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Sustainable resource production for manufacturing bioactives from micro- and macroalgae: Examples from harvesting and cultivation in the Nordic region

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Abstract

Micro- and macroalgae are a great and important source of raw material for manufacturing of bioactives and ingredients for food, feed, cosmetics, or pharmaceuticals. Macroalgae (or seaweeds) have been harvested locally from wild stocks in smaller volumes for a long time, and a production chain based on cultivated seaweed for the harvest of considerably larger amounts is in progress for several species. Microalgae and cyanobacteria such as *Spirulina* have been produced in "backyard ponds" for use in food and feed also for a long time, and now we see the establishment of large production plants to control the cultivation process and increase the production yields. There is also a shift from harvesting or cultivation centered in warmer, sunnier areas to increasing exploitation of natural resources in temperate to boreal regions. In locations with strong seasonal variations in solar irradiance and temperatures, we need to develop procedures to maximize the biomass production in the productive seasons and ensure efficient stabilization of the biomass for year-round processing and product manufacturing. Industrialized biomass production and large-scale manufacturing of bioactives also mean that we must employ sustainable, cost-effective, and environmentally friendly processing methods, including stabilization and extraction methods such as ensiling and subcritical water extraction (SWE) and advanced analytic tools to characterize the products. These topics are focus areas of the Nordic Centre of Excellence (NCoE) NordAqua, and here we present a review of current activities in the field of micro- and macroalgae biomass production sectors illustrated with some of our experiences from the NordAqua consortium.

1 | INTRODUCTION

A growing need exists for food and feed ingredients such as proteins and marine oils, to satisfy an increasing, global population and to substitute the nonsustainable feed ingredients in a growing aquaculture industry. There is also an expanding interest for sustainable exploitation of natural resources and, at the same time, a growing concern for how we exploit them (Duffy et al., 2019). Aquatic environments provide increasing amounts of resources from wild seafood catch, harvesting of wild algae resources and aquaculture. In 2018, the global aquaculture sector produced 114.5 million tonnes of wet weight (ww) of various seafood, including 32.4 million tonnes of algae (wet weight, mostly macroalgae) at a value of USD 13.3 billion (FAO, 2020). China and other Asian countries are the major contributors with 97% of the aquatic plant production, but macroalgae farming is gaining more interest also in Europe and other Western countries. Cultivation of macroalgae has a long tradition in Asian countries like China, Indonesia, Japan, Korea, and the Philippines, and algae constitute a large and natural part of people's diet. A close relative to the kelp *Saccharina latissima* cultivated in Norway is *S. japonica* and the first attempts to cultivate *S. japonica* occurred in northern China in the 1930–1940s, with the breakthrough coming at the end of the 1950s with the horizontal longline method (Su et al., 2017). Approximately 220 species of seaweed are of commercial value, while the number of species that are intensively cultivated is relatively low, posing a challenge to finding new species that can offer novel products (Hafting et al., 2015). The most common seaweed taxa to cultivate are the brown algae *S. japonica* (kombu), *Undaria pinnatifida* (wakame), and *Sargassum fusiforme* (hiziki), together with the red algae *Euchema* spp. and *Kappaphycus alvarezii* (both for carrageenan), *Gracilaria* spp. (for agar) and *Porphyra/Pyropia* spp. (for nori).

Industrial production of microalgae is also increasing globally, and according to FAO, China accounted for almost all the 87 000 tonnes ww of farmed microalgae and cyanobacteria that were produced in 2018 (FAO, 2020). The global production of microalgae is somewhat larger than this number, and the understating is due to unavailable data from many producers and the present system of reporting microalgae outside aquaculture registers. In the EU report on Blue Biotechnology from 2018, “algae” are listed under the Blue economy emerging sector, and algae biomass production (mainly macroalgae) employed 14 000 people and had a value of EUR 1.69 billion in 2018 according to the industry itself (EU, 2018). Increased production and use of micro- and macroalgae are also followed by legislative issues, such as regulations on food and feed additives, pharmaceuticals, or biostimulants or cosmetics (Lähteenmäki-Uutela et al., 2021) and commercialization and patenting (Ritala et al., 2017).

