Environmental Chemistry Letters
https://doi.org/10.1007/s10311-020-01124-4

REVIEW

Biorefinery of marine macroalgae into high-tech bioproducts: a review

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Received: 16 June 2020 / Accepted: 17 October 2020

Abstract
Pollution and climate change induced by fossil fuel usage are calling for the development of a circular bioeconomy based on carbon neutral resources such as marine macroalgae, also named seaweeds. Macroalgal biomass can generate biofuels and valuable bioproducts such as hydrocolloids and other unique biomolecules. Biorefinery of marine macroalgae involves a minimum use of energy and chemicals, and low waste generation, as demonstrated in recent laboratory-scale studies. Here, we review biorefinery of marine macroalgae with focus on non-energy bioproducts and advances in the separation of biomolecules. We found that metabolites with bioactive properties are in high demand for food, cosmetic, medicine and pharmaceutical industries. These metabolites can be obtained together with energy products to improve macroalgae valorization. Emerging extraction methods facilitate the generation of more qualitative bioproducts in higher yields with less energy.

Keywords Marine macroalgae · Biorefinery · Biobased products · Bioresource · Bioeconomy · Circular economy

Introduction

The increasing demand for fossil fuel resources, which is likely to expand the carbon emissions by 26% until 2030 (BP Global 2013), as well as the finite nature of this feedstock, indicates that urgent solutions are required to find renewables that can provide an alternative in order to ensure a sustainable future and meet society's growing demands. A suitable replacing feedstock would need to address environmental and economic issues related to climate change, energy security and oil prices, as well as to support the transition to a circular economy.

In the quest of changing a fossil-based economy for a bioeconomy, algae have gained more and more attention (Jung et al. 2013). The advantages of algal biomass production and processing have been acknowledged in many studies (Milledge et al. 2014; Scaife et al. 2015; Ghadiryanfar et al. 2016; Kawai and Murata 2016; Schiener et al. 2016). In comparison with first and second generation biofuels obtained from lignocellulosic biomass, the third generation biofuels which are generated from micro- and macroalgae, constitute a better alternative due to the lack or very little amount of lignin in the chemical structure of algae and the fact that their growth does not interfere with terrestrial food production processes (Wang et al. 2016; Peng et al. 2019; Patle et al. 2020).

Although up to date, marine macroalgae biomass has been mostly used as food or has been processed to produce hydrocolloids (alginate, carrageenan, agar), the potential of this feedstock is far greater. Approximately 83–90% of the current global value of marine macroalgae industry is based on their use as food products (Wei et al. 2013). However, marine macroalgae could play a key role in generating both energy and valuable bioproducts.

Over the last years, there has been a growing demand for natural antioxidants and replacement of synthetic molecules in food, cosmetics and pharmaceuticals (Agregán et al. 2018). Marine macroalgae include in their chemical structure important molecules, some of which unique in the natural world, and could be used for the production of functional foods (Holdt and Kraan 2011), cosmetics (Thomas and Kim 2013), pharmaceuticals (Smit 2004; Silva et al. 2012; Vo et al. 2012; Liu et al. 2015; Raposo et al. 2015),

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Published online: 15 November 2020

biochemical (Alvarado-Morales et al. 2015) and biobased polyesters (Noreen et al. 2016).

One major obstacle in making biofuels from marine macroalgae feasible is represented by the high cost required. It is estimated that just the costs for feedstock generation would need approximately a 75% decrease (Bruton et al. 2009). In this regard, biorefinery approach is suggested for an integrated production of biofuels and value-added co-products for successful, efficient and cost-effective valorization of macroalgae biomass (Bruton et al. 2009; Trivedi et al. 2015; Masarin et al. 2016). A biorefinery perspective also implies the transformation of the feedstock in a sustainable and environmentally friendly way (Jung et al. 2013). Therefore, integrated processing has strongly emerged as a topic of interest in the development of the marine macroalgae-based industries aiming to find feasible and optimized combinations of sequential processes. A report on developing a Norwegian bioeconomy based on cultivation and processing of seaweeds, points out the importance of identifying key product combinations that can ensure the implementation of an economically feasible biorefinery (Skjermo et al. 2014).

Although many research endeavours have been fulfilled for the study of algae, and increasingly more in case of marine macroalgae, there are still many gaps to fill in order to develop successfully the applications of this valuable biomass and fulfil the sustainability criteria. This is valid even more in the European countries which have less experience in this area compared to Asian ones and need to develop and adapt available technology and know-how to their own environment. Fortunately, the number of studies concerning the integrated processing of marine macroalgae has been growing exponentially (Balboa et al. 2015; Yuan and Macquarrie 2015a; Masarin et al. 2016; Sunwoo et al. 2016).

Since there is already a number of reviews and studies regarding the methods for biofuels obtaining from marine macroalgae (Milledge et al. 2014; Bharathiraja et al. 2015; Ghadiryanfar et al. 2016; Lee and Lee 2016; Sudhakar et al. 2018), the current review deals with the latest results in the development of marine macroalgae biorefinery with a focus on the generation of value-added bioproducts. The innovations in the processing techniques and the advances regarding an integrated approach are also highlighted.

Wild and cultivated marine macroalgae resources for biorefinery

Marine macroalgae represent a very diverse group of large multicellular organisms with 1549 species identified only in Europe (Mineur et al. 2015). Marine macroalgae are macroscopic organisms classified into three main groups: red (*Rhodophyta*), brown (*Phaeophyta*) and green (*Chlorophyta*) (Santos et al. 2018). All macroalgae have in common a cellulosic cell wall and the presence of *chlorophyll a* in their structure. Each class of seaweeds has also characteristic types of pigments that give the different colours and the specific group name, as well as unique molecules that cannot be found in the chemical structure of terrestrial plants. Marine macroalgae have the capacity to store a large amount of carbon through their photosynthesis processes (Popa et al. 1974).

The current seaweed industry is based on the harvesting of either wild or cultivated resources and it is much more developed in the Asian countries, where most of the produced algae are obtained through aquaculture, than in Europe where marine macroalgae are mostly harvested from natural stocks or imported (Bak et al. 2018). Out of 10,000 species of marine macroalgae that exist around the world, 101 species are destined for hydrocolloids production (Barbosa et al. 2019). All three types of marine macroalgae (red, green and brown) are harvested in Europe (Mineur et al. 2015). Norway, Ireland and France are the main countries where seaweeds are collected for commercial purposes (Vieira et al. 2018), while Portugal, Spain and UK have developed a smaller industry. *Laminaria* species are especially harvested in these countries. In France, harvests of *Laminaria* are around 60,000 tonnes (wet weight) per year (Kostas et al. 2017), while in Ireland there is also some harvesting activity with *Ascophyllum* as the most collected genus (29,000 wet tonnes in 2006) (Bruton et al. 2009). The concern for identifying more macroalgae species that can be successfully cultivated, harvested and processed generating a high production rate, as well as increasing the yields obtained from seaweeds with already established commercial value, represents important objectives for researchers and industries in the field.

Apart from the cultivated stocks, some studies have taken into consideration the so-called drift seaweed resources that are annually washed ashore on the European coasts like *Laminaria hyperborea* or the "green tides" generated by eutrophication, the algal blooming phenomenon consisting mostly of green macroalgae (*Ulva* spp.). Climate change will further increase the algal blooms due to ocean warming and acidification. In terms of biochemical composition, a study on the effects of climate change on *Ulva rigida* concluded that the protein and lipids content will increase, while carbohydrate levels will decrease (Gao et al. 2017). This is a very important aspect to consider for the development of marine macroalgae biorefinery based on algal blooms as feedstock. From an economic point of view, these resources are not so reliable for a sustainable business model, unless they are processed in local units, for the development of the local economy. Also, from an environmental point of view, algal feedstocks generated by eutrophication are not desirable for the health of the marine waters on long term. Their development indicates

an imbalance in the marine ecosystem that should be prevented, rather than fixed.

Although available natural resources of marine macroalgae are abundant, the necessary supplies for their use in biorefineries are very high and seaweeds cultivation is therefore required. The cultivation and harvesting of macroalgae are considered the most expensive and energy-consuming steps of the biorefinery process flow (Bruton et al. 2009; Tedesco and Daniels 2018). Reported methods of macroalgae cultivation include near-shore systems, off-shore systems, open ponds or land-based facilities (Langlois et al. 2012). Due to the very high percentage of water present in macroalgae biomass, around 70–90% fresh wt. (Jung et al. 2013), large amounts of harvested seaweeds are required for biorefinery. This implies extensive areas of cultivation and generates concerns regarding their establishment in coastal areas, one of the most important issues in Europe being the biofouling phenomenon (Matsson et al. 2019). A viable option remains the off-shore cultivation of marine macroalgae (Bak et al. 2018).

The need to make aquaculture practices environmentally sustainable has turned the attention onto cultivating macroalgae for feed and bioremediation purposes together with commercialized fish, into the IMTA system (Filote et al. 2015). Traditional aquaculture practices can cause environmental degradation through faces, uneaten food, dead fishes and other pollutants generated in the excretion process, which leads to the generation of high concentrations of nitrogen and phosphorous, causing eutrophication. This approach would ensure the treatment of the nutrient-enriched wastewaters derived from aquaculture by accumulation in the macroalgal biomass, which afterwards could be used for obtaining valuable products. Seaweeds could become in this way the main protein source for fish feed, replacing smaller fish provided as food, which have become threatened because of their overexploitation (FAO 2012; Marinho et al. 2013).

Cultivation of macroalgae in an IMTA system can significantly reduce the costs of biomass generation for biorefinery purposes. Furthermore, in comparison with freshwater microalgae and terrestrial plants, cultivation of marine macroalgae entails using sea water and thus, avoids the consumption of large amounts of fresh water resources. Among the marine macroalgae that have been successfully cultivated and used as biofilters in an IMTA pilot system are also *Mastocarpus stellatus*, a red alga which produces carrageenan (Domingues et al. 2015), *Ulva lactuca* (Ben-Ari et al. 2014) and *Saccharina latissima* cultivated in Danish waters (Marinho et al. 2015a).

An important aspect that should be taken into consideration for biorefinery is the amount in which valuable biomolecules can be found in cultivated macroalgae that can differ from those identified in wild species. In order to successfully produce macroalgal biomass, certain conditions must be taken into consideration: lighting, nutrients, water depth, turbidity and temperature (Aravind et al. 2020). When selecting a specific seaweed for cultivation and valorization in a biorefinery system, its chemical composition and stability should therefore be taken into consideration as it can significantly influence the production yields (Skjermo et al. 2014). The relationship of the cultivated species with other organisms from the marine ecosystems is also very important to have in mind in order to avoid population declines of native species which can cause serious negative outcomes on the environment and consequently on human health (Ali and Khan 2017).

The highest sugar contents of marine macroalgae have been recorded for biomass harvested from late spring to middle summer (Alvarado-Morales et al. 2015). Agar from red algae *Gracillaria verrucosa* had the highest yield for the biomass collected in July, while the lowest was recorded for the algae harvested in May (Kumar et al. 2013). Alginates with higher mannuronic/guluronic acid ratio (M/G) were generated from wild macroalgae collected during spring (Fawzy et al. 2017). The protein content reaches the highest amount in winter–spring and registers the lowest values during summer–autumn (Vieira et al. 2018). Studies indicate that macroalgae cultivated in an IMTA system have a more stable protein chemical composition than the ones that grow in a wild environment (Abreu et al. 2009). Macroalgae cultivated in high nitrogen conditions are not suitable for bioenergy production, unless additional pre-treatment steps are applied to the biomass, which implies increased costs. Therefore, in a biorefinery system, the protein fraction should be separated before generating bioenergy products from IMTA-derived macroalgae biomass. A study regarding the potential of cultivated *Ulva lactuca* for the production of methane indicated that the green algae deprived of nitrogen gave better results than the algae that were provided with high concentrations (Bruhn et al. 2011).

Chemical components of marine macroalgae

Polysaccharides

Polysaccharides represent the largest part of the macroalgae biomass with percentages ranging from 4 to 76% d.w. (dry weight) (Kraan 2013; Kadam et al. 2015a; Noreen et al. 2016). The most common carbohydrates of brown algae are fucoidan, cellulose, alginate and laminarin (or laminaran). Out of these, a high proportion of the d.w. is represented by alginate, an important cell wall constituent, 40%, and laminarin, 35% (Sambusiti et al. 2015).

Alginates have a chemical composition comprised of β-D mannuronic acid (M) and α-L guluronic acid (G)

(Andriamanantoanina and Rinaudo 2010; Abraham et al. 2019) and are generally extracted for commercial purposes from *Ecklonia maxima*, *Laminaria* species, *Macrocystis pyrifera*, *Ascophyllum nodosum* and *Durvillea antarctica*. High quantities of alginate are stored especially in the macroalgal cell wall (Rinaudo 2014). Most of its current use is in the food and biomedical industries (Lee and Mooney 2012). Alginates have a molecular weight between 500 and 1000 kDa (Pérez et al. 2016). The molecular weight and M/G ratio of alginate play an important part in the determination of their chemical and physical properties. Alginates with a higher amount of G blocks than M units have demonstrated higher viscosity and a high antioxidant activity (Fawzy et al. 2017).

Fucoidan amounts range from 25 to 30% d.w. and are polymers of disaccharide units of α-1,3- and α-1,4-linked fucose residues (Rodriguez-Jasso et al. 2011). Its composition includes 34–44% fucose and less than 10% monosaccharides like xylose, uronic acid, mannose and galactose. The sulphated components of fucoidan influence its biological characteristics, a high degree of sulphation of the fucoidan structure determining a higher bioactivity of this compound. Other factors that play a key role in determining the biological activity of fucoidan are monosaccharide composition, polymer chain structure and molecular weight (Vishchuk et al. 2011; Hahn et al. 2012; Atashrazm et al. 2015; Saravana et al. 2018). Based on their chemical composition, there are two types of fucoidan namely galactofucans which present fucosyl, galactosyl and sulphate chemical groups and uronofucans which have a high quantity of fucose and uronic acid and a lower quantity of sulphate (Lorbeer et al. 2015b). These can sometimes be found in the same alga. The brown seaweeds containing fucoidan are traditionally consumed in Asia, especially in Japan, China and Korea (Atashrazm et al. 2015).

Laminarans are β-glucans with low molecular weight, with reported values between 4 and 6 kDa (Menshova et al. 2014; Kadam et al. 2015a). It is a storage polysaccharide with glucose as its main monosaccharide unit (Ghadiryanfar et al. 2016). Unlike alginate, it is a brown macroalgae-derived polysaccharide without gelling and thickening properties (Kadam et al. 2015a). Mannitol is a sugar alcohol which can be found in the composition of most types of plants, including algae (Dai et al. 2017). In brown algae, it can reach 20–30% of d.w. (Xia et al. 2015). Cellulose content ranges from 1 to 8% algal d.w. in brown algae (Deniaud-Bouët et al. 2014). It is a polysaccharide found in both macroalgae and terrestrial plants and it plays an important part in the chemical structure of the cell wall (Popa 1975). In filamentous green algae, it can reach up to 20–30 wt% and even more. In *Cladophora glomerata*, it reached 45 wt% (Mihranyan 2011).

Agar and carrageenan are major polysaccharides characteristic to all red algae species. Agar is an important constituent, commonly extracted for commercial purposes from *Gracillaria* and *Gelidium* algae (McHugh 2003). This compound is composed of α-1,3 and β-1,4 alternating units, with 3,6-anhydro-L-galactopyranose present in its structure (Rhein-Knudsen et al. 2015). A large number of studies have researched the variation of agar characteristics in correlation with environmental conditions, geographical source, extraction procedures used and seaweed species (Romero et al. 2008). Carrageenans represent a family of sulphated galactans which can be classified depending on the amount of sulphated groups (25–35%) and their position into λ-, κ-, ι-, ε- and μ-carrageenans (Campo et al. 2009; Manuhara et al. 2016; Gereniu et al. 2018). Among these, k-carrageenan is used as a thickening agent, whereas j- and i-carrageenans are used for their gelling properties (Campo et al. 2009). Some red algae among which *Kappaphycus*, *Chondrus*, *Hypnea*, *Gigartina* and *Eucheuma* can contain a carrageenan content of 50% d.w. (Youssouf et al. 2017). Generally, carrageenan content ranges between 30 and 75% d.w. (Shi et al. 2017). Porphyrans represent another type of sulphated polysaccharides characteristic to *Porphyra sp.* red algae species and have reported antioxidant activity (Zhang et al. 2010). Red algae also contain other carbohydrates that cannot be found in green or brown algae, namely floridean starch and floridoside (Jung et al. 2013).

One of the main polysaccharides found in green algae is ulvan which is part of the cell wall. This sulphated polysaccharide is composed of smaller fractions such as xylose, glucose, rhamnose, iduronic acid, glucuronic acid and smaller amounts of galactose. Their content ranges between 8 and 29% d.w. and have molecular weights of approximately 189–8200 kD. The polysaccharide has a branched structure comprised of repeating L-rhamnose disaccharide units coupled with either D-guluronic acid residue, L-iduronic acid residue, D-xylose 4-sulphate residue or D-xylose residue (Trivedi et al. 2016; Shi et al. 2017).

Agars, carrageenans and alginates are regularly used in the food industry because of their gelling and thickening properties. The sulphated polysaccharides from *Ulva fasciata* have been characterized as having similar potential (Shao et al. 2014). Furthermore, applications in removal of pollutants have been reported, algae being regarded as part of the non-conventional adsorbents group (Crini et al. 2019). Adsorbents based on agar and alginate have improved removal capacity owing to the functional groups present in these biocompounds. Alginate, which is very efficient due to its many carboxyl functional groups, has been recently demonstrated to reduce the swelling degree ratio of an agar-based aerogel. The synthesized dual-network aerogel thus showed improved properties, with an increase in adsorption

capacity from 71.6 mg/g for the agar aerogel to 171.7 mg/g for the ion cross-linked aerogel (Huang et al. 2019).

Polyhydroxybutyrate (PHB), a natural biodegradable polymer that can be applied in bioplastic production, was found in the composition of green algae *Cladophora rupestris* (Stabili et al. 2014) and red algae *Gracilariopsis longissima* (Stabili et al. 2012). PHB was also identified and isolated from red macroalga *Plocamium cartilagineum*. Owing to properties such as ultraviolet resistance, acid and bases resistance, chloroform and chlorinated hydrocarbons solubility and good oxygen permeability, PHB can be a good and viable alternative to toxic options for applications in pharmaceutics, medicine and packaging industries (Stabili et al. 2012).

Proteins

Macroalgae are also an important source of proteins, having significant quantities of threonine, lysine, tryptophan, methionine, cysteine and histidine, amino acids which can be found also in cereals and vegetables (Holdt and Kraan 2011). Furthermore, they contain a high amount of essential amino acids which can make them a good alternative for the human diet (Kazir et al. 2019). *Porphyra complex*, *Undaria pinnatifida* and *Saccharina latissima* are edible seaweeds that contain reported amino acids in amounts similar to those from beef (Marinho et al. 2015b). Lysine, an amino acid that is found in small concentrations in terrestrial plants, is abundant in marine macroalgae (Kazir et al. 2019). In fact, red and green algae have been demonstrated to have higher quantities of proteins than terrestrial biomass (Polikovsky et al. 2016).

The digestibility of macroalgae proteins in human diet was evaluated through simulated gastro-intestinal processes using *Ulva* sp. and *Gracilaria* sp. and positive results were generated, yielding at least 89% potential proteolysis (Kazir et al. 2019). On the other hand, depending on the separation method some food allergens such as troponin C, superoxide dismutase (SOD), aldolase A and thioredoxin h were detected in protein extracts from *Ulva* sp. (Polikovsky et al. 2019). More research is required while the amino acid content of marine macroalgae has potential to become a suitable protein source for human consumption and nutraceuticals production.

Macroalgal proteins have been especially isolated from red algae, where the amounts can reach up to 47% of d.w. (Dumay et al. 2013; Kadam et al. 2017; Vieira et al. 2018). Research on the characterization of proteins from brown macroalgae *Laminaria digitata*, *Saccharina latissima* and *A. esculenta* has been recommended in the literature (Masarin et al. 2016). The high protein content in macroalgae, as well as their functions including anticoagulant, antioxidant, antihypertensive, immune-modulatory properties and so forth (Polikovsky et al. 2016), are all arguments in favour of their separation and valorization in macroalgae biorefinery.

