, Gallic acid, Vanillic acid, Protocatechuic acid, Caffeic acid, Syringic acid, Chlorogenic acid, Coumaric acid, Phlorotannins, Fuhalols, Phlorethols, Hydroxyfuhalols, Monofuhalol A,	
Other compounds	Halogenated compounds, Halogenated ketones, 1,1-dibromo-3-iodo-2-propanone, 1,3-dibromo-2-propanone, 1,3-dibromo-1-chloro-2-propanone ( $\pm$ ) form, Halogenated carboxylic acids, Dibromoacetic acid, Bromochloroacetic acid, Dibromoacrylic acid, Halogenated alkanes, Bromoform, Dibromochloromethane	Serine protease	Long chain aliphatic alcohols	Tetrapernyltaluquinol meroterpenoid with a chrome moiety	Squalene
Reference	[72–74]	[75,76]	[77]	[78]	[79,80]

Finally, these compounds also show immune-stimulating properties in both in vitro and in vivo models. Sulfated galactan obtained from *C. fragile* stimulated murine macrophages RAW264.7 cell line, increasing the levels of nitric oxide and both pro-inflammatory and anti-inflammatory cytokines, which are fundamental for the host immune response [81–83]. In head kidney cells, SPs had a stimulatory effect on immune genes, including interleukin (IL)-1 $\beta$ , IL-8, TNF- $\alpha$ , interferon (IFN)- $\gamma$ , and lysozyme [84]. Immuno-stimulant properties have been also observed in human peripheral blood dendritic cells and T cells, which were activated by SPs. This suggests that these compounds could be candidates for products aimed to enhance human immune system [85].

*S. muticum* is a source of several valuable polysaccharides, such as fucoidans, alginate, guluronic and mannuronic acids, laminarin, and their derivatives [86]. Alginate obtained from *S. muticum* has been demonstrated to possess anticancer properties, stimulating cell death in A549 cells (epithelial lung adenocarcinoma), PSN1 cells (pancreatic adenocarcinoma), HCT-116 cells (colon carcinoma), and T98G cells (glioblastoma) [87].

Finally, *G. vermiculophylla* and *G. turuturu* are being used in the phycocolloid industry for obtaining agar and carrageenan, respectively, turning them into valuable matrixes [88,89]. Recently, polysaccharide extracts from *G. turuturu* have shown antimicrobial properties against *Escherichia coli* and *Staphylococcus aureus* [90].

### 3.2. Lipids

Starting with *A. armata*, it has been reported that these macroalgae contain some sterols such as cholesta-5,25-diene-3,24-diol, (3 $\beta$ ,24S)-form [91], palmitic and stearic fatty acids, and cholestanol [64]. Recently, different crude extracts and fractions of this species were demonstrated to present antibacterial and antifouling properties. In the crude extract and most active fractions, several compounds were identified, including hexadecanoic, dodecanoic, octadecanoic, and tetradecanoic acids, which may be involved in this activity [92,93].

Regarding *C. fragile*, clerosterol (a derivative of cholesterol) was found in several extracts. This compound shows antioxidant properties, since it attenuated UVB-induced oxidative damage in human immortalized keratinocyte HaCaT cells and BALB/c mice models, reducing lipid and protein oxidation [94]. In addition, clerosterol stimulated apoptosis in A2058 human melanoma cells [95] and modulated several apoptotic factors in human leukemia cells [96]. Recently, a study observed that *C. fragile* displayed neuroprotective effects on neuroblastoma cell line SH-SY5Y. In the most bioactive fractions, several lipid compounds, among others, were identified. Although more research is needed, the authors considered that lipids are involved in the neuroprotective effect [97].

*G. vermiculophylla* contains high quantity of cholesterol (473.2 mg/kg dry weight), cholesterol derivatives, long-chain aliphatic alcohols, and monoglycerides, including 1-tetradecanol, 1-hexadecanol, 1-octadecanol, 1-eicosanol, and 1-docosanol [77]. Other lipids of great interest for nutraceutical and biotechnological industries include phospholipids, glycolipids, and eicosapentaenoic acid, present in high levels in this alga [79]. For example, three sphingolipids (gracilarioside, and gracilamides A and B) isolated from *G. vermiculophylla* (accepted name of *G. asiatica*) showed moderate cytotoxic effects against human A375-S2 melanoma cell line [98].

### 3.3. Proteins

To our knowledge, only *G. vermiculophylla* presents bioactive compounds of protein nature. This alga can absorb UV-A and UV-B radiations and decrease free radicals-induced effects, resulting from its high content in mycosporine-like amino acids [99].

### 3.4. Pigments

Siphonaxanthin from *C. fragile* has shown anticancer properties, stimulating the apoptosis of A549 lung cancer cells and modulating apoptotic factors in human leukemia cells [95,96]. Moreover, the anti-angiogenic effect of siphonaxanthin has been described in human umbilical vein endothelial cells as well as in a rat aortic ring angiogenic model [100], which suggests that this biomolecule could be an alternative to prevent pro-angiogenic diseases such as cancer. In addition, this alga also contains  $\beta$ -carotene [76].

In recent years, fucoxanthin has received a great deal of interest from the scientific community and industry due to the many beneficial health properties attributed to it, including anti-inflammatory [101]. Fucoxanthin extracted from *S. muticum* inhibited the lipopolysaccharide-induced nitric oxide production in RAW 264.7 macrophages and inhibited the expression of pro-inflammatory cytokines [102,103].

At industrial scale, *G. turuturu* is also used to produce R-phycoerythrin, a pink-purple pigment soluble in water present in large quantities, which presents diverse biological properties and potential industrial applications [89,104].

### 3.5. Vitamins

Different vitamins have been identified in the selected macroalgae, except in *A. armata*. In *C. fragile*, high levels of tocopherols have been reported (1617.6  $\mu$ g/g lipid), including  $\alpha$ ,  $\beta$ ,  $\gamma$ , and  $\delta$  tocopherol and  $\gamma$ -tocotrienol [76]. *G. vermiculophylla* showed a considerable  $\alpha$ -tocopherol content (28.4  $\mu$ g/g of extract) [105]. Regarding *G. turuturu*, a chemical analysis revealed the presence of  $\alpha$ -tocopherol and phytonadione (vitamin K1) [80]. Finally,



*S. muticum* contains high amounts of  $\alpha$ - and  $\gamma$ -tocopherol, 218 and 20.8  $\mu\text{g/g}$  of extract, respectively [105].

### 3.6. Phenolic Compounds

Phenolic content has been evaluated in several species, although not all the studies have identified the target compounds. In the case of *A. armata*, phenolic content was determined by the Folin–Ciocalteu spectrophotometry method, which showed that it represented  $1.13 \pm 0.05\%$  of dry weight [106]. Different extracts of *C. fragile* also contain phenolic compounds, mainly flavonoids and, to a lesser extent, tannins. These compounds showed a correlation with the antioxidant activity of the macroalgae [75]. The previous study of Farvin and Jacobsen (2013) identified several phenolic acids in both *G. vermiculophylla* aqueous extracts (gallic, protocatechuic, hydroxybenzoic, vanillic, syringic, and salicylic acids) and ethanolic extracts (gallic, protocatechuic, and gentisic acids). In correspondence with its content in phenolic compounds, a high antioxidant capacity has been demonstrated for these macroalgae according to the 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and the ferric antioxidant power (FRAP) methods. In addition, *G. vermiculophylla* extracts inhibited lipid peroxidation [105]. Finally, some authors have reported the presence of phenolic compounds in *S. muticum*, including (ordered from highest to lowest concentration): hydroxybenzoic and gallic acids, *p*-hydroxybenzaldehyde, vanillic acid, 3,4-dihydroxybenzaldehyde and protocatechuic, ferulic, *p*-coumaric, caffeic, syringic, and chlorogenic acids [107]. Several bioactivities of *S. muticum*, such as antioxidant, antimicrobial, anticancer, or anti-inflammatory, have been attributed to the presence of phenolic compounds with high antioxidant capacity, particularly to phlorotannins (e.g., phloroglucinol, diphlorethol, bifuhalol), which are exclusively found in marine seaweed [78,108–111].

### 3.7. Other Minor Compounds

The invasive species *A. armata* presents high levels of halogenated secondary metabolites with recognized antibiotic activity [112]. They act as chemical defense against grazers and epibiota [113] and may be suitable for a wide range of applications [114,115]. For instance, the major metabolites bromoform and dibromoacetic acid, along with dibromochloromethane, bromochloroacetic acid, and dibromoacrylic acid, have shown high antifouling potential [72–74]. They can decrease the density of six bacteria strains on the algae surface: two marine (*Vibrio harveyi* and *V. alginolyticus*) and four biomedical strains (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermis*, and *Escherichia coli*) [116]. Recently, several brominated compounds, such as tribromomethanol, were found in the crude extract and fractions of *A. armata*, which showed antimicrobial antifouling potential [92,93].

A serine protease extracted from *C. fragile* was demonstrated to exert in vitro and in vivo anticoagulant and fibrinolytic activity [117]. Finally, it was found that *G. turuturu* contains squalene, which was reported to exert several beneficial activities [80].

## 4. Current Strategies to Obtain Bioactive Compounds from Algae

Algae have been considered as potential sources for the extraction of bioactive compounds with applications in food, cosmetic, pharmaceutical, or other industrial sectors. However, one of the most limiting steps when referring to obtaining bioactive compounds from natural sources is the extraction system, and, thus, upscale and downstream processes in the case of its industrial application [118]. Table 4 summarizes some examples of extraction techniques applied for the recovery of bioactive compounds from the studied invasive species.

For the final purpose of extracting bioactive compounds, several techniques of pretreatments and extraction have been thoroughly described. Traditionally, pretreatments consist of using hot air drying, chemical treatments with acids, salts, or surfactants. Nevertheless, novel extraction techniques (explained below) have also been successfully applied as pretreatments for algae [119].

