



Review article

Macroalgae biorefineries as a sustainable resource in the extraction of value-added compounds

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ABSTRACT

Beyond the commercial exploitation of macroalgae as food and as a source of phycocolloids, this bioresource could represent a third-generation feedstock to obtain a wide range of bioactive compounds as well as biostimulants and bioenergy from biomass valorization. However, seaweed biorefineries are less advanced than those based on terrestrial biomass and validation of this concept must address not only technical feasibility but also environmental and economic sustainability. In this context, the valorization of macroalgae should be demonstrated as a cost-effective alternative, where it would be possible to produce several target products with reduced operational costs and environmental burdens compared to their counterparts. This review aims to address a comparative study including the most recent extraction options based on a sequence of cascading stages of both conventional and advanced techniques. The potential products from the valorization of macroalgae considered in this review correspond to pigments, lipids, proteins, polysaccharides, biostimulants and biogas. Each of these has been evaluated separately to identify which technologies have been used for their extraction/production, analyzing their main advantages and disadvantages, and giving an overview of which technological aspects are most relevant to ensure their potential in the market value chain. This review also provides valuable information on the current macroalgae valorization facilities being developed, in different TRLs, and with the identification of the market sectors of the products obtained. It is hoped that this critical review will be useful to evaluate the possibility of using macroalgae as feedstock in production systems within a biorefinery approach.

1. Introduction

Population growth has resulted in the consumption of non-renewable fossil resources, reaching unsustainable levels. The environmental problems associated with the use of fossil resources are obvious: threat of climate change, pollution in different environmental compartments and waste generation. In this approach, the concept of circular economy could help in a very positive way, as it promotes the valorisation of waste streams into products with high added value in the market, *i.e.*, it supports the concept of giving a second life to unusable resources. Furthermore, the use of renewable and natural resources to obtain multi-products in the framework of biorefinery is of particular interest [1,2]. On the other hand, another aspect to take into account is the growing consumer awareness regarding not only product quality, but also information on how the product is produced, its geographical origin and the social and economic characteristics associated with the production process.

In this scenario, the use of macroalgae as feedstock for the development of a biorefinery process is considered as a high potential alternative in the food, pharmaceutical, medical and energy sectors. However, as with other natural resources, it is necessary to carry out pre-treatment processes to make their molecular structure accessible. In this sense, extraction processes can be applied based on conventional techniques or so-called green technologies.

Therefore, this manuscript addresses the review of the available literature on the valorisation of macroalgae as a resource for the extraction of products with high market potential. The analysis focuses on the extraction of pigments, lipids, proteins and carrageenan, and the subsequent valorisation of the biomass into biostimulants and bioenergy. This review could be described as a comprehensive manuscript highlighting the traditional and the most developed and emerging technologies for the extraction of bioactive compounds from macroalgae. In addition, a discussion on the potentialities of scaling up extraction procedures from a laboratory scale to a larger production

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Table 1
Number of published reports and their classification on the valorization of macroalgae for the production of the selected bio-products.

	Pigment	Lipids	Proteins	Polysaccharides	Biostimulant	Biogas
Number of publications	260	420	695	101	42	130
Type of research document						
Article	193	341	569	51	23	89
Review	36	48	73	29	13	21
Book chapter	14	15	28	12	2	7
Conference paper	14	13	19	5	3	12
Editorial	2		1	1		
Book	1	1	1			
Others		2	4	3	1	1

Data from 2012 to 2021 both included. Source: SCOPUS database.

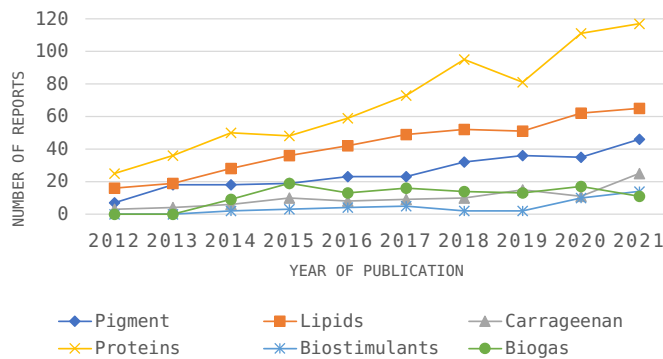


Fig. 1. Trends in macroalgae valorization research from 2012 to 2021. Data source: SCOPUS database.

capacity is included. In this sense, it is expected that the information gathered and critically analyzed in this review will be valuable in the evaluation of large-scale biotechnology processes by stakeholders and policy makers.

2. Methods

The revision of the available literature on the valorization of macroalgae for the extraction and production of high value-added compounds has been carried out using the SCOPUS database. In order to provide a focus on the latest trends and potentials of the macroalgae extraction processes, research reports from the last 10 years, i.e., from 2012 to 2021, both included, have been considered. In addition, as search criteria, the main value-added components from macroalgae for the development of large-scale processes have been considered; that is, pigments, lipids, proteins, carrageenan, biostimulants and biogas, as these are the ones on which the most recent research has focused. Thus, the search pattern has been as follows: TITLE-ABS-KEY (macroalgae AND “XX”) AND PUBYEAR>2011 AND PUBYEAR<2022, with XX being each of the bioproducts mentioned.

Table 1 includes the number of manuscripts published for each of the bioproduct categories, including the type of research work. The publication of research reports in SCI-indexed journals is the most prominent category, although the number of published reviews and participation in conferences is also significant. Fig. 1 shows the trend in the production of research reports over the last 10 years, with the valorization of macroalgae for the extraction of proteins, lipids and pigments being the preferred topic. On the other hand, it is important to mention that in recent years, specifically since 2019, interest in the use of macroalgae for biostimulants and carrageenan has increased significantly. In

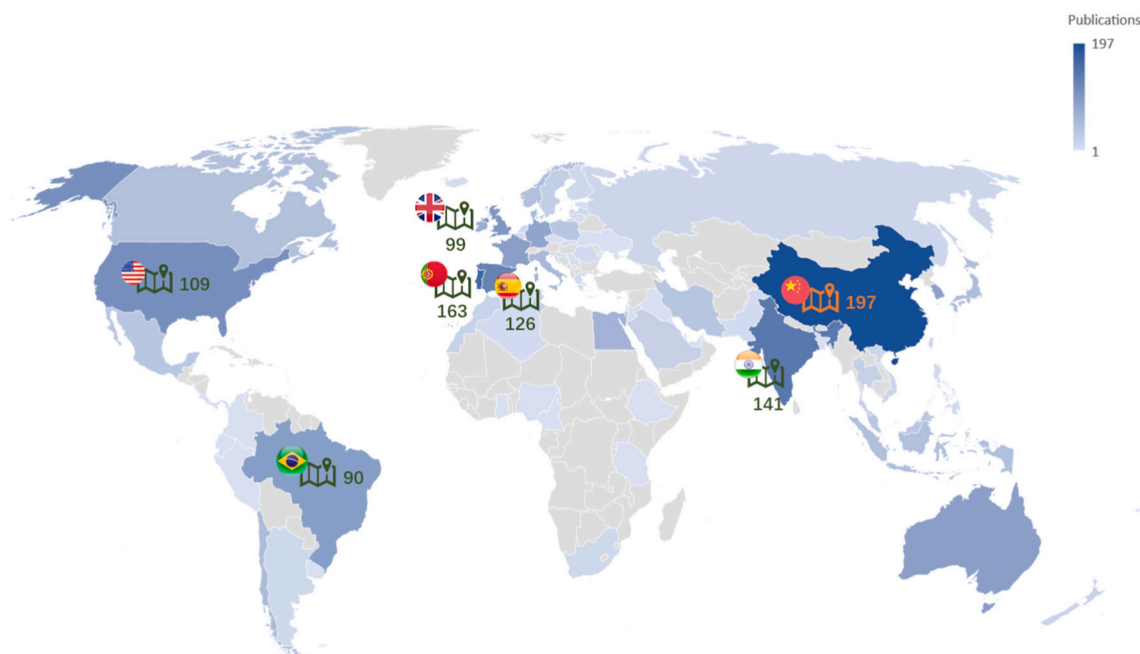


Fig. 2. Publications on macroalgae valorization per territory under the period 2012–2021.

contrast, the research on biogas production from algae has experienced a certain decline.