Lipids

Lipids represent a small part of macroalgae, typically between 1 and 5% of the d.w. (van Ginneken et al. 2011; Schmid et al. 2018), but their fatty acids are considered superior to those derived from terrestrial plants (Kumari et al. 2010). Some brown algae can have even higher amounts of lipidic compounds, 10–20 wt.% per d.w. (Miyashita et al. 2013). Important amounts of C18 and C20 fatty acids were identified in brown algae, while green and red algae showed significant amounts of either C18 fatty acids or C20 (Kumari et al. 2010). Large amounts of arachidonic acid and eicosapentaenoic acid (EPA) were determined in brown and red seaweeds, respectively, and docosahexaenoic acid (DHA) in green macroalgae. Generally, the amounts of DHA in the macroalgae biomass can reach 50% (Saravana et al. 2019).

Interest in lipophilic compounds has increased especially due to their antioxidant properties and owing to their dietary and health benefits. Macroalgae have generally demonstrated an optimum ω-6:ω-3 ratio of fatty acids, which according to the World Health Organisation should be lower than 10 (van Ginneken et al. 2011). The ratio value in marine macroalgae has usually been recorded around 1 (Schmid et al. 2018) and this is due to the high content of ω-3 fatty acids present in the biomass. Seaweeds are the main source of polyunsaturated fatty acids (PUFAs) for fish and the total content is comparable to that of terrestrial plants (van Ginneken et al. 2011). This makes macroalgae lipids suitable and popular for use in nutraceuticals, pharmaceuticals, functional foods and cosmetics markets. Of course, in order to be applied in the health and food sectors, more research is required in order to evaluate the stability of these compounds in different conditions (Schmid et al. 2016). Polyunsaturated fatty acids (PUFAs), for example, have in their chemical structure double bonds that can react with oxygen and this can affect the ω-3 quality. The diversity of lipidic constituents in seaweeds has been under intense development over the last years. Da Costa et al. (2015) reported, for the first time, the occurrence of sulphoquinovosylmonoacylglycerols, phosphatidylinositols, and species of monoacyl betaine lipids in green algae.

Other than their antioxidant and nutritional characteristics, macroalgae lipids also have demonstrated antimicrobial activity. A research study performed by Stabili et al. (2014) assayed the antimicrobial potential of lipidic extract from Mediterranean *Cladophora rupestris*. The detected antibacterial activity was mainly attributed to α-linoleic acid.

Pigments

Marine macroalgae contain various pigments including carotenoids (α- and β-carotene), xanthophylls (lutein, zeaxanthin, neoxanthin, antheraxanthin, etc.) and chlorophyll (de Quirós et al. 2010; Ragonese et al. 2014; Aryee et al. 2018), with important bioactive properties.

Chlorophylls are the most important type of pigments in the macroalgae chemical composition. They play a key role in the photosynthetic activity of all types of macroalgae and have antioxidant properties (Ragonese et al. 2014). Chlorophyll-a is common to all three major categories of macroalgae.

Fucoxanthin is a xanthophyll found in brown algae and its functional role has been intensely researched so far (Aryee et al. 2018). Its concentrations have shown to vary in different anatomical parts of the macroalgae, with a higher content detected in the blade, approximately 20–50%, in comparison with the sporophyll (Fung et al. 2013). The biological activities of fucoxanthin include anticarcinogenic (Nakazawa et al. 2009; Kim et al. 2010), anti-inflammatory (Heo et al. 2010), anti-photoageing (Heo et al. 2009), antihypertensive, antidiabetic (Nishikawa et al. 2012; Zaharudin et al. 2019), antioxidant (Fung et al. 2013) and antiobesity effects (Hosokawa et al. 2010; Woo et al. 2010; Hu et al. 2012; Gammone and D'Orazio 2015).

Phycobilins represent a group of pigments such as phycoerythrin, phycocyanin and allophycocyanin which are found in red algae and are commonly used as fluorescent reagents or as colourants in the food, dyes and cosmetic industries (Ragonese et al. 2014; Mittal et al. 2017). Phycobiliproteins are heat-sensitive pigment–protein complexes (Le Guillard et al. 2016; Mittal et al. 2017) with stable properties around 4–40 °C and pH values of 6–7 (Saluri et al. 2019). Furthermore, these macroalgae biomolecules are known to have antioxidant, antidiabetic, anti-inflammatory and other medical properties (Ragonese et al. 2014; Mittal et al. 2017).

Polyphenols

Recently, research regarding algae-derived polyphenols has especially increased due to the request to replace harmful and synthetic compounds, like butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), used in the food production industry. Furthermore, brown macroalgae polyphenolic extracts have demonstrated a bacterial growth inhibitory capacity similar to that of additives such as sodium benzoate and sodium nitrite (Cox et al. 2010). Polyphenols removal is necessary for bioethanol and biogas production, since it has an inhibitory effect on the fermentation processes (Bruton et al. 2009). In the alginate industry, they are also usually extracted using formaldehyde before alginate isolation but, as this is a carcinogenic compound, other more green alternatives are necessary. Considering these aspects, the separation of polyphenols from macroalgae fulfils an important role in an integrated biorefinery processing. Their isolation represents a key step in the optimization of the overall chemical conversion of the biomass and the production of purified extracts.

In order to obtain the maximum yield of polyphenolic compounds from macroalgae, the conditions of the pretreatment processes must be carefully selected since they can reduce the potential outcome. Oven-drying is one such process that contributes to the reduction of polyphenolic content and its antioxidant characteristics (Balboa et al. 2015; Agregán et al. 2017). On the other hand, the extraction yield seems to be higher in case of oven-dried biomass, in comparison with freeze-dried and microwave-dried.

Polyphenolic compounds derived from macroalgae have demonstrated antioxidant (Saravana et al. 2017; Dinh et al. 2018), antiageing (Ferreres et al. 2012), anti-inflammatory, antidiabetic (Lee and Jeon 2013), antiallergic (Ferreres et al. 2012), antimicrobial (Eom et al. 2012) and anticarcinogenic (Ganesan et al. 2019) properties. The use of ethanol and acetone for extraction enhances the antimicrobial activity of polyphenols separated from red and green macroalgae, whereas the one of the methanolic extract is much lower (Cox et al. 2010). Brown algae have usually registered higher amounts of phenolic compounds than the other two macroalgae categories. They have a polyphenolic content of up to 14% d.w. (Agregán et al. 2018).

According to most researches, phlorotannins represent the largest group of polyphenols and antioxidants in brown seaweeds (de Quirós et al. 2010; Fung et al. 2013). Many studies have identified phlorotannins as the only polyphenolic group present in brown algae (Budhiyanti et al. 2012; Ferreres et al. 2012). They are phloroglucinol-based polyphenols superior to the ones contained by terrestrial plants, presenting eight interconnected rings, in comparison with three or four rings found in the plant biomass (Wang et al. 2009). Furthermore, phlorotannins have also been identified recently in green algae *Ulva rigida* (Mezghani et al. 2016). Their molecular weight varies between 126 and 650 kDa (Sathya et al. 2017).

Generally, the investigation has demonstrated that among brown algae, fucoid algae species have a higher concentration of phlorotannins (Cox et al. 2010), of high molecular weight and with the highest lipid peroxidation inhibitory activity (Ferreres et al. 2012) and antioxidant activity. Phlorotannins have attracted the attention of many researchers trying to identify their structure and potential applications in the industry. However, there are some difficulties concerning this aspect due to the fact that commercial standards are not available for their determination (Ferreres et al. 2012). Still, the bioactivity of phlorotannins and their health beneficial role (Wijesekara et al. 2011), their antimicrobial (Eom et al.

2012) and antidiabetic effect (Lee and Jeon 2013), potential for cosmeceuticals application (Sanjeewa et al. 2016) have been reviewed. Although their bioactivity has been extensively studied, more work is required to achieve a thorough characterization and make these biocompounds marketable (Barbosa et al. 2019).

Other phenolic compounds that have been identified in marine macroalgae are flavonoids, bromophenols and phenolic acids (de Quirós et al. 2010).

Advanced processing technologies

Separation of biomolecules in primary biorefinery

Non-conventional solvents

According to the six principles of green extraction (Table 1), the selection of a sustainable solvent should be made based on workers and process safety, effect on final product safety and the environmental impact. The sustainable options considered for biomass processing, including macroalgae, are ionic liquids, deep eutectic solvents, supercritical fluids, agro-solvents and water. These provide an alternative to a series of problems raised by conventional solvents due to their high volatility and flammability (Bubalo et al. 2018).

Ionic liquids (ILs) have been suggested to replace traditional harmful solvents. They are stable in high thermal conditions, having a melting temperature below 100 °C (Yi et al. 2015; Lee et al. 2020). Although having a lower volatility, the water solubility of ILs represents a threat to the aqueous environment (Pham et al. 2010; Thamke et al. 2019). Furthermore, the degradability of ionic liquids is dependant on their structure. In some cases, the issue can be fixed using microbial organisms. However, for hydrophobic ionic liquids, this option is not viable (Castillo et al. 2016; Thamke et al. 2019).

In comparison with ILs, deep eutectic solvents (DESs) have lower costs and an easier synthesis process, being produced with high purity, are less harmful for the environment and present less toxicity (Benvenutti et al. 2019; Kostić and Divac 2019). DESs are characterized by a lower melting point than the initial constituents (Florindo et al. 2017; Krishnan et al. 2020). There are two types of deep eutectic solvents: ionic and non-ionic (Huang et al. 2019) and the synthesis of various DESs has already been reviewed (Khandelwal et al. 2016).

Although DESs have emerged as greener alternatives than ILs, there are still aspects that require improvement in order to increase their sustainability. This is of utmost importance when it comes to the solvents used in the separation of natural bioactive molecules destined for food, cosmetics or pharmaceuticals. Fortunately, the disadvantages posed by ILs and DESs in terms of toxicity and impact are combated by natural deep eutectic solvents (NADESs). These green solvents are obtained by mixing two or more natural constituents (plant primary metabolites) at optimal molar ratio, generating a solvent with a lower melting point. NADESs are not only safer due to their natural origin, but they have a higher solubility power for biocompounds (Aroso et al. 2017). Since their definition in 2011, they underwent intense research with 150 NADES combinations already developed (Vanda et al. 2018).

Ionic liquids (ILs) and deep eutectic solvents (DESs) have already been applied in several studies for the extraction of biomolecules from marine macroalgae. From red macroalgae biomass, agarose was separated using imidazolium-based ionic liquids (Trivedi and Kumar 2014). NADESs

Table 1 Principles of green extraction and how they are fulfilled by marine macroalgae processing through non-conventional technologies (Chemat et al. 2012)

Green extraction principles	How non-conventional extraction of macroalgal compounds fulfils the green extraction principles
Innovation by selection of varieties and use of renewable plant resources	Algae have fast growth and are renewable marine resources
Use of alternative solvents and principally water or agro-solvents	This type of solvents have already been successfully applied for the separation of algae biomolecules
Reduce energy consumption by energy recovery and using innovative technologies	Research on green or innovative extraction methods for macroalgal compounds separation has shown a decrease in time and/or temperature and a reduction in energy consumption accordingly
Production of co-products instead of waste to include the bio- and agro-refining industry	Biorefinery of marine macroalgae enables the co-production of biofuels and added-value bioproducts, with minimum waste
Reduce unit operations and favour safe, robust and controlled processes	Biorefinery of seaweeds facilitates the integration under one dedicated unit for derived biofuels and biomolecules
Aim for a non-denaturated and biodegradable extract without contaminants	Advances in the separation techniques and characterization methods enable a good control of the degree of macroalgal extract contamination. Higher quality of generated bioproducts is now possible

have been applied for the isolation of biocompounds from various types of plant materials, including macroalgae. So far, ten types of NADES were applied for the extraction of phlorotannins from brown algae *Fucus vesiculosus* and *Ascophyllum nodosum* (Obluchinskaya et al. 2019).

Novel extraction methods

The development of green chemistry in the last years has determined a paradigm shift, and thus, environmentally safe procedures have been in great demand (Armenta et al. 2015). The integrated valorization of marine macroalgae biomass can be improved by developing and optimizing the extraction methods and process conditions. The growing concern over chemicals has supported the development of more natural products (that include bioactive compounds of high-quality), and thus, the development of extraction methods that generate maximum yield and minimum environmental impacts has accelerated (Goto et al. 2015). Although the potential applications of macroalgae biomolecules have been extensively evaluated, research studies performed so far, at pilot or industrial scale, have used mainly conventional extraction methods. However, these separation techniques are becoming more and more ignored, since they are time-consuming and entail high costs. Moreover, the traditional methods are often not able to extract the maximum potential yield of the targeted molecules. For example, algal residue obtained after agar extraction, has demonstrated to still contain approximately 48% carbohydrates (Cesário et al. 2018). A synthesis of the improvements as well as the drawbacks of the innovative extraction technologies in comparison with the traditional separation methods is included in Table 2.

The use of the so-called green or innovative extraction methods that are characterized as having an important reduction of the environmental footprint (Pollet et al. 2014) promises a change of the industrial processes into more sustainable ones that can fulfil better the circular economy principles and develop the bioeconomy. Innovative extraction methods include supercritical water extraction (SWE), supercritical fluid extraction (SFE), microwave-assisted extraction (MAE), ultrasound-assisted extraction (UAE), enzyme-assisted extraction (EAE), pulsed electric field-assisted extraction (PEF) and pressurized liquid extraction (PLE). The application of these methods could also significantly reduce the costs and improve the development of the macroalgae-based industry. Table 3 summarizes the innovative extraction methods that can be applied for macroalgae biomolecules separation.

The growing interest in the development and application of innovative extraction methods for macroalgae processing has also been proven by the reviews focused on valuable compounds from marine biomass (Grosso et al. 2015)

Table 2 Advantages and disadvantages of non-conventional extraction methods over the conventional ones (Talmaciu et al. 2015; Herrero and Ibánez 2018; Okolie et al. 2019)

Advantages	Disadvantages
Increased cell membrane permeability	High overall costs of use
Higher selectivity for extracted compounds	High energy consumption and associated costs
Moderate or shorter extraction times	Difficulty in scaling
Uses so-called GRAS solvents which are more sustainable	High costs of enzymes or some GRAS solvents
Increased extraction yields	
Reduced use of toxic solvents	
Faster energy transfer	
Reduced waste	
Higher purity of extracts	

Table 3 Innovative extraction methods for separation of macroalgae biomolecules

Novel extraction methods	Supercritical water extraction (SWE)	Supercritical fluid extraction (SFE)	Microwave-assisted extraction (MAE)	Ultrasound-assisted extraction (UAE)	Enzyme-assisted extraction (EAE)	Pulsed electric field-assisted extraction (PEF)	Pressurized liquid extraction (PLE)
Biomolecules separated from macroalgae	Lipids	Lipids	Lipids	Lipids	Lipids	Lipids	Lipids
	Carotenoids	Carotenoids	Carotenoids	Carotenoids	Carotenoids	Carotenoids	Carotenoids
	Polyphenolic compounds	Polyphenolic compounds	Polyphenolic compounds	Polyphenolic compounds	Polyphenolic compounds	Polyphenolic compounds	Polyphenolic compounds
			Polysaccharides		Polysaccharides	Polysaccharides	Polysaccharides
			Proteins		Proteins	Proteins	Proteins

in general, as well as micro- and macroalgae (Kadam et al. 2013; Michalak and Chojnacka 2014). In some cases, different innovative technologies are combined in order to improve the results. Thus, an ultrasound-assisted enzymatic hydrolysis of red macroalgae, *Grateloupia turuturu*, generated 20% higher yields (Le Guillard et al. 2016). Also, ultrasounds were used as pre-treatment before a supercritical fluid extraction performed for isoflavones extraction (Klejdus et al. 2010). Moreover, a microwave-assisted aqueous two-phase extraction (Cao et al. 2018) or a supercritical water extraction (SWE) and pressurized liquid extraction (PLE) (Gereniu et al. 2018) have been reported recently.

Extraction of macroalgae biomolecules using innovative techniques

Polysaccharides extraction: Most of the conducted studies concerning the use of innovative extraction techniques to isolate polysaccharides from macroalgae have focused on the extraction of hydrocolloids such as agar, carrageenan and alginate, aiming to reduce the time, solvent quantity and energy consumption, thus, leading to the optimization of the general processing.

The use of microwave-assisted extraction (MAE) entails the use of microwaves ranging from 0.3 to 300 GHz (Gude and Martinez-Guerra 2018; Tang et al. 2020) and has demonstrated several benefits when applied for the isolation of seaweeds-derived compounds in comparison with the results obtained with traditional methods, namely: reduced solvent quantity used in the process, improved extraction yields and higher quality of the extracted compounds (Charoensiddhi et al. 2015). Moreover, in comparison with conventional heating processes, the use of microwave conditions avoids heat losses at high temperatures (Uy et al. 2005). This is even more important for the extraction of macroalgae compounds such as carrageenan that have low energy transfer capacity. Agar from IMTA cultivated *Gracilaria vermiculophylla* extracted using hot water and microwaves demonstrated higher yields than those generated by the conventional extraction method, as well as improved gel strength (Sousa et al. 2010).

The advantages of applying a subcritical water extraction (SWE) together with ionic liquids for the isolation of k-carrageenan from *Kappaphycus alvarezii* were recently tested (Gereniu et al. 2018). Studies published so far demonstrate that ionic liquids enhance the solubility of the targeted extracted compounds. The optimized result is even higher than the values registered for the same algae specie by separation of carrageenan through ultrasound-assisted extraction (UAE) (Youssouf et al. 2017) or even other deep eutectic solvent, 10% hydrated choline chloride-glycerol and MAE. However, the 50–55% yield obtained by UAE (Youssouf et al. 2017) for the carrageenan extract was generated in approximately half the time required for SWE with and without ionic liquids.

The extraction of alginate from acid pre-treated *Sacorrhiza polyschides* was studied using MAE and HCl as co-solvent (Silva et al. 2015). The use of microwaves decreased ten times the extraction time in comparison with the applied conventional extraction. In another study (Youssouf et al. 2017), alginates were extracted from brown seaweeds using ultrasound, and the yield of extracted polysaccharide doubled in 30 min. Chemical characterization of alginates revealed that the use of ultrasounds does not affect the M/G ratio up to a 30 min extraction time, fact which was pointed out by NMR analysis (Youssouf et al. 2017). The highest alginate extraction yield obtained by the same study was 54%, whereas the most influencing parameters were ultrasound and pH.

Other types of macroalgal polysaccharides with potential market value, that have been separated using the green extraction techniques, are fucoidan and laminarin. Commercialized seaweeds *Ascophyllum nodosum* and *Laminaria hyperborea* were used as feedstocks to isolate laminarin through UAE and traditional solid–liquid extraction. The highest yields, 5.82% for *A. nodosum* and 6.24% for *L. hyperborea*, were obtained using HCl as solvent and ultrasounds (Kadam et al. 2015b).

The extraction of fucoidan from brown seaweeds using MAE has been studied for various conditions, such as temperature, extraction time, alga/liquid ratio and pressure (Rodriguez-Jasso et al. 2011; Yuan and Macquarrie 2015b). The use of microwaves for the isolation of fucoidan (Lorbeer et al. 2015b) determined a faster extraction rate up to a 6 min time limit in comparison with the conventional method. Also, it was noticed that the galactose content of the generated fucoidan decreased with extraction time, whereas the glucuronic acid amounts increased. Another study applied an UAE for the isolation of fucoidan fractions and compared the results with the ones generated by applying a conventional solid–liquid extraction (SLE). Although the outcome in terms of extraction yield was similar for both methods (4.8–12%), the use of ultrasounds reduced the necessary separation time by more than 20 times. The applied temperature was also considerably lower for the innovative process which also leads to a reduction in energy consumption. In terms of bioactivity, the same study reports a similar anticancer activity for both the conventional and unconventional generated fucoidan fractions (Hmelkov et al. 2018). The separation of fucoidan and alginate from *Saccharina japonica* using subcritical water hydrolysis (SWH) combined with the addition of DES to the water almost doubled the generated yields in comparison with the use of water/HCl as solvent mixture (Saravana et al. 2018).

Macroalgae have a strong cell wall composed of carbohydrates and proteins. In some brown algae species, alginate

can constitute even more than 70% of the cell wall components. Therefore, different carbohydrases or proteinases can be applied to break down the algae cell wall and release certain bioactive compounds or to increase the generated yield. For the isolation of polysaccharides, specific enzymes produced from the marine biomass have been applied. These include agarases, carrageenases or porphyranases for red algae, ulvan-lyases for green algae and glucuronan-lyases and laminarinases for brown algae (Hardouin et al. 2016). The method can be used to efficiently isolate polysaccharides from macroalgae together with water or organic solvents, since the conventional methods do not have the same efficiency when used individually for obtaining the bioactive compounds (Wijesinghe and Jeon 2012). Biomolecules obtained from seaweeds using enzyme-assisted extraction (EAE) have a higher yield, as well as a higher radical scavenging activity than the ones generated using only organic solvents (Heo et al. 2003).