#### 4.1. Conventional Extraction Techniques

Conventional extraction techniques were deeply investigated during the past decades for their easiness of application and low requirements, but, also for this reason, they continue to be the most used [120]. As it can be seen in Table 4, the techniques that have been more frequently applied are maceration, Soxhlet, and heat assisted extraction (HAE). These methodologies are applied using different solvents, heat, and/or stirring in some cases. Moreover, in the case of Soxhlet extraction, the recircularization of the solvent during longer time periods is aimed at improving the extraction yield [121]. Additionally, heat favors the mass transfer of the bioactive compounds to the solvent through the disruption of cell walls [122].

**Table 4.** Extraction techniques for obtaining bioactive compounds from the invasive macroalgae in northwest Spain.

Method	Conditions	Compounds	Activities	Model/Assay	Ref.
<i>Asparagopsis armata</i>					
Soxhlet	Chloroform-methanol (3:2), dichloromethane (100%), methanol (100%), and water (100%), 8 h	-	Anti-Herpes Simplex Virus and cytotoxicity	Neutral red dye method on Vero cells.	[63]
Mac	Hexane, dichloromethane, and ethanol	Halogenated compounds	Antiprotozoal	<i>Leishmania donovani</i> promastigotes cultures	[123]
Mac	0.025 g/mL; methanol, 16 h, 20 °C	Phenolic compounds	Antioxidant and neuroprotective	DPPH, CCA, ICA, AChE, BuChE, TYRO inhibition. In vivo MTT assay on SH-SY5Y cells on H <sub>2</sub> O <sub>2</sub> induced cytotoxicity.	[124]
HAE	0.04 g/mL; distilled water, 5 h, 96 °C	Polysaccharides	Anti-HIV	Human immunodeficiency virus (HIV) induced syncytium formation on MT4 cells.	[62]
PLE	Dichloromethane methanol (1:1; v:v); 75 °C, 1500 psi, 7 min (×2)	Phenolic compounds	Antioxidant and cytotoxicity	Radical-scavenging activity (DPPH). Reducing activity. Daudi, Jurkat and K562 cell lines.	[106]
<i>Codium fragile</i>					
Mac	80% methanol (×3). Butanol and ethyl-acetate fractions.	Clerosterol	Antioxidant and anti-inflammatory	In vivo MTT assay on human keratinocyte HaCaT cells irradiated with UVB and BALB/c mice models. Expression of pro-inflammatory proteins and mediators	[94]
Mac	Hexane, ethyl, and methanol (×3)	-	Antioxidant and anti-hypertensive	DPPH and ABTS inhibition. In vitro ACE inhibitory assay	[75]
Mac	80% methanol	-	Anti-inflammatory	Lipopolysaccharide-stimulated RAW 264.7	[125]
Mac	80% methanol	-	Anti-cancer	Human breast cancer cell line MDA-MB-231	[126]
HAE	0.02 g/mL; water, 12 h, 60 °C	Polysaccharides	Anticoagulant	APTT assay on human blood	[68]
HAE	10 vol, distilled water, 1 h, 95 °C	-	Anti-inflammatory and anti-edema	LPS-stimulated RAW 264.7 and carrageenan-induced paw edema in male Sprague-Dawley rats.	[127]
HAE	Ethanol 96% (v/v), 3 h, 70 °C (×3)	-	Anti-inflammatory	LPS-stimulated RAW 264.7.	[128]
HAE	Distilled water, 4 h, 90 °C.	-	Anti-inflammatory, alleviation of cartilage destruction	Primary chondrocytes cells, osteoarthritis rat model.	[129]
<i>Gracilaria vermiculophylla</i>					
Mac	0.1 g/mL; water or ethanol, 96%, 12 h, room temperature.	Phenolic compounds	Antioxidant	In vitro assays (DPPH, FRAP, ferrous ion-chelating) and liposome model system.	[105]
Soxhlet	0.3 g/mL; ethyl acetate; 72 h.	-	Antimicrobial	Strains of <i>S. enteritidis</i> , <i>P. Aeruginosa</i> and <i>L. innocua</i>	[121]

Table 4. Cont.

Method	Conditions	Compounds	Activities	Model/Assay	Ref.
<i>Grateloupia turututu</i>					
S/L	1/20 ratio (w/v), water, 20 min, phosphate buffer (20 mM, pH 7.1)	-	Antibacterial	European abalone pathogen <i>Vibrio harveyi</i>	[130]
<i>Sargassum muticum</i>					
Mac	0.01 g/mL; 80% methanol, 24 h, RT.	Fucoanthin	Anti-inflammatory	LPS-stimulated RAW 264.7 macrophages	[103]
Mac	0.1 g/mL; Water or ethanol, 96%, 12 h, RT.	Phenolic compounds	Antioxidant	In vitro assays (DPPH, FRAP, ferrous ion-chelating) and liposome model system	[105]
Mac	Dichloromethane or methanol, 1:4 (w/v), 12 h.	Phenolic compounds	Antioxidant and cytoprotective effect	In vitro assays (DPPH and ORAC) Protective effect on MCF-7 cells	[131]
HAE	Methanol:water (1:10), 3 h, 65 °C (×3)	Chromane meroterpenoid	Photodamage attenuation	Human dermal fibroblasts	[132]
SFE	CO <sub>2</sub> , 10% ethanol, 15.2 MPa, 60 °C, 90 min (static)	-	Antioxidant	Not reported	[133]
PLE	Ethanol:water (95:5); 160 °C, 10.3 MPa, 20 min (×2)	Phlorotannins	Antiproliferative	HT-29 adenocarcinoma colon cancer cells	[134]
UAE	Water at S/L ratio of 1:20; 5–30 min, RT (25 °C), 5 A, 150 W and 40 Hz.	Alginate	Cytotoxic effect	A549, HCT- 116, PSN1, and T98G cells	[87]
Autohydrolysis	96% ethanol	-	Antioxidant, anti-inflammatory and anti-irritant	In vitro assays (FRAP, DPPH and ABTS). Reconstructed human epidermis test method. Irritability assays with the Episkin test.	[108]
Autohydrolysis	RT, formaldehyde 1% (15 h), sulfuric acid 0.2 N (4 h), and sodium carbonate 1% (15 h).	Phlorotannins	Anti-tumor and anti-inflammatory	A549, HCT-116, PSN1, and T98G cells. Neutrophils' oxidative burst oxidation of luminol.	[78]

Extraction method: PLE: pressurized liquid extraction; S/L: solid–liquid; SFE: supercritical fluid extraction; UAE: ultrasound assisted extraction; Mac: maceration; RT: room temperature. Assays: DPPH: 1,1-Diphenyl-2-picrylhydrazyl; ABTS: 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); CCA: copper chelating activity; ICA: iron chelating activity; AChE: acetylcholinesterase; BuChE: butyrylcholinesterase; TYRO: tyrosinase; ACE: angiotensin converting enzyme; APTT: activated partial thromboplastin Time; ORAC: oxygen radical absorbent capacity; FRAP: ferric antioxidant power. Cell lines: Vero: African green monkey kidney cell line; MT4: leukemia cell line; HaCaT: aneuploid immortal keratinocyte cell line; RAW 264.7: murine macrophage cell line; MCF-7: human breast cancer cell line; A549: adenocarcinomic human alveolar basal epithelial cells; HCT-116: human colon cancer cell line; PSN1: human pancreatic cancer cell line; T98G: glioblastoma cell line.

#### 4.2. Novel Extraction Techniques

On the other hand, emerging or novel techniques are also increasing as new methods directed towards a more sustainable process, with lower times and energy consumption or higher yields. Among them, some examples must be highlighted: microwave assisted extraction (MAE), ultrasounds assisted extraction (UAE), pressurized liquid assisted extraction (PLE), enzyme assisted extraction (EAE), high pressure assisted extraction (HPAE), pulsed electric field (PEF), supercritical fluid extraction (SFE), and hydrothermal liquefaction. At last, new options are being explored that combine approaches of different techniques [119]. Table 4 shows some of the examples when these techniques have been applied on invasive species.

Considering the information collected, obtaining processes of bioactive compounds from these invasive species utilizes a wide range of conventional and novel sample preparation and extraction techniques. Once the extraction has been performed, it is necessary to characterize and quantify the compounds present in the extract. To carry out this process, the most used techniques are based on chromatographic methods [135]. These methods are regularly evolving and currently coupled to different detectors. Nuclear magnetic resonance, mass spectrometry, vibrational spectrometry, or a combination of several tech-

niques are some of the approaches currently applied. All of them are focused on separating, detecting, characterizing, and quantifying those bioactive molecules as well as elucidating their structures and their function on the metabolic pathways they are involved in [136].

## 5. Algae as Supplement of Diets in Aquaculture

Aquaculture has grown very fast in the last decades, reaching expansion rates higher than other major food production sectors. By 2016, the aquaculture relevance as an animal protein source was underlined by its huge global production that reached nearly 80 million tons. Among the European countries, Spain is expected to reach more than 0.3 Mt of annual production [137]. This exponential growth has been prompted by the low feed conversion ratio that aquaculture species exhibit, 1.1–1.6 kg of feed/kg of edible fish, against livestock, which can reach maximum ratios of 9 kg of feed/kg of beef [138,139]. However, for the aquaculture sector to continue growing at a constant rate, the supply of nutrients and feed will have to grow at a similar rate [140]. Finding appropriate ingredients to substitute the limited marine resources generally used in aquaculture feeds has been challenging the sector for decades. Therefore, it is necessary to develop new and more sustainable food sources for aquaculture use. In this sector, macroalgae has been proposed as a possible protein source in the fish feed but also as a source of bioactive compounds, which may improve the nutritional values and exert beneficial effects on animal health, including antioxidant, antimicrobial, or positive effects on immune system [141]. Invasive algae may be possible candidates for these uses. This kind of exploitation will permit obtaining compounds from sustainable sources for industrial application while reducing the population of invasive species, providing double profit. However, several limitations of the use of macroalgae species in aquaculture feeds have been identified. For example, from a nutritional point of view, it would be necessary to eliminate compounds that may be anti-nutritive or to develop methods to reduce polysaccharides to increase the digestibility [142]. In addition, in some cases, knowledge gaps about the compounds involved in the observed effects and the mechanisms of action still persist. Therefore, the use of some species in aquaculture is still limited, and more research is necessary before their application.