If we shift our perspective from the global aqua industries, where algae-related economy is relatively moderate in terms of economic turnover, to research and technology, we see a different picture. There is an abundant library of knowledge about micro- and macroalgae to be found in published works over many years and not enough room for an extensive list here, but we have selected references to illustrate how the field is being developed both for micro- and macroalgae throughout the text (Buschmann et al., 2017; Garrido-Cardenas et al., 2018). Algae as a source for biofuel production sparked the interest in the last half of the 20th century, and financial support from the US Energy department was the engine of algae research for several decades (Roesijadi et al., 2010; Sheehan et al., 2009). In later years, significant effort has been directed towards production, processing, and characterization of algae biomass for fuel production again (Vassilev & Vassileva, 2016), but other applications are receiving more attention and there has also been a shift in the production companies from focus on biofuels to high-value, low-volume markets (Barsanti & Gualtieri, 2018; Chauton et al., 2015). Algae biomass and refined ingredients are now considered for human food consumption and nutraceuticals (Cotas et al., 2020; García et al., 2017; Vigani et al., 2015), pharmaceuticals (Barbosa et al., 2014; Galasso et al., 2019), cosmetics (Ariede et al., 2017), and animal feed (Øverland et al., 2019; Wan et al., 2019) or prebiotics (de Jesus Raposo et al., 2016). Furthermore, algae are also considered for large-scale processes such as water remediation, both in closed systems (Andreotti et al., 2020) and in the field (Fossberg et al., 2018), resource recirculation using macroalgae (Seghetta et al., 2016) or microalgae (Santos et al., 2020), or carbon capturing and climate change abatements (Laurens et al., 2020). Now that algae are being “domesticated” for intensive production, we see that the topic of genetics and breeding is rapidly evolving and introduction of gene editing tools is accelerating this field (Mikami, 2014; Nymark et al., 2016). Introduction of non-native seaweed species may lead to gene mixing from “crop-to-wild” and alter the wild-type genome, and like mono-species crops in agriculture, genetically uniform populations are vulnerable to diseases and pests (Loureiro et al., 2015). Gene sequencing of model species may also help us to understand the complex metabolic pattern which lead to synthesis of desired compounds (Lin & Qin, 2014).

Phototrophic micro- and macroalgae share many traits in terms of genealogy and cellular physiology, for example, they use light energy to fuel their cell metabolism, and harvest CO_2 and nutrients from the ambient water to build their cell constituents (Figure 1). As raw materials, they have in common a bulk biochemical profile of variable concentrations of proteins, carbohydrates, and lipids, and complementary compounds such as pigments (Novoveská et al., 2019), mycosporines (Llewellyn & Airs, 2010; Orfanoudaki et al., 2019), vitamins (Shannon & Abu-Ghannam, 2019), polyphenols/phlorotannins (Zolotareva et al., 2019), iodine (Roleda et al., 2018), and other minerals which are considered as highly valuable in nutritional and health aspects (Wells et al., 2017). Natural products from micro- and macroalgae remain largely unexplored compared to terrestrial agriculture plants. Nevertheless, there are several promising compounds from both sources that exhibit a wide array of bioactivities, including antioxidant, anti-inflammatory, antitumor, antiviral, antibacterial, and antimalarial properties (Michalak & Chojnacka, 2015).

There are also significant differences such as size (unicellular, microscopic algae vs. pluricellular, and large macroalgae), structural properties (different cell coatings or cell walls, and supportive materials) and life cycles. Microalgae have high growth rates and reproduce to a large extent by cell division, while macroalgae commonly grow over several seasons or years and usually reproduce sexually with, in some cases, quite complex processes. When discussing how to exploit macro- and microalgae in industrial terms, we can make use of some of these common traits in the processing part and explore, for example, cell wall crushing methods, stabilization, and biorefining protocols which may be applicable for both micro- and macroalgae biomass resources. Also, some of the interesting bioactives can come from both sources, for example, fucoxanthin from brown macroalgae or the heterokont lineage of microalgae (Kanazawa et al., 2008; Peng