The influence of the enzymatic treatment on the chemical composition of freeze-dried red algae *Chondrus crispus* and green algae *Codium fragile* using carbohydrases and proteases was studied and results indicated an increase in all the analysed components (ash, uronic acids, neutral sugars, proteins, polysaccharides) in the enzymatic hydrolysates in comparison with the water extracts (Kulshreshtha et al. 2015). Significant improvements were noticed, for example, in the polysaccharides amount (from 40 to 75% for *Chondrus crispus*). Enzyme-assisted extraction (EAE) using cellulase, laminarase and alginate lyase is recommended in the literature for the isolation of fucoidan (Hahn et al. 2012) due to the fact that it improves the bioactivity of this compound. Ultrasounds and the use of enzymes were combined for the isolation of sulphated polysaccharides from *Gracillaria birdiae* (Fidelis et al. 2014). The best yield was obtained using both sonication and proteolysis and NaOH as solvent. The use of a mix of carbohydrases, and a cellulase to isolate *Ulva armoricana* extracts generated a higher content of neutral sugars and a polysaccharide fraction with higher molecular weight than the ones obtained by conventional extraction methods or the use of endo-proteases (Hardouin et al. 2016). A similar yield was obtained with both the carbohydrases and the cellulase.

The application of microwaves for the extraction of cellulose nanocrystal (CNC) from red algae was also studied. The extraction time was reduced by 30 min and the additional dewaxing step was removed, demonstrating to be a greener process than the conventional one (Singh et al. 2017). The application of pressurized liquid extraction (PLE) was also demonstrated to be an efficient method for increasing the yield of polysaccharides from macroalgae (Saravana et al. 2016). Studies regarding the isolation of ulvan using the innovative extraction methods are scarce. The optimization of ultrasound-assisted extraction (UAE) of ulvan from *Ulva intestinalis* was performed and demonstrated a maximum yield of 8.3% (Rahimi et al. 2016). Table 4 resumes the applications of "green" technologies reported in the literature for the extraction of different macroalgae polysaccharides.

Proteins extraction: The literature regarding the use of innovative extraction methods for macroalgal proteins is scarce. However, enzymatic-assisted extraction, ultrasound-assisted extraction and pulsed electric field extraction were used and some studies have been reported. Table 5 presents green extraction techniques used for macroalgae proteins separation.

Enzymatic-assisted extraction has demonstrated to be advantageous when it is applied to wet algae, thus reducing costs, time and water consumption in the protein separation process (Dumay et al. 2013). Usually, polysaccharides mixture or only cellulase was used as single treatment or as pre-treatment associated with ultrasound-assisted extraction. The use of polysaccharidases showed a clear improvement of the extraction yields (Kulshreshtha et al. 2015).

Ultrasounds were tested for the enhancement of acid, alkali and combined acid–alkali extractions of proteins from brown algae (Kadam et al. 2017). A two-step extraction process, with both acid and alkaline solvents being used sequentially, led to the highest yield. The result generated by the single-step alkaline extraction was lower, but very close to the first one, 57%. Ultrasounds were also applied to enhance the efficiency of maceration and homogenization processes for the separation of phycobiliproteins (Mittal et al. 2017).

Other studies used pulsed electric field extractions for the separation of protein compounds from green (Polikovsky et al. 2019) and red macroalgae (Martínez et al. 2019). PEF extraction applies pulses of electric fields ranging from 100–300 V/cm to 20–80 kV/cm that disrupt the cell wall temporarily or permanently through electroporation, releasing valuable compounds from the processed biomass (Barba et al. 2015). It is a non-thermal processing technology that can be used at industrial scale in various fields, including biotechnology, medicine, food and pharmaceuticals (Robin et al. 2018). The electric pulses have a duration ranging between nanoseconds and milliseconds and determine lower energy consumption (Barbosa-Pereira et al. 2018). The estimated energy consumption depends on the type of biomass, but it is estimated to be somewhere between 1 and 15 kJ/kg (Fauster et al. 2018). Reducing emissions generated by energy consumption is very important in the climate change mitigation process since these are a major contributing factor to the greenhouse gas levels (Fawzy et al. 2020). So far there are only a few published studies that applied the pulsed electric field technology for the treatment of marine macroalgae. The application of PEF extraction for the isolation of proteins from *Ulva* made possible the separation of proteins that

Table 4 Applications of green extraction technologies for the isolation of macroalgae polysaccharides. MAE: microwave-assisted extraction, UAE: ultrasound-assisted extraction, SWE: subcritical water extraction, DES: deep eutectic solvents, PLE: pressurized liquid extraction, IL: ionic liquids, EAE: enzyme-assisted extraction, MAATPE: microwave-assisted aqueous two-phase extraction

Macroalgae	Method	Operating conditions	Ref
Alginate			
S. polyschides [a]	MAE	HCl 1 M, 100 °C, 20 min, magnetron power 100%	Silva et al. (2015)
S. binderi	UAE	S/L 10–30 g/l, pH 8–12 (NaOH), 20–40 min Optimized conditions: pH 12, 90 ºC, S/L 10 g/l, 150 W	Youssouf et al. (2017)
S. japonica	SWE + DES	150 ºC, 19.85 bar, 70% water content, S/L 27.17 g/l	Saravana et al. (2018)
Reducing sugars			
L. japonica	SWE	200–280 °C, 1.3–6.0 MPa, 28–42 min, 1% acetic acid[b]	Park et al. (2012)
Fucoidan			
A. nodosum	MAE	HCl 0.1 M, 90–150 °C, 5–30 min	Yuan and Macquarrie (2015b)
F. vesiculosus	MAE	Distilled water, 30–120 psi, 1–31 min, S/L 40–200 g/l Optimized conditions: 120 psi, 1 min, 40 g/l	Rodriguez-Jasso et al. (2011)
E. radiata	MAE	HCl solution, pH 2, 60 ºC, 0–3 h, S/L 33 g/l	Lorbeer et al. (2015b)
S. japonica	PLE	Different solvents[c], S/L 60 g/l, 80–200 ºC, 5–100 bar, 5 min	Rahimi et al. (2016)
S. muticum	UAE	Water, 150 W, 40 kHz, 25 °C, 5–30 min, S/L 50 g/l	Flórez-Fernández et al. (2017)
F. evanescens	UAE[d]	Water, 15 min	Hmelkov et al. (2018)
S. japonica	SWE + DES	150 ºC, 19.85 bar, 70% water content[e], S/L 27.17 g/l	Saravana et al. (2018)
Laminarin			
A. nodosum, *L. hyperborea*	UAE	HCl 0.1 M and Water, 60% ultrasonic power amplitude, 15 min	Kadam et al. (2015b)
Carrageenan			
E. denticulatum, *K. alvarezii*	MAE[f]	Acetone, ethanol, methanol, 2-propanol and water, 800 W, 2450 MHz, atmospheric pressure, 30 min	Uy et al. (2005)
K. alvarezii, *E. denticulatum*	UAE	Water, 10 g/l, pH 7, 150 W, 90 ºC, 15–30 min	Youssouf et al. (2017)
K. alvarezii	SWE + IL[g]	Different ILs (0.1–2.0%)[h], 60–180 ºC; 5 MPa; 30–40 min	Gereniu et al. (2018)
Agar			
G. vermiculophylla	MAE	Water, 85 ºC, 2 h, magnetron power 100%	Sousa et al. (2010)
Polysaccharides/Carbohydrates			
G. birdiae [i]	UAE + EAE	Water and 0.1 M NaOH; 30 min, 60 ºC, 60 W + 12 h, 60 ºC, pH 8.0	Fidelis et al. (2014)
L. japonica	UAE	Water, 15–75 min, 450–1050 W, 40–90 ℃, S/L 14–50 g/l Optimized conditions: 54 min, 1050 W, 80 ℃, S/L 20 g/l	Wan et al. (2015)
S. pallidum	MAATPE[j]	ATPS[k], S/L 16.7 g/l, 5–25 min, 50–100 ºC, 200–1000 W	Cao et al. (2018)
U. armoricana [l]	EAE	3 h, 50 ºC; Denaturation: 90 ºC, 15 min	Hardouin et al. (2016)
Ulvan			
U. intestinalis	UAE[m]	30–100 ºC, S/L 12.5–100 g/l, 10–70 min, pH 4–9 Optimized conditions: 66 °C, 40 min, 20 g/l, pH 7.0	Saravana et al. (2016)
Cellulose nanocrystal			
G. aceroso	MAE	2.5 M NaOH, 30 min, 360 W	Singh et al. (2017)

[a]Acid pre-treatment; [b] catalyst; [c] distilled water, 0.1% sodium hydroxide, 0.1% formic acid, 70% ethanol, 50% ethanol and 25% ethanol; [d] Defatting: 70% ethanol, 23 ºC, 10 days; [e] SWE combined with DES extraction (DES mixed with water at various concentration levels); [f] extracted compounds: l-carrageenan and k-carrageenan; [g] extracted compound: k-carrageenan; [h] BMIMAc, [BMIM][PO4], BMIM-BF4, EMIM Br, EMIMBF4, BMIMCl and ChCl; [i] extracted compounds: sulphated polysaccharides; [j] microwave-assisted aqueous two-phase extraction; [k] Aqueous two-phase system: ethanol (19–27% w/w)/ammonium sulphate (20–24% w/w); [l] extracted compounds: total carbohydrates; [m] Pre-treatment: 80% ethanol

otherwise could not be extracted through the control method using water as solvent (Polikovsky et al. 2016).

Lipophilic compounds isolation: Although marine macroalgae present a very small lipids amount, there are already a few studies that applied innovative extraction methods for the isolation of this class of compounds. Table 6 presents the applications of some green techniques for the extraction of lipidic compounds from macroalgae biomass.

Table 5 Applications of green extraction techniques for macroalgae proteins separation. UAE: ultrasound-assisted extraction, M/H: maceration/homogenization, EAE: Enzyme-assisted extraction, PEF: pulsed electric field-assisted extraction

Macroalgae	Method	Operating conditions	Ref
Phycobiliproteins			
G. pusillum	UAE + M/H [a, b]	0.1 M phosphate buffer, pH 6.8, ultrasonication amplitude 60–120 µm, 1–10 min, 30–45 °C, S/L100 g/l Optimized conditions: 30 °C, 120 µm, 10 min	Mittal et al. (2017)
G. turuturu	EAE, UAE, UAE [c]	Enzymatic cocktail [d], pH 5.5, 40 °C, 6 h, 350–400 W [e]	Le Guillard et al. (2016)
P. palmata	EAE	Acetate buffer 50 mM, pH 5, S/L 100 g/l, 10–40 °C, 30–360 min, 16.5 g/kg d.w. of xylanase and E/S [f] 5–25 g/kg d.w Optimized conditions: 24 °C, 320 min, E/S 17.8 g/kg d.w	Dumay et al. (2013)
F. lumbricalis	EAE [g]	Cellulases, xylanases and β-galactosidase; citrate buffer (50 mM in 0.025% NaN_3), pH 5–7, S/L 5 g/l	Saluri et al. (2019)
F. lumbricalis	UAE [g]	Citrate buffer (50 mM in 0.025% NaN_3), pH 6, 4 °C, 3.5 h, 35 rpm; ultrasonic bath, 37 kHz, 30 min in darkness	Saluri et al. (2019)
Proteins			
U. rigida, *U. rotundata*	EAE	Cellulases and polysaccharidases; Phosphate buffer 0.1 M, pH 6, 30 °C, 2 h	Fleurence et al. (1995)
Ulva sp.	PEF	2.964 kV cm^{-1}, pulse duration 5.70 ± 0.30 µs, 0.5 Hz, 35.5 °C (maximum observed), 75 pulses	Polikovsky et al. (2016)
A. nodosum	UAE	0.1 M HCl, 0.1 M NaOH, S/L 66.7 g/l, 10 min (ultrasound) + 1 h (stirring), 4 °C	Kadam et al. (2017)
Red, brown and green seaweeds [h]	UAE	0.2 M perchloric acid, S/L 10 g/l, 30 min + 10 min (two-sonication extraction steps)	Vieira et al. (2018)
Ulva sp., *Gracillaria sp.*	UAE	Water, S/L 10 g/l, 1 h; stirring overnight 4 °C; centrifugation; 2 cycles	Kazir et al. (2018)
Ulva sp., *Gracillaria sp*	UAE	NaOH (10% w/v), 2 h; centrifugation (4 °C), 2 cycles	Kazir et al. (2018)
Ulva sp.	PEF	0–75 pulses of 2.2–7.2 µs, 12 or 26 kV (1.56 or 7.26 kV/cm field strength), 0.5 Hz Optimized parameters: 50 pulses of 2.3 µs, 26 kV, 7.26 kV/cm field strength	Polikovsky et al. (2019)

[a]Extracted compounds: R-phycoerythrin (R-PE) and R-phycocyanin (R-PC); [b]M/H—maceration/homogenization; [c]extracted compound: R-phycoerythrin; [d]comprised of Sumizyme TG, Sumizyme MC, Multifect® CX 15 L, Ultraflo® XL, 0.2% w/w concentration of each enzyme; [e]actual power 300-340 W; [f]E/S—enzyme/substrate ratio; [g]extracted compounds: R-phycoerythrin and allophycocyanin; [h]Red seaweeds: *C. crispus*, *Gracilaria sp.*, *O. pinnatifida* and *Porphyra spp.*; Brown seaweeds: *A. nodosum*, *F. spiralis*, *S. polyschides* and *U. pinnatifida*; Green seaweeds: *Ulva spp.*

Ultrasounds and a buffered solvent system were applied to improve three conventional lipids extraction methods using green macroalgae (*Ulva fasciata*), red macroalgae (*Gracillaria corticata*) and brown algae (*Sargassum tenerrimum*) (Kumari et al. 2011). The sonication treatment did not show relevant results, whereas the use of buffer proved to be the most appropriate to obtain the best outcome.

Most of the published research on this topic has focused though on the isolation of fucoxanthin which has already been intensely analysed and has gained a lot of popularity owing to its bioactive properties. The use of alginate lyase enzyme facilitated the degradation of the cell wall of brown algae *Undaria pinnatifida* releasing the targeted component (Billakanti et al. 2013). Its use increased the fucoxanthin yield by up to 15% more in comparison with untreated samples, in wet or dry form. On the downside, the applied procedure generated a high non-lipid material. The addition of ethanol as a co-solvent determined a significant improvement of the generated yield, over 80%, but the extracts included higher amounts of non-lipid compounds.

Process parameters such as time and temperature can significantly influence the yield values of fucoxanthin separation, as it is a heat-sensitive compound. A temperature above 60 °C determined a decrease in the generated yield for *Undaria pinnatifida* processing (Goto et al. 2015). In an optimization study, performed for the PLE of fucoxanthin, it was demonstrated that ethanol concentration had the highest influence on the separation process, followed by extraction temperature (Shang et al. 2011).

In terms of co-solvents used in supercritical CO_2 extraction, sunflower oil determined the highest fucoxanthin content and stability, as well as antioxidant activity, when compared to the simple supercritical CO_2 process (Saravana et al. 2017). The simultaneous extraction of oil from roasted coffee and fucoxanthin from brown algae, significantly increased the extraction yield of the carotenoid and

Table 6 Applications of green extraction technologies for macroalgae lipophilic compounds isolation. SFE: supercritical fluid extraction, EAE: enzyme-assisted extraction, UAE: ultrasound-assisted extraction, PLE: pressurized liquid extraction

Macroalgae	Method	Operating conditions	Ref
Oils			
L. japonica	SFE (SCO_2)[a]	35–55 °C, 15–25 MPa, 2 h, CO_2 26.81 g/min Optimized conditions: 55 °C, 25 MPa	Park et al. (2012)
Fucoxanthin and lipids rich in PUFAs			
U. pinnatifida	EAE	Alginate lyase (100 mM sodium phosphate buffer, pH 6.2), 2 h, 37 °C; DME[b], EtOH and DME/EtOH extraction	Billakanti et al. (2013)
Carotenoids and lipids			
U. pinnatifida	SFE (SCO_2)[a]	DME (co-solvent), 40–80 °C, 20–40 MPa	Goto et al. (2015)
Lipids			
Green, red and brown seaweeds [c]	UAE	Total lipid fraction: Chloroform/methanol (2:1, v/v), S/L 100 g/l, 20 min, 25 °C Triacylglycerol fraction: Hexane, S/L 75 g/l	Ragonese et al. (2014)
U. fasciata, *G. corticata*, *S. tenerrimum*	UAE	Chloroform/methanol (1:2 + 1:1), Chloroform/methanol (2:1 + 1:1, v/v), Dichloromethane/methanol (2:1 + 1:1, v/v), with/without sonication (2 min on ice) and buffer	Kumari et al. (2011)
Fucoxanthin			
S. japonica	SFE(SCO_2)[a]	Sunflower oil (SFO), soybean oil, canola oil, ethanol, water (co-solvents); 45–55 °C, 200–300 bar, co-solvent flow rate 0.50–2.00% of CO_2 (w/w) Optimized conditions: 50.62 °C, 300 bar and 2.00% of SFO	Saravana et al. (2017)
E. bicyclis	PLE	Ethanol in water (50, 100%), 40 and 100 °C, 5 and 15 min, 1000 and 2500 psi Optimized conditions: 110 °C, 90% ethanol concentration	Shang et al. (2011)
S. japonica	SFE(SCO_2)[a]	40–50 °C, 200–300 bar, SJ/RC[d] 25–75%, CO_2 flow rate 27 g/min, 3 h Optimized conditions: 40 °C, 300 bar, SJ/RC 75:25	Getachew et al. (2018)

[a]Supercritical carbon dioxide extraction process; [b]DME—dimethyl ether; [c]Green seaweeds: *E. intestinalis* and *U. rigida;* Red seaweeds: *A. taxiformis* and *P. capilacea*; Brown seaweeds: *S. scoparium, C. sinuosa, C. brachicarpa, D. dicotoma;* [d] mixing ratio of *Saccharina japonica* (SJ) with roasted coffee (RC)

favoured the attenuation of the algae flavour, making the mixture more suitable for nutraceuticals, cosmetics and pharmaceuticals production (Getachew et al. 2018).

Polyphenols isolation: As already confirmed in the scientific literature, the applied extraction method influences greatly the determined total polyphenolic content (TPC), antimicrobial and antioxidant activity of the polyphenols (Cox et al. 2010; Keyrouz et al. 2011). Various types of innovative extraction methods, including SFE, MAE, UAE and EAE, have been lately more and more studied concerning the isolation of polyphenols from macroalgae biomass. Table 7 presents the applications of these technologies for the extraction of polyphenolic compounds from marine macroalgae.

The effect of ultrasounds on polyphenols extraction was tested and compared for a series of brown macroalgae and microalgae species (Agregán et al. 2018). Seaweeds registered significantly higher TPC values (16–20 g of PGE, phloroglucinol equivalents, per 100 g of extract) in comparison with microalgae (4.3–4.7 g PGE/100 g extract) and the antioxidant activity determined for the extracts was in correlation with the generated TPC values. The sonication process determines the release of soluble biomolecules due to the creation of cavitations at the macroalgae cell wall level which generate its degradation (Lazar et al. 2016). UAE is a good extraction method for the separation of heat-sensitive biomolecules, including polyphenols. The use of ultrasounds avoids degradation of the desired compounds and facilitates the generation of a high yield in low temperature conditions (Mittal et al. 2017; Lazar et al. 2016). An optimization study for the application of UAE demonstrated that among the influencing parameters, the extraction time and temperature had the highest effect on the TPC and antioxidant activity of isolated polyphenols from brown macroalgae *Hormosira banksii* (Dang et al. 2017). The use of ultrasounds also increased the extraction of high molecular weight polyphenols (total phenolics) from *Ascophyllum nodosum* (Kadam et al. 2015c).