Regarding the selected invasive algae species, different examples along the scientific literature reported their beneficial effects in the nutrition of several aquaculture animals. The use of *A. armata*, under the commercial powder presentation named after Ysaline<sup>®</sup>100, was assessed for the development of *Sparus aurata* larvae. Among the experimental parameters analyzed—growth, survival, anti-bacterial activity, microbiota quantification, digestive capacity, stress level, and non-specific immune—the last three were not affected when *A. armata*-based feed was utilized. Besides, this diet significantly reduced the amount of Vibrionaceae present in water and larval gut and enhanced growth rate. It was suggested that mortality produced when high concentrations of *A. armata*-based feed were used will improve if lower amounts are used until 10 days after hatching, promoting a safer rearing environment [143]. Recently, extracts of *A. armata* were used to supplement the feed of the whiteleg shrimp (*Penaeus vannamei*). The results showed that the formulation increased the survival rate in presence of *Vibrio parahaemolyticus* (causative agent of acute hepatopancreatic necrosis disease) and reduced the food contamination caused by fungus [144].

As previously mentioned, a recent study stated the protective effect of SPs extracted from *C. fragile* against free radicals. These molecules were demonstrated to suppress the oxidative damage induced by oxygen peroxide in the main fish live model, zebrafish. Embryos at 7–9 h post-fertilization stage were incubated with different concentrations of SPs from *C. fragile* for 1 h and then exposed to the pro-oxidant agent for another 14 h. Obtained results indicated that the pre-treatment of zebrafish with *C. fragile* SPs can protect animals against oxidative stress by reducing reactive oxygen species, minimizing cell death and lipid peroxidation. This antioxidant capacity of *C. fragile* SPs can be relevant for the development of innovative fishmeal [67]. In another study, *C. fragile* SPs exerted immuno-stimulating effects on olive flounder (*Paralichthys olivaceus*), up-regulating the

expression of interleukins 1 $\beta$  and 8, TNF- $\alpha$ , interferon- $\gamma$ , and lysozyme genes, all of them involved in the immune response. Thus, this species could be used as feed additive to improve the immune system of the fish [84].

*G. vermiculophylla* has been repeatedly tested in experimental diets, especially aimed at freshwater fish species such as rainbow trout (*Oncorhynchus mykiss*). The apparent digestibility coefficient for trout of proteins and lipids from a *G. vermiculophylla* based diet was like that of the reference diets [145]. Additionally, another work in which *G. vermiculophylla* was utilized for designing experimental diets for rainbow trout demonstrated some benefits for animal health that also reflect an economical benefit for improving the quality of the finally commercialized product. The inclusion of this invasive alga in 5% doubled the flesh iodine levels, which ultimately improved the fillet color intensity and juiciness since it enhanced the carotenoid deposition, which can be also associated with a better conservation of the final product for the antioxidant properties related to carotenoid pigments [146]. In another study, the inclusion of 5% of this species in the diet of *O. mykiss* was reported to enhance the immune system of the animals by increasing lysozyme, peroxidase, and complementing system activities, which play a key role in the defense against pathogens [147]. Finally, the effect of supplementation of heat-treated *G. vermiculophylla* was evaluated in gilthead sea bream (*Sparus aurata*) submitted to acute hypoxia and successive recovery. Compared to the control, the dietary inclusion of the macroalgae reduced the antioxidant stress caused by the hypoxia, and the survival rate was higher [148]. More recently, the immunomodulatory effect of *G. vermiculophylla* has been evaluated in the shrimp *Litopenaeus vannamei*. Co-culture with diverse macroalgae species (including *G. vermiculophylla*) improved the immune response of the shrimps against the pathogen *V. parahaemolyticus* and white spot virus, increasing the production of hemocytes and the activity of superoxide dismutase (SOD) and catalase (CAT) compared to control [149].

Very scarce information regarding the development of experimental diets formulated with *S. muticum* has been found. However, at least one study performed its inclusion and tested its effect in African catfish, *Clarias gariepinus*. As in previous works, they added 5% of alga and fed animals for 12 weeks. In the skin of fish fed with probiotics diet, an improved glutathione S-transferase (GST) and SOD activity and less CAT activity were recorded, whereas in the livers from fishes fed with *S. muticum*, a better oxidative status with improved GST and CAT activities were displayed. This positive effect on antioxidant enzyme activity has been suggested to ultimately improve the resistance of animals against bacterial infections [150]. Other species belonging to the *Sargassum* genus have been described as immunomodulators and growth promoters for great sturgeon (*Huso huso*) and as immunobooster for shrimp (*Fenneropenaeus chinensis*) to which they also provide specific resistance to vibriosis [151,152].

Finally, experimental diets aimed to feed cultivated hybrid abalone cross (*Haliotis rubra* and *Haliotis laevigata*) were designed using several macroalgae, i.e., *G. turuturu* together with *Ulva australis* and/or *U. laetevirens*. Treatment applied for 12 weeks period provided a significant higher growth rate of abalone in terms of length and weight. Besides, it improved abalone health and its nutritional composition, since animals showed, by the end of the assay, tissues with higher carbohydrate/protein ratio, ash content, and lower lipid amount [153]. Other studies in which *G. turuturu* mixed with *P. palmata* was used as feed for the European abalone *Haliotis tuberculata* demonstrated that the combination of algae did not produce animals' mortality, and it improved growth rates (in length and weight) while increasing the final content of lipid in the abalone [154]. Besides, in another work, the capacity of *G. turuturu* was underlined for inhibiting, in a quantity of 16%, the growth of the main pathogen of the *H. tuberculata*, that is, *Vibrio harveyi* [130]. Therefore, the inclusion of this invasive alga in experimental diets may provide nutritional value to abalone but also antibacterial activity which ultimately reduces mortalities.

## 6. Future Perspectives and Conclusions

According to the compiled studies, *Asparagopsis armata*, *Codium fragile* subs. *tomentosoides*, *Grateloupia turuturu*, *Sargassum muticum*, and *Gracilaria vermiculophylla* can be considered as alternative sources of bioactive compounds which could be further used for industrial applications. Thus, revalorization strategies will make it possible to obtain new compounds from sustainable sources but also reduce the population of invasive species, generating a double benefit. Nevertheless, two key concerns limit their further use. From the scientific and the technological points of view, more research is still required to increase the profitability of the extraction process. Therefore, the applicability of different techniques needs to be further investigated to assess which is the most favorable process, comparing both conventional and modern extraction techniques. In addition, in some cases, it is still necessary to identify the specific compounds responsible for the observed activities and to determine their action mechanisms. Nevertheless, the development of invasive algae harvesting methods generates a series of drawbacks. The main one is that the revalorization of invasive algae could lead to an increase of their populations instead of eliminating them due to the economic benefits that could be obtained from their use. In fact, this economic revenue would not be difficult to achieve, since these invasive algae are often characterized by a high reproductive rate. Considering this drawback, the collection of invasive species should be subjected to a strict policy. A principle that should be considered is that the only legal collectors of invasive algae should be those companies whose activity is reduced by the presence of these organisms (e.g., shellfish catchers/farmers, inshore fishermen, diving companies, etc.). This would prevent the harvesters themselves from “planting” more invasive algae to further increase their profits.

**Author Contributions:** Conceptualization, M.A.P. and J.S.-G.; methodology, A.G.P., C.L.-L., M.C., M.F.-C., P.G.-O.; formal analysis, A.G.P., C.L.-L., M.C., M.F.-C., P.G.-O.; investigation, A.G.P., C.L.-L., M.C., M.F.-C., P.G.-O.; writing—original draft preparation, A.G.P., C.L.-L., M.C., M.F.-C., P.G.-O.; writing—review and editing, M.A.P. and J.S.-G.; supervision, M.A.P. and J.S.-G.; project administration, M.A.P. and J.S.-G. All authors have read and agreed to the published version of the manuscript.

**Funding:** The research leading to these results was funded by Xunta de Galicia supporting the Axudas Conecta Peme, the IN852A 2018/58 NeuroFood Project, and the program EXCELENCIA-ED431F 2020/12; to Ibero-American Program on Science and Technology (CYTED—AQUA-CIBUS, P317RT0003) and to the Bio Based Industries Joint Undertaking (JU) under grant agreement No 888003 UP4HEALTH Project (H2020-BBI-JTI-2019). The JU receives support from the European Union’s Horizon 2020 research and innovation program and the Bio Based Industries Consortium. The project SYSTEMIC Knowledge hub on Nutrition and Food Security has received funding from national research funding parties in Belgium (FWO), France (INRA), Germany (BLE), Italy (MIPAAF), Latvia (IZM), Norway (RCN), Portugal (FCT), and Spain (AEI) in a joint action of JPI HDHL, JPI-OCEANS, and FACCE-JPI launched in 2019 under the ERA-NET ERA-HDHL (n° 696295).