On the other hand, an evaluation of research articles published by country and territory has also been considered. As can be seen in Fig. 2, China leads in the number of manuscripts in the field of macroalgae valorization, reaching a total of 197. It is closely followed by Portugal, India and Spain, with 163, 141 and 126 publications respectively, also showing very active research in this scientific field. The United States, the United Kingdom and Brazil also have a significant number of research papers, around 100 in the time period considered.

2.1. Macroalgae as bio-resource for pigments

The main pigments of macroalgae are differentiated by the algal species. Green algae (*Chlorophyta*), brown algae (*Phaeophyta*) and red algae (*Rhodophyta*) have natural pigments characteristic of the macroalgal species. Furthermore, the difference between the molecular structures of the pigments is based on the variations in their substituents, while they have an analogous basic molecular structure [3].

Phycocerythrin represents one of the most promising bioactive compounds from red algae used as a dye and its antioxidant and nutritional properties [4]. It has attracted considerable research and search interest, leading to a large number of patents: 314 [5], and to a projected market of \$6.3 million dollars by 2025 [6]. The most widespread methods for pigment extraction from macroalgae are tissue or cell disruption and solvent extraction [7]. As for cell disruption alternatives, the most commonly used are freeze thawing [8], sonication and/or enzymatic hydrolysis with lysozyme. Some of the drawbacks of the freezing process are the time required for cell lysis and the required operating temperatures: $-20\text{ }^{\circ}\text{C}$ [9], which will significantly affect the energy requirements of these steps and the associated environmental impacts [10]. However, the amount of phycocerythrin extracted by freeze-drying achieves a significantly higher value but also a higher purity [11]. As for the use of an enzymatic procedure, an incubation time of 24 h is required for a relatively high enzyme load: 2 g/L [9]. It should be noted that the use of such an amount of enzymes could be considered as a bottleneck and a disadvantage in demonstrating the economic feasibility of the process. In this regard, the most common extraction procedure is sonication, based on the application of high frequency in the form of sound waves for a short time (10 min). Furthermore, in terms of process efficiency, freezing treatment leads to the highest yield in phycocerythrin extraction, requiring the addition of sodium phosphate buffer [9,11]. Regarding phosphate buffer, it has also been used as solvent for phycobilliprotein extraction, and the extraction yields and purity indexes for red pigments using this solvent are suitable [12]. However, when comparing with greener solvents, as distilled water, productivity and quality results are even higher, from 0.028 mg/mL of phycocerythrin extracted with phosphate buffer to 0.039 mg/L when using distilled water [13].

Emerging green technologies have also been considered as alternatives for phycocerythrin extraction such as microwave (MAE) and ultrasound (UAE) methodologies, while MAE is recognized for its extraction capacity by using heat sources without the addition of solvents, UAE stands out for the superior potential to perform cell disruption, allowing better accessibility to the extraction of bioactive compounds [14–16]. Better yields and process capacities have reported for both technologies, in comparison with conventional extraction techniques [6], with UAE ranking first [17]. However, when selecting one or the other, scale-up must be considered, since although UAE is still a proven technology on a large scale, MAE is in a developmental stage [6].

After the centrifugation stage, different options for the downstream processing have been investigated. Ammonium sulphate precipitation is the most commonly used [18,19], but aqueous two-phase partitioning and ultrafiltration have also been evaluated. Comparatively, the best results were obtained when using phosphate buffer as solvent and ammonium sulphate precipitation [20]. Other authors have evaluated

alternative procedures for pigment purification. When it comes to obtain a higher purity, better results were obtained when considering anion exchange chromatography [21–24]. Another innovative method that has proven to be efficient is a heat-sensitive aqueous biphasic micellar system (AMPT) based on the use of surfactants and ionic liquids [25]. In this framework, two sequentially mixed AMTPS units and an ultrafiltration stage are required to obtain a surfactant-poor phase with a high content of the R-phycocerythrin pigment with a purity above 80 % [25].

In the case of brown algae, the most abundant pigments found in their structure are pheophytin a, which is a compound derived from chlorophyll, and fucoxanthin, identified as a carotenoid [26] with valuable antioxidant, anti-inflammatory and neuroprotective properties [27,28]. The extraction of fucoxanthin with ethanol attained optimal results in terms of maximum fucoxanthin concentration for an ethanol/solid ratio of 20:1, $45\text{ }^{\circ}\text{C}$ and an extraction time of 60 min [29].

Three extraction technologies: Soxhlet, liquefied dimethyl ether (DME) and supercritical CO_2 for the extraction of fucoxanthin were compared [30]. The most promising values were obtained by the liquefied DME, as it only requires 0.72 h for the extraction at room temperature, achieving a fucoxanthin yield of 390 $\mu\text{g/g}$, which is significantly higher than that obtained by conventional Soxhlet extraction (50 $\mu\text{g/g}$) at $78\text{ }^{\circ}\text{C}$ and extended period of 12 h. Another important advantage of this liquefied DME method is that it does not require a pre-treatment step for macroalgae cell disruption. On the other hand, the efficiency of supercritical CO_2 extraction could be increased by using ethanol as entrainer to favor CO_2 saturation, obtaining a fucoxanthin yield of 995 $\mu\text{g/g}$ [30]. Ultrasound-assisted extraction (UAE) has also been shown to be a suitable extraction strategy [31]. The optimal conditions selected were an extraction time of 27 min, $75\text{ }^{\circ}\text{C}$, leading to an extraction yield of 698 $\mu\text{g/g}$, using green solvents such as ethyl lactate, limonene or vegetable oil.

It has been identified that one of the main challenges in the extraction of fucoxanthin from brown macroalgae is the downstream processing. The use of complex techniques such as HPLC can be a limitation in the development of large-scale processes due to their high cost and complexity [32]. In the search for alternative purification strategies, a sustainable and efficient approach based on the combination of an octadecyl silyl open column chromatography (ODS) with ethanol precipitation has been reported, achieving 75 % recovery of a high purity product (91 %).

For this last step, the addition of ethanol and phosphate is required, with the aim of removing carotenoids, chlorophylls and lipids, obtaining a fluid lower phase with these compounds, and an upper phase with at least 50 % purity and a fucoxanthin recovery of 70 % [33].

Aqueous two-phase system separation (ATPS) has also been assessed as a purification method, due to the high recovery efficiency achieved. The overall process is divided into five main stages, starting with centrifugation, filtration of the extract, liquid-liquid extraction using hexane as the extraction solvent. For this last stage, the addition of ethanol and phosphate is required, with the aim of separating two fractions: the fraction in the bottom poor in carotenoids, chlorophylls and lipids, and the upper phase rich in fucoxanthin [33].