In terms of solvents, generally polyphenols are obtained from macroalgae using aqueous mixtures of methanol, ethanol, acetone, hexane and ether (Cox et al. 2010; Ferreres et al. 2012). However, water was found to be better than solvent mixtures like ethanol/water (80:20) and acetone/water (80:20) for phenols extracted from Irish macroalgae (*Ascophyllum nodosum*, *Pelvetia canaliculata*, *Fucus spiralis* and *Ulva intestinalis*) (Tierney et al. 2013). Water is

Table 7 Applications of green extraction technologies for macroalgae polyphenols isolation. MAE: microwave-assisted extraction, UAE: ultrasound-assisted extraction, SWE: subcritical water extraction, IL: ionic liquids, S: supercritical

Macroalgae	Method	Operating conditions	Ref
Phenolic compounds			
Polisiphonia sp., Ulva sp., Cladophora sp.	MAE	Water, 25–60 °C, 30 min	Michalak et al. (2015)
A. nodosum, F. vesiculosus, B. bifurcata	UAE	Water/ethanol (50:50, *v/v*), S/L 100 g/l, room temperature, 30 min	Agregán et al. (2018)
C. racemosa	MAE	Ethanol (20–100%), 100–600 W, 20–70 °C, 5–60 min, S/L 20–100 g/l Optimized conditions: 200 W, 60% Ethanol, 40 °C, 25 g/l	Li et al. 2012
S. japonica	SWE + IL	[C4C1im][BF4] (SWE catalyst, 0.25–1.00 M), 100–250 °C	Dinh et al. (2018)
A. nodosum	UAE	HCl (0–0.06 M), 5–25 min, ultrasound amplitude 22.8–114 µm, 20 kHz	Kadam et al. (2015c)
U. rigida	UAE	Water, 250 g/l (fresh sample)	Mezghani et al. (2016)
H. banksii	UAE	Ethanol 70% (v/v), 150–250 W, S/L 20 g/l, 30–50 °C, 20–60 min Optimized conditions: 30 °C, 60 min and 150 W	Dang et al. (2017)
P. palmata[a]	EAE	Water, S/L 40 g/l, 10 min incubation, different enzymes (enzymatic hydrolysis 24 h), boiling at 100 °C, 10 min	Wang et al. (2010)
Phlorotannins			
C. flexuosum, E. radiata	MAE	Water, acetone, ethanol, propan-1-ol, ethyl acetate, S/L 25–200 g/l, 135–185 °C, 1–20 min Optimized conditions: S/L 33 g/l, 160 °C, 3 min	Magnusson et al. (2017)
S. japonica	SCO_2	Sunflower oil, soybean oil, canola oil, ethanol and water (co-solvents), 45–55 °C, 200–300 bar, co-solvent flow rate 0.50–2.00% of CO_2 (w/w) Optimized conditions: 48.98 °C, 300 bar and 2% of water	Saravana et al. (2017)
Isoflavones			
Brown and red seaweeds[b]	SCO_2 + UAE	CO_2 modified by 3% (v/v) MeOH/H_2O 9:1 (v/v), 30–60 min; 35–75° C, 10–40 MPa Optimized conditions: 35 MPa, 40 °C, 60 min	Klejdus et al. (2010)

[a]Polyphenols and other hydrophilic antioxidant compounds; [b] *S. muticum*, *S. vulgare*, *H. spinella*, *Porphyra sp.*, *U. pinnatifida*, *C. crispus*, *H. incurvus*

also a preferable solvent in comparison with organic ones from a toxicological point of view (Agregán et al. 2017). The highest TPC values of polyphenolic extracts isolated from green macroalgae *Ulva rigida,* by using various solvents and applying ultrasounds, were registered for the ethyl acetate extract (582.93 ± 0.8 mg GAE g^{-1}) and for the hydrolysed water extract (457.12 ± 4.8 mg GAE g^{-1}), while the sonicated water extract registered a lower value (Mezghani et al. 2016).

Common phenolic compounds that can be found also in terrestrial feedstock have been successfully extracted in higher amounts through SWE with and without the use of ionic liquids than through a conventional method (Dinh et al. 2018). The antioxidant activity tests of the obtained phenolic compounds (gallic, chlorogenic, gentisic, protocatechuic, p-hydroxybenzoic and caffeic acids) indicated as well high values and were also correlated with the TPC results. The application of the ionic liquid [C4C1im][BF4] (1-butyl-3-methylimidazolium tetrafluoroborate) led to an increase in both quantity and antioxidant activity of the polyphenolic content in comparison with the use of the simple SWE method. However, the qualitative analysis of the extract determined a decomposing effect on the vanillic acid and a slight reduction in quantity for the p-hydroxybenzoic acid.

The influence of various parameters was studied in order to determine the optimum conditions for MAE of phenolic compounds from *Caulerpa racemosa* (Li et al. 2012). The highest influence on the process yield was exerted by the microwave power, followed by extraction time, extraction temperature, ethanol concentration and solvent-to-material ratio. Increased polyphenolic extraction yields (up to 70%) were registered when microwaves were applied (Magnusson et al. 2017). However, the physico-chemical properties of extracts can be affected by this fast process and the high temperatures and pressures involved. The effect that MAE can have on the structural properties and bioactivity of heat-sensitive compounds has been pointed out by various authors (Rodriguez-Jasso et al. 2011; Hahn et al. 2012; Talmaciu et al. 2015). Therefore, increasing the yield sometimes might generate a less qualitative bioproduct.

Furthermore, several commercial enzymes were applied for the improved separation of polyphenols from *Palmaria*

palmata (Wang et al. 2010). Water-soluble extracts with antioxidant activity and polyphenolic content were obtained using various proteases and carbohydrases (Heo et al. 2005). Enzymatic-assisted extraction coupled with the power of microwaves was applied for the separation of polyphenolic content from brown macroalgae *Ecklonia radiata* generating significantly higher yields than the used conventional methods, up to 20%. The combined innovative methods determined also higher TPC values in comparison with the single use of the EAE process (Charoensiddhi et al. 2015).

Integrated processing of marine macroalgae

Macroalgal biorefinery has been often referred to as a potential solution for making biofuels and bioproducts marketable (Alvarado-Morales et al. 2015). Identifying key products and processes combinations is essential in this regard. Fortunately, more and more dedicated studies have been reported in last years.

A scientific review of available research studies regarding marine macroalgae biorefinery has been performed aiming to offer a perspective on this topic. The analysis was carried out using Web of Knowledge platform from 2013 to 2019. The database reveals 137 articles generated for "seaweeds biorefinery" keywords, followed by "macroalgae biorefinery" with 131 articles.

So far, several authors have tested various processes for the isolation of important metabolites and the production of bioenergy in an integrated approach. The common processes of marine macroalgae biorefinery are summarized in Fig. 1.

Many performed studies achieved a complete biomass conversion, leading the path towards a zero-waste biorefinery. After the isolation of macroalgal extractives like pigments (Balboa et al. 2015; Francavilla et al. 2015; Baghel et al. 2016) or polysaccharides (Kumar et al. 2013; Yuan and Macquarrie 2015a; Masarin et al. 2016) and the production of bioethanol (Kumar et al. 2013; Baghel et al. 2015, 2016) or biogas (Alvarado-Morales et al. 2015), the residue was converted into biochar (Francavilla et al. 2015; Yuan and Macquarrie 2015a), biosorbent for heavy metals (Sunwoo et al. 2016; Filote et al. 2019) or studied for its potential as soil conditioner (Baghel et al. 2016). Table 8 presents up-to-date information regarding the studies that have been performed so far on this topic and the obtained results.

Overall, reported results show different situations in terms of generated yields of the macroalgae compounds. In some cases, the results obtained through sequential and integrated processing were similar to the ones recorded for individual, direct processing (Trivedi et al. 2016), whereas in other cases, lower values were reported (Yuan and Macquarrie 2015a). Ulvan isolated in a biorefinery approach after the separation of mineral-rich extract and lipids, registered different values in the studies performed so far, ranging from 19.90% dw to 39% dw (Trivedi et al. 2016; Gajaria et al. 2017). Separation of alginate from brown algae through a

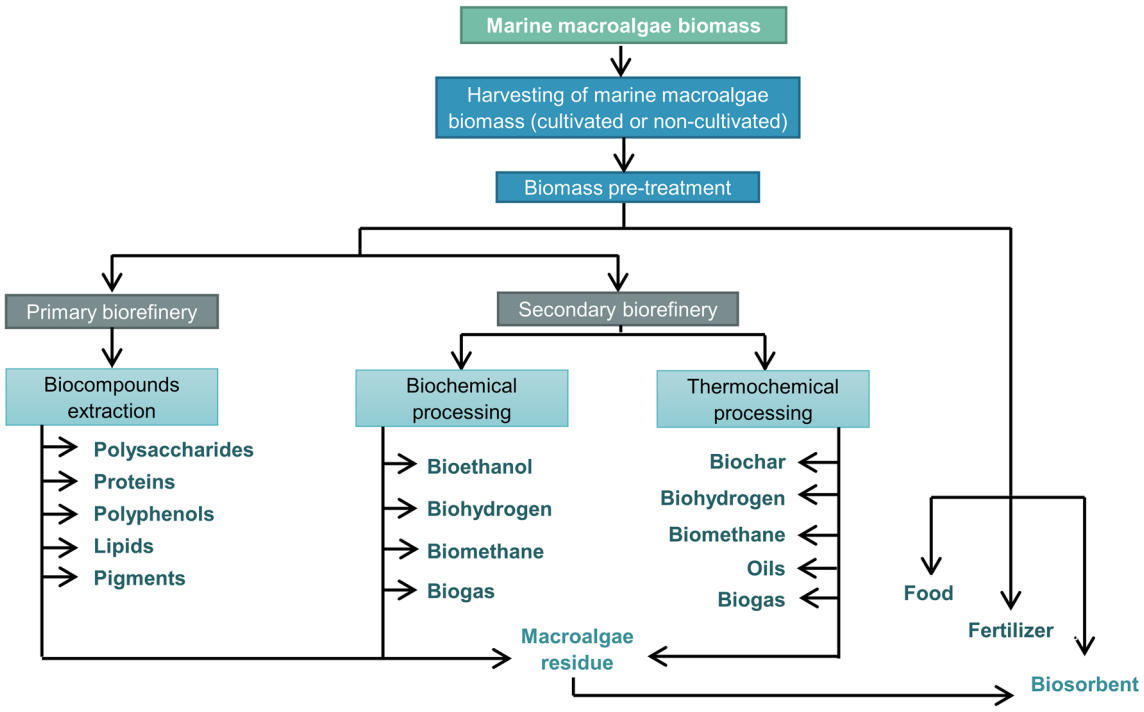

Fig. 1 Flowsheet of common processes of marine macroalgae biorefinery

Table 8 Marine macroalgae conversion through biorefinery. SLE: solid-liquid extraction, MAE: microwave-assisted extraction, SC: supercritical

Algae	Process	Process conditions	Generated products	Reference
Red algae (Rhodophyta)				
G. acerosa, *G. pusillum* *G. dura*	SLE	0.1 M phosphate buffer (pH 6.8), incubation 12 h at 4 °C, S/L 500 g/l (fresh); centrifugation (6300 g, 4 °C, 15 min)	Phycobilin pigments (R-PE, R-PC) Liquid fertilizer	Baghel et al. (2015)
	SLE	Chloroform/methanol (1:2 v/v), centrifugation (2000 g, 4 °C, 20 min)	Lipids	
	SLE	Water (S/L 1:5[a]), autoclaving (120 °C, 1.5 h), centrifugation (6300 g, 6 min)	Agar	
	SLE	Acetate buffer (1:15 w/v) with 36% $NaClO_2$ (for bleaching), 60 °C, 8 h	Cellulose	
	Enzymatic hydrolysis of cellulose and Fermentation	Commercial enzyme cellulase 2% v/v, in sodium acetate buffer (pH 4.8), 36 h, 45 ºC *Saccharomyces cerevisiae* yeast, 28 °C, 120 rpm, 48 h	Bioethanol	
G. corticata	SLE	Water, 12 h, 4 °C; UMF[b], 200 kDa cut-off poly sulphone membrane	Pigments (R-PE and R-PC) Mineral-rich water	Baghel et al. (2016)
	SLE	Chloroform/methanol (1:2 v/v), room temperature, 30 min	Lipids	
	SLE	Water, 1:35 ratio, 1.5 h, 120 °C; centrifugation (6300 g, 6 min)	Agar	
	Enzymatic hydrolysis and fermentation	Commercial enzyme cellulase, 2% in sodium acetate buffer (pH 4.8); *Saccharomyces cerevisiae*, 28 °C, 120 rpm, 12 h	Bioethanol	
G. gracilis	SLE	S/L 50 g/l, 1 M acetic acid–sodium acetate buffer (pH 5.5) with 0.01% of sodium azide, 30 min (dark); grinding 5 min; centrifugation (5 °C, 15,000 rpm, 20 min)	Phycobiliproteins (R-PE, PC[c], APC[d])	Francavilla et al. (2015)
	Fast pyrolysis	400, 500 and 600 °C, heating rate 50 ºC/s, atmospheric pressure, inert atmosphere	Char Liquid Non-condensable gas	

Table 8 (continued)

Algae	Process	Process conditions	Generated products	Reference
G. verrucosa	Water Extraction	Pre-treatment (5% NaOH, 80 °C, 2 h); neutralization (1.5% H_2SO_4, 2 h); water extraction at boiling temperature (90 min), S/L 50 g/l	Agar	Kumar et al. (2013)
	Enzymatic Hydrolysis	0.05 M citrate phosphate buffer (pH 5), 50 °C, 2 h; commercial cellulase (*Trichoderma reesei*) and β-glucosidase (*Aspergillus niger*), 50 ºC	–	
	Fermentation	*Saccharomyces cerevisiae* yeast (6.0% v/v), pH 6.0	Bioethanol	
G. verrucosa, *K. alvarezii* and *E. denticulatum*	Thermal acid hydrolysis	30–110 mM H_2SO_4, 30–120 min, 121 °C, hydrolysates adjusted to pH 5.0 with NaOH	Ethanol	Sunwoo et al. (2016)
	Enzymatic saccharification	Saccharification, 45 °C, 150 rpm, 48 h with 16 units/mL of mixed enzymes (commercial cellulase, and cellulase/β-glucanase		
	Fermentation	*Saccharomyces cerevisiae* adapted to 80 g/L galactose		
	Biosorption	pH 5, 30 °C and 150 rpm for 2 h	Biosorbent for Cd(II), Pb(II) and Cu(II)	
K. alvarezii (brown and red strains)	Cold alkali transformation and distilled water extraction	6% KOH solution (w/v), 24 h, 25 °C; water extraction, 65 °C, 120 rpm, 2 h	Carrageenan	Masarin et al. (2016)
	Enzymatic hydrolysis	Commercial enzyme preparations, 50 mM sodium-acetate buffer (pH 4.8), 45 °C, 120 rpm	Glucose	
Brown algae (Phaeophyta)				
A. nodosum	MAE	0.1 M HCl, microwave irradiation, 15 min, 90 °C; Alginate removal by 2% $CaCl_2$; Fucoidan precipitation by ethanol	Fucoidan	Yuan and Macquarrie (2015a)
	MAE	0.1 M Na_2CO_3, microwave irradiation, extraction time 10 min, 100 °C; Precipitation by ethanol	Alginate	
	Acid hydrolysis	0.4 M H_2SO_4, microwave irradiation, 1 min, 150 °C	Reducing sugars Biochar (algal residue)	

Table 8 (continued)

Algae	Process	Process conditions	Generated products	Reference
L. digitata	Enzymatic hydrolysis	Cellulase and β-glucosidase enzymes, 50 °C, 150 rpm, 48 h	Succinic acid	Alvarado-Morales et al. (2015)
	Fermentation	Anaerobic conditions, 37 °C, 150 rpm, 48 h; using *A. succinogenes*	Biogas	
L. digitata	Enzymatic hydrolysis	Enzyme loading: 10% v/w Celluclast 1.5L + 0.5% w/w alginate lyase;	Bioethanol	Hou et al. (2015)
	Separate Hydrolysis and Fermentation (SHF)	S/L 50 g/l, MilliQ water and ampicillin sodium salt, pH 5, 10% (v/w) of Celluclast 1.5L and 0.25% (w/w) of alginate lyase, 250 rpm, 50 °C; cooling to room temperature; 1 g/L *S. cerevisiae*; second incubation, 30 °C, 120 rpm, 48 h		
	Determination of nitrogen content	Calculated based on ammonia amount (oxidation and conversion of nitrogen into ammonia)	Total proteins and amino acids in the residue	
	Determination of amino acid composition	ISO 13,903:2005 protocol		
S. muticum	Ethanolic extraction and SC-CO_2 [f]	Pilot plant extractor, 1 h, 50 °C, 10 and 35 MPa, 25 g CO_2 min^{-1}	Fucoxanthin	Balboa et al. (2015)
	Autohydrolysis [g]	Three different reactors; non-isothermal conditions	Alginate	
S. axillaris, *M. pyrifera*, *D. potatorum*, *E. radiata*, *E. radiata*, *E. radiata*	SLE	Ethanol, 3 h (repeated twice)	Ethanolic extract	Lorbeer et al. (2015a), Lorbeer et al. (2017)
	SLE	HCl, pH 1, 42 °C, 159 min	Fucoidan	
	SLE	0.2 M Na_2CO_3, 120 min, 45 °C (incubator)	Alginate	
S. japonica	SLE	0.5–4.0 wt% sodium carbonate, S/L 100 g/l, 40–80 °C, 60–120 min	Alginate	Ryu and Oh (2017)
	Enzymatic Hydrolysis	Commercial hydrolase, Celluclast (1.5 L) and Novozymes 188, 100 mM sodium citrate buffer (pH 4.8), 50 °C, 120 rpm, 48 h	Glucose	

Table 8 (continued)

Algae	Process	Process conditions	Generated products	Reference
L. digitata	SLE	0.1 M HCl (pH 2–2.5), 70 °C, 1 h, 250 rpm; centrifugation (5000 rpm, 15 min); precipitation of alginate with 1% (w/v) $CaCl_2$; precipitation of fucoidan with Ethanol (4 °C, 24 h)	Fucoidan and Alginate	Kostas et al. (2017)
	Hydrolysis and Fermentation	1.5 M H_2SO_4 and water-based auto-hydrolysis, S/L 250 g/l, 24 min, 121 °C, autoclave); enzymatic hydrolysis, Novozymes Cellic®, 50 mM sodium citrate buffer, 50 °C, 48 h, 120 rpm	Bioethanol	
L. digitata	Enzymatic liquefaction	50.0 mM Acetate buffer (pH 5.0), S/L 70–80 g/l, 50 °C, 400 rpm, 72 h, admixture of the commercial hydrolase enzyme[e]	Lipids	Masri et al. (2018)
	Yeast cultivation	Cultivation of *C. oleaginosus* with different enzymatic hydrolysates. 0.2 L min^{-1} filtered air, 28 °C, 120 rpm, 5 d		
	Lipids extraction	Lyophilization, cell destruction with a high-pressure homogenizer, sequential solvent extraction (3 times) with Folch solution		
	Biosorption	S/L 0.01 g/L, 3 h incubation time (room temperature), centrifugation 10 000 g, 10 min	Biosorbent for Ce^{+3}, Pb^{+2}, Cu^{+2} and Ni^{+2}	
D. potatorum	SLE	0.025–0.1 M HCl, S/L 50 g/L, 60 ºC, 3 h	Fucoidan + Laminarin	Abraham et al. (2019)
	SLE	28% Na_2CO_3, 2 h, 60 ºC	Alginate	
L. japonica	SLE	Biomass autoclaved at 120 °C (20 min), 40 g/l; Extraction with 2% (w/v) of Na_2CO_3 (60 °C, 5 h) or with water (70 °C, 5 h)	Alginate	Kim et al. (2019)
	SLE	Chloroform/methanol (2:1, v/v)	Lipids	

Table 8 (continued)

Algae	Process	Process conditions	Generated products	Reference
Green algae (Chlorophyta)				
U. fasciata	SLE	Water, S/L 500 g/l, grinding	MRLE (mineral-rich liquid extract)	Trivedi et al. (2016)
	SLE	Chloroform/methanol (1:2), S/L 50 g/l, vortexing, centrifugation (4000 rpm, 4 °C, 20 min); repetition 2–3 times until a clear supernatant	Lipid fraction	
	SLE	Water, S/L 44.5 g/l, autoclaving 2 h, 90 °C; precipitation with chilled isopropyl alcohol (24 h, -40 °C)	Ulvan	
	SLE	Acetate buffer, S/L 25 g/l, containing $NaClO_2$ for bleaching (60 °C, 6–8 h); neutralization with water; alkaline treatment (0.5 M NaOH 60 °C, 8–10 h), washing, suspension in HCl 5% v/v; heating to 100 °C	Cellulose	
	Enzymatic hydrolysis and fermentation	Cellulose and residual biomass as substrates, saccharification with commercial cellulase (2% v/v), 45 °C, 36 h; cellulose hydrolysate enriched with peptone (5 g/L) and yeast extract (3 g/L), fermentation with fresh *S. cerevisiae,* 12 h, 28 ± 2 °C, 120 rpm	Bioethanol	
U. lactuca	SLE	S/L 500 g/l, Water, crushing (biomass mechanically disintegrated into tiny particles) and filtration	Sap	Gajaria et al. (2017)
	SLE	Chloroform/methanol solution (1:2), agitation, 3 h	Lipids	
	SLE	Incubation in water, 90 °C, 2 h; precipitation with iso-propanol	Ulvan	
	SLE	1 N NaOH, 80 °C; Neutralization with 6 N HCl	Proteins	
	SLE	36% w/w NaClO, pH 3; incubation overnight, 65–70 °C	Cellulose	
U. lactuca	SLE	Demineralized water, S/L 100 g/l, 60 °C, 45 min	Sap	Mhatre et al. (2019)
	SLE	Acidified water (1 M HCl, pH 2), S/L 62.5 g/l, 95 °C, 3 h	Ulvan	
	SLE	0.25 M NaOH (optimized alkali concentration), S/L 50 g/l, 60 °C, 1 h	Proteins	

Table 8 (continued)

Algae	Process	Process conditions	Generated products	Reference
U. lactuca	Enzymatic liquefaction	50.0 mM Acetate buffer (pH 5.0), S/L 70–80 g/l, 50 °C, 400 rpm, 72 h, admixture of the commercial hydrolase enzyme[e]	Lipids	Masri et al. (2018)
	Yeast cultivation	Cultivation of *C. oleaginosus* with different enzymatic hydrolysates. 0.2 L min^{-1} filtered air, 28 °C, 120 rpm, 5 d		
	Lipids extraction	Lyophilization, cell destruction with a high-pressure homogenizer, sequential solvent extraction (3 times) with Folch solution		
	Biosorption	S/L 0.01 g/L, 3 h incubation time (room temperature), centrifugation 10 000 g, 10 min	Biosorbent for Ce^{+3}, Pb^{+2}, Cu^{+2} and Ni^{+2}	

[a]Mixing ratio of residue with distilled water (based on primary biomass weight); [b]ultra-membrane filtration; [c]PC-phycocyanin, [d]APC—Allophycocyanin; [e]Cellic CTec 2®, Cellic HTec®, Novozymes 188®, exo-Laminarase and α-Amylase®, [f]supercritical carbon dioxide purification; [g]subcritical water extraction

biorefinery processing gave a lower yield due to potential fractions (being isolated together with fucoidan in a previous acidic extraction). However, applying the separation of alginate first would determine the co-extraction of fucoidan since the uronic acids sequence of alginate is part of the macroalgal cell wall (Yuan and Macquarrie 2015a). In another study, the yield of the agar isolated from the residual biomass demonstrated to be significantly higher than the one obtained directly from feedstock (Baghel et al. 2016; Trivedi et al. 2016).