**Institutional Review Board Statement:** Not applicable.

**Data Availability Statement:** Not applicable.

**Acknowledgments:** The research leading to these results was supported by MICINN supporting the Ramón y Cajal grant for M.A. Prieto (RYC-2017-22891); by Xunta de Galicia for supporting the post-doctoral grant of M. Fraga-Corral (ED481B-2019/096), the pre-doctoral grants of P. García-Oliveira (ED481A-2019/295) and Antía González Pereira (ED481A-2019/0228); by University of Vigo for the predoctoral grant of M. Carpena (Uvigo-00VI 131H 6410211) and by UP4HEALTH Project that supports the work of C. Lourenço-Lopes.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Máximo, P.; Ferreira, L.M.; Branco, P.; Lima, P.; Lourenço, A. Secondary metabolites and biological activity of invasive macroalgae of southern Europe. *Mar. Drugs* **2018**, *16*, 265. [[CrossRef](#)]
2. Shackleton, R.T.; Shackleton, C.M.; Kull, C.A. The role of invasive alien species in shaping local livelihoods and human well-being: A review. *J. Environ. Manag.* **2019**, *229*, 145–157. [[CrossRef](#)]

3. Pyšek, P.; Hulme, P.E.; Simberloff, D.; Bacher, S.; Blackburn, T.M.; Carlton, J.T.; Dawson, W.; Essl, F.; Foxcroft, L.C.; Genovesi, P.; et al. Scientists' warning on invasive alien species. *Biol. Rev.* **2020**, *95*, 1511–1534. [[CrossRef](#)] [[PubMed](#)]
4. Otero, M.; Cebrian, E.; Francour, P.; Galil, B.; Savini, D. *Monitoring Marine Protected in Mediterranean Invasive Species Areas (MPAs)—A Strategy and Practical Guide for Managers*; IUCN: Malaga, Spain, 2013.
5. Commission European. *Invasive Alien Species of Union Concern*; Commission European: Luxembourg, 2020.
6. Milledge, J.J.; Nielsen, B.V.; Bailey, D. High-value products from macroalgae: The potential uses of the invasive brown seaweed, *Sargassum muticum*. *Rev. Environ. Sci. Biotechnol.* **2015**, *15*, 67–88. [[CrossRef](#)]
7. Davoult, D.; Surget, G.; Stiger-Pouvreau, V.; Noisette, F.; Riera, P.; Stagnol, D.; Androuin, T.; Poupart, N. Multiple effects of a *Gracilaria vermiculophylla* invasion on estuarine mudflat functioning and diversity. *Mar. Environ. Res.* **2017**, *131*, 227–235. [[CrossRef](#)]
8. Pinteus, S.; Lemos, M.F.L.; Alves, C.; Neugebauer, A.; Silva, J.; Thomas, O.P.; Botana, L.M.; Gaspar, H.; Pedrosa, R. Marine invasive macroalgae: Turning a real threat into a major opportunity—the biotechnological potential of *Sargassum muticum* and *Asparagopsis armata*. *Algal Res.* **2018**, *34*, 217–234. [[CrossRef](#)]
9. Machmudah, S.; Diono, W.; Kanda, H.; Goto, M. Supercritical fluids extraction of valuable compounds from algae: Future perspectives and challenges. *Eng. J.* **2018**, *22*, 13–30. [[CrossRef](#)]
10. Buschmann, A.H.; Camus, C.; Infante, J.; Neori, A.; Israel, Á.; Hernández-González, M.C.; Pereda, S.V.; Gomez-Pinchetti, J.L.; Golberg, A.; Tadmor-Shalev, N.; et al. Seaweed production: Overview of the global state of exploitation, farming and emerging research activity. *Eur. J. Phycol.* **2017**, *52*, 391–406. [[CrossRef](#)]
11. Fernández-Segovia, I.; Lerma-García, M.J.; Fuentes, A.; Barat, J.M. Characterization of Spanish powdered seaweeds: Composition, antioxidant capacity and technological properties. *Food Res. Int.* **2018**, *111*, 212–219. [[CrossRef](#)] [[PubMed](#)]
12. Gómez-Zavaglia, A.; Prieto Lage, M.A.; Jiménez-López, C.; Mejuto, J.C.; Simal-Gándara, J. The Potential of Seaweeds as a Source of Functional Ingredients of Prebiotic and Antioxidant Value. *Antioxidants* **2019**, *8*, 406. [[CrossRef](#)]
13. Gomez, L.P.; Alvarez, C.; Zhao, M.; Tiwari, U.; Curtin, J.; Garcia-Vaquero, M.; Tiwari, B.K. Innovative processing strategies and technologies to obtain hydrocolloids from macroalgae for food applications. *Carbohydr. Polym.* **2020**, *248*, 116784. [[CrossRef](#)]
14. Camacho, F.; Macedo, A.; Malcata, F. Potential industrial applications and commercialization of microalgae in the functional food and feed industries: A short review. *Mar. Drugs* **2019**, *17*, 312. [[CrossRef](#)]
15. Matos, Á.P. The Impact of Microalgae in Food Science and Technology. *JAOCS J. Am. Oil Chem. Soc.* **2017**, *94*, 1333–1350. [[CrossRef](#)]
16. Soleymani, M.; Rosentrater, K.A. Techno-economic analysis of biofuel production from macroalgae (Seaweed). *Bioengineering* **2017**, *4*, 92. [[CrossRef](#)] [[PubMed](#)]
17. Culaba, A.B.; Ubando, A.T.; Ching, P.M.L.; Chen, W.H.; Chang, J.S. Biofuel from microalgae: Sustainable pathways. *Sustainability* **2020**, *12*, 9. [[CrossRef](#)]
18. Milano, J.; Ong, H.C.; Masjuki, H.H.; Chong, W.T.; Lam, M.K.; Loh, P.K.; Vellayan, V. Microalgae biofuels as an alternative to fossil fuel for power generation. *Renew. Sustain. Energy Rev.* **2016**, *58*, 180–197. [[CrossRef](#)]
19. Shuba, E.S.; Kifle, D. Microalgae to biofuels: 'Promising' alternative and renewable energy, review. *Renew. Sustain. Energy Rev.* **2018**, *81*, 743–755. [[CrossRef](#)]
20. Blunt, J.W.; Carroll, A.R.; Copp, B.R.; Davis, R.A.; Keyzers, R.A.; Prinsep, M.R. Marine natural products. *Nat. Prod. Rep.* **2018**, *35*, 8–53. [[CrossRef](#)] [[PubMed](#)]
21. Holdt, S.L.; Kraan, S. Bioactive compounds in seaweed: Functional food applications and legislation. *J. Appl. Phycol.* **2011**, *23*, 543–597. [[CrossRef](#)]
22. Silva, A.; Silva, S.A.; Carpena, M.; Garcia-Oliveira, P.; Gullón, P.; Barroso, M.F.; Prieto, M.A.; Simal-Gandara, J. Macroalgae as a source of valuable antimicrobial compounds: Extraction and applications. *Antibiotics* **2020**, *9*, 642. [[CrossRef](#)]
23. Gopeechund, A.; Bhagooli, R.; Neergheen, V.S.; Bolton, J.J.; Bahorun, T. Anticancer activities of marine macroalgae: Status and future perspectives. In *Biodiversity and Biomedicine*; Ozturk, M., Egamberdieva, D., Pešić, M., Eds.; Academic Press: Cambridge, MA, USA, 2020; pp. 257–275. ISBN 9780128195413.
24. Cikoš, A.-M.; Jerković, I.; Molnar, M.; Šubarić, D.; Jokić, S. New trends for macroalgal natural products applications. *Nat. Prod. Res.* **2019**, 1–12. [[CrossRef](#)]
25. Kim, S.K. *Marine Cosmeceuticals: Trends and Prospects*, 1st ed.; Kim, S.K., Ed.; Taylor & Francis Group: Boca Raton, FL, USA, 2012; ISBN 9781439860281.
26. Bedoux, G.; Hardouin, K.; Burlot, A.S.; Bourgougnon, N. Bioactive components from seaweeds: Cosmetic applications and future development. In *Advances in Botanical Research*; Academic Press: Cambridge, MA, USA, 2014.
27. Verdy, C.; Branka, J.-E.; Mekideche, N. Quantitative assessment of lactate and progerin production in normal human cutaneous cells during normal ageing: Effect of an *Alaria esculenta* extract. *Int. J. Cosmet. Sci.* **2011**, *33*, 462–466. [[CrossRef](#)]
28. Nizard, C.; Friguet, B.; Moreau, M.; Bulteau, A.-L.; Saunois, A. Use of *Phaeodactylum* Algae Extract as Cosmetic Agent Promoting the Proteasome Activity of Skin Cells and Cosmetic Composition Comprising Same. U.S. Patent 7,220,417, 22 May 2007.
29. Hwang, E.; Park, S.Y.; Sun, Z.; Shin, H.S.; Lee, D.G.; Yi, T.H. The Protective Effects of Fucosterol Against Skin Damage in UVB-Irradiated Human Dermal Fibroblasts. *Mar. Biotechnol.* **2014**, *16*, 361–370. [[CrossRef](#)] [[PubMed](#)]