In the case of green macroalgae, analogous to brown algae, two main pigments have been identified: chlorophylls a and b, and the carotenoid xanthophyll [26]. Chlorophylls are one of the most widely used natural food dyes, but their properties allow them to be used in pharmaceuticals due to their chemical similarity to haemoglobin [34]. Moreover, the only difference between the two types of chlorophylls is the substitution of a methyl group for a formyl group at position 3 in the case of type b [34]. The extraction of chlorophylls from green macroalgae starts with an initial dehydration and desalting of the macroalgae, followed by the extraction process, using organic solvent extraction and supercritical fluid extraction (SFE) as the most widespread alternatives [34]. Solvent screening identifies acetone as the best solvent in contrast to methanol, which is preferred for red and brown algae [35], but in the case of green algae the use of liquefied dimethyl ether also leads to good yield and

selectivity. Comparing the potential of both solvents: acetone and DME for the extraction of chlorophyll and carotenoids, it was observed that the use of DME leads to higher selectivity, efficiency and yield and lower solvent residue content in the extract [36].

Emerging green technologies, such as SFE with CO₂, UAE and MAE with ethanol as solvent have been included in comparative studies with conventional Soxhlet extraction [37–39]. Higher extraction yields of chlorophyll a and b, lower cost, shorter process time and better environmental sustainability were favorable for UAE and MAE technologies. The use of surfactant ionic liquids as extraction solvents to replace the conventional ethanol extraction process has also been evaluated [40]. The results obtained showed that the use of a chloride ionic liquid (250 mM) leads to the maximum yield, with a value of 5.96 mg chlorophyll/g of dried green macroalgae. Furthermore, in terms of economic evaluation, the use of ionic liquids is 1.7 times less costly, demonstrating its potential for the development of a sustainable extraction technology.

2.2. Macroalgae as a bio-resource for the extraction of proteins

The protein content of macroalgae depends on the species, with concentration ranging from 15 % for brown algae, <26 % for green algae and reaching values of 47 % for red macroalgae [41]. In fact, one of the most widespread bioresources as a source of protein is soybean, with a protein content of 35–50 % by weight, which has gained market value due to its availability and low cost but is also one of the causes of deforestation in producer countries, such as the United States, Brazil and Argentina. Therefore, other alternative biological resources should be considered as raw materials for protein extraction, with seaweed being a potential and suitable candidate, as it does not cause deforestation and does not require the use of fertilizers. However, as in the case of soybean, an efficient extraction process needs to be developed to separate the proteins from the algae. The use of subcritical water may be an alternative for the extraction of protein fractions from harvested red macroalgae biomass after agar extraction [42].

Extraction with subcritical water has proven to be an efficient method to carry out extraction processes, since under these conditions it presents adequate hydrolysis properties to be considered as an extraction solvent, since almost 100 % of the protein content is extracted [42]. In fact, water at high temperatures and pressures reaches dielectric constant values that imply a behavior similar to that of methanol or ethanol, being as efficient as those chemical compounds in dissolving organic molecular structures. Moreover, by using water as a solvent, hazardous chemicals and pollutants are avoided, thus reducing the environmental impacts caused by them.

The possibility of using a sequence of extraction steps based on acidic or basic media has also been evaluated as an alternative to organic solvents. Three main solvents: deionized water, hydrochloric acid and citric acid [43] and sodium hydroxide [44] have been considered for the extraction of proteins from brown macroalgae species. No significant differences were detected between the solvents, as similar yield results were obtained in both cases. However, it should be noted that the selection of the macroalgae species has a direct impact on the extraction yield of the process. While *Ascophyllum nodosum* leads to a yield value of 31–38 %, a yield of 50 % is achieved with *Fucus vesiculosus* [43]. It is the case of red macroalgae *P. palmata*, using a solvent mixture of NaOH with sodium dodecyl sulphate, higher protein extraction yield is obtained, reaching a value of 95 % [45].

Emerging technologies have also been used as techniques for protein extraction from macroalgae. It has also been reported the application of enzyme-based treatment and pulse electric field (PEF). In the case of considering an enzymatic process, the use of cellulases, amylases and pectinases has been considered, concluding that the use of cellulases is the most efficient, as its hydrolytic activity is the highest [46]. This extraction technology leads to the production of a purified protein extract, just after the acetone precipitation and lyophilization stages. However, although the results were promising, large extraction

residence times are required to allow enzymatic attack, which could be considered a bottleneck in large-scale production [47].

PEF technology has also been considered for the valorization of algae following a biorefinery approach, as it is a time-efficient process. It could be considered as a technique for starch and protein extraction using the green macroalgae species *Ulva ohnoi* as feedstock. In addition to PEF, a mechanical press pre-treatment was performed for cell disruption, aiming at increasing the yield of the extractive process. After a filtration stage, the solid retained will be used for starch extraction, following a water extraction procedure. On the other hand, also an extract rich in proteins is also obtained just after the filtration step [48].

Ultrasound Assisted Extraction (UAE) and Microwave Assisted Extraction (MAE) have also been considered as green extraction technologies [49]. The UAE process could be divided into three main stages: a pre-treatment, to remove the fat fraction from the algal biomass, an extraction stage at 4 °C and a downstream phase based on a shaking water bath and various centrifugation cycles. In the case of MAE, promising results were also obtained, with yield levels of 80 % for a very short time: 3 min. The main advantage of MAE is based on the lack of pre-treatment steps. Therefore, even though the yield value using the UAE is slightly higher (84 %), the difference in process time and the absence of pre-treatment steps could be key factors in the selection of MAE technology over UAE.

It is important to note that, in addition to the extraction processes, the purification strategy is also of great importance in defining the stages of the production process, as the quality of the protein obtained will directly depend on the downstream processing stage. In general, one of the main challenges in the purification steps is the co-presence of polysaccharides and proteins in the extract. One of the methods that has been identified as the most promising for their separation is the ion exchange process, using a negatively charged resin, so that the retained molecules can be subsequently released by elution with salt concentrations. A basic medium is also required for the proteins to bind to the resin and, in turn, separate from the polysaccharides present in the medium, thus facilitating effective separation. This effect occurs because the polysaccharides have a higher negative charge, so their separation from the ion exchange resin will be more complex, with the proteins then eluting first down the upward salt gradient [50].

2.3. Macroalgae as bio-resource for polysaccharide extraction

Functional foods with antioxidant, antimicrobial and anti-inflammatory properties could be developed using polysaccharides extracted from marine macroalgae. Their non-toxic, bio-compatible and bio-degradable makes them suitable candidates for various applications in the food, medical and pharmaceutical sectors [51]. Each of the seaweed species is characterized by providing high molecular weight polysaccharides: carrageenan for red algae, fucoidan, for brown algae and ulva for green macroalgae.

Carrageenan is a high molecular weight galactose-based protein found in the cell wall of red macroalgae [52,53]. Its widespread use is based on the beneficial properties it provides: antimicrobial, antiviral, antioxidant and anti-inflammatory capabilities [54,55]. The use of carrageenan in the formulation of bioactive edible films also stands out [56,57]. For their extraction, subcritical water using ionic liquids as catalysts has recently been evaluated as a highly efficient technology, providing a carrageenan extract with enhanced antioxidant activities and low impurities. For its extraction, subcritical water using ionic liquids as catalysts has been recently assessed as a highly effective technology, providing a carrageenan extract with enhanced antioxidant activities and low impurities [58].