Furthermore, an improvement in the structural and functional properties of the biomolecules has also been observed. Gel strength of agar obtained through an integrated biorefinery system proved to be approximately 1.5–3 times higher than that of the compound generated through direct extraction (Baghel et al. 2015). Gelling temperature, melting temperature and extraction yield remained however similar in its values. A biorefinery approach also showed an effect on the molecular weight of the generated bioactive compounds. For instance, the sequential extraction of polyphenols, fucoidan and alginate from *Ascophyllum nodosum* determined a decrease in the molecular weight of alginate from 195.3 kDa to 75.13 kDa (Yuan and Macquarrie 2015a). Multiple sequential processes applied to macroalgae increase the degradation of the chemical structures of the primary biomass, and thus, extracts with lower molecular weight can be generated from the residue.

The laboratory-scale integrated processing of brown, red and green macroalgae biomass performed so far in available biorefinery studies is summarized in Figs. 2, 3 and 4, respectively, considering the types of bioproducts obtained and the types of processes used for their generation.

One of the main concerns of co-producing hydrocolloids and energy bioproducts is the reduction of fermentable sugars from the algal biomass (Tedesco and Stokes 2017). However, monosaccharide analysis of the biorefinery residue, generated after the separation of polysaccharides with functional properties from *Laminaria digitata,* showed a considerable increase in glucose (161.9 mg/g of residue), which confirms the potential of this residue for bioethanol production (Kostas et al. 2017). Glucose amounts from the initial biomass of two strains of *Kappaphycus alvarezii* (brown and red) and the biomass obtained after KOH pretreatment and water extraction were analysed and the results obtained after the enzymatic hydrolysis of the samples indicated the highest concentrations of glucose in the residues which thus could be more suitable for the production of bioethanol (Masarin et al. 2016).

Biogas obtained from brown macroalgae residues after the extraction of value-added compounds has a high potential, with *Laminaria* and *Fucus* species showing the highest values. Further pre-treatments to improve the biodegradability of the macroalgae waste are necessary though, since the

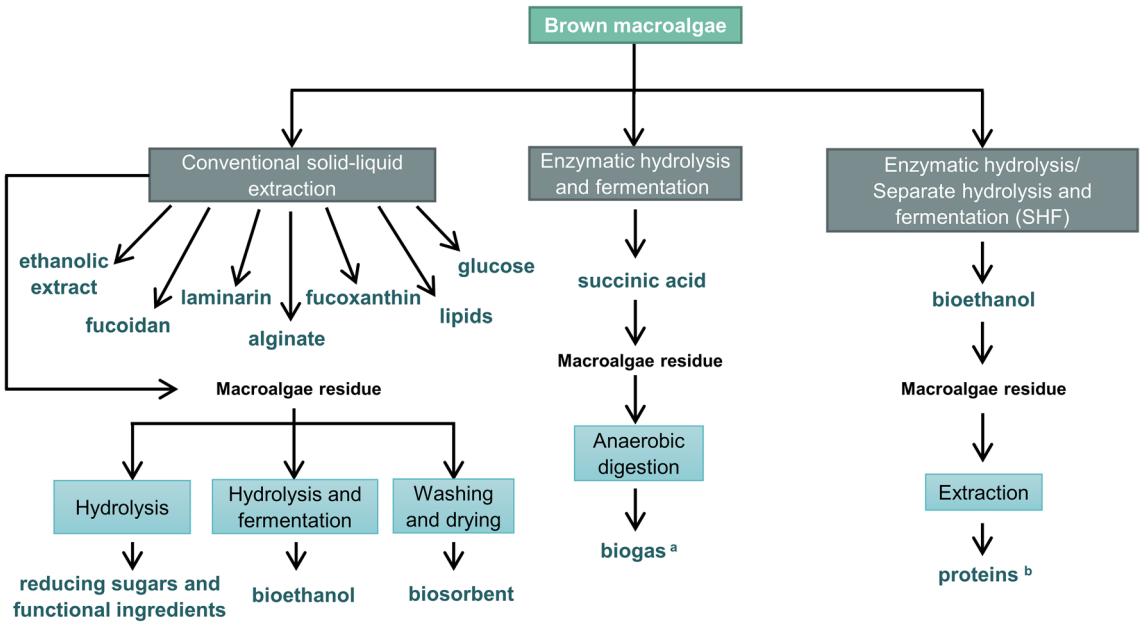

Fig. 2 Laboratory-scale integrated processing of brown macroalgae biomass performed so far in available biorefinery studies; [a]biogas potential by biochemical methane potential (BMP) analysis (Alvarado-Morales et al. 2015); [b]total proteins content analysis (Hou et al. 2015)

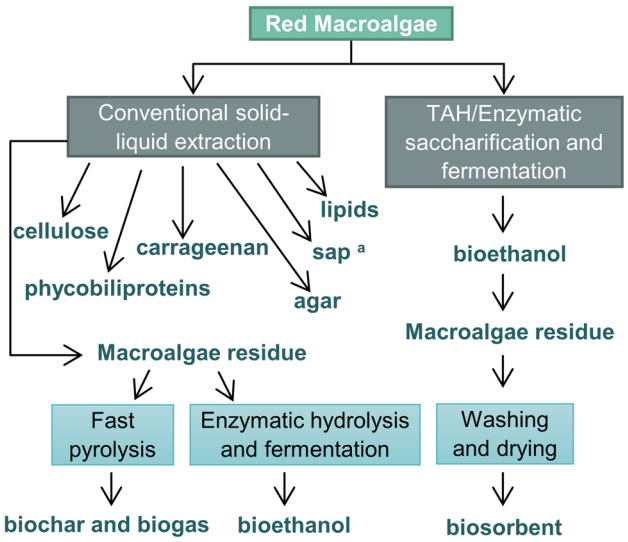

Fig. 3 Laboratory-scale integrated processing of red macroalgae biomass performed so far in available biorefinery studies; [a]sap—algal extract composed of amino acids, vitamins, minerals, trace nutrients

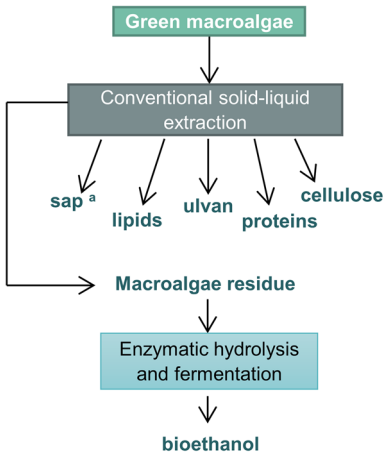

Fig. 4 Laboratory-scale integrated processing of green macroalgae biomass performed so far in available biorefinery studies; [a]sap—algal extract composed of amino acids, vitamins, minerals, trace nutrients

actual yields have demonstrated to be 50% lower than the theoretical ones (Tedesco and Stokes 2017).

Another study focused on an integrated conversion of brown algae *Laminaria digitata* into bioethanol, with the co-production of proteins (Fig. 1) (Hou et al. 2015). Maximum ethanol potential yield of 77.7% was obtained by applying the Separate Hydrolysis and Fermentation (SHF) method. Furthermore, the fermentation processes determined a 2.7 times increase in the protein content with glutamic acid and aspartic acid as the most abundant amino acids.

A different approach has been the use of red algae biomass for bioethanol production coupled with testing the macroalgae waste for heavy metals removal. The residue generated after the enzymatic hydrolysis was successfully applied in biosorption studies for the removal of Cd(II),

Pb(II) and Cu(II) (Sunwoo et al. 2016). Marine macroalgae have had their high bioadsorptive capacity proven in many research studies, but most of the conducted experiments used the primary biomass as adsorbent. The use of the algal waste for pollutant removal after extracting important bioactive compounds and generating other energy or non-energy bioproducts in comparison with the simple processing of raw macroalgae clearly makes more sense for a sustainable use of this bioresource and the fulfilment of the circular economy principles.

A biorefinery approach for the production of succinic acid and bioenergy from *Laminaria digitata* biomass was also analysed. Succinic acid is a product of the petrochemical industry and is used in various sectors of production as block chemical, but biobased succinic acid requires high production costs (Alvarado-Morales et al. 2015). The integrated production could reduce thus the costs associated with both succinic acid and bioenergy providing in this way a feasible alternative to the use of the petroleum refinery. Moreover, the biobased synthesis of succinic acid by fermentation is a more sustainable option also due to CO_2 consumption. The macroalgal biomass rich in carbohydrate content with a determined sugar yield of 77.6% (w/w), registered an overall productivity of the succinic acid production process of 0.50 g L^{-1} h^{-1}. The synthesis process also generated a high yield, 86.49% (g g^{-1} of total sugars), and a low titre of fermentation (5.65 g L^{-1}). The performed hydrolysis determined an increase in the amino acid content by 3.5 times, as well as in the lipid bioavailability, by 8.6 times. These increments recommend the residual biomass for a diverse range of applications, particularly in functional foods industry, fish food industry and for biodiesel production. In terms of bioenergy production, the study compared the biological biomethane potential of the dried initial biomass, the fermentation broth and the residual biomass concluding that they all generated values similar to those obtained by other research studies using *Laminaria digitata* as substrate (around 285–298 NmL of CH_4 per g of volatile solids added).

Another good result was obtained for green macroalgae. Biomethane potential yields obtained from *Ulva lactuca* after the separation of sap and ulvan were approximately double than the result from the primary biomass (408 ± 20.02 mL CH_4 per g of volatile solids) (Mhatre et al. 2019). The generated value was also significantly higher than the results from other studies on the production of biomethane from marine macroalgae and microalgae, including biomass treated through mechanical, chemical, biochemical and thermochemical processes, respectively.

Biochar obtained from the biorefinery residue of *Gracillaria gracilis* presented a higher carbon content than the biochar generated from the original biomass, as well as other important inorganic elements including Fe, Ca, Mg, P and K. These results indicate very interesting properties of the bioproduct, with applications in agriculture and to improve soil qualities, especially of acidic ones (Francavilla et al. 2015). The generated bio-oil, however, showed N-levels above the limit established for its use as biofuel, further pretreatment processes being required.

Some research work has also integrated the non-conventional technologies into the applied biorefinery processes. Supercritical carbon dioxide (SC-CO_2) was used to purify fucoxanthin extract from *Sargassum muticum* (Balboa et al. 2015). Microwave-assisted extraction (MAE) was applied for a better isolation of fucoidan and alginate from *Ascophyllum nodosum* (Yuan and Macquarrie 2015a). The latter study also includes a comparison between fucoidan extraction using solely a conventional method and the microwave-assisted process. The results obtained indicated that the chemical composition of fucoidan is especially affected by temperature and pressure. Moreover, MAE was much faster in comparison with the conventional method, while maintaining a very similar chemical composition.

Supercritical fluids technology has been proven to separate an extract with less impurities, therefore obtaining a more qualitative one (Pérez-López et al. 2014). Supercritical carbon dioxide, for example, generates clean, solvent-free extracts and has a high selectivity for the targeted compounds (Akalin et al. 2016). The application of innovative extraction methods can still lead to more environmentally friendly processes by reducing the extraction temperature and required chemicals when comparing with the conventional techniques (Dumay et al. 2013; Singh et al. 2017; Hmelkov et al. 2018).

The reduction in chemicals consumption also occurs due to the application of integrated sequential processes which determine the concentration of targeted molecules in the reduced residual biomass (Trivedi et al. 2016). Cellulose extraction from red algae performed after several biorefinery steps required an amount of chemicals reduced by 85% (Baghel et al. 2015). For the cellulose separation from green alga *Ulva fasciata* after the separation of mineral-rich liquid extract (MRLE), total lipids and ulvan, a 30–40% reduction in the required chemicals was calculated (Trivedi et al. 2016). Furthermore, the integrated processing can determine a decrease in the environmental impact by diminishing the generated waste (Sunwoo et al. 2016; Masri et al. 2018) or by fulfilling even the zero-waste approach (Pérez-López et al. 2014).

Lastly, although most life cycle assessment studies (LCA) of marine macroalgae valorization have focused on biofuels production (Alvarado-Morales et al. 2013; Aitken et al. 2014; Czyrnek-Delêtre et al. 2017; Ertem et al. 2017; Parsons et al. 2019), there are also a few that took into consideration the generation of bioproducts (Pérez-López et al. 2014; Ghosh et al. 2015; Anand et al. 2018). The sustainability of marine macroalgae processing for co-production

of energy as well as non-energy products has been evaluated only briefly (Pechsiri et al. 2016; Seghetta et al. 2016).

Conclusion

The identification of key processes for the integrated production of biofuels and bioproducts from marine macroalgae has been an important goal of recent years in order to address the issue of depleting petrochemical resources and the development of the circular economy.

At present, the following key initiatives are ongoing: European Biofuels Technology Platform, dedicated to the development of cost-competitive world-class biofuels value chains and creation of a vibrant and lasting biofuels industry; European Energy Research Alliance—Joint Programme on Bioenergy (EERA Bioenergy), aimed at aligning the major European research institutes in the area of bioenergy with a particular focus on biofuels; IEA Bioenergy Task 42 Biorefining, with focus on the sustainable processing of biomass into biobased products and bioenergy. All these initiatives are focused on second and third generation of biofuels with special attention on macroalgae biomass. In this regard, marine macroalgae biorefinery will exhibit a development in the near future.

This strategic aim will be achieved through an update, consolidation and share of knowledge with all the European and international research communities. All the relevant, local and regional initiatives can be channelled for achieving this joint goal.

In order to ensure the demand of a macroalgae-based industry, cultivation and harvesting techniques need to be further developed. Until now, biomass generated from eutrophication processes or harvesting of naturally grown seaweeds alone cannot provide the necessary consistent amounts of feedstock for a macroalgae-based biorefinery. Furthermore, seaweeds cultivation and harvesting are well established in Asian countries, while in Europe it is yet to be developed to a similar status. Solutions still need to be further analysed and tested in order to understand the variability of the macroalgae chemical composition and how to manage it in order to have predictable and traceable results.

Except for alginate, carrageenan and agar, the markets for other marine macroalgae co-products still need to be developed, tested and applied in various industries where they can become optimal natural alternatives or innovative components. Optimization of the purification steps required to isolate different bioactive molecules is also necessary in some cases. The extraction and purification processes should be carefully studied and applied in order to preserve the functional properties of the isolated biomolecules as well as to obtain a maximum yield. The emerging innovative extraction techniques can support the development of marketable bioproducts with potential increased yields and bioactive properties. The use of the novel separation methods and solvents can play an important role in reducing the environmental impact of the production processes through a decrease in solvents, pre-treatments and extraction time. However, more environmental impact studies such as life cycle assessment (LCA) analysis and environmental footprint studies are necessary in order to have a full perspective regarding this aspect. Although they determine increased yields and bioactivities, some of these methods, including supercritical fluid extraction and microwaves have shown a high energy consumption which can also increase the overall biorefinery processing costs and environmental impact. Therefore, whether or not the "green" or innovative techniques are worth being applied or when they can really bring added-value to the overall biorefinery process is still debatable. Different scenarios in terms of costs and environmental sustainability need to be further analysed.

In terms of integrated processing, tests performed so far demonstrated an improvement of the yields of bioenergy products generated from macroalgae residues after the separation of non-energy products. More sequential extractions of biomolecules from cultivated macroalgae should be performed in order to improve the biorefinery systems and determine optimal process flows, together with a complete chemical characterization of the studied biomass and bioactivity analysis. Also, studies for large-scale macroalgae biorefineries are required in order to develop this industry. All in all, the integrated approach of macroalgae refining represents a promising strategy in order to develop the marine macroalgae-based industry and fulfil the circular economy principles.

Funding This study is part of the Ph.D. thesis carried out by the first author within the Laboratory of Bioresources (Med-Res) at "Gheorghe Asachi" Technical University of Iasi. Ph.D. scholarship was awarded by Romanian Government. This work was also partially financed by: Base Funding—UIDB/50,020/2020 of the Associate Laboratory LSRE-LCM—funded by national funds through FCT/MCTES (PIDDAC). S. Santos acknowledges postdoctoral scholarship (SFRH/BPD/117,387/2016), awarded by the Portuguese Science and Technology Foundation (FCT) and financed by National Funds and by the European Social Fund (ESF) through the Human Capital Operational Programme (POCH).

Compliance with ethical standards

Conflict of interest The authors have no conflict of interest to declare related to the content of this article.