30. Joe, M.J.; Kim, S.N.; Choi, H.Y.; Shin, W.S.; Park, G.M.; Kang, D.W.; Yong, K.K. The inhibitory effects of eckol and dieckol from *Ecklonia stolonifera* on the expression of matrix metalloproteinase-1 in human dermal fibroblasts. *Biol. Pharm. Bull.* **2006**, *29*, 1735–1739. [[CrossRef](#)] [[PubMed](#)]
31. Le Lann, K.; Surget, G.; Couteau, C.; Coiffard, L.; Cérantola, S.; Gaillard, F.; Larnicol, M.; Zubia, M.; Guérard, F.; Poupart, N.; et al. Sunscreen, antioxidant, and bactericide capacities of phlorotannins from the brown macroalga *Halidrys siliquosa*. *J. Appl. Phycol.* **2016**, *28*, 3547–3559. [[CrossRef](#)]
32. Sanjeewa, K.K.A.; Kim, E.A.; Son, K.T.; Jeon, Y.J. Bioactive properties and potentials cosmeceutical applications of phlorotannins isolated from brown seaweeds: A review. *J. Photochem. Photobiol. B Biol.* **2016**, *162*, 100–105. [[CrossRef](#)] [[PubMed](#)]
33. Ryu, B.M.; Qian, Z.J.; Kim, M.M.; Nam, K.W.; Kim, S.K. Anti-photoaging activity and inhibition of matrix metalloproteinase (MMP) by marine red alga, *Corallina pilulifera* methanol extract. *Radiat. Phys. Chem.* **2009**, *78*, 98–105. [[CrossRef](#)]
34. Heo, S.-J.; Jeon, Y.-J. Protective effect of fucoxanthin isolated from *Sargassum siliquastrum* on UV-B induced cell damage. *J. Photochem. Photobiol. B Biol.* **2009**, *95*, 101–107. [[CrossRef](#)]
35. Fernando, I.P.S.; Dias, M.K.H.M.; Madusanka, D.M.D.; Han, E.J.; Kim, M.J.; Jeon, Y.J.; Ahn, G. Fucoïdan refined by *Sargassum confusum* indicate protective effects suppressing photo-oxidative stress and skin barrier perturbation in UVB-induced human keratinocytes. *Int. J. Biol. Macromol.* **2020**, *164*, 149–161. [[CrossRef](#)]
36. Guinea, M.; Franco, V.; Araujo-Bazán, L.; Rodríguez-Martín, I.; González, S. In vivo UVB-photoprotective activity of extracts from commercial marine macroalgae. *Food Chem. Toxicol.* **2012**, *50*, 1109–1117. [[CrossRef](#)]
37. Pozharitskaya, O.N.; Obluchinskaya, E.D.; Shikov, A.N. Mechanisms of Bioactivities of Fucoïdan from the Brown Seaweed *Fucus vesiculosus* L. of the Barents Sea. *Mar. Drugs* **2020**, *18*, 275. [[CrossRef](#)]
38. Choi, J.S.; Moon, W.S.; Choi, J.N.; Do, K.H.; Moon, S.H.; Cho, K.K.; Han, C.J.; Choi, I.S. Effects of seaweed *Laminaria japonica* extracts on skin moisturizing activity in vivo. *J. Cosmet Sci.* **2013**, *64*, 193–205. [[PubMed](#)]
39. Leelapornpisid, P.; Mungmai, L.; Sirithunyalug, B.; Jiranusornkul, S.; Peerapornpisal, Y. A novel moisturizer extracted from freshwater macroalga [*Rhizoclonium hieroglyphicum* (C. Agardh) Kützinger] for skin care cosmetic. *Chiang Mai J. Sci* **2014**, *41*, 1195–1207.
40. Kim, S.-K.; Babitha, S.; Kim, E.-K. Effect of Marine Cosmeceuticals on the Pigmentation of Skin. In *Marine Cosmeceuticals*; CRC Press: Boca Raton, FL, USA, 2011; pp. 63–65.
41. Wang, H.D.; Chen, C.; Huynh, P.; Chang, J. Exploring the potential of using algae in cosmetics. *Bioresour. Technol.* **2015**, *184*, 355–362. [[CrossRef](#)] [[PubMed](#)]
42. Sahin, S.C. The potential of *Arthrospira platensis* extract as a tyrosinase inhibitor for pharmaceutical or cosmetic applications. *S. Afr. J. Bot.* **2018**, *119*, 236–243. [[CrossRef](#)]
43. Ariede, M.B.; Candido, T.M.; Jacome, A.L.M.; Velasco, M.V.R.; de Carvalho, J.C.M.; Baby, A.R. Cosmetic attributes of algae—A review. *Algal Res.* **2017**, *25*, 483–487. [[CrossRef](#)]
44. Bak, S.S.; Ahn, B.N.; Kim, J.A.; Shin, S.H.; Kim, J.C.; Kim, M.K.; Sung, Y.K.; Kim, S.K. *Ecklonia cava* promotes hair growth. *Clin. Exp. Dermatol.* **2013**, *38*, 904–910. [[CrossRef](#)]
45. Atzori, G.; Nissim, W.G.; Rodolfi, L.; Niccolai, A.; Biondi, N.; Mancuso, S.; Tredici, M.R. Algae and Bioguanos as promising source of organic fertilizers. *J. Appl. Phycol.* **2020**, *32*, 3971–3981. [[CrossRef](#)]
46. Akila, V.; Manikandan, A.; Sahaya Sukeetha, D.; Balakrishnan, S.; Ayyasamy, P.M.; Rajakumar, S. Biogas and biofertilizer production of marine macroalgae: An effective anaerobic digestion of *Ulva* sp. *Biocatal. Agric. Biotechnol.* **2019**, *18*, 101035. [[CrossRef](#)]
47. Hashem, H.A.; Mansour, H.A.; El-Khawass, S.A.; Hassanein, R.A. The potentiality of marine macro-algae as bio-fertilizers to improve the productivity and salt stress tolerance of canola (*Brassica napus* L.) plants. *Agronomy* **2019**, *9*, 146. [[CrossRef](#)]
48. Stirk, W.A.; Rengasamy, K.R.R.; Kulkarni, M.G.; Staden, J. Plant Biostimulants from Seaweed. In *The Chemical Biology of Plant Biostimulants*; Geelen, D., Lin, X., Eds.; Wiley: Chichester, UK, 2020; pp. 31–55.
49. Leandro, A.; Pereira, L.; Gonçalves, A.M.M. Diverse applications of marine macroalgae. *Mar. Drugs* **2020**, *18*, 17. [[CrossRef](#)] [[PubMed](#)]
50. Maia, M.R.G.; Fonseca, A.J.M.; Cortez, P.P.; Cabrita, A.R.J. In vitro evaluation of macroalgae as unconventional ingredients in ruminant animal feeds. *Algal Res.* **2019**, *40*, 101481. [[CrossRef](#)]
51. Bansemmer, M.S.; Qin, J.G.; Harris, J.O.; Duong, D.N.; Hoang, T.H.; Howarth, G.S.; Stone, D.A.J. Growth and feed utilisation of greenlip abalone (*Haliotis laevis*) fed nutrient enriched macroalgae. *Aquaculture* **2016**, *452*, 62–68. [[CrossRef](#)]
52. Sáez, M.I.; Vizcaino, A.; Galafat, A.; Anguís, V.; Fernández-Díaz, C.; Balebona, M.C.; Alarcón, F.J.; Martínez, T.F. Assessment of long-term effects of the macroalgae *Ulva ohnoi* included in diets on Senegalese sole (*Solea senegalensis*) fillet quality. *Algal Res.* **2020**, *47*, 101885. [[CrossRef](#)]
53. Valente, L.M.P.; Gouveia, A.; Rema, P.; Matos, J.; Gomes, E.F.; Pinto, I.S. Evaluation of three seaweeds *Gracilaria bursa-pastoris*, *Ulva rigida* and *Gracilaria cornea* as dietary ingredients in European sea bass (*Dicentrarchus labrax*) juveniles. *Aquaculture* **2006**, *252*, 85–91. [[CrossRef](#)]
54. Passos, R.; Correia, A.P.; Ferreira, I.; Pires, P.; Pires, D.; Gomes, E.; do Carmo, B.; Santos, P.; Simões, M.; Afonso, C.; et al. Effect on health status and pathogen resistance of gilthead seabream (*Sparus aurata*) fed with diets supplemented with *Gracilaria gracilis*. *Aquaculture* **2021**, *531*, 735888. [[CrossRef](#)]