Red macroalgae species *Gracilaria manilaensis* and *Kappaphycus alvarezii* have also been considered as resources for carrageenan extraction, using potassium and sodium hydroxides as extracting agents. Alkaline extraction conditions has also been considered, with a first pre-treatment, based on washing, soaking and grinding of *Kappaphycus*

alvarezii macroalgae [59]. After extraction, filtration is performed, obtaining a viscous filtrate containing the extracted carrageenan. The subsequent purification step requires several stages: neutralization with HCl, heating, coagulation with KCl, soaking in alcohol, filtration and drying. The extraction yield obtained depends directly on the concentration of KCl used in the coagulation stage, with the highest value of 44 % being obtained with an HCl concentration of 3.5 % [59]. Tuvikene et al. have considered a different procedure for the separation and purification of carrageenan, using a single precipitation step with 95 % v/v ethanol, obtaining similar results [60].

Response surface methodology has been studied as a method for optimize the extraction process of carrageenan from *Kappaphycus alvarezii*. The advantage of this methodology is that the first alkaline pre-treatment is avoided, thus reducing the process time and chemical consumption, and it is possible to use ethanol as a precipitating agent in the subsequent step for the purification of the extracted carrageenan. Moreover, the method used is aqueous extraction, without the need of introducing other chemicals. The main drawbacks identified are the process time required, which amounts to 4 h, and the constant temperature of 74 °C [61]. Both values could have a significant environmental impact, as a fairly high amount of energy will be required to maintain this temperature, which could reduce the viability of this extraction alternative. However, it is true that the lack of a pre-treatment step and the non-use of chemical solvents are clear advantages compared to other strategies.

Looking for more sustainable alternatives, green extraction technologies have been also assessed by some authors, being UAE and MAE the ones that have led to better process yields and efficiencies [62]. Some authors have assessed how ultrasonic power and extraction temperature affect the extraction yield of carrageenan [63]. A pre-treatment stage is required, based on the addition of ethanol, followed by filtration and washing stages. The extraction is performed in a water bath at neutral pH, applying ultrasounds with a power of 150 W during 15 min. Afterwards, the carrageenan solution is hot filtered, gelled at 4 °C and freeze-dried for isolation and purification [63]. Under these process conditions, an extraction yield of 55 % is achieved, which is analogous to conventional strategies, but requires significantly reduced operating times and chemical agents.

Deep eutectic solvents (DES) were used as efficient agents for the extraction of k-carrageenan from the red macroalga *K. alvarezii*. Their main advantage and suitability lie in the ease of the process, which is higher compared to conventional methods, and in the quality of the product, since using water as the main solvent avoids impurities. The highest extraction yield: 60.25 %, is obtained when using 10 % of DES hydrated chlorine-chloride-glycerol 1:2 [64].

Fucoidans are the characteristic polysaccharides of brown macroalgae. Their composition includes the presence of sulphated compounds, which are available in the algal cell walls, with fucoses as their main monomeric units, covering >70 % of all monosaccharides found in their structure [65]. On the other hand, variations in their composition and heterogeneity of structure have been observed depending on the extraction method used, harvesting sites and climate conditions of cultivation. Another interesting property of sulphated polysaccharides is their antioxidant capacity. In fact, according to research work by Choi et al., fucoidans obtained from *Sargassum fulvellum* brown seaweeds even have a higher antioxidant capacity than commercial tocopherols or BHA antioxidants. This is based on their ability to act as NO scavengers [66].

As previously mentioned, one of the most relevant properties of fucoidans from brown macroalgae is its high sulphate content, which is beneficial for anticancer action. *Fucus vesiculosus* is one of the most studied brown macroalgae for the extraction of this polysaccharide, that even with low molecular weight fucoidans extractants, its beneficial properties are not diminished [65,67]. Considering the possible alternatives for fucoidan extraction, one of the most effective methods is solid-phase extraction, with efficiencies as high as 95.5 % [68].

Sargassum binderi has also been evaluated for the extraction of fucoidans by enzymatic hydrolysis using the commercial enzyme cocktail Celluclast, a constant acid pH, a 24-h incubation and a temperature of 50 °C. After completion of the enzymatic reaction, ethanol has been used to allow precipitation of the polysaccharides, which are finally lyophilized and separated by anion exchange chromatography [69]. This extraction procedure yields an extract with a high fucose content and a strong sulphate composition compared to that of commercial fucoidan products, which increases the benefits of using *S. binderi* brown algae as a bioresource for the production of a bioactive compound with enhanced anti-inflammatory properties [69]. Enzymatic extraction has also been used by Lee et al., using *Ecklonia cava* as brown seaweed species [70]. A comparison between hot water (HWE) and enzymatic extraction procedure has been conducted.

In the case of HWE, 24 h and a constant temperature of 70 °C are required. In the case of enzymatic extraction, the main difference with respect to the description of the previous enzymatic process is that the extraction agent used just after the enzymatic extraction is CaCl₂. The comparison between the two extraction methods concludes that the yield using HWE is lower than that of enzymatic extraction (30.3 % and 40.6 % respectively), and also higher values of fucose are obtained when enzymes are used, with a 10 times higher proportion than that obtained with HWE. In the case of sulphate content, the trends are similar, with 12.5 % obtained with enzymatic extraction compared to 7.5 % obtained with HWE [70].

Regarding the use of novel extraction techniques, Saravana et al. have considered the use of deep eutectic solvents in a subcritical water hydrolysis extraction [71]. The brown seaweed species used for this research was *Saccharina japonica*, an abundant macroalgae from South Korea, widely consumed in Asian food sectors, and also in medical uses, as its high vitamin and mineral content has shown positive effects on woman health [72]. The results showed that the deep eutectic solvent consisting of choline chloride and glycerol has a higher overall yield for polysaccharide extraction and, as for the optimal process conditions, a temperature of 150 °C, 20 bar and a liquid-to-solid ratio of 36.81 mL/g achieved the best extraction yields [72].

Ulva polysaccharide is found in the cell walls of algae and its commercial uses range from the pharmaceutical sector, due to its bioactivity properties and antioxidant capacity [73], to biomedical applications, as it can be used to produce natural-based polymers for encapsulation or drug delivery [74,75], thanks to its biodegradability and biocompatibility characteristics [76–78]. Another beneficial property of Ulva is its adaptability to different climatic conditions, which translates into its ability to grow and propagate with high productivity and yield values in a wide diversity of environmental conditions [79,80].

One of the bio-based methods used for their extraction is an enzyme-assisted procedure, which is considered to be a more environmentally friendly strategy. Kevin et al. have used *Ulva armoricana* as a green alga for the extraction of ulva polysaccharide using six different commercial enzyme cocktails, namely proteases and carbohydrases [81]. The reaction is carried out at 50 °C for 3 h, and then the temperature is increased to 90 °C, to allow denaturation, for 15 min. The next step is the filtration and centrifugation of the bioreactor output stream, obtaining an insoluble pellet and a soluble extract. The results obtained showed that the use of proteases gives a higher value for the extraction yield, amounting to a score between 70 and 88 %, compared to 45 % obtained for carbohydrases [81]. On the other hand, proteases also give an extracted polysaccharide with higher antiradical activities (i.e. antioxidant capacities), which makes *U. armoricana* an effective bio-based raw material as a good candidate to be used as an organoleptic compound for food preservation and as an additional product to be used in the cosmetic and pharmaceutical sectors. Even higher extraction yield values are obtained when a hot water extraction process is developed, requiring a constant process temperature of 130 °C for 2 h, leading to a recovery value amounting to 97.6 wt% [82].