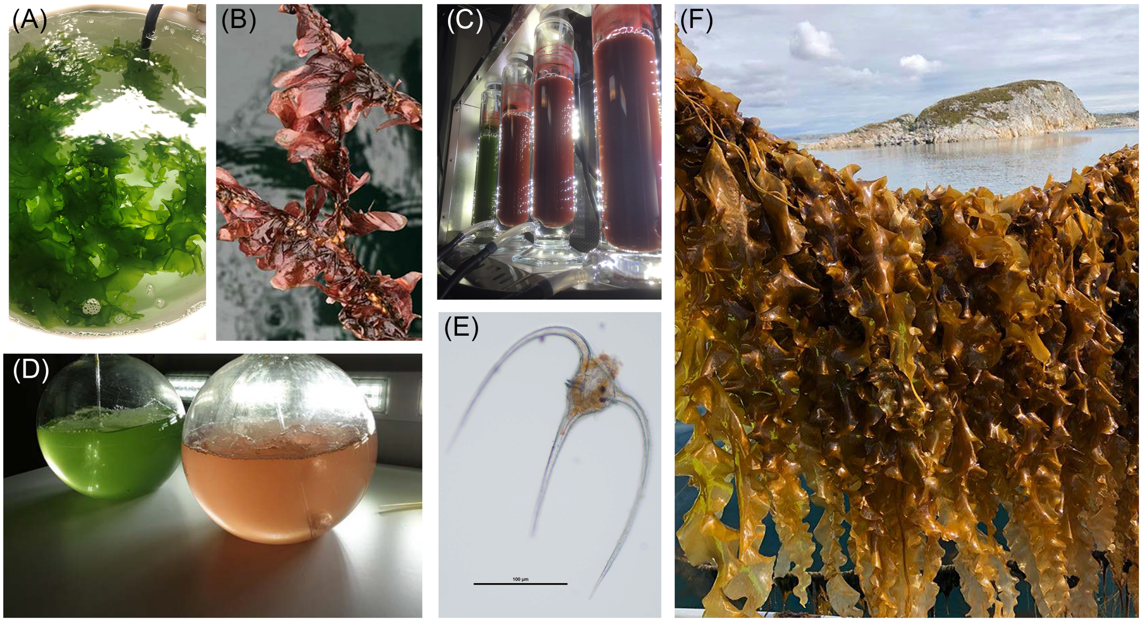

FIGURE 1 Morphological diversity and size variations in micro- and macroalgae. (A) Green macroalga *Ulva* sp. collected from the field and kept in lab, (B) red macroalga *Palmaria palmata* cultivated on nets in the sea, (C) green microalgae *Haematococcus lacustris* in lab bioreactors (green vegetative cells and astaxanthin-rich red spores), (E) cultures of green microalgae *Dunaliella* sp. and cryptophyte *Rhodomonas* sp. in lab, (F) microscope image of the dinoflagellate *Tripos* cf. *longipes* (scale bar 100 μm), (F) brown macroalgae *Saccharina latissima* cultivated on ropes at location in mid-Norway. Picture rights: Sintef

et al., 2011). For preparation of other compounds like phlorotannins, macroalgae yield a much higher output than microalgae (Agregán et al., 2018) and vice-versa, essential omega 3-oils are preferentially refined from microalgae. Other issues such as area usage, production systems, harvesting methods, and biomass yields, are fundamentally different between the two algae groups.

Here, we review the status of algae biomass production and applications in the Nordic region, exemplified with results from the Nordic Centre of Excellence (NCoE) NordAqua project activities and collaborations between the research groups. This project focuses on the exploitation of locally adapted strains and improved biomass production of microalgae using nutrient-rich side streams from other productions in photobioreactors, or sustainable cultivation and harvesting of macroalgae from natural resources. Further downstream in the value chain, we investigate stabilization and processing of the raw material using ensiling and optimized extraction using subcritical water extraction (SWE). Pre-processed biomass or extracted fractions are characterized using advanced analytics such as high-resolution nuclear magnetic resonance spectroscopy (HR-NMR) or mass spectroscopy to study changes in composition during different storage conditions. Refined fractions or compounds are also tested in the project (but outside the scope of this paper) using bioactivity assays to investigate potential applications. Finally, techno-economical improvements and LCA on algae biorefinery systems using nutrient recirculation and water remediation from other productions is used in the project as a tool to further understanding and optimizing the value chain.

2 | ADVANCING BIOBASED RESOURCE PRODUCTION IN THE NORDIC REGION

2.1 | Cultivation and biomass yield optimization

The Nordic countries have access to abundant water resources, spanning from brackish water in the Bothnic gulf to full seawater in the North Sea and along the Norwegian coast where coastal water merges with the waters from the North-East Atlantic Ocean. Sweden and Finland have particularly extensive inland lakes and river systems, and Norway also has abundant freshwater sources. However, the boreal location and climate make light a limited resource for long periods during winter. One way to increase the potential of algae biomass production in these areas, is to exploit the already adapted local strains (Cheregi et al., 2019; Pankratz et al., 2019). A collection of Nordic strains of microalgae and cyanobacteria is found within the collections of the Norwegian Culture Collection of Algae (NORCCA), the Finnish biological research centre HAMBI bank, and the Culture Collection at Umeå University (UMEA). Collections which contain macroalgae are few and lack an international coordination (Wade et al., 2020). For future projections of biomass production and area/nutrients exploitation, we must also consider the expected climate change which in this region of the world is expected to result in warmer, wetter, and windier conditions (Hanssen-Bauer et al., 2017). From the point of view of biomass production, higher water temperature may increase the growth of some species and extend the areas which are suitable (Marbà et al., 2017), but it may also restrict reproduction, growth, and distribution of other species (Clark et al., 2020; Khan et al., 2018; Park, 2017).