55. Boletín Oficial del Estado. *Real Decreto 630/2013, de 2 de Agosto, por el que se Regula el Catálogo Español de Especies Exóticas Invasoras*; Boletín Oficial del Estado: Madrid, Spain, 2013.
56. Mulas, M.; Bertocci, I. Devil's tongue weed (*Grateloupia turuturu* Yamada) in northern Portugal: Passenger or driver of change in native biodiversity? *Mar. Environ. Res.* **2016**, *118*, 1–9. [[CrossRef](#)]
57. Altamirano, M.; Muñoz, A.R.; de la Rosa, J.; Barrajón-Mínguez, A.; Barrajón-Domenech, A.; Moreno-Robledo, C.; del Arroyo, M.C. The invasive species *Asparagopsis taxiformis* (Bonnemaisoniales, Rhodophyta) on andalusian coasts (Southern Spain): Reproductive stages, new records and invaded communities. *Acta Botánica Malacit.* **2008**, *23*, 5–15. [[CrossRef](#)]
58. Bellissimo, G.; Galfo, F.; Nicastro, A.; Costantini, R.; Castriota, L. First record of the invasive green alga *Codium fragile* ssp. *fragile* (Chlorophyta, Bryopsidales) in Abruzzi waters, central Adriatic sea. *Acta Adriat.* **2018**, *59*, 207–212. [[CrossRef](#)]
59. Gennaro, P.; Piazzini, L. The indirect role of nutrients in enhancing the invasion of *Caulerpa racemosa* var. *cylindracea*. *Biol. Invasions* **2014**, *16*, 1709–1717. [[CrossRef](#)]
60. Ornano, L.; Sanna, C.; Serafini, M.; Bianco, A.; Donno, Y.; Ballero, M. Phytochemical study of *Caulerpa racemosa* (Forsk.) J. Agarth, an invading alga in the habitat of La Maddalena Archipelago. *Nat. Prod. Res.* **2014**, *28*, 1795–1799. [[CrossRef](#)]
61. Capdevila-Argüelles, L.; Zilletti, B.; Suárez Álvarez, V.Á. *Plan. Extratético galego de Xestión das Especies Exóticas Invasoras e Para o Desenvolvemento Dun Sistema Esandarizado de Análise de Riscos Para as Especies Exóticas en Galicia*; Xunta de Galicia: Santiago, Chile; Galicia, Spain, 2012.
62. Haslin, C.; Lahaye, M.; Pellegrini, M.; Chermann, J.C. In Vitro Anti-HIV Activity of Sulfated Cell-Wall Polysaccharides from Gametic, Carposporic and Tetrasporic Stages of the Mediterranean Red Alga *Asparagopsis armata*. *Planta Med.* **2001**, *67*, 301–305. [[CrossRef](#)] [[PubMed](#)]
63. Bouhlal, R.; Riadi, H.; Bourgougnon, N. Antiviral activity of the extracts of Rhodophyceae from Morocco. *Afr. J. Biotechnol.* **2010**, *9*, 7968–7975. [[CrossRef](#)]
64. Andrade, P.B.; Barbosa, M.; Pedro, R.; Lopes, G.; Vinholes, J.; Mouga, T.; Valentão, P. Valuable compounds in macroalgae extracts. *Food Chem.* **2013**, *138*, 1819–1828. [[CrossRef](#)]
65. Kolsi, R.B.A.; Fakhfakh, J.; Sassi, S.; Elleuch, M.; Gargouri, L. Physico-chemical characterization and beneficial effects of seaweed sulfated polysaccharide against oxydatif and cellular damages caused by alloxan in diabetic rats. *Int. J. Biol. Macromol.* **2018**, *117*, 407–417. [[CrossRef](#)]
66. Kolsi, R.B.A.; Jardak, N.; Hajkacem, F.; Chaaben, R.; Jribi, I.; El Feki, A.; Rebai, T.; Jamoussi, K.; Fki, L.; Belghith, H.; et al. Anti-obesity effect and protection of liver-kidney functions by *Codium fragile* sulphated polysaccharide on high fat diet induced obese rats. *Int. J. Biol. Macromol.* **2017**, *102*, 119–129. [[CrossRef](#)]
67. Wang, L.; Oh, J.Y.; Je, J.G.; Jayawardena, T.U.; Kim, Y.S.; Ko, J.Y.; Fu, X.; Jeon, Y.J. Protective effects of sulfated polysaccharides isolated from the enzymatic digest of *Codium fragile* against hydrogen peroxide-induced oxidative stress in in vitro and in vivo models. *Algal Res.* **2020**, *48*, 101891. [[CrossRef](#)]
68. Athukorala, Y.; Lee, K.W.; Kim, S.K.; Jeon, Y.J. Anticoagulant activity of marine green and brown algae collected from Jeju Island in Korea. *Bioresour. Technol.* **2007**, *98*, 1711–1716. [[CrossRef](#)] [[PubMed](#)]
69. Ciancia, M.; Quintana, I.; Vizcargüénaga, M.I.; Kasulin, L.; de Dios, A.; Estevez, J.M.; Cerezo, A.S. Polysaccharides from the green seaweeds *Codium fragile* and *C. vermilara* with controversial effects on hemostasis. *Int. J. Biol. Macromol.* **2007**, *41*, 641–649. [[CrossRef](#)]
70. Surayot, U.; You, S.G. Structural effects of sulfated polysaccharides from *Codium fragile* on NK cell activation and cytotoxicity. *Int. J. Biol. Macromol.* **2017**, *98*, 117–124. [[CrossRef](#)]
71. Park, S.H.; Kim, J.L.; Jeong, S.; Kim, B.R.; Na, Y.J.; Jo, M.J.; Yun, H.K.; Jeong, Y.A.; Kim, D.Y.; Kim, B.G.; et al. *Codium fragile* F2 sensitize colorectal cancer cells to TRAIL-induced apoptosis via c-FLIP ubiquitination. *Biochem. Biophys. Res. Commun.* **2019**, *508*, 1–8. [[CrossRef](#)]
72. Marshall, R.A.; Hamilton, J.T.G.; Dring, M.J.; Harper, D.B. Do vesicle cells of the red alga *Asparagopsis* (*Falkenbergia* stage) play a role in bromocarbon production? *Chemosphere* **2003**, *52*, 471–475. [[CrossRef](#)]
73. McConnell, O.; Fenical, W. Halogen chemistry of the red alga *asparagopsis*. *Phytochemistry* **1977**, *16*, 367–374. [[CrossRef](#)]
74. Woolard, F.X.; Moore, R.E.; Roller, P.P. Halogenated acetic and acrylic acids from the red alga *asparagopsis taxiformis*. *Phytochemistry* **1979**, *18*, 617–620. [[CrossRef](#)]
75. Kolsi, R.B.A.; Salah, H.B.; Hamza, A.; El feki, A.; Allouche, N.; El feki, L.; Belguith, K. Characterization and evaluating of antioxidant and antihypertensive properties of green alga (*Codium fragile*) from the coast of Sfax. *J. Pharmacogn. Phytochem.* **2017**, *6*, 186–191.
76. Ortiz, J.; Uquiche, E.; Robert, P.; Romero, N.; Quitral, V.; Llantén, C. Functional and nutritional value of the Chilean seaweeds *Codium fragile*, *Gracilaria chilensis* and *Macrocystis pyrifera*. *Eur. J. Lipid Sci. Technol.* **2009**, 320–327. [[CrossRef](#)]
77. Santos, S.A.O.; Vilela, C.; Freire, C.S.R.; Abreu, M.H.; Rocha, S.M.; Silvestre, A.J.D. Chlorophyta and Rhodophyta macroalgae: A source of health promoting phytochemicals. *Food Chem.* **2015**, *183*, 122–128. [[CrossRef](#)] [[PubMed](#)]
78. Casas, M.P.; Rodríguez-Hermida, V.; Pérez-Larrán, P.; Conde, E.; Liveri, M.T.; Ribeiro, D.; Fernandes, E.; Domínguez, H. In vitro bioactive properties of phlorotannins recovered from hydrothermal treatment of *Sargassum muticum*. *Sep. Purif. Technol.* **2016**, *167*, 117–126. [[CrossRef](#)]
79. Kendel, M.; Barnathan, G.; Fleurence, J.; Rabesaotra, V.; Wielgosz-Collin, G. Non-methylene interrupted and hydroxy fatty acids in polar lipids of the alga *Grateloupia turuturu* over the four seasons. *Lipids* **2013**, *48*, 535–545. [[CrossRef](#)]

80. Kendel, M.; Couzinet-Mossion, A.; Viau, M.; Fleurence, J.; Barnathan, G.; Wielgosz-Collin, G. Seasonal composition of lipids, fatty acids, and sterols in the edible red alga *Grateloupia turuturu*. *J. Appl. Phycol.* **2013**, *25*, 425–432. [[CrossRef](#)]
81. Lee, J.B.; Ohta, Y.; Hayashi, K.; Hayashi, T. Immunostimulating effects of a sulfated galactan from *Codium fragile*. *Carbohydr. Res.* **2010**, *345*, 1452–1454. [[CrossRef](#)] [[PubMed](#)]
82. Shi, Q.; Wang, A.; Lu, Z.; Qin, C.; Hu, J.; Yin, J. Overview on the antiviral activities and mechanisms of marine polysaccharides from seaweeds. *Carbohydr. Res.* **2017**, 453–454, 1–9. [[CrossRef](#)] [[PubMed](#)]
83. Fernández, P.V.; Arata, P.X.; Ciancia, M. *Polysaccharides from Codium Species*; Elsevier: Amsterdam, The Netherlands, 2014; Volume 71, ISBN 9780124080621.
84. Yang, Y.; Park, J.; You, S.G.; Hong, S. Immuno-stimulatory effects of sulfated polysaccharides isolated from *Codium fragile* in olive flounder, *Paralichthys olivaceus*. In *Fish Shellfish Immunology*; Elsevier Inc.: Alpharetta, GA, USA, 2019; Volume 87, pp. 609–614. [[CrossRef](#)]
85. Zhang, W.; Hwang, J.; Park, H.; Lim, S.; Go, S. Human Peripheral Blood Dendritic Cell and T Cell Activation by *Codium fragile* Polysaccharide. *Mar. Drugs* **2020**, *18*, 535. [[CrossRef](#)] [[PubMed](#)]
86. Sánchez-Camargo, P.; Montero, L.; Stiger-pouvreau, V.; Tanniou, A.; Cifuentes, A.; Herrero, M.; Ibáñez, E. Considerations on the use of enzyme-assisted extraction in combination with pressurized liquids to recover bioactive compounds from algae. *Food Chem.* **2016**, *192*, 67–74. [[CrossRef](#)] [[PubMed](#)]
87. Flórez-Fernández, N.; Domínguez, H.; Torres, M.D. A green approach for alginate extraction from *Sargassum muticum* brown seaweed using ultrasound-assisted technique. *Int. J. Biol. Macromol.* **2019**, *124*, 451–459. [[CrossRef](#)]
88. Martínez-Lüscher, J.; Holmer, M. Potential effects of the invasive species *Gracilaria vermiculophylla* on *Zostera marina* metabolism and survival. *Mar. Environ. Res.* **2010**, *69*, 345–349. [[CrossRef](#)]
89. Pereira, L. *Edible Seaweeds of the World*; CRC Press: Boca Raton, FL, USA, 2016.
90. Cardoso, I.; Cotas, J.; Rodrigues, A.; Ferreira, D.; Osório, N.; Pereira, L. Extraction and analysis of compounds with antibacterial potential from the red alga *Grateloupia turuturu*. *J. Mar. Sci. Eng.* **2019**, *7*, 220. [[CrossRef](#)]
91. Sheu, J.; Huang, S.; Duh, C. Cytotoxic Oxygenated Desmosterols of the Red Alga *Galaxaura marginata*. *J. Nat. Prod.* **1996**, *59*, 23–26. [[CrossRef](#)] [[PubMed](#)]
92. Pinteus, S.; Lemos, M.F.L.; Alves, C.; Silva, J.; Pedrosa, R. The marine invasive seaweeds *Asparagopsis armata* and *Sargassum muticum* as targets for greener antifouling solutions. *Sci. Total Environ.* **2021**, *750*, 141372. [[CrossRef](#)] [[PubMed](#)]
93. Pinteus, S.; Lemos, M.F.L.; Simões, M.; Alves, C.; Silva, J.; Gaspar, H.; Martins, A.; Rodrigues, A.; Pedrosa, R. Marine invasive species for high-value products' exploration—Unveiling the antimicrobial potential of *Asparagopsis armata* against human pathogens. *Algal Res.* **2020**, *52*, 102091. [[CrossRef](#)]
94. Lee, C.; Park, G.H.; Ahn, E.M.; Kim, B.A.; Park, C.I.; Jang, J.H. Protective effect of *Codium fragile* against UVB-induced pro-inflammatory and oxidative damages in HaCaT cells and BALB/c mice. *Fitoterapia* **2013**, *86*, 54–63. [[CrossRef](#)]
95. Kim, A.D.; Lee, Y.; Kang, S.H.; Kim, G.Y.; Kim, H.S.; Hyun, J.W. Cytotoxic effect of clerosterol isolated from *Codium fragile* on A2058 human melanoma cells. *Mar. Drugs* **2013**, *11*, 418–430. [[CrossRef](#)]
96. Ganesan, P.; Noda, K.; Manabe, Y.; Ohkubo, T.; Tanaka, Y.; Maoka, T.; Sugawara, T.; Hirata, T. Siphonaxanthin, a marine carotenoid from green algae, effectively induces apoptosis in human leukemia (HL-60) cells. *Biochim. Biophys. Acta Gen. Subj.* **2011**, *1810*, 497–503. [[CrossRef](#)]
97. Silva, J.; Martins, A.; Alves, C.; Pinteus, S.; Gaspar, H.; Alfonso, A.; Pedrosa, R. Natural Approaches for Neurological Disorders—The Neuroprotective Potential of *Codium tomentosum*. *Molecules* **2020**, *25*, 5478. [[CrossRef](#)]
98. Sun, Y.; Xu, Y.; Liu, K.; Hua, H.; Zhu, H.; Pei, Y. Gracilarioid and gracilamides from the Red alga *Gracilaria asiatica*. *J. Nat. Prod.* **2006**, *69*, 1488–1491. [[CrossRef](#)]
99. Barceló-villalobos, M.; Figueroa, F.L.; Korbee, N. Production of Mycosporine-Like Amino Acids from *Gracilaria vermiculophylla* (Rhodophyta) Cultured Through One Year in an Integrated Multi-trophic Aquaculture (IMTA) System. *Mar. Biotechnol.* **2017**, *19*, 246–254. [[CrossRef](#)] [[PubMed](#)]
100. Ganesan, P.; Matsubara, K.; Ohkubo, T.; Tanaka, Y.; Noda, K.; Sugawara, T.; Hirata, T. Anti-angiogenic effect of siphonaxanthin from green alga, *Codium fragile*. *Phytomedicine* **2010**, *17*, 1140–1144. [[CrossRef](#)]
101. Lourenço-Lopes, C.; Garcia-Oliveira, P.; Carpena, M.; Fraga-Corral, M.; Jimenez-Lopez, C.; Pereira, A.G.; Prieto, M.A.; Simal-Gandara, J. Scientific approaches on extraction, purification and stability for the commercialization of fucoxanthin recovered from brown algae. *Foods* **2020**, *9*, 1113. [[CrossRef](#)] [[PubMed](#)]
102. Heo, S.J.; Yoon, W.J.; Kim, K.N.; Ahn, G.N.; Kang, S.M.; Kang, D.H.; Affan, A.; Oh, C.; Jung, W.K.; Jeon, Y.J. Evaluation of anti-inflammatory effect of fucoxanthin isolated from brown algae in lipopolysaccharide-stimulated RAW 264.7 macrophages. *Food Chem. Toxicol.* **2010**, *48*, 2045–2051. [[CrossRef](#)] [[PubMed](#)]
103. Yang, E.-J.; Moon, J.-Y.; Kim, S.S.; Yang, K.-W.; Lee, W.J.; Lee, N.H.; Hyun, C.-G. Jeju seaweeds suppress lipopolysaccharide-stimulated proinflammatory response in RAW 264.7 murine macrophages. *Asian Pac. J. Trop. Biomed.* **2014**, *4*, 529–537. [[CrossRef](#)] [[PubMed](#)]
104. Le Guillard, C.; Dumay, J.; Donnay-Moreno, C.; Bruzac, S.; Ragon, J.Y.; Fleurence, J.; Bergé, J.P. Ultrasound-assisted extraction of R-phycoerythrin from *Grateloupia turuturu* with and without enzyme addition. *Algal Res.* **2015**, *12*, 522–528. [[CrossRef](#)]
105. Sabeena Farvin, K.H.; Jacobsen, C. Phenolic compounds and antioxidant activities of selected species of seaweeds from Danish coast. *Food Chem.* **2013**, *138*, 1670–1681. [[CrossRef](#)] [[PubMed](#)]