Ulva fasciata and *Ulva lactuca* species has also been reported as green

seaweed for sulphated polysaccharide extraction. These macroalgae are mainly found in the Mediterranean Sea and are harvested and dried before processing for Ulva extraction. A recent research report has used water extraction methodology for polysaccharide recovery, requiring a medium temperature, 80 °C, and a reaction time of 4 h. Then, to separate the ulva, a filtration and precipitation step is required, for which ethanol is used as solvent, requiring an additional step based on dehydration with diethyl ether, in order to increase the purity of the extract [83]. The use of ethanol also implies a purification of the extracted compounds, as it facilitates the removal of other co-extracted products, such as some pigments or low molecular weight polysaccharides, which are soluble in the ethanol solution [84]. This manuscript studies the capacity of this polysaccharide as a biostimulant for plant growth. *U. fasciata* seems to have a higher stimulating capacity, both in the germination stage and in shoot and root growth. Therefore, its applicability as a biofertilizer is also feasible [83].

As mentioned above, the use of filtration and precipitation steps is the most common procedure in the extraction of polysaccharides from green seaweed [85]. But, looking for a more purified product, a multi-step purification process could be developed, based on a first stage of ultrafiltration, followed by ion exchange and ending with the precipitation of the remaining proteins [86]. Right after this procedure, neutralization with sodium hydroxide and recovery with a sodium salt are required to obtain the sulphated polysaccharides in a proper way. With this extraction sequence, the ulva polysaccharides obtained will have a strong anticoagulant capacity, in fact even superior to that of the commercial anticoagulant Lovenox® [86]. This anticoagulant activity is the result of the mechanism of action of the sulphated polysaccharides, based on direct inhibition of thrombin and potentiation of the activity of heparin cofactor II [85].

2.4. Macroalgae as bio-resource for lipids extraction

The use of macroalgae has been considered as a high potential alternative for the extraction of lipids, which have a wide spectrum of applications in the market as an ingredient in food, cosmetics and nutraceuticals. Lipids are primary natural metabolites found in a percentage of 0.2–8 % of the dry weight in macroalgae, depending on the species. Although their abundance is not so high, macroalgae can provide omega-3 and PUFA as the main high value-added products associated with lipids [87]. Another important advantage to be considered is the antioxidant activity they provide, together with anti-inflammatory and chemoprotective properties.

Different extraction methods have been evaluated for lipid recovery. The most widespread conventional method is based on the use of chloroform (CHCl₃) [88,89], but as many restrictions have been imposed on the use of this chemical, due to its harmful effects on health and the environment, it is necessary to find substitutes for this solvent. One option is the use of dichloromethane, which although not a natural and totally safe chemical, its restrictions and effects on health and the environment are significantly lower [90]. The use of propan-2-ol could also be considered as an alternative, but for sustainability, health and environmental protection, it would be desirable to avoid the use of chemical agents, with supercritical CO₂ extraction being a plausible and efficient alternative technology. Analogous performance values were obtained when comparing CHCl₃ and propan-2-ol, concluding that considering this substitution as a good alternative [91]. In the case of supercritical CO₂ extraction, the yield values were slightly lower.

Methanol and CHCl₃ were used as extraction solvents for the recovery of lipids from the green macroalga *Utricularia rigida* after freezing steps and biomass grinding [92]. Subsequently, for the separation and purification of the extracted lipids, centrifugation is required, thus obtaining an organic lower phase, in which the 202 polar lipid species are melted, to be recovered as solid powder after a drying step [93].

Instead of CHCl₃, a mixture of dichloromethane and methanol (2:1 v/v) could also be considered [92,94]. However, a previous

polysaccharide (MPS) extraction using the solvent mixture is required. This first extraction of MPS is based on a hot water extraction with a solid/liquid ratio of 30 g: 1 L. Once extracted, to allow purification, an ethanol precipitation is performed, which requires 4 °C and 24 h, centrifugation and drying to obtain a powder. This powder is used for re-extraction with CH₂Cl₂ and CH₃OH, using a sonicator equipment, with subsequent centrifugation and evaporation stages for purification and recovery of the solvent [94]. Other extraction technologies are based on a direct transesterification method [95] which allows lipid extraction with lower loss and better recovery [96,97].

The co-production of the pigment lutein and lipids by direct dimethyl ether (DME) extraction has been studied [98]. The main advantage of this strategy is that no pre-treatment steps, i.e., drying and cell disruption, are necessary, as the method is sufficiently efficient without prior extraction steps [30]. The yield results obtained were like those of Soxhlet and conventional extraction with chloroform and methanol, so the potential of this more environmentally friendly alternative could be considered high. Three main pieces of equipment are required to perform this extraction scheme: DME is added to the extraction column at 35 °C and 0.79 MPa. After extraction, the mixture passes through a filtration stage and the DME is recycled by evaporation [98].

In the case of so-called green extraction technologies, pressurized liquid extraction (PLE) is one of the most widespread at 100 bar for 10 min. Different solvents have been evaluated, but ethanol: water (1:1) has been recognized as the best extraction, achieving yields ranging from 35 % to 57 %, depending on the process temperature: 80 °C and 160 °C respectively [99].

Microwave hydrolysis, together with yeast fermentation, has been used as a procedure to recover lipids from brown, green and red macroalgae [100]. Pre-treatment methods comprise freezing, freeze-drying and milling prior to suspension of the macroalgae in 5 % deionized water, for which microwave extraction will be performed, requiring 190 °C and 15 min holding time. Subsequently, a product with a high polysaccharide content is obtained, which will be treated in a second stage, based on an enzymatic hydrolysis using a cellulase for an incubation time of 20 h. Finally, for fermentation, *Metschnikowia pulcherrima* strain is used as culture medium and mannitol and *Saccharina latissimi* as hydrolysates. Aeration and agitation are provided to the fermenter to maintain a dissolved oxygen concentration with an air saturation of 80 %. With these process conditions, a final lipid content of 37.2 % is obtained, which is higher than that obtained by other lignocellulosic inputs commonly used as bioresources, such as wheat straw or distillers grains [100]. In this way, the use of macroalgae for lipid extraction seems to be a potential alternative renewable resource.