References

Abraham RE, Su P, Puri M, Raston CL, Zhang W (2019) Optimisation of biorefinery production of alginate, fucoidan and laminarin from brown seaweed *Durvillaea potatorum*. Algal Res 38:101389. https://doi.org/10.1016/j.algal.2018.101389

Abreu MH, Varela DA, Henríquez L, Villarroel A, Yarish C, Sousa-Pinto I, Buschmann AH (2009) Traditional vs. integrated multi-trophic aquaculture of *Gracilaria chilensis* C. J. Bird, J. McLachlan & E. C. Oliveira: productivity and physiological performance. Aquaculture 293:211–220. https://doi.org/10.1016/j.aquaculture.2009.03.043

Agregán R, Munekata PES, Franco D, Dominguez R, Carballo J, Lorenzo JM (2017) Phenolic compounds from three brown seaweed species using LC-DAD-ESI-MS/MS. Food Res Int 99:979–985. https://doi.org/10.1016/j.foodres.2017.03.043

Agregán R, Munekata PES, Franco D, Carballo J, Barba FJ, Lorenzo JM (2018) Antioxidant potential of extracts obtained from macro- (*Ascophyllum nodosum*, *Fucus vesiculosus* and *Bifurcaria bifurcata*) and micro-algae (*Chlorella vulgaris* and *Spirulina platensis*) assisted by ultrasound. Medicines 5:33–41. https://doi.org/10.3390/medicines5020033

Aitken D, Bulboa C, Godoy-Faundez A, Turrion-Gomez JL, Antizar-Ladislao B (2014) Life cycle assessment of macroalgae cultivation and processing for biofuel production. J Clean Prod 75:45–56. https://doi.org/10.1016/j.jclepro.2014.03.080

Akalin MK, Tekin K, Karagöz S (2017) Supercritical fluid extraction of biofuels from biomass. Environ Chem Lett 15:29–41. https://doi.org/10.1007/s10311-016-0593-z

Ali H, Khan E (2017) Environmental chemistry in the twenty-first century. Environ Chem Lett 15:329–346. https://doi.org/10.1007/s10311-016-0601-3

Alvarado-Morales M, Boldrin A, Karakashev AB, Holdt SL, Angelidaki I, Astrup T (2013) Life cycle assessment of biofuel production from brown seaweed in Nordic conditions. Bioresour Technol 129:92–99. https://doi.org/10.1016/j.biortech.2012.11.029

Alvarado-Morales M, Gunnarsson IB, Fotidis IA, Vasilakou E, Lyberatos G, Angelidaki I (2015) *Laminaria digitata* as a potential carbon source for succinic acid and bioenergy production in a biorefinery perspective. Algal Res 9:126–132. https://doi.org/10.1016/j.algal.2015.03.008

Anand KGV, Eswaran K, Ghosh A (2018) Life cycle impact assessment of a seaweed product obtained from *Gracilaria edulis*—a potent plant biostimulant. J Clean Prod 170:1621–1627. https://doi.org/10.1016/j.jclepro.2017.09.241

Andriamanantoanina H, Rinaudo M (2010) Characterization of the alginates from five madagascan brown algae. Carbohydr Polym 82:555–560. https://doi.org/10.1016/j.carbpol.2010.05.002

Aravind S, Senthil Kumar P, Kumar NS, Siddarth N (2020) Conversion of green algal biomass into bioenergy by pyrolysis. A review Environ Chem Lett 18:829–849. https://doi.org/10.1007/s10311-020-00990-2

Armenta S, Garrigues S, de la Guardia M (2015) The role of green extraction techniques in green analytical chemistry. TRAC-Trend Anal Chem 71:2–8. https://doi.org/10.1016/j.trac.2014.12.011

Aroso IM, Paiva A, Reis RL, Duarte ARC (2017) Natural deep eutectic solvents from choline chloride and betaine—physicochemical properties. J Mol Liq 241:654–661. https://doi.org/10.1016/j.molliq.2017.06.051

Aryee ANA, Agyei D, Akanbi TO (2018) Recovery and utilization of seaweed pigments in food processing. Curr Opin Food Sci 19:113–119. https://doi.org/10.1016/j.cofs.2018.03.013

Atashrazm F, Lowenthal RM, Woods GM, Holloway AF, Dickinson JL (2015) Fucoidan and cancer: a multifunctional molecule with anti-tumor potential. Mar Drugs 13(4):2327–2346. https://doi.org/10.3390/md13042327

Baghel RS, Trivedi N, Gupta V, Neori A, Reddy CRK, Lali A, Jha B (2015) Biorefining of marine macroalgal biomass for production of biofuel and commodity chemicals. Green Chem 17:2436–2443. https://doi.org/10.1039/c4gc02532f

Baghel RS, Trivedi N, Reddy CRK (2016) A simple process for recovery of a stream of products from marine macroalgal biomass. Bioresour Technol 203:160–165. https://doi.org/10.1016/j.biortech.2015.12.051

Bak UG, Mols-Mortensen A, Gregersen O (2018) Production method and cost of commercial-scale offshore cultivation of kelp in the Faroe Islands using multiple partial harvesting. Algal Res 33:36–47. https://doi.org/10.1016/j.algal.2018.05.001

Balboa EM, Moure A, Domínguez H (2015) Valorization of *Sargassum muticum* biomass according to the biorefinery concept. Mar Drugs 13:3745–3760. https://doi.org/10.3390/md13063745

Barba FJ, Parniakov O, Pereira SA, Wiktor A, Grimi N, Boussetta N, Saraiva JA, Raso J, Martin-Belloso O, Witrowa-Rajchert D, Lebovka N, Vorobiev E (2015) Current applications and new opportunities for the use of pulsed electric fields in food science and industry. Food Res Int 77:773–798. https://doi.org/10.1016/j.foodres.2015.09.015

Barbosa M, Lopes G, Andrade PB, Valentão P (2019) Bioprospecting of brown seaweeds for biotechnological applications: phlorotannin actions in inflammation and allergy network. Trends Food Sci Technol 86:153–171. https://doi.org/10.1016/j.tifs.2019.02.037

Barbosa-Pereira L, Guglielmetti A, Zeppa G (2018) Pulsed electric field assisted extraction of bioactive compounds from cocoa bean shell and coffee silverskin. Food Bioprocess Tech 11:818–835. https://doi.org/10.1007/s11947-017-2045-6

Ben-Ari T, Neori A, Ben-Ezra D, Shauli L, Odintsov V, Shpigel M (2014) Management of *Ulva lactuca* as a biofilter of mariculture effluents in IMTA system. Aquaculture 434:493–498. https://doi.org/10.1016/j.aquaculture.2014.08.034

Benvenutti L, Ferreira Zielinski AA, Salvador Ferreira SR (2019) Which is the best food emerging solvent: IL, DES or NADES? Trends Food Sci Technol 90:133–146. https://doi.org/10.1016/j.tifs.2019.06.003

Bharathiraja B, Chakravarthy M, Kumar RR, Yogendran D, Yuvaraj D, Jayamuthunagai J, Kumar RP, Palani S (2015) Aquatic biomass (algae) as a future feed stock for bio-refineries: a review on cultivation, processing and products. Renew Sust Energ Rev 47:634–653. https://doi.org/10.1016/j.rser.2015.03.047

Billakanti JM, Catchpole OJ, Fenton TA, Mitchell KA, MacKenzie AD (2013) Enzyme-assisted extraction of fucoxanthin and lipids containing polyunsaturated fatty acids from *Undaria pinnatifida* using dimethyl ether and ethanol. Process Biochem 48:1999–2008. https://doi.org/10.1016/j.procbio.2013.09.015

BP Global (2013) BP Energy Outlook 2030. https://www.bp.com/content/dam/bp/business-sites/en/global/corporate/pdfs/energy-economics/energy-outlook/bp-energy-outlook-2013.pdf

Bruhn A, Dahl J, Nielsen HB, Nikolaisen L, Rasmussen MB, Markager S, Olesen B, Arias C, Jensen PD (2011) Bioenergy potential of *Ulva lactuca*: Biomass yield, methane production and combustion. Bioresour Technol 102:2595–2604. https://doi.org/10.1016/j.biortech.2010.10.010

Bruton T, Lyons H, Lerat Y, Stanley M, Rasmussen MB (2009) A Review of the potential of marine algae as a source of biofuel in Ireland. Sustainable Energy Ireland. https://www.leanbusinessireland.ie/includes/documents/SEIalgae%20Report.pdf

Bubalo MC, Vidović S, Redovniković IR, Jokić S (2018) New perspective in extraction of plant biologically active compounds

by green solvents. Food Bioprod Process 109:52–73. https://doi.org/10.1016/j.fbp.2018.03.001
Budhiyanti SA, Raharjo S, Marseno DW, Lelana IYB (2012) Antioxidant activity of brown algae *Sargassum* species extract from the coastline of Java Island. AJABS 7(3):337–346. https://doi.org/10.3844/ajabssp.2012.337.346
Campo VL, Kawano DF, da Silva Jr. DB, Carvalho I, (2009) Carrageenans: biological properties, chemical modifications and structural analysis—a review. Carbohydr Polym 77(2):167–180. https://doi.org/10.1016/j.carbpol.2009.01.020
Cao C, Huang Q, Zhang B, Li C, Fu X (2018) Physicochemical characterization and *in vitro* hypoglycemic activities of polysaccharides from *Sargassum pallidum* by microwave-assisted aqueous two-phase extraction. Int J Biol Macromol 109:357–368. https://doi.org/10.1016/j.ijbiomac.2017.12.096
Castillo ASR, Guihéneuf S, Le Guével R, Biard P-F, Paquin L, Amrane A, Couvert A (2016) Synthesis and toxicity evaluation of hydrophobic ionic liquids for volatile organic compounds biodegradation in a two-phase partitioning bioreactor. J Hazard Mater 307:221–230. https://doi.org/10.1016/j.jhazmat.2015.12.043
Cesário MT, da Fonseca MMR, Marques MM, de Almeida MCMD (2018) Marine algal carbohydrates as carbon sources for the production of biochemicals and biomaterials. Biotechnol Adv 36:798–817. https://doi.org/10.1016/j.biotechadv.2018.02.006
Charoensiddhi S, Franco C, Su P, Zhang W (2015) Improved antioxidant activities of brown seaweed *Ecklonia radiata* extracts prepared by microwave-assisted enzymatic extraction. J Appl Phycol 27(5):2049–2058. https://doi.org/10.1007/s10811-014-0476-2
Chemat F, Vian MA, Cravotto G (2012) Green extraction of natural products: concept and principles. Int J Mol Sci 13:8615–8627. https://doi.org/10.3390/ijms13078615
Cox S, Abu-Ghannam N, Gupta S (2010) An assessment of the antioxidant and antimicrobial activity of six species of edible Irish seaweeds. Int Food Res J 17:205–220
Crini G, Lichtfouse E, Wilson LD, Morin-Crini N (2019) Conventional and non-conventional adsorbents for wastewater treatment. Environ Chem Lett 17:195–213. https://doi.org/10.1007/s10311-018-0786-8
Czyrnek-Delêtre MM, Rocca S, Agostini A, Giuntoli J, Murphy JD (2017) Life cycle assessment of seaweed biomethane, generated from seaweed sourced from integrated multi-trophic aquaculture in temperate oceanic climates. Appl Energy 196:34–50. https://doi.org/10.1016/j.apenergy.2017.03.129
da Costa E, Melo T, Moreira ASP, Alves E, Domingues P, Calado R, Abreu MH, Domingues MR (2015) Decoding bioactive polar lipid profile of the macroalgae *Codium tomentosum* from a sustainable IMTA system using a lipidomic approach. Algal Res 12:388–397. https://doi.org/10.1016/j.algal.2015.09.020
Dai Y, Meng Q, Mu W, Zhang T (2017) Recent advances in the applications and biotechnological production of mannitol. J Funct Foods 36:404–409. https://doi.org/10.1016/j.jff.2017.07.022
Dang TT, Vuong QV, Schreider MJ, Bowyer MC, Van Altena IA, Scarlett CJ (2017) Optimisation of ultrasound-assisted extraction conditions for phenolic content and antioxidant activities of the alga *Hormosira banksii* using response surface methodology. J Appl Phycol 29:3161–3173. https://doi.org/10.1007/s10811-017-1162-y
Deniaud-Bouët E, Kervarec N, Michel G, Tonon T, Kloareg B, Hervé C (2014) Chemical and enzymatic fractionation of cell walls from Fucales: Insights into the structure of the extracellular matrix of brown algae. Ann Bot 114(6):1203–1216. https://doi.org/10.1093/aob/mcu096
de Quirós ARB, Frecha-Ferreiro S, Vidal-Pérez AM, López-Hernández J (2010) Antioxidant compounds in edible brown seaweeds. Eur Food Res Technol 231:495–498. https://doi.org/10.1007/s00217-010-1295-6
Dinh TV, Saravana PS, Woo HC, Chun BS (2018) Ionic liquid-assisted subcritical water enhances the extraction of phenolics from brown seaweed and its antioxidant activity. Sep Purif Technol 196:287–299. https://doi.org/10.1016/j.seppur.2017.06.009
Domingues B, Abreu MH, Sousa-Pinto I (2015) On the bioremediation efficiency of *Mastocarpus stellatus* (Stackhouse) Guiry, in an integrated multi-trophic aquaculture system. J Appl Phycol 27:1289–1295. https://doi.org/10.1007/s10811-014-0414-3
Dumay J, Clément N, Morançais M, Fleurence J (2013) Optimization of hydrolysis conditions of *Palmaria palmata* to enhance R-phycoerythrin extraction. Bioresour Technol 131:21–27. https://doi.org/10.1016/j.biortech.2012.12.146
Eom SH, Kim YM, Kim SK (2012) Antimicrobial effect of phlorotannins from marine brown algae. Food Chem Toxicol 50(9):3251–3255. https://doi.org/10.1016/j.fct.2012.06.028
Ertem FC, Neubauer P, Junne S (2017) Environmental life cycle assessment of biogas production from marine macroalgal feedstock for the substitution of energy crops. J Clean Prod 140:977–985. https://doi.org/10.1016/j.jclepro.2016.08.041
FAO (2012) The state of world fisheries and aquaculture. https://www.fao.org/3/i2727e/i2727e.pdf
Fauster T, Schlossnikl D, Rath F, Ostermeier R, Teufel F, Toepfl S, Jaeger H (2018) Impact of pulsed electric field (PEF) pretreatment on process performance of industrial French fries production. J Food Eng 235:16–22. https://doi.org/10.1016/j.jfoodeng.2018.04.023
Fawzy MA, Gomaa M, Hifney AF, Abdel-Gawad KM (2017) Optimization of alginate alkaline extraction technology from *Sargassum latifolium* and its potential antioxidant and emulsifying properties. Carbohydr Polym 157:1903–1912. https://doi.org/10.1016/j.carbpol.2016.11.077
Fawzy S, Osman AI, Doran J, Rooney DW (2020) Strategies for mitigation of climate change. Environ Chem Lett. https://doi.org/10.1007/s10311-020-01059-w
Ferreres F, Lopes G, Gil-Izquierdo A, Andrade PB, Sousa C, Mouga T, Valentão P (2012) Phlorotannin extracts from Fucales characterized by HPLC-DAD-ESI-MS^n: approaches to Hyaluronidase inhibitory capacity and antioxidant Properties. Mar Drugs 10(12):2766–2781. https://doi.org/10.3390/md10122766
Fidelis GP, Camara RBG, Queiroz MF, Costa MSSP, Santos PC, Rocha HAO, Costa LS (2014) Proteolysis, NaOH and ultrasound-enhanced extraction of anticoagulant and antioxidant sulfated polysaccharides from the edible seaweed, *Gracilaria birdiae*. Molecules 19:18511–18526. https://doi.org/10.3390/molecules191118511
Filote C, Popa VI, Volf I (2017) Marine algae biomass potential for obtaining biofuels and bioproducts. In: Strategic Synergies in the Black Sea Basin, proceedings of the XIIth edition of the annual conference "The Academic Days of A.T.S.R.", pp 452–457
Filote C, Volf I, Santos SCR, Botelho CMS (2019) Bioadsorptive removal of Pb(II) from aqueous solution by the biorefinery waste of *Fucus spiralis*. Sci Total Environ 648:1201–1209. https://doi.org/10.1016/j.scitotenv.2018.08.210
Fleurence J, Le Coeur C, Mabeau S, Maurice M, Landrein A (1995) Comparison of different extractive procedures for proteins from the edible seaweeds *Ulva rigida* and *Ulva rotundata*. J Appl Phycol 7(6):577–582
Florindo C, Branco LC, Marrucho IM (2017) Development of hydrophobic deep eutectic solvents for extraction of pesticides from aqueous environments. Fluid Phase Equilib 448:135–142. https://doi.org/10.1016/j.fluid.2017.04.002
Flórez-Fernández N, López-García M, González-Muñoz MJ, Vilariño JML, Domínguez H (2017) Ultrasound-assisted extraction of fucoidan from *Sargassum muticum*. J Appl Phycol 29:1553–1561. https://doi.org/10.1007/s10811-016-1043-9

Francavilla M, Manara P, Kamaterou P, Monteleone M, Zabaniotou A (2015) Cascade approach of red macroalgae *Gracilaria gracilis* sustainable valorization by extraction of phycobiliproteins and pyrolysis of residue. Bioresour Technol 184:305–313. https://doi.org/10.1016/j.biortech.2014.10.147

Fung A, Hamid N, Lu J (2013) Fucoxanthin content and antioxidant properties of *Undaria pinnatifida*. Food Chem 136:1055–1062. https://doi.org/10.1016/j.foodchem.2012.09.024

Gajaria TK, Suthar P, Baghel RS, Balar NB, Sharnagat P, Mantri VA, Reddy CRK (2017) Integration of protein extraction with a stream of byproducts from marine macroalgae: a model forms the basis for marine bioeconomy. Bioresour Technol 243:867–873. https://doi.org/10.1016/j.biortech.2017.06.149

Gammone MA, D'Orazio N (2015) Anti-obesity activity of the marine carotenoid fucoxanthin. Mar Drugs 13:2196–2214. https://doi.org/10.3390/md13042196

Ganesan AR, Tiwari U, Rajauria G (2019) Seaweed nutraceuticals and their therapeutic role in disease prevention. Food Sci Hum Wellness 8:252–263. https://doi.org/10.1016/j.fshw.2019.08.001

Gao G, Clare AS, Rose C, Caldwell GS (2017) Eutrophication and warming-driven green tides (*Ulva rigida*) are predicted to increase under future climate change scenarios. Mar Pollut Bull 114:439–447. https://doi.org/10.1016/j.marpolbul.2016.10.003

Gereniu CRN, Saravana PS, Chun BS (2018) Recovery of carrageenan from Solomon Islands red seaweed using ionic liquid-assisted subcritical water extraction. Sep Purif Technol 196:309–317. https://doi.org/10.1016/j.seppur.2017.06.055

Getachew AT, Saravana PS, Cho YJ, Woo HC, Chun BS (2018) Concurrent extraction of oil from roasted coffee (*Coffea arabica*) and fucoxanthin from brown seaweed (*Saccharina japonica*) using supercritical carbon dioxide. J CO_2 Util 25:137–146. https://doi.org/https://doi.org/10.1016/j.jcou.2018.03.018

Ghadiryanfar M, Rosentrater KA, Keyhani A, Omid M (2016) A review of macroalgae production, with potential applications in biofuels and bioenergy. Renew Sust Energ Rev 54:473–481. https://doi.org/10.1016/j.rser.2015.10.022

Ghosh A, Anand KGV, Seth A (2015) Life cycle impact assessment of seaweed based biostimulant production from onshore cultivated *Kappaphycus alvarezii* (Doty) Doty ex Silva—is it environmentally sustainable? Algal Res 12:513–521. https://doi.org/10.1016/j.algal.2015.10.015

Goto M, Kanda H, Wahyudiono MS (2015) Extraction of carotenoids and lipids from algae by supercritical CO_2 and subcritical dimethyl ether. J Supercrit Fluids 96:245–251. https://doi.org/10.1016/j.supflu.2014.10.003

Grosso C, Valentão P, Ferreres F, Andrade PB (2015) Alternative and efficient extraction methods for marine-derived compounds. Mar Drugs 13(5):3182–3230. https://doi.org/10.3390/md13053182

Gude VG, Martinez-Guerra E (2018) Green chemistry with process intensification for sustainable biodiesel production. Environ Chem Lett 16:327–341. https://doi.org/10.1007/s10311-017-0680-9

Hahn T, Lang S, Ulber R, Muffler K (2012) Novel procedures for the extraction of fucoidan from brown algae. Process Biochem 47(12):1691–1698. https://doi.org/10.1016/j.procbio.2012.06.016

Hardouin K, Bedoux G, Burlot AS, Donnay-Moreno C, Bergé JP, Nyvall-Collén P, Bourgougnon N (2016) Enzyme-assisted extraction (EAE) for the production of antiviral and antioxidant extracts from the green seaweed *Ulva armoricana* (Ulvales, Ulvophyceae). Algal Res 16:233–239. https://doi.org/10.1016/j.algal.2016.03.013

Heo SJ, Jeon YJ, Lee JH, Kim HT, Lee KW (2003) Antioxidant effect of enzymatic hydrolyzate from a kelp. *Ecklonia cava* Algae 18(4):341–347. https://doi.org/10.4490/ALGAE.2003.18.4.341

Heo SJ, Park EJ, Lee KW, Jeon YJ (2005) Antioxidant activities of enzymatic extracts from brown seaweeds. Bioresour Technol 96:1613–1623. https://doi.org/10.1016/j.biortech.2004.07.013

Heo SJ, Ko SC, Cha SH, Kang DH, Park HS, Choi YU, Jeon YJ (2009) Effect of phlorotannins isolated from *Ecklonia cava* on melanogenesis and their protective effect against photo-oxidative stress induced by UV-B radiation. Toxicol Vitr 23(6):1123–1130. https://doi.org/10.1016/j.tiv.2009.05.013