106. Zubia, M.; Fabre, M.; Deslandes, E.; Shannon, C. Antioxidant and cytotoxic activities of some red algae (Rhodophyta) from Brittany coasts (France). *Botanica Mar.* **2009**, *52*, 268–277. [[CrossRef](#)]
107. Klejdus, B.; Plaza, M.; Snóblová, M.; Lojková, L. Development of new efficient method for isolation of phenolics from sea algae prior to their rapid resolution liquid chromatographic—tandem mass spectrometric determination. *J. Pharm. Biomed. Anal.* **2017**, *135*, 87–96. [[CrossRef](#)] [[PubMed](#)]
108. Balboa, E.M.; Luisa, M.; Nogueira, D.R.; González-lópez, N.; Conde, E.; Moure, A.; Pilar, M. Potential of antioxidant extracts produced by aqueous processing of renewable resources for the formulation of cosmetics. *Ind. Crop. Prod.* **2014**, *58*, 104–110. [[CrossRef](#)]
109. Agregán, R.; Munekata, P.E.S.; Franco, D.; Dominguez, R.; Carballo, J.; Lorenzo, J.M. Phenolic compounds from three brown seaweed species using LC-DAD—ESI-MS/MS. *Food Res. Int.* **2017**, *99*, 979–985. [[CrossRef](#)] [[PubMed](#)]
110. Casas, M.P.; Conde, E.; Domínguez, H.; Moure, A. Ecofriendly extraction of bioactive fractions from *Sargassum muticum*. *Process Biochem.* **2019**, *79*, 166–173. [[CrossRef](#)]
111. Pérez-Larrán, P.; Torres, M.D.; Flórez-Fernández, N.; Balboa, E.M.; Moure, A.; Domínguez, H. Green technologies for cascade extraction of *Sargassum muticum* bioactives. *J. Appl. Phycol.* **2019**, *31*, 2481–2495. [[CrossRef](#)]
112. Mata, L.; Silva, J.; Schuenhoff, A.; Santos, R. The effects of light and temperature on the photosynthesis of the Asparagopsis armata tetrasporophyte (*Falkenbergia rufolanosa*), cultivated in tanks. *Aquaculture* **2006**, *252*, 12–19. [[CrossRef](#)]
113. Jacinto, M.S.C.; Monteiro, H.R.; Lemos, M.F.L. Impact of the invasive macroalgae *Asparagopsis armata* on coastal environments: An ecotoxicological assessment. *Curr. Opin. Biotechnol.* **2013**, *24S*, S75. [[CrossRef](#)]
114. De Nys, R.; Steinberg, P.D.; Willemsen, P.; Dworjanyan, S.A.; Gabelish, C.L.; King, R.J. Broad spectrum effects of secondary metabolites from the red alga *Delisea pulchra* in antifouling assays. *Biofouling* **1995**, *8*, 259–271. [[CrossRef](#)]
115. Schuenhoff, A.; Mata, L.; Santos, R. The tetrasporophyte of *Asparagopsis armata* as a novel seaweed biofilter. *Aquaculture* **2006**, *252*, 3–11. [[CrossRef](#)]
116. Paul, N.; Nys, R. De Chemical defence against bacteria in the red alga *Asparagopsis armata*: Linking structure with function. *Mar. Ecol. Prog. Ser.* **2006**, *306*, 87–101. [[CrossRef](#)]
117. Choi, J.H.; Sapkota, K.; Park, S.E.; Kim, S.; Kim, S.J. Thrombolytic, anticoagulant and antiplatelet activities of codiase, a bi-functional fibrinolytic enzyme from *Codium fragile*. *Biochimie* **2013**, *95*, 1266–1277. [[CrossRef](#)]
118. Alhazzaa, R.; Nichols, P.D.; Carter, C.G. Sustainable alternatives to dietary fish oil in tropical fish aquaculture. *Rev. Aquac.* **2019**, *11*, 1195–1218. [[CrossRef](#)]
119. Ummat, V.; Sivagnanam, S.P.; Rajauria, G.; O'Donnell, C.; Tiwari, B.K. Advances in pre-treatment techniques and green extraction technologies for bioactives from seaweeds. *Trends Food Sci. Technol.* **2021**, *110*, 90–106. [[CrossRef](#)]
120. Picot-Allain, C.; Mahomoodally, M.F.; Ak, G.; Zengin, G. Conventional versus green extraction techniques—A comparative perspective. *Curr. Opin. Food Sci.* **2021**. [[CrossRef](#)]
121. Mendes, M.; Pereira, R.; Sousa Pinto, I.; Carvalho, A.P.; Gomes, A.M. Antimicrobial activity and lipid profile of seaweed extracts from the North Portuguese Coast. *Int. Food Res. J.* **2013**, *20*, 3337–3345.
122. Kamarudin, A.A.; Mohd, E.N.; Saad, N.; Sayuti, N.H.; Nor, N.A. Heat assisted extraction of phenolic compounds from *Eleutherine bulbosa* (Mill.) bulb and its bioactive profiles using response surface methodology. *Ind. Crops Prod.* **2020**, *144*, 112064. [[CrossRef](#)]
123. Genovese, G.; Tedone, L.; Hamann, M.T.; Morabito, M. The Mediterranean Red Alga *Asparagopsis*: A Source of Compounds against Leishmania. *Mar. Drugs* **2009**, *7*, 361–366. [[CrossRef](#)] [[PubMed](#)]
124. Custódio, L.; Silvestre, L.; Rocha, M.I.; Rodrigues, M.J.; Vizetto-duarte, C.; Pereira, H.; Barreira, L.; Varela, J.; Custódio, L.; Silvestre, L.; et al. Methanol extracts from *Cystoseira tamariscifolia* and *Cystoseira nodicaulis* are able to inhibit cholinesterases and protect a human dopaminergic cell line from hydrogen peroxide-induced cytotoxicity from hydrogen peroxide-induced cytotoxicity. *Pharm. Biol.* **2016**, *54*, 1687–1696. [[CrossRef](#)]
125. Kang, C.-H.; Choi, Y.H.; Park, S.-Y.; Kim, G.-Y. Anti-Inflammatory Effects of Methanol Extract of *Codium fragile* in Lipopolysaccharide-Stimulated RAW 264.7 Cells. *J. Med. Food* **2011**, *15*, 44–50. [[CrossRef](#)]
126. Dilshara, M.G.; Jayasooriya, R.G.P.T.; Kang, C.H.; Choi, Y.H.; Kim, G.Y. Methanol extract of *Codium fragile* inhibits tumor necrosis factor- $\alpha$ -induced matrix metalloproteinase-9 and invasiveness of MDA-MB-231 cells by suppressing nuclear factor- $\kappa$ B activation. *Asian Pac. J. Trop. Med.* **2016**, *9*, 535–541. [[CrossRef](#)]
127. Lee, S.A.; Moon, S.M.; Choi, Y.H.; Han, S.H.; Park, B.R.; Choi, M.S.; Kim, J.S.; Kim, Y.H.; Kim, D.K.; Kim, C.S. Aqueous extract of *Codium fragile* suppressed inflammatory responses in lipopolysaccharide-stimulated RAW264.7 cells and carrageenan-induced rats. *Biomed. Pharmacother.* **2017**, *93*, 1055–1064. [[CrossRef](#)]
128. Yoon, H.-D.; Jeong, E.-J.; Choi, J.-W.; Lee, M.-S.; Park, M.-A.; Yoon, N.-Y.; Kim, Y.-K.; Cho, D.-M.; Kim, J.-I.; Kim, H.-R. Anti-inflammatory Effects of Ethanolic Extracts from *Codium fragile* on LPS-Stimulated RAW 264.7 Macrophages via Nuclear Factor  $\kappa$ B Inactivation. *Fish. Aquat. Sci.* **2012**, *14*, 267–274. [[CrossRef](#)]
129. Moon, S.M.; Lee, S.A.; Han, S.H.; Park, B.R.; Choi, M.S.; Kim, J.S.; Kim, S.G.; Kim, H.J.; Chun, H.S.; Kim, D.K.; et al. Aqueous extract of *Codium fragile* alleviates osteoarthritis through the MAPK/NF- $\kappa$ B pathways in IL-1 $\beta$ -induced rat primary chondrocytes and a rat osteoarthritis model. *Biomed. Pharmacother.* **2018**, *97*, 264–270. [[CrossRef](#)]