2.5. Macroalgae as bio-resource for biostimulants production

Biostimulants are natural compounds that enable plant growth, favoring plant tolerance to abiotic and biotic stresses [101]. The ability of macroalgae extract to act as biostimulants is the result of its composition in bioactive compounds, specifically those that are plant growth hormones; cytokinins, auxins, abscisic acid and gibberellins, among others [102]. While auxins provide the potentiality for plant ageing and plant tissue growth, cytokinins are involved in cell division and nutrient transport and stand out as the most promising plant biostimulator [103]. As for gibberellins, their main advantage is seed germination and fruit development, and in the case of abscisic acid, their effects focus on the response to stress factors [102,104]. These stimulating activities are the main advantage, and also the differences, compared to chemical-based fertilizers. While the latter only provide nutrients for normal plant growth, biostimulants support and regulate plant elongation and fruit production from a metabolic pathway. The brown algae *Ascophyllum nodosum* is a well-established plant biostimulant, as it uses agricultural crops increases the nutrient availability, thus improving crop growth and productivity. It is rich in auxins and cytokinins and it provides other benefits on crops yield, as it could increase plant resistance

and tolerance to pests and diseases. Several companies such as Acadian Agritech, Agri Gro Marketing Inc., MainStream Organics, etc. have developed commercial plant growth biostimulants using *A. nodosum* as seaweed [105–107]. *Kappaphycus alvarezii* and *Sargassum vulgare*, red and brown seaweeds respectively, have also been combined in a commercial biostimulant called Reabilit Algas®, developed by Nutimax Fertilizantes company. This macroalgae bioextract has been used by Melo et al. to evaluate its capacity to stimulate the growth and metabolism of peppers (*Capsicum annuum* L.) [101]. The results obtained show an increase in nutrient uptake as a direct effect of the application of the algal biostimulant. The green seaweed *Enteromorpha intestinalis* has also been used as biostimulant for further improve cucumber plants growth and production yields. The high nitrogen concentration of this seaweed leads to an increase on plant length, leaf number and productivity, together with its auxin and gibberellin content. In fact, in comparison with Algreen® (a commercial stimulant), the results obtained are better [108].

Another interesting fact about the consideration of macroalgae as a source of biostimulants lies in their safety requirements when introducing them into the market, as compared to the production of food additives, pharmaceuticals, antioxidants or PUFAS, their requirements are significantly lower, being mostly minimal [109].

For the extraction of biostimulants from macroalgae, the most widespread method is supercritical CO₂ extraction. It requires high pressure conditions, with mild temperatures, with an approximate CO₂ consumption of 100 kg/kg of macroalgae biomass loaded into the reactor [102]. MAE has also been reported as a green technology and method for the extraction of bioactive compounds to be applied in agricultural activities. As with supercritical CO₂ extraction, it is also necessary to apply mild temperatures with MAE. The reason for this is based on the fact that low temperatures favor the extraction of bioactive compounds, such as phenolics, while higher temperatures lead to the decomposition of those, thus decreasing the biostimulant potential of the macroalgae extract [110].

Among the macroalgae species, brown macroalgae are the most common for the extraction of biostimulants, and also the ones with the largest market presence [101,111]. However, the most recent research reports are focusing on assessing the efficiency of this algae biostimulants in the growth phase of crops, in order to evaluate its potential to be used in the harvesting processes on agriculture activities [101,112–115].

2.6. Macroalgae as bio-resource for biogas production

The spent biomass of seaweed after extraction can be treated in an anaerobic digester to produce biogas due to its low lignin content and the high amount of polysaccharides in its molecular structure [116–118], which facilitates the hydrolysis stage [119]. However, the high molecular weight structure of macroalgae requires pre-treatment technologies to increase the bioavailability of carbohydrates and the release of fermentable sugars. In this sense, physical, thermal, enzymatic, chemical or biological stages, or even a combination of them can be applied [120]. It has been evaluated more environmentally friendly alternatives for the preparation and pre-treatment of macroalgae, as using beaten and ball milling as conventional techniques in combination with microwave [119]. Two main aspects were considered as comparable characteristics, firstly the productivity of biogas production, and the energy balance of the process, considering the amount of energy produced versus consumed when applying the pre-treatment step. According to these, the results have shown that the use of the beaten pre-treatment leads to the best process performance and is also the only one for which excess energy is available, as the amount of energy required for this pre-treatment alternative is lower than that obtained by anaerobic digestion.

Chadiryfar et al. have studied the use of macroalgae to produce bioenergy, considering all the life cycle stages, from the seaweed

cultivation and production to the final product [121]. Harvesting stages should be considered as, according to some studies, only 6 % of the total seaweed consumed are obtained by natural stocks. Once produced, pre-treatment methods are required before being used as biorefinery inputs. These methods encompassed washing, milling and drying, which helps to process productivity due to the increase of the surface area for reaching higher reaction/fermentation efficiencies and to reduce the energy consumption in transport, storage or process stages due to the high-water content [121,122].

Besides, regarding the macroalgae species that has experience greater attraction to be considered as feedstock for the production of biofuels, both biogas, biomethane and/or bioethanol, is brown macroalgae. This tendency is based on the fact that red and green macroalgae are commonly used on food and hydrocolloid production, whereas brown macroalgae has less applications in those areas [123].

One main drawback that could be identified when using macroalgae as feedstock is the dependence on its productivity by the seasonal period of its harvesting. The carbohydrates content is directly dependent on the season in which macroalgae is harvested [124]. But, for solving this problem, the use of pre-treatment stages could enhance the effective use of the carbohydrates available, acquiring process yields that could be improved by a 47 % with respect to the untreated feedstock.

In the scope of environmental awareness, LCA studies on the production of biogas from macroalgae has also been assessed. Different system boundaries were considered by some authors when developing the environmental loads of the process, but the most common are the ones based on cradle-to-gate and cradle-to-grave approaches, considering all the stages between the harvesting to the production or use stage, respectively [125,126]. The LCA results showed that the use of macroalgae for biogas production is favorable and leads to reduced environmental impacts in comparison with its counterparts, i.e. the use of agricultural feedstocks as resources for biogas production.

Looking for biorefinery approaches, some authors have thought different scenarios on the valorisation of macroalgae as feedstock for bioenergy production [127,128]. The simplest is the one in which only one product is obtained, just after a first mechanical pre-treatment and an anaerobic digestion stage, biogas is produced. Nonetheless another co-product could be easily obtained by using the digestate obtained from anaerobic digestion, a fertilizer compound, adequate for agricultural purposes. Still, another scenario could be performed, in the case of considering an intermediate stage between the pre-treatment and the anaerobic digestion. This middle stage is a fermentation one, in which bioethanol could be obtained, which after its purification could be used as fuel additive. In this case, three co-products could be obtained by using the same macroalgae feedstock: bioethanol, biogas and a fertilizer compound. This is the scenario proposed by the research of [129], in which it has demonstrated, by applying an environmental analysis, the suitability and potentiality of macroalgae as feedstock for biorefinery approaches.

3. How about the industrial scale-up of emerging technologies? Is it possible?

In the need to develop efficient production processes, to meet the criteria and objectives set to reduce environmental damage, to be sustainable and to promote the basis of the circular economy concepts, the approach of the valorization of macroalgae in the development of biotechnological processes can be considered as a production strategy with high potential [25,42]. However, it is still an enormous challenge the transition from the small-scale methods and protocols to an industrial scale-up [5,117].