Heo SJ, Yoon WJ, Kim KN, Ahn GN, Kang SM, Kang DH, Affan A, Oh C, Jung WK, Jeon YJ (2010) Evaluation of anti-inflammatory effect of fucoxanthin isolated from brown algae in lipopolysaccharide-stimulated RAW 264.7 macrophages. Food Chem Toxicol 48:2045–2051. https://doi.org/10.1016/j.fct.2010.05.003

Herrero M, Ibañez E (2018) Green extraction processes, biorefineries and sustainability: Recovery of high added-value products from natural sources. J Supercrit Fluids 134:252–259. https://doi.org/10.1016/j.supflu.2017.12.002

Hmelkov AB, Zvyagintseva TN, Shevchenko NM, Rasin AB, Ermakova SP (2018) Ultrasound-assisted extraction of polysaccharides from brown alga *Fucus evanescens*. Structure and biological activity of the new fucoidan fractions. J Appl Phycol 30:2039–2046. https://doi.org/10.1007/s10811-017-1342-9

Holdt SL, Kraan S (2011) Bioactive compounds in seaweed: functional food applications and legislation. J Appl Phycol 23:543–597. https://doi.org/10.1007/s10811-010-9632-5

Hosokawa M, Miyashita T, Nishikawa S, Emi S, Tsukui T, Beppu F, Okada T, Miyashita K (2010) Fucoxanthin regulates adipocytokine mRNA expression in white adipose tissue of diabetic/obese KK-A^Y mice. Arch Biochem Biophys 504:17–25. https://doi.org/10.1016/j.abb.2010.05.031

Hou X, Hansen JH, Bjerre AB (2015) Integrated bioethanol and protein production from brown seaweed *Laminaria digitata*. Bioresour Technol 197:310–317. https://doi.org/10.1016/j.biortech.2015.08.091

Hu X, Li Y, Li C, Fu Y, Cai F, Chen Q, Li D (2012) Combination of fucoxanthin and conjugated linoleic acid attenuates body weight gain and improves lipid metabolism in high-fat diet-induced obese rats. Arch Biochem Biophys 519:59–65. https://doi.org/10.1016/j.abb.2012.01.011

Huang J, Guo X, Xu T, Fan L, Zhou X, Wu S (2019) Ionic deep eutectic solvents for the extraction and separation of natural products. J Chromatogr A 1598:1–19. https://doi.org/10.1016/j.chroma.2019.03.046

Huang D, Quan Q, Zheng Y, Tang W, Zhang Z, Qiang X (2020) Dual-network design to enhance the properties of agar aerogel adsorbent by incorporating in situ ion cross-linked alginate. Environ Chem Lett 18:251–255. https://doi.org/10.1007/s10311-019-00932-7

Jung KA, Lim SR, Kim Y, Park JM (2013) Potentials of macroalgae as feedstocks for biorefinery. Bioresour Technol 135:182–190. https://doi.org/10.1016/j.biortech.2012.10.025

Kadam SU, Tiwari BK, O'Donnell CP (2013) Application of novel extraction technologies for bioactives from marine algae. J Agric Food Chem 61(20):4667–4675. https://doi.org/10.1021/jf400819p

Kadam SU, Tiwari BK, O'Donnell CP (2015) Extraction, structure and biofunctional activities of laminarin from brown algae. Int J Food Sci Technol 50:24–31. https://doi.org/10.1111/ijfs.12692

Kadam SU, O'Donnell CP, Rai DK, Hossain MB, Burgess CM, Walsh D, Tiwari BK (2015) Laminarin from Irish brown seaweeds *Ascophyllum nodosum* and *Laminaria hyperborea*: Ultrasound assisted extraction, characterization and bioactivity. Mar Drugs 13:4270–4280. https://doi.org/10.3390/md13074270

Kadam SU, Tiwari BK, Smyth TJ, O'Donnell CP (2015) Optimization of ultrasound assisted extraction of bioactive components

from brown seaweed *Ascophyllum nodosum* using response surface methodology. Ultrason Sonochem 23:308–316. https://doi.org/10.1016/j.ultsonch.2014.10.007

Kadam SU, Álvarez C, Tiwari BK, O'Donnell CP (2017) Extraction and characterization of protein from Irish brown seaweed *Ascophyllum nodosum*. Food Res Int 99:1021–1027. https://doi.org/10.1016/j.foodres.2016.07.018

Kawai S, Murata K (2016) Biofuel production based on carbohydrates from both brown and red macroalgae: recent developments in key biotechnologies. Int J Mol Sci 17:145–161. https://doi.org/10.3390/ijms17020145

Kazir M, Abuhassira Y, Robin A, Nahor O, Luo J, Israel A, Golberg A, Livney YD (2019) Extraction of proteins from two marine macroalgae, *Ulva sp.* and *Gracilaria sp.*, for food application, and evaluating digestibility, amino acid composition and antioxidant properties of the protein concentrates. Food Hydrocoll 87:194–203. https://doi.org/10.1016/j.foodhyd.2018.07.047

Keyrouz R, Abasq ML, Le Bourvellec C, Blanc N, Audibert L, ArGall E, Hauchard D (2011) Total phenolic contents, radical scavenging and cyclic voltammetry of seaweeds from Brittany. Food Chem 126(3):831–836. https://doi.org/10.1016/j.foodchem.2010.10.061

Khandelwal S, Tailor YK, Kumar M (2016) Deep eutectic solvents (DESs) as eco-friendly and sustainable solvent/catalyst systems in organic transformations. J Mol Liq 215:345–386. https://doi.org/10.1016/j.molliq.2015.12.015

Kim KN, Heo SJ, Kang SM, Ahn G, Jeon YJ (2010) Fucoxanthin induces apoptosis in human leukemia HL-60 cells through a ROS-mediated Bcl-xL pathway. Toxicol in Vitro 24:1648–1654. https://doi.org/10.1016/j.tiv.2010.05.023

Kim GY, Seo YH, Kim I, Han JI (2019) Co-production of biodiesel and alginate from *Laminaria japonica*. Sci Total Environ 673:750–755. https://doi.org/10.1016/j.scitotenv.2019.04.049

Klejdus B, Lojková L, Plaza M, Šnóblová M, Štěrbová D (2010) Hyphenated technique for the extraction and determination of isoflavones in algae: Ultrasound-assisted supercritical fluid extraction followed by fast chromatography with tandem mass spectrometry. J Chromatogr A 1217:7956–7965. https://doi.org/10.1016/j.chroma.2010.07.020

Kostas ET, White DA, Cook DJ (2017) Development of a bio-refinery process for the production of specialty chemical, biofuel and bioactive compounds from *Laminaria digitata*. Algal Res 28:211–219. https://doi.org/10.1016/j.algal.2017.10.022

Kostić MD, Divac VM (2019) Green solvents in organoselenium chemistry. Environ Chem Lett 17:897–915. https://doi.org/10.1007/s10311-018-00848-8

Kraan S (2013) Mass-cultivation of carbohydrate rich macroalgae, a possible solution for sustainable biofuel production. Mitig Adapt Strat Gl 18:27–46. https://doi.org/10.1007/s11027-010-9275-5

Krishnan A, Gopinath KP, Vo DVN, Malolan R, Nagarajan VM, Arun J (2020) Ionic liquids, deep eutectic solvents and liquid polymers as green solvents in carbon capture technologies: a review. Environ Chem Lett. https://doi.org/10.1007/s10311-020-01057-y

Kulshreshtha G, Burlot AS, Marty C, Critchley A, Hafting J, Bedoux G, Bourgougnon N, Prithiviraj B (2015) Enzyme-assisted extraction of bioactive material from *Chondrus crispus* and *Codium fragile* and its effect on *Herpes simplex* virus (HSV-1). Mar Drugs 13:558–580. https://doi.org/10.3390/md13010558

Kumar S, Gupta R, Kumar G, Sahoo D, Kuhad RC (2013) Bioethanol production from *Gracilaria verrucosa*, a red alga, in a biorefinery approach. Bioresour Technol 135:150–156. https://doi.org/10.1016/j.biortech.2012.10.120

Kumari P, Kumar M, Gupta V, Reddy CRK, Jha B (2010) Tropical marine macroalgae as potential sources of nutritionally important PUFAs. Food Chem 120:749–757. https://doi.org/10.1016/j.foodchem.2009.11.006

Kumari P, Reddy CRK, Jha B (2011) Comparative evaluation and selection of a method for lipid and fatty acid extraction from macroalgae. Anal Biochem 415:134–144. https://doi.org/10.1016/j.ab.2011.04.010

Langlois J, Sassi JF, Jard G, Steyer JP, Delgenes JP, Hélias A (2012) Life cycle assessment of biomethane from offshore-cultivated seaweed. Biofuel Bioprod Bior 6:387–404. https://doi.org/10.1002/bbb.1330

Lazar L, Talmaciu AI, Volf I, Popa VI (2016) Kinetic modeling of the ultrasound-assisted extraction of polyphenols from *Picea abies* bark. Ultrason Sonochem 32:191–197. https://doi.org/10.1016/j.ultsonch.2016.03.009

Lee KY, Mooney DJ (2012) Alginate: properties and biomedical applications. Prog Polym Sci 37:106–126. https://doi.org/10.1016/j.progpolymsci.2011.06.003

Lee SH, Jeon YJ (2013) Anti-diabetic effects of brown algae derived phlorotannins, marine polyphenols through diverse mechanisms. Fitoterapia 86(1):129–136. https://doi.org/10.1016/j.fitote.2013.02.013

Lee OK, Lee EY (2016) Sustainable production of bioethanol from renewable brown algae biomass. Biomass Bioenergy 92:70–75. https://doi.org/10.1016/j.biombioe.2016.03.038

Lee SY, Khoiroh I, Vo DVN, Kumar PS, Show PL (2020) Techniques of lipid extraction from microalgae for biofuel production: a review. Environ Chem Lett. https://doi.org/10.1007/s10311-020-01088-5

Le Guillard C, Bergé JP, Donnay-Moreno C, Bruzac S, Ragon JY, Baron R, Fleurence J, Dumay J (2016) Soft liquefaction of the red seaweed *Grateloupia turuturu* Yamada by ultrasound-assisted enzymatic hydrolysis process. J Appl Phycol 28:2575–2585. https://doi.org/10.1007/s10811-015-0788-x

Li Z, Wang B, Zhang Q, Qu Y, Xu H, Li G (2012) Preparation and antioxidant property of extract and semipurified fractions of *Caulerpa racemosa*. J Appl Phycol 24:1527–1536. https://doi.org/10.1007/s10811-012-9813-5

Liu J, Zhan X, Wan J, Wang Y, Wang C (2015) Review for carrageenan-based pharmaceutical biomaterials: favourable physical features *versus* adverse biological effects. Carbohydr Polym 121:27–36. https://doi.org/10.1016/j.carbpol.2014.11.063

Lorbeer AJ, Lahnstein J, Bulone V, Nguyen T, Zhang W (2015) Multiple-response optimization of the acidic treatment of the brown alga *Ecklonia radiata* for the sequential extraction of fucoidan and alginate. Bioresour Technol 197:302–309. https://doi.org/10.1016/j.biortech.2015.08.103

Lorbeer AJ, Lahnstein J, Fincher GB, Su P, Zhang W (2015) Kinetics of conventional and microwave-assisted fucoidan extractions from the brown alga, *Ecklonia radiata*. J Appl Phycol 27:2079–2087. https://doi.org/10.1007/s10811-014-0446-8

Lorbeer AJ, Charoensiddhi S, Lahnstein J, Lars C, Franco CMM, Bulone V, Zhang W (2017) Sequential extraction and characterization of fucoidans and alginates from *Ecklonia radiata*, *Macrocystis pyrifera*, *Durvillaea potatorum*, and *Seirococcus axillaris*. J Appl Phycol 29:1515–1526. https://doi.org/10.1007/s10811-016-0990-5

Magnusson M, Yuen AKL, Zhang R, Wright JT, Taylor RB, Maschmeyer T, de Nys R (2017) A comparative assessment of microwave assisted (MAE) and conventional solid-liquid (SLE) techniques for the extraction of phloroglucinol from brown seaweed. Algal Res 23:28–36. https://doi.org/10.1016/j.algal.2017.01.002

Manuhara GJ, Praseptiangga D, Riyanto RA (2016) Extraction and characterization of refined K-carrageenan of Red Algae [*Kappaphycus alvarezii* (Doty ex P.C. Silva, 1996)] originated from Karimun Jawa Islands. Aquat Procedia 7:106–111. https://doi.org/10.1016/j.aqpro.2016.07.014

Marinho G, Nunes C, Sousa-Pinto I, Pereira R, Rema P, Valente LMP (2013) The IMTA-cultivated Chlorophyta *Ulva spp.* as a sustainable ingredient in *Nile tilapia* (*Oreochromis niloticus*) diets. J Appl Phycol 25:1359–1367. https://doi.org/10.1007/s10811-012-9965-3

Marinho GS, Holdt SL, Birkeland MJ, Angelidaki I (2015) Commercial cultivation and bioremediation potential of sugar kelp, *Saccharina latissima*, in Danish waters. J Appl Phycol 27:1963–1973. https://doi.org/10.1007/s10811-014-0519-8

Marinho GS, Holdt SL, Angelidaki I (2015) Seasonal variations in the amino acid profile and protein nutritional value of *Saccharina latissima* cultivated in a commercial IMTA system. J Appl Phycol 27(5):1991–2000. https://doi.org/10.1007/s10811-015-0546-0

Martínez JM, Delso C, Álvarez I, Raso J (2019) Pulsed electric field permeabilization and extraction of phycoerythrin from *Porphyridium cruentum*. Algal Res 37:51–56. https://doi.org/10.1016/j.algal.2018.11.005

Masarin F, Cedeno FRP, Chavez EGS, de Oliveira LE, Gelli VC, Monti R (2016) Chemical analysis and biorefinery of red algae *Kappaphycus alvarezii* for efficient production of glucose from residue of carrageenan extraction process. Biotechnol Biofuels 9:122. https://doi.org/10.1186/s13068-016-0535-9

Masri MA, Jurkowski W, Shaigani P, Haack M, Mehlmer N, Brück T (2018) A waste-free, microbial oil centered cyclic bio-refinery approach based on flexible macroalgae biomass. Appl Energy 224:1–12. https://doi.org/10.1016/j.apenergy.2018.04.089

Matsson S, Christie H, Fieler R (2019) Variation in biomass and biofouling of kelp, *Saccharina latissima*, cultivated in the Arctic, Norway. Aquaculture 506:445–452. https://doi.org/10.1016/j.aquaculture.2019.03.068

McHugh DJ (2003) A Guide to the Seaweed Industry. FAO Fisheries Technical Paper. https://www.fao.org/3/a-y4765e.pdf

Menshova RV, Ermakova SP, Anastyuk SD, Isakov VV, Dubrovskaya YV, Kusaykin MI, Zvyagintseva TN (2014) Structure, enzymatic transformation and anticancer activity of branched high molecular weight laminaran from brown alga *Eisenia bicyclis*. Carbohydr Polym 99:101–109. https://doi.org/10.1016/j.carbpol.2013.08.037

Mezghani S, Csupor D, Bourguiba I, Hohmann J (2016) Characterization of phenolic compounds of *Ulva rigida* (Chlorophycae) and its antioxidant activity. Euro J Med Plants 12(1):1–9. https://doi.org/10.9734/ejmp/2016/22935

Mhatre A, Gore S, Mhatre A, Trivedi N, Sharma M, Pandit R, Anil A, Lali A (2019) Effect of multiple products extraction on biomethane potential of marine macrophytic green alga *Ulva lactuca*. Renew Energy 132:742–751. https://doi.org/10.1016/j.renene.2018.08.012

Michalak I, Chojnacka K (2014) Algal extracts: technology and advances. Eng Life Sci 14:581–591. https://doi.org/10.1002/elsc.201400139

Michalak I, Tuhy Ł, Chojnacka K (2015) Seaweed extract by microwave assisted extraction as plant growth biostimulant. Open Chem 13(1):1183–1195. https://doi.org/10.1515/chem-2015-0132

Mihranyan A (2011) Cellulose from Cladophorales Green Algae: from environmental problem to high-tech composite materials. J Appl Polym Sci 119:2449–2460. https://doi.org/10.1002/app.32959

Milledge JJ, Smith B, Dyer PW, Harvey P (2014) Macro-algae derived biofuel: a review of methods of energy extraction from seaweed biomass. Energies 7:7194–7222. https://doi.org/10.3390/en7117194

Mineur F, Arenas F, Assis J, Davies AJ, Engelen AH, Fernandes F, Malta EJ, Thibaut T, Nguyen TV, Vaz-Pinto F, Vranken S, Serrão EA, De Clerck O (2015) European seaweeds under pressure: consequences for communities and ecosystem functioning. J Sea Res 98:91–108. https://doi.org/10.1016/j.seares.2014.11.004

Mittal R, Tavanandi HA, Mantri VA, Raghavarao KSMS (2017) Ultrasound assisted methods for enhanced extraction of phycobiliproteins from marine macro-algae *Gelidium pusillum* (*Rhodophyta*). Ultrason Sonochem 38:92–103. https://doi.org/10.1016/j.ultsonch.2017.02.030

Miyashita K, Mikami M, Hosokawa M (2013) Chemical and nutritional characteristics of brown seaweed lipids: a review. J Funct Foods 5:1507–1517. https://doi.org/10.1016/j.jff.2013.09.019

Nakazawa Y, Sashima T, Hosokawa M, Miyashita K (2009) Comparative evaluation of growth inhibitory effect of stereoisomers of fucoxanthin in human cancer cell lines. J Funct Foods 1(1):88–97. https://doi.org/10.1016/j.jff.2008.09.015

Nishikawa S, Hosokawa M, Miyashita K (2012) Fucoxanthin promotes translocation and induction of glucose transporter 4 in skeletal muscles of diabetic/obese KK-A^Y mice. Phytomedicine 19:389–394. https://doi.org/10.1016/j.phymed.2011.11.001

Noreen A, Zia KM, Zuber M, Ali M, Mujahid M (2016) A critical review of algal biomass: a versatile platform of bio-base polyesters from renewable resources. Int J Biol Macromol 86:937–949. https://doi.org/10.1016/j.ijbiomac.2016.01.067

Obluchinskaya ED, Daurtseva AV, Pozharitskaya ON, Flisyuk EV, Shihov AN (2019) Natural deep eutectic solvents as alternatives for extracting phlorotannins from brown algae. Pharm Chem J 53:243–247. https://doi.org/10.1007/s11094-019-01987-0

Okolie CL, Akanbi TO, Mason B, Udenigwe CC, Aryee ANA (2019) Influence of conventional and recent extraction technologies on physicochemical properties of bioactive macromolecules from natural sources: a review. Food Res Int 116:827–839. https://doi.org/10.1007/s11094-019-01987-0

Park JN, Shin TS, Lee JH, Chun BS (2012) Production of reducing sugars from *Laminaria japonica* by subcritical water hydrolysis. APCBEE Procedia 2:17–21. https://doi.org/10.1016/j.apcbee.2012.06.004

Parsons S, Allen MJ, Abeln F, McManus M, Chuck CJ (2019) Sustainability and life cycle assessment (LCA) of macroalgae-derived single cell oils. J Clean Prod 232:1272–1281. https://doi.org/10.1016/j.jclepro.2019.05.315

Patle DS, Pandey A, Srivastava S, Sawarkar AN, Kumar S (2020) Ultrasound-intensified biodiesel production from algal biomass: a review. Environ Chem Lett. https://doi.org/10.1007/s10311-020-01080-z

Pechsiri JS, Thomas JBE, Risén E, Ribeiro MS, Malmström ME, Nylund GM, Jansson A, Welander U, Pavia H, Gröndahl F (2016) Energy performance and greenhouse gas emissions of kelp cultivation for biogas and fertilizer recovery in Sweden. Sci Total Environ 573:347–355. https://doi.org/10.1016/j.scitotenv.2016.07.220

Peng L, Fu D, Chu H, Wang Z, Qi H (2019) Biofuel production from microalgae: a review. Environ Chem Lett 18:285–297. https://doi.org/10.1007/s10311-019-00939-0

Pérez MJ, Falqué E, Domínguez H (2016) Antimicrobial action of compounds from Marine Seaweed. Mar Drugs 14:52. https://doi.org/10.3390/md14030052

Pérez-López P, Balboa EM, González-García S, Domínguez H, Feijoo G, Moreira MT (2014) Comparative environmental assessment of valorization strategies of the invasive macroalgae *Sargassum muticum*. Bioresour Technol 161:137–148. https://doi.org/10.1016/j.biortech.2014.03.013

Pham TPT, Cho CW, Yun YS (2010) Environmental fate and toxicity of ionic liquids: a review. Water Res 44:352–372. https://doi.org/10.1016/j.watres.2009.09.030

Polikovsky M, Fernand F, Sack M, Frey W, Müller G, Golberg A (2016) Towards marine biorefineries: selective proteins extractions from marine macroalgae *Ulva* with pulsed electric

fields. Innov Food Sci Emerg Technol 37:194–200. https://doi.org/10.1016/j.ifset.2016.03.013

Polikovsky M, Fernand F, Sack M, Frey W, Müller G, Golberg A (2019) *In silico* food allergenic risk evaluation of proteins extracted from macroalgae *Ulva sp.* with pulsed electric fields. Food Chem 276:735–744. https://doi.org/10.1016/j.foodchem.2018.09.134

Pollet P, Davey EA, Ureña-Benavides EE, Eckert CA, Liotta CL, Sheldon RA, Liotta CL (2014) Solvents for sustainable chemical processes. Green Chem 16:1034–1055. https://doi.org/10.1039/c3gc42302f

Popa V, Rusan V, Simionescu C (1974) Chimia algelor marine. Editura Academiei Republicii Socialiste România.