130. García-Bueno, N.; Decottignies, P.; Turpin, V.; Dumay, J.; Paillard, C.; Stiger-Pouvreau, V.; Kervarec, N.; Pouchus, Y.-F.; Marín-Atucha, A.A.; Fleurence, J. Seasonal antibacterial activity of two red seaweeds, *Palmaria palmata* and *Grateloupia turuturu*, on European abalone pathogen *Vibrio harveyi*. *Aquat. Living Resour.* **2014**, *27*, 83–89. [[CrossRef](#)]
131. Pinteus, S.; Silva, J.; Alves, C.; Horta, A.; Fino, N.; Rodrigues, A.I.; Mendes, S.; Pedrosa, R. Cytoprotective effect of seaweeds with high antioxidant activity from the Peniche coast (Portugal). *Food Chem.* **2017**, *218*, 591–599. [[CrossRef](#)] [[PubMed](#)]
132. Balboa, E.M.; Li, Y.; Ahn, B.; Eom, S.; Domínguez, H.; Jiménez, C.; Rodríguez, J. Photodamage attenuation effect by a tetraprenyltoluquinol chromane meroterpenoid isolated from *Sargassum muticum*. *J. Photochem. Photobiol. B Biol.* **2015**, *148*, 51–58. [[CrossRef](#)] [[PubMed](#)]
133. Ibáñez, E.; Mendiola, J.A.; Castro-Puyana, M. *Supercritical Fluid Extraction*; Academic Press: Cambridge, MA, USA, 2016; ISBN 9780123849472.
134. Montero, L.; Sánchez-Camargo, A.P.; García-Cañas, V.; Tanniou, A.; Stiger-Pouvreau, V.; Russo, M.; Rastrelli, L.; Cifuentes, A.; Herrero, M.; Ibáñez, E. Anti-proliferative activity and chemical characterization by comprehensive two-dimensional liquid chromatography coupled to mass spectrometry of phlorotannins from the brown macroalga *Sargassum muticum* collected on North-Atlantic coasts. *J. Chromatogr. A* **2016**, *1428*, 115–125. [[CrossRef](#)] [[PubMed](#)]
135. Misra, N.N.; Rai, D.K.; Hossain, M. Analytical techniques for bioactives from seaweed. In *Seaweed Sustainability: Food and Non-Food Applications*; Elsevier Inc.: Amsterdam, The Netherlands, 2015; pp. 271–287. ISBN 9780124199583.
136. Fraga-Corral, M.; Carpena, M.; Garcia-Oliveira, P.; Pereira, A.G.; Prieto, M.A.; Simal-Gandara, J. Analytical Metabolomics and Applications in Health, Environmental and Food Science. *Crit. Rev. Anal. Chem.* **2020**, 1–23. [[CrossRef](#)] [[PubMed](#)]
137. Gutiérrez, E.; Lozano, S.; Guillén, J. Efficiency data analysis in EU aquaculture production. *Aquaculture* **2020**, *520*, 734962. [[CrossRef](#)]
138. FAO. *The State of World Fisheries and Aquaculture 2018—Meeting the Sustainable Development Goals*; FAO: Rome, Italy, 2018; Volume 35, ISBN 9789251060292.
139. Jones, S.W.; Karpol, A.; Friedman, S.; Maru, B.T.; Tracy, B.P. Recent advances in single cell protein use as a feed ingredient in aquaculture. *Curr. Opin. Biotechnol.* **2020**, *61*, 189–197. [[CrossRef](#)]
140. Tacon, A.G.J.; Hasan, M.R.; Metian, M. *Demand and Supply of Feed Ingredients for Farmed Fish and Crustaceans: Trends and Prospects*; FAO: Rome, Italy, 2011; Volume 564, ISBN 9789251069332.
141. Øverland, M.; Mydland, L.T.; Skrede, A. Marine macroalgae as sources of protein and bioactive compounds in feed for monogastric animals. *J. Sci. Food Agric.* **2019**, *99*, 13–24. [[CrossRef](#)] [[PubMed](#)]
142. Davies, S.J.; Soler-vila, A.; Fitzgerald, R.; Johnson, M.P. Macroalgae as a sustainable aquafeed ingredient. *Rev. Aquaculture* **2019**, *11*, 458–492. [[CrossRef](#)]
143. Castanho, S.; Califano, G.; Soares, F.; Costa, R.; Mata, L.; Pousão-Ferreira, P.; Ribeiro, L. The effect of live feeds bathed with the red seaweed *Asparagopsis armata* on the survival, growth and physiology status of *Sparus aurata* larvae. *Fish. Physiol. Biochem.* **2017**, *43*, 1043–1054. [[CrossRef](#)]
144. Félix, R.; Félix, C.; Januário, A.P.; Carmona, A.M.; Baptista, T.; Gonçalves, R.A.; Sendão, J.; Novais, S.C.; Lemos, M.F.L. Tailoring shrimp aquafeed to tackle Acute Hepatopancreatic Necrosis Disease by inclusion of industry-friendly seaweed extracts. *Aquaculture* **2020**, *529*, 735661. [[CrossRef](#)]
145. Pereira, R.; Valente, L.M.P.; Sousa-Pinto, I.; Rema, P. Apparent nutrient digestibility of seaweeds by rainbow trout (*Oncorhynchus mykiss*) and Nile tilapia (*Oreochromis niloticus*). *Algal Res.* **2012**, *1*, 77–82. [[CrossRef](#)]
146. Valente, L.M.P.; Rema, P.; Ferraro, V.; Pintado, M.; Sousa-Pinto, I.; Cunha, L.M.; Oliveira, M.B.; Araújo, M. Iodine enrichment of rainbow trout flesh by dietary supplementation with the red seaweed *Gracilaria vermiculophylla*. *Aquaculture* **2015**, *446*, 132–139. [[CrossRef](#)]
147. Araújo, M.; Rema, P.; Sousa-Pinto, I.; Cunha, L.M.; Peixoto, M.J.; Pires, M.A.; Seixas, F.; Brotas, V.; Beltrán, C.; Valente, L.M.P. Dietary inclusion of IMTA-cultivated *Gracilaria vermiculophylla* in rainbow trout (*Oncorhynchus mykiss*) diets: Effects on growth, intestinal morphology, tissue pigmentation, and immunological response. *J. Appl. Phycol.* **2016**, *28*, 679–689. [[CrossRef](#)]
148. Magnoni, L.J.; Martos-Sitcha, J.A.; Queiroz, A.; Caldach-Giner, J.A.; Gonçalves, J.F.M.; Rocha, C.M.R.; Abreu, H.T.; Schrama, J.W.; Ozorio, R.O.A.; Perez-Sanchez, J. Dietary supplementation of heat-treated *Gracilaria* and *Ulva* seaweeds enhanced acute hypoxia tolerance in gilthead sea bream (*Sparus aurata*). *Biol. Open* **2017**, *6*, 897–908. [[CrossRef](#)] [[PubMed](#)]
149. Anaya-Rosas, R.E.; Rivas-Vega, M.E.; Miranda-Baeza, A.; Piña-Valdez, P.; Nieves-Soto, M. Effects of a co-culture of marine algae and shrimp (*Litopenaeus vannamei*) on the growth, survival and immune response of shrimp infected with *Vibrio parahaemolyticus* and white spot virus (WSSV). *Fish. Shellfish Immunol.* **2019**, *87*, 136–143. [[CrossRef](#)] [[PubMed](#)]
150. Abdul-Qadir, A.-M.; Mohammed, A.-P.; Adamu, K.M.; Abdulraheem, A.-A. Inclusion of *Sargassum muticum* and *Parkia biglobosa* in diets for African Catfish (*Clarias gariepinus*) elevates feed utilization, growth and immune parameters. *Afr. J. Agric. Res.* **2020**, *15*, 134–139. [[CrossRef](#)]
151. Yeganeh, S.; Adel, M. Effects of dietary algae (*Sargassum ilicifolium*) as immunomodulator and growth promoter of juvenile great sturgeon (*Huso huso* Linnaeus, 1758). *J. Appl. Phycol.* **2019**, *31*, 2093–2102. [[CrossRef](#)]
152. Huang, X.; Zhou, H.; Zhang, H. The effect of *Sargassum fusiforme* polysaccharide extracts on vibriosis resistance and immune activity of the shrimp, *Fenneropenaeus chinensis*. *Fish. Shellfish Immunol.* **2006**, *20*, 750–757. [[CrossRef](#)]

- 
153. Mulvaney, W.J.; Winberg, P.C.; Adams, L. Comparison of macroalgal (*Ulva* and *Grateloupia* spp.) and formulated terrestrial feed on the growth and condition of juvenile abalone. *J. Appl. Phycol.* **2013**, *25*, 815–824. [[CrossRef](#)]
  154. García-Bueno, N.; Turpin, V.; Cognie, B.; Dumay, J.; Morañais, M.; Amat, M.; Pédrón, J.-M.; Atucha, A.M.; Fleurence, J.; Decottignies, P. Can the European abalone *Haliotis tuberculata* survive on an invasive algae? A comparison of the nutritional value of the introduced *Grateloupia turuturu* and the native *Palmaria palmata*, for the commercial European abalone industry. *J. Appl. Phycol.* **2016**, *28*, 2427–2433. [[CrossRef](#)]