One of the main drawbacks that has been identified for the scale-up of some of the green emerging or more environmentally friendly technologies are the large investments needed to be implemented in high production industrial facilities: the largest scale process considered, the highest costs associated [42]. Also, the lack of common extraction

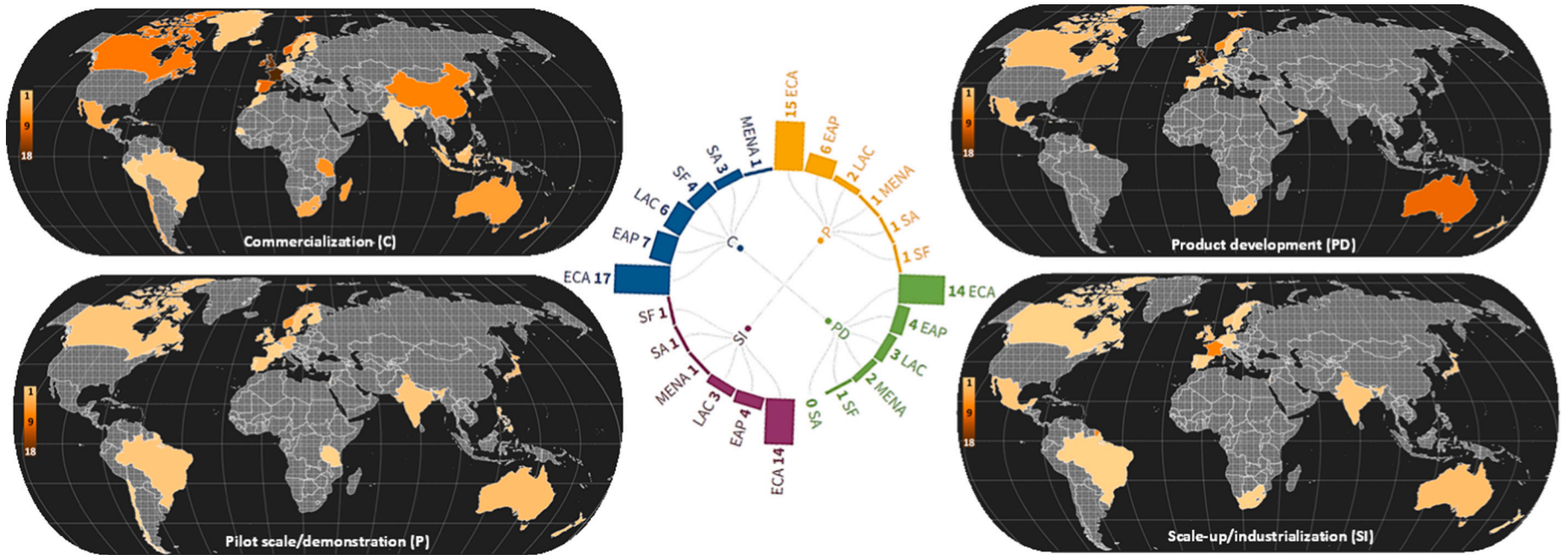


Fig. 3. Worldwide most important facilities working on algae valorization within different TRLs: commercialization, pilot scale/demonstration, product development and scale-up/industrialization. Acronyms: EAP (East Asia and Pacific), ECA (Europe and Central Asia), LAC (Latin America & the Caribbean), SF (Sub-Saharan Africa), SA (South Asia).

Table 2
Worldwide facilities using macroalgae as feedstock classified by commercial sector.

Industry	Country	Species	Food sector	Plant & soil nutrition	Cosmetics/ personal care products	Nutraceutical/ pharmaceutical	Animal feed	Bioenergy	Biopolymers
Algaia	France	<i>Laminaria digitata/hyperborea</i>	X	X	X	X			
Algamar	Spain	<i>Laminaria sp., Palmaria sp., Porphyra sp., Undaria sp.</i>		X		X	X		
Algamar Mexico (Algas Marinas S.A.)	Mexico	<i>Macrocystis pyrifera, Ecklonia sp.</i>		X	X	X	X		
ALGAplus Lda	Portugal	<i>Codium tomentosum, Gracilaria gracilis, Palmaria palmata, Porphyra dioica, Porphyra umbilicalis, Ulva rigida</i>		X					
AlgAran	Ireland	<i>Alaria esculenta, Chondrus crispus, Himanthalia elongata, Laminaria digitata, Palmaria palmata, Porphyra umbilicalis, Ulva sp.</i>	X		X				
Algea	Norway	<i>Ascophyllum nodosum</i>		X			X		
Algea (Valagro/Syngenta)	Norway	<i>Ascophyllum nodosum</i>		X			X		
Alginor	Norway	<i>Laminaria hyperborea</i>				X			
Arramara Teo	Ireland	<i>Ascophyllum nodosum</i>		X			X		
Atlantic Mariculture Ltd/Tangled Greens	UK	<i>Alaria esculenta, Saccharina latissima</i>	X	X					
BioAtlantis Limited	Ireland	<i>Laminaria hyperborea/digitata, Ascophyllum nodosum</i>		X		X	X		
Carbonwave	USA	<i>Sargassum sp.</i>	X	X	X				
CH4Global	USA	<i>Asparagopsis sp.</i>	X				X		
C-weed aquaculture	France	<i>Alaria esculenta, Saccharina latissima, Undaria sp.</i>	X		X	X	X		
EstAgar	Estonia	<i>Furcellaria lumbicalis</i>	X		X				
Fearless Fund	USA	<i>Ulva sp., Sargassum sp., Ulva lactuca, Gracilaria sp., Fucus sp.</i>	X		X			X	
FMC	USA	<i>Ascophyllum nodosum</i>		X					
Fujian Shenshilian Foods	China	<i>Porphyra yezoensis</i>	X						
Gelymar	Chile	<i>Sarcothalia crispata, Sarcopeltis skottsbergii, Mazzaella laminarioides, Chondracanthus chamissoi, Chondrus crispus/canaliculatus, Lessonia berteriana/trabeculata, Macrocystis pyrifera, Durvillaea incurvata</i>	X		X				
Marinova	Australia	<i>Undaria pinnatifida, Fucus vesiculosus</i>	X		X	X			
Mediterranean Algae	Spain	<i>Ulva sp.</i>	X	X	X				
Naas Food	Canada	<i>Macrocystis sp.</i>	X						
North Atlantic Organics	Canada	<i>Laminaria sp.</i>		X	X				
Nutramara	Ireland	<i>Fucus vesiculosus, Ascophyllum nodosum, Saccharina latissima</i>	X		X	X	X		
Nutrimar AS	Norway	<i>Laminaria hyperborea</i>	X			X			
NZ Kelp	New Zealand	<i>Macrocystis pyrifera</i>		X			X		
Oceana minerals	Brazil	<i>Lithothamnium sp.</i>		X			X		
Oilean Glas Teoranta	Ireland	<i>Ascophyllum nodosum</i>		X			X		
OLMIX	France	<i>Solieria sp., Ulva sp.</i>	X	X	X	X	X		
Organic Seaweed	Denmark	<i>Fucus sp.</i>			X	X			
Origin by Ocean	Finland	<i>Fucus vesiculosus, Sargassum sp., Saccharina latissima, Rugulopteryx okamurae</i>	X	X	X				X
Prospersea	Brazil	<i>Kappaphycus alvarezii</i>	X	X		X			
Redrose Developments Ltd	Ireland	<i>Saccharina latissima, Ascophyllum nodosum, Laminaria digitata, Fucus serratus/vesiculosus</i>	X	X	X	X	X		
Renovare	Mexico	<i>Sargassum sp.</i>							X
Rhodomaxx	Malaysia	<i>Kappaphycus alvarezii</i>		X			X		X
Salgax	Mexico	<i>Sargassum sp.</i>		X	X				X
SeaChange Biochemistry	Canada	<i>Ascophyllum nodosum</i>	X	X	X				X
SEADLING	Malaysia	<i>Kappaphycus alvarezii</i>	X	X			X		
Seakura	Israel	<i>Ulva sp., Gracilaria sp.</i>	X	X	X	X			

(continued on next page)

Table 2 (continued)