Popa V (1975) Cercetări în domeniul chimiei algelor marine (PhD Thesis). Institutul Politehnic "Gh Asachi", Facultatea de Chimie și Inginerie Chimică, p.14.

Ragonese C, Tedone L, Beccaria M, Torre G, Cichello F, Cacciola F, Mondello L (2014) Characterisation of lipid fraction of marine macroalgae by means of chromatography techniques coupled to mass spectrometry. Food Chem 145:932–940. https://doi.org/10.1016/j.foodchem.2013.08.130

Rahimi F, Tabarsa M, Rezaei M (2016) Ulvan from green algae *Ulva intestinalis*: optimization of ultrasound-assisted extraction and antioxidant activity. J Appl Phycol 28:2979–2990. https://doi.org/10.1007/s10811-016-0824-5

Raposo MFJ, Morais AMB, Morais RMSC (2015) Marine polysaccharides from algae with potential biomedical applications. Mar Drugs 13:2967–3028. https://doi.org/10.3390/md13052967

Rhein-Knudsen N, Ale MT, Meyer AS (2015) Seaweed hydrocolloid production: an update on enzyme assisted extraction and modification technologies. Marine Drugs 13:3340–3359. https://doi.org/10.3390/md13063340

Rinaudo M (2014) Biomaterials based on a natural polysaccharide: alginate. TIP 17(1):92–96. https://doi.org/10.1016/S1405-888X(14)70322-5

Robin A, Sack M, Israel A, Frey W, Müller G, Golberg A (2018) Deashing macroalgae biomass by pulsed electric field treatment. Bioresour Technol 255:131–139. https://doi.org/10.1016/j.biortech.2018.01.089

Rodriguez-Jasso RM, Mussatto SI, Pastrana L, Aguilar CN, Teixeira JA (2011) Microwave-assisted extraction of sulfated polysaccharides (fucoidan) from brown seaweed. Carbohydr Polym 86:1137–1144. https://doi.org/10.1016/j.carbpol.2011.06.006

Romero JB, Villanueva RD, Montano MNE (2008) Stability of agar in the seaweed *Gracilaria eucheumatoides* (Gracilariales, Rhodophyta) during postharvest storage. Bioresour Technol 99(17):8151–8155. https://doi.org/10.1016/j.biortech.2008.03.017

Ryu HJ, Oh KK (2017) Combined de-algination process as a fractionation strategy for valorization of Brown Macroalga *Saccharina japonica*. Appl Biochem Biotechnol 182:238–249. https://doi.org/10.1007/s12010-016-2323-1

Saluri M, Kaldmäe M, Tuvikene R (2019) Extraction and quantification of phycobiliproteins from the red alga *Furcellaria lumbricalis*. Algal Res 37:115–123. https://doi.org/10.1016/j.algal.2018.11.013

Sambusiti C, Bellucci M, Zabaniotou A, Beneduce L, Monlau F (2015) Algae as promising feedstocks for fermentative biohydrogen production according to a biorefinery approach: a comprehensive review. Renew Sust Energ Rev 44:20–36. https://doi.org/10.1016/j.rser.2014.12.013

Sanjeewa KKA, Kim EA, Son KT, Jeon YJ (2016) Bioactive properties and potentials cosmeceutical applications of phlorotannins isolated from brown seaweeds: a review. J Photochem Photobiol B 162:100–105. https://doi.org/10.1016/j.jphotobiol.2016.06.027

Santos SCR, Ungureanu G, Volf I, Boaventura RAR, Botelho CMS (2018) Macroalgae biomass as sorbent for metal ions. In: Popa V, Volf I (eds) Biomass as renewable raw material to obtain bioproducts of high-tech value. Elsevier, Amsterdam, The Netherlands, pp 69–112. https://doi.org/10.1016/B978-0-444-63774-1.00003-X

Saravana PS, Cho YJ, Park YB, Woo HC, Chun BS (2016) Structural, antioxidant, and emulsifying activities of fucoidan from *Saccharina japonica* using pressurized liquid extraction. Carbohydr Polym 153:518–525. https://doi.org/10.1016/j.carbpol.2016.08.014

Saravana PS, Getachew AT, Cho YJ, Choi JH, Park YB, Woo HC, Chun BS (2017) Influence of co-solvents on fucoxanthin and phlorotannin recovery from brown seaweed using supercritical CO_2. J Supercrit Fluids 120:295–303. https://doi.org/10.1016/j.supflu.2016.05.037

Saravana PS, Cho YN, Woo HC, Chun BS (2018) Green and efficient extraction of polysaccharides from brown seaweed by adding deep eutectic solvent in subcritical water hydrolysis. J Clean Prod 198:1474–1484. https://doi.org/10.1016/j.jclepro.2018.07.151

Saravana PS, Shanmugapriya K, Gereniu CRN, Chae SJ, Kang HW, Woo HC, Chun BS (2019) Ultrasound-mediated fucoxanthin rich oil nanoemulsions stabilized by κ-carrageenan: process optimization, bio-accessibility and cytotoxicity. Ultrason Sonochem 55:105–116. https://doi.org/10.1016/j.ultsonch.2019.03.014

Sathya R, Kanaga N, Sankar P, Jeeva S (2017) Antioxidant properties of phlorotannins from brown seaweed *Cystoseira trinodis* (Forsskål) C. Agardh Arab J Chem 10:2608–2614. https://doi.org/10.1016/j.arabjc.2013.09.039

Scaife MA, Merkx-Jacques A, Woodhall DL, Armenta RE (2015) Algae biofuels in Canada: status and potential. Renew Sust Energ Rev 44:620–642. https://doi.org/10.1016/j.rser.2014.12.024

Schiener P, Atack T, Wareing R, Kelly MS, Hughes AD (2016) The by-products from marine biofuels as a feed source for the aquaculture industry: a novel example of the biorefinery approach. Biomass Convers Biorefinery 6:281–287. https://doi.org/10.1007/s13399-015-0190-6

Schmid M, Guihéneuf F, Stengel DB (2016) Evaluation of food grade solvents for lipid extraction and impact of storage temperature on fatty acid composition of edible seaweeds *Laminaria digitata* (Phaeophyceae) and *Palmaria palmata* (Rhodophyta). Food Chem 208:161–168. https://doi.org/10.1016/j.foodchem.2016.03.123

Schmid M, Kraft LGK, van der Loos LM, Kraft GT, Virtue P, Nichols PD, Hurd CL (2018) Southern Australian Seaweeds: a promising resource for omega-3 fatty acids. Food Chem 265:70–77. https://doi.org/10.1016/j.foodchem.2018.05.060

Seghetta M, Hou X, Bastianoni S, Bjerre AB, Thomsen M (2016) Life cycle assessment of macroalgal biorefinery for the production of ethanol, proteins and fertilizers—a step towards a regenerative bioeconomy. J Clean Prod 137:1158–1169. https://doi.org/10.1016/j.jclepro.2016.07.195

Shang YF, Kim SM, Lee WJ, Um BH (2011) Pressurized liquid method for fucoxanthin extraction from *Eisenia bicyclis* (Kjellman) Setchell. J Biosci Bioeng 111(2):237–241. https://doi.org/10.1016/j.jbiosc.2010.10.008

Shao P, Qin M, Han L, Sun P (2014) Rheology and characteristics of sulfated polysaccharides from chlorophytan seaweeds *Ulva fasciata*. Carbohydr Polym 113:365–372. https://doi.org/10.1016/j.carbpol.2014.07.008

Shi Q, Wang A, Lu Z, Qin C, Hu J, Yin J (2017) Overview on the antiviral activities and mechanisms of marine polysaccharides from seaweeds. Carbohydr Res 453–454:1–9. https://doi.org/10.1016/j.carres.2017.10.020

Silva TH, Alves A, Popa EG, Reys LL, Gomes ME, Sousa RA, Silva SS, Mano JF, Reis RL (2012) Marine algae sulphated

polysaccharides for tissue engineering and drug delivery approaches. Biomatter 2(4):278–289. https://doi.org/10.4161/biom.22947

Silva M, Gomes F, Oliveira F, Morais S, Delerue-Matos C (2015) Microwave-assisted alginate extraction from Portuguese *Saccorhiza polyschides*—influence of acid pretreatment. Int J Chem Nucl Metall Mater Eng 9(1):30–33. https://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.688.198&rep=rep1&type=pdf

Singh S, Gaikwad KK, Park SI, Lee YS (2017) Microwave-assisted step reduced extraction of seaweed (*Gelidiella aceroso*) cellulose nanocrystals. Int J Biol Macromol 99:506–510. https://doi.org/10.1016/j.ijbiomac.2017.03.004

Skjermo J, Aasen IM, Arff J, Broch OJ, Carvajal A, Christie H, Forbord S, Olsen Y, Reitan KI, Rustad T, Sandquist J, Solbakken R, Steinhovden KB, Wittgens B, Wolff R, Handå A (2014) A new Norwegian bioeconomy based on cultivation and processing of seaweeds: opportunities and R&D needs. SINTEF Fish Aquacult. https://sintef.brage.unit.no/sintef-xmlui/handle/11250/2448125

Smit AJ (2004) Medicinal and pharmaceutical uses of seaweed natural products: a review. JAppl Phycol 16:245–262. https://doi.org/10.1023/B:JAPH.0000047783.36600.ef

Sousa AMM, Alves VD, Morais S, Delerue-Matos C, Gonçalves MP (2010) Agar extraction from integrated multitrophic aquacultured *Gracilaria vermiculophylla*: evaluation of a microwave-assisted process using response surface methodology. Bioresour Technol 101(9):3258–3267. https://doi.org/10.1016/j.biortech.2009.12.061

Stabili L, Acquaviva MI, Biandolino F, Cavallo RA, De Pascali SA, Fanizzi FP, Narracci M, Petrocelli A, Cecere E (2012) The lipidic extract of the seaweed *Gracilariopsis longissima* (Rhodophyta, Gracilariales): a potential resource for biotechnological purposes? N Biotechnol 29(3):443–450. https://doi.org/10.1016/j.nbt.2011.11.003

Stabili L, Acquaviva MI, Biandolino F, Cavallo RA, De Pascali SA, Fanizzi FP, Narracci M, Cecere E, Petrocelli A (2014) Biotechnological potential of the seaweed *Cladophora repestris* (Chlorophyta, Cladophorales) lipidic extract. N Biotechnol 31(5):436–444. https://doi.org/10.1016/j.nbt.2014.05.002

Sudhakar K, Mamat R, Samykano M, Azmi WH, Ishak WFW, Yusaf T (2018) An overview of marine macroalgae as bioresource. Renew Sust Energ Rev 91:165–179. https://doi.org/10.1016/j.rser.2018.03.100

Sunwoo IY, Ra CH, Jeong G, Jeong GT, Kim SK (2016) Evaluation of ethanol production and bioadsorption of heavy metals by various red seaweeds. Bioprocess Biosyst Eng 39:915–923. https://doi.org/10.1007/s00449-016-1571-3

Talmaciu AI, Volf I, Popa VI (2015) A comparative analysis of the "Green" techniques applied for polyphenols extraction from bioresources. Chem Biodivers 12:1635–1651. https://doi.org/10.1002/cbdv.201400415

Tang DYY, Yew GY, Koyande AK, Chew KW, Vo DVN, Show PL (2020) Green technology for the industrial production of biofuels and bioproducts from microalgae: a review. Environ Chem Lett. https://doi.org/10.1007/s10311-020-01052-3

Tedesco S, Stokes J (2017) Valorisation to biogas of macroalgal waste streams: a circular approach to bioproducts and bioenergy in Ireland. Chem Pap 71:721–728. https://doi.org/10.1007/s11696-016-0005-7

Tedesco S, Daniels S (2018) Optimisation of biogas generation from brown seaweed residues: compositional and geographical parameters affecting the viability of a biorefinery concept. Appl Energy 228:712–723. https://doi.org/10.1016/j.apenergy.2018.06.120

Thamke VR, Chaudhari AU, Tapase SR, Paul D, Kodam KM (2019) *In vitro* toxicological evaluation of ionic liquids and development of effective bioremediation process for their removal. Environ Pollut 250:567–577. https://doi.org/10.1016/j.envpol.2019.04.043

Thomas NV, Kim SK (2013) Beneficial effects of marine algal compounds in cosmeceuticals. Mar Drugs 11(1):146–164. https://doi.org/10.3390/md11010146

Tierney MS, Smyth TJ, Rai DK, Soler-Vila A, Croft AK, Brunton N (2013) Enrichment of polyphenol contents and antioxidant activities of Irish brown macroalgae using food-friendly techniques based on polarity and molecular size. Food Chem 139(1–4):753–761. https://doi.org/10.1016/j.foodchem.2013.01.019

Trivedi TJ, Kumar A (2014) Efficient extraction of agarose from red algae using ionic liquids. Green Sustain Chem 4:190–201. https://doi.org/10.4236/gsc.2014.44025

Trivedi J, Aila M, Bangwal DP, Kaul S, Garg MO (2015) Algae based biorefinery—how to make sense? Renew Sust Energ Rev 47:295–307. https://doi.org/10.1016/j.rser.2015.03.052

Trivedi N, Baghel RS, Bothwell J, Gupta V, Reddy CRK, Lali AM, Jha B (2016) An integrated process for the extraction of fuel and chemicals from marine macroalgal biomass. Sci Rep 6:30728. https://doi.org/10.1038/srep30728

Uy SF, Easteal AJ, Farid MM, Keam RB, Conner GT (2005) Seaweed processing using industrial single-mode cavity microwave heating: a preliminary investigation. Carbohydr Res 340(7):1357–1364. https://doi.org/10.1016/j.carres.2005.02.008

Vanda H, Dai Y, Wilson EG, Verpoorte R, Choi YH (2018) Green solvents from ionic liquids and deep eutectic solvents to natural deep eutectic solvents. C R Chim 21:628–638. https://doi.org/10.1016/j.crci.2018.04.002

van Ginneken VJT, Helsper JPFG, de Visser W, van Keulen H (2011) Brandenburg WA Polyunsaturated fatty acids in various macroalgal species from north Atlantic and tropical seas. Lipids Health Dis 10(1):104. https://doi.org/10.1186/1476-511X-10-104

Vieira EF, Soares C, Machado S, Correia M, Ramalhosa MJ, Oliva-teles MT, Carvalho AP, Domingues VF, Antunes F, Oliveira TAC, Morais S, Delerue-Matos C (2018) Seaweeds from the Portuguese coast as a source of proteinaceous material: total and free amino acid composition profile. Food Chem 269:264–275. https://doi.org/10.1016/j.foodchem.2018.06.145

Vishchuk OS, Ermakova SP, Zvyagintseva TN (2011) Sulfated polysaccharides from brown seaweeds *Saccharina japonica* and *Undaria pinnatifida*: isolation, structural characteristics, and antitumor activity. Carbohydr Res 346:2769–2776. https://doi.org/10.1016/j.carres.2011.09.034

Vo T, Ngo D, Kim S (2012) Marine algae as a potential pharmaceutical source for anti-allergic therapeutics. Process Biochem 47:386–394. https://doi.org/10.1016/j.procbio.2011.12.014

Wan P, Yang X, Cai B, Chen H, Sun H, Chen D, Pan J (2015) Ultrasonic extraction of polysaccharides from *Laminaria japonica* and their antioxidative and glycosidase inhibitory activities. J Ocean Univ China 14(4):651–662. https://doi.org/10.1007/s11802-015-2648-3

Wang T, Jónsdóttir R, Ólafsdóttir G (2009) Total phenolic compounds, radical scavenging and metal chelation of extracts from Icelandic seaweeds. Food Chem 116(1):240–248. https://doi.org/10.1016/j.foodchem.2009.02.041

Wang T, Jónsdóttir R, Kristinsson HG, Hreggvidsson GO, Jónsson JÓ, Thorkelsson G, Ólafsdóttir G (2010) Enzyme-enhanced extraction of antioxidant ingredients from red algae *Palmaria palmata*. LWT Food Sci Technol 43:1387–1393. https://doi.org/10.1016/j.lwt.2010.05.010

Wang D, Yun EJ, Kim S, Kim DH, Seo N, An HJ, Kim J-H, Cheong NY, Kim KH (2016) Efficacy of acidic pretreatment for the saccharification and fermentation of alginate from brown macroalgae. Bioprocess Biosyst Eng 39:959–966. https://doi.org/10.1007/s00449-016-1575-z

Wei N, Quarterman J, Jin YS (2013) Marine macroalgae: an untapped resource for producing fuels and chemicals. Trends Biotechnol 31(2):70–77. https://doi.org/10.1016/j.tibtech.2012.10.009

Wijesekara I, Pangestuti R, Kim S-K (2011) Biological activities and potential health benefits of sulfated polysaccharides derived from marine algae. Carbohydr Polym 84:14–21. https://doi.org/10.1016/j.carbpol.2010.10.062

Wijesinghe WAJP, Jeon YJ (2012) Enzyme-assistant extraction (EAE) of bioactive components: a useful approach for recovery of industrially important metabolites from seaweeds: a review. Fitoterapia 83:6–12

Woo MN, Jeon SM, Kim HJ, Lee MK, Shin SK, Shin YC, Park YB, Choi MS (2010) Fucoxanthin supplementation improves plasma and hepatic lipid metabolism and blood glucose concentration in high-fat fed C57BL/6N mice. Chem Biol Interact 186:316–322. https://doi.org/10.1016/j.cbi.2010.05.006

Xia A, Jacob A, Herrmann C, Tabassum MR, Murphy JD (2015) Production of hydrogen, ethanol and volatile fatty acids from the seaweed carbohydrate mannitol. Bioresour Technol 193:488–497. https://doi.org/10.1016/j.biortech.2015.06.130

Yi YB, Lee JW, Chung Ch (2015) Conversion of plant materials into hydroxymethylfurfural using ionic liquids. Environ Chem Lett 13:173–190. https://doi.org/10.1007/s10311-015-0503-9

Youssouf L, Lallemand L, Giraud P, Soulé F, Bhaw-Luximon A, Meilhac O, D'Hellencourt CL, Jhurry D, Couprie J (2017) Ultrasound-assisted extraction and structural characterization by NMR of alginates and carrageenans from seaweeds. Carbohydr Polym 166:55–63. https://doi.org/10.1016/j.carbpol.2017.01.041

Yuan Y, Macquarrie DJ (2015a) Microwave assisted step-by-step process for the production of fucoidan, alginate sodium, sugars and biochar from *Ascophyllum nodosum* through a biorefinery concept. Bioresour Technol 198:819–827. https://doi.org/10.1016/j.biortech.2015.09.090

Yuan Y, Macquarrie D (2015b) Microwave assisted extraction of sulfated polysaccharides (fucoidan) from *Ascophyllum nodosum* and its antioxidant activity. Carbohydr Polym 129:101–107. https://doi.org/10.1016/j.carbpol.2015.04.057

Zaharudin N, Staerk D, Dragsted LO (2019) Inhibition of α-glucosidase activity by selected edible seaweeds and fucoxanthin. Food Chem 270:481–486. https://doi.org/10.1016/j.foodchem.2018.07.142

Zhang Z, Zhang Q, Wang J, Song H, Zhang H, Niu X (2010) Regioselective syntheses of sulphated porphyrans from *Porphyra haitanensis* and their antioxidant and anticoagulant activities *in vitro*. Carbohydr Polym 79:1124–1129. https://doi.org/10.1016/j.carbpol.2009.10.055