Industry	Country	Species	Food sector	Plant & soil nutrition	Cosmetics/ personal care products	Nutraceutical/ pharmaceutical	Animal feed	Bioenergy	Biopolymers
Seastock	Australia	<i>Asparagopsis sp.</i>	X			X			
Seaweed & Co	UK	<i>Ascophyllum nodosum</i>	X			X			
Seaweed Sheycheles	Sheycheles	<i>Sargassum sp.</i>		X		X			
SJOBORG AS	Norway	<i>Ascophyllum nodosum</i>				X			
SMO Solar Process	Guadeloupe	<i>Sargassum sp.</i>		X				X	
Tekslo Seafood	Norway	<i>Laminaria hyperborea, Chondrus crispus, Himanthalia sp., Palmaria sp., Ulva lactuca, Alaria esculenta, Saccharina latissima, Ascophyllum nodosum</i>	X	X	X	X	X		
Waikaitu	New Zealand	<i>Undaria Pinnatifida</i>		X			X		
Wild Irish Seaweeds	Ireland	<i>Laminaria digitata, Palmaria palmata, Saccharina latissima, Chondrus crispus, Himanthalia elongata, Porphyra umbilicalis, Alaria sp., Fucus vesiculosus, Ulva intestinalis, Ascophyllum nodosum, Ulva lactuca, Fucus serratus</i>	X		X	X			

Table 3

Classification of commercial macroalgae valorization facilities according to the region and annual production capacity.

Region	Annual production capacity (ton/year)					
	0–10	10–10 ²	10 ² –10 ³	10 ³ –10 ⁴	10 ⁴ –10 ⁵	10 ⁵ –10 ⁶
East Asia and Pacific	4	6	4	2	4	1
Europe and Central Asia	14	8	8	2	4	1
Latin America & the Caribbean	1	2	2	5	1	2
Middle East and North Africa		1		1		
South Asia		1	4		1	
Sub-Saharan Africa	2	2	2	3	2	
Total	21	20	20	13	12	4

protocols could also be considered as an impediment to its spreading [49,50]. While good extraction results are obtained at laboratory scale, most of them are far away for be considered for developing in an industrial scale with a commercial perspective [5]. Extraction procedures that has been recently developed in a lab-scale level entails the sequence of several extraction stages, that requires significant amount of buffers and solvents, resulting in complex protocols with a high demand of both chemicals and energy [7]. In this regard, optimization procedures are required, not only for increase process effectiveness in terms of chemicals and energy needs, but also to enhance the recovery and purification stages [33,100].

Regarding the assessment of the possibility of integrating green emerging technologies in industrial large-scale production procedures, ultrasound assisted extraction could be considered as a proven technology, with high efficiency on macroalgae bioactive extraction [31,63], but with high costs associated [6,37]. Besides the huge investment capital required for it installation, also large energy requirements are needed for it operation, which further increases the capital required for this technology [26]. In the case of microwave, also promising results were obtained at lab-scale protocols, but it is a technology currently founded at a development stage to be applied at an industrial level. The reasons for this lack of scaled up, even the good extraction yields that could be achieved, is based on the optimization needed to enhance the wave penetration, the capital investment and the deeply knowledge required to control the microwave equipment, as inadequate process

control could lead to product degradation [26,52]. Subcritical water extraction procedure has also achieved promising extraction yields and recoveries, even though optimization assessments should be developed with the aim of improve the energetic efficiency of the process, it could be considered as a greener technology when comparing with conventional ones, as Soxhlet or maceration. In fact, it has been proven that it scale-up is economically profitable [42]. Another technology that has been extensively evaluated and developed by numerous researchers at the laboratory level has been pressurized liquid extraction. It is defined as a fast, efficient method, with low degradation level and through which high purity products are acquired [90,99]. However, the high energy demand required to maintain the working pressures, together with the expensive and sophisticated equipment required to be implemented, are the main impediments to being used on a larger industrial scale [90,115]. Once again, the economic constraints appeared as one of the bottlenecks on the way of using this more efficient technologies in a larger scale [109].

Another impediment that can be identified is the fact that, even though compounds of high added value are obtained from the valorization of macroalgae, their criteria and conditions for its use and application are still at a very early stage of development, depending on a higher level of knowledge of both the product itself and the technology required to obtain it [5]. It is important to mention that any product intended to be applied for human consumption, whether in the form of cosmetic or pharmaceutical products or as natural food additives, must meet strict evaluations and comply with the requirements established by law, to guarantee its benefits.

Besides, beyond the extraction processes, the purification processes of the extracted product are also important, which are essential in the commercialization. A recent study has concluded that the use of a column chromatography in combination with ethanol precipitation would be an efficient purification method, obtaining a high purity product. Even though it has been performed on a small scale, it is considered as an easily scalable, cost-effective and low environmental impact process strategy [32]. But a higher level of research is required in these downstream stages for its implementation at larger production levels.

Given these weaknesses in the path of using macroalgae as inputs for the production of high value-added products on a large scale, many authors have concluded that the best solution to the problem would be based on the development of biorefinery processes [26,94,100,109,117]. The multiplicity of products obtained using the same raw material would favor a higher yield of the overall process, as well as a higher economic profitability. This statement is based on the

fact that the greater the quantity of products obtained, the greater the profits and, therefore, a gross margin sufficient to compensate the costs associated to the process. But, nevertheless, a more exhaustive analysis and more studies are necessary to ensure the effectiveness and suitability of macroalgae biorefineries, not only from a technological or economic point of view, but also from an environmental approach.

4. Current state on algae valorization. From lab-scale to commercial

In order to know the current status of the use of macroalgae as raw material at different technological levels (TRLs), from the laboratory scale to the industrial process at commercial scale, Fig. 3 represents the most important facilities worldwide, classified by TRL level and economic sector. Europe, Asia and the Pacific regions stand out in terms of number of facilities. On the other hand, it should be noted that, although the largest number of installations are available at commercial scale, there are such a significant number of processes under development. This is a reflection of the importance of macroalgae as a valuable feedstock for future emerging technologies and facilities, with the goal of reducing dependence on fossil resources. On the other hand, seeking to identify which are the main algae species used and the commercial sectors in which the products obtained are established, Table 3 is included, in which the most important and gross macroalgae valorization facilities are represented. Finally, to show the potential production capacity of current macroalgae facilities, Table 2 shows that most of the major production industries are located in Europe and Central Asia and that their production capacities are limited, mainly between 10 and 10³ tons/year.

5. Discussion

This review evaluates the potential of green, brown and red macroalgae for the extraction of high value-added compounds with a wide range of applications in the agro-industrial, food, pharmaceutical and medical sectors. Focus has been paid to the main value products: lipids, proteins, carrageenan, biostimulants and biogas, as well as the main extraction technologies, comprising both conventional and green techniques. In order to achieve sustainability and circular economy approaches, biorefinery and biotechnology procedures need to be applied at industrial level, taking into account both process productivity, i.e., extraction yields, by-product recovery and environmental indicators. In this sense, future research studies should focus on the optimization of green extraction technologies, for better scalability in large-scale processes, and on the evaluation of production strategies that allow for multi-product yields, to achieve better productivities, market opportunities and profits.

CRediT authorship contribution statement

Ana Arias: Methodology, Formal analysis, Investigation, Writing – original draft. **Gumersindo Feijoo:** Writing – review & editing. **Maria Teresa Moreira:** Conceptualization, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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