The Norwegian coastline covers more than 10° in latitude and provides a range of abiotic and biotic conditions for successful macroalgal farming. The cultivation is still in a preliminary phase, but seaweed farmers along the Norwegian coast cultivated and harvested 176 tonnes ww of brown seaweeds (kelp) in 2018. In 2019, the production was reduced to 117 tonnes ww while the commercial value had increased significantly, according to the Directorate of Fisheries (Fiskeridirektoratet, 2020). There are also several companies and research institutes cultivating macroalgae in the other Scandinavian countries, and the emerging interest for macroalgal biomass for multiple purposes is evident (Bak et al., 2018; Bruhn et al., 2016; Visch et al., 2020). The most common kelp cultivation practice today consists of collecting sporophytes (mother plants) near the cultivation site, and either induce fertility (especially outside the reproduction season) or use fertile tissue (sori) for releasing spores directly (Forbord et al., 2012). The juvenile seedlings are produced either by seeding the spores directly on a substrate (e.g., a rope) or using the spores to produce gametophyte cultures which may be upscaled and maintained for years until used for seeding (Forbord et al., 2018). The seeded substrates are incubated in a land-based hatchery for several weeks under favorable conditions until the seedlings are large enough for deployment at sea farms. The use of local populations for the production of seedlings is highly recommended in the Scandinavian countries at present, and breeding is not used as a tool to obtain desired traits in macroalgae due to the precautionary principle and possible negative influence on native species if the modified strains spread into the wild habitats (Goecke et al., 2020; Hasselström et al., 2018). However, there are several ongoing European research projects that are focusing on how to use breeding for value creation (e.g. The Horizon 2020 Blue Growth project GENIALG and The Research Council of Norway's Large-scale Programme on Aquaculture Research project Breed4Kelp2Feed). Developing cultivars for improved traits like high biomass production, increased content of valuable compounds and low affinity for biofouling could be of great importance for the future industry and are of current interest. Obtaining sporophytes that do not hybridize with natural populations is also essential for the survival of a responsible and sustainable industry, an approach the agriculture industry has used for several commercial species (e.g., banana, melon, grapes).

In addition to light and CO_2, algae use macronutrients such as nitrogen (N) and phosphor (P) to build important biomolecules and run their cell machinery. Dissolved, inorganic N and P is efficiently scavenged from the surrounding water, and both can become a limiting factor for cell growth. In microalgae, biomass production N and P are added in appropriate ratios, and in the laboratory, we can use commercially available, high-quality chemicals without any concerns regarding costs. However, in large-scale production increasing interest in nutrient recycling from other sources exists, both to reduce the costs and because it is a water remediation strategy. Cultivation substrate (mineral-rich medium) for algae cultivation in bioreactors or open systems can come from many sources such as household wastewater (Neveux et al., 2016; Wang et al., 2017), digestate from biogas production (Sebök & Hanelt, 2020; Yu et al., 2019), animal husbandry (Ji et al., 2013), food and dairy industry (Navarro-López et al., 2020; Van Den Hende et al., 2016), aquaculture (Andreotti et al., 2020; Marinho-Soriano et al., 2009) or greenhouse productions, to mention some. Also, both micro- and macroalgae are used as biofilters in productions of other aquatic organisms (Wang et al., 2007; Xing et al., 2018), integrated productions such as aquaponics (Han et al., 2019; Kotzen et al., 2019) or integrated multitrophic aquaculture (IMTA; Buck et al., 2018; Fossberg et al., 2018; Knowler et al., 2020).

2.2 | Case story: Cultivation of seaweed along the Norwegian coast: The importance of site selection and hatchery treatment for obtaining high biomass yield and protein content

Several methods exist to influence biomass yield and chemical composition of the harvestable macroalgal biomass. If the goal is to produce biomass with a high content of internal nitrogen-components such as protein, cultivation during periods of high ambient nitrate is essential (Forbord et al., 2020). This occurs during the period from late fall to spring along the Norwegian coastline, depending on the latitude (Broch et al., 2019). Nitrogen enrichment can also be accomplished by pumping deep water into land-based tank systems (Jevne et al., 2020) or by moving the cultivation lines to deeper depths when the nutrients are depleted in the surface layer due to microalgae blooms. However, if the main goal is to produce the highest harvestable yield, adequate light must be provided to the sporophytes, together with high ambient N, to increase their length and weight. The hatchery phase also impacts the biomass productivity. Incubation of seed lines with spores for 42 days in the hatchery before deployment at sea promotes the highest possible yield compared to seeding with gametophytes or juvenile sporophytes (Forbord et al., 2020). Recent experiments with the brown kelp *Saccharina latissima* along the Norwegian coast revealed an evident south-north gradient in biomass development during spring and summer, with the southern location reaching maximum frond length and biomass yield two months earlier than the northernmost location (Forbord et al., 2020). Irrespective of latitude, which clearly has a huge influence on growth and chemical content due to large differences in essential resources such as nutrients and light, site selection in general must be considered before deployment and large-scale cultivation.

2.3 | Biomass harvesting and preservation

Historically, seaweed harvesting has been performed for direct consumption from the shore, or in smaller amounts for drying and storage. The new plans for large-scale cultivation and harvesting in offshore areas require the development of tools and vessels for efficient harvesting, and efficient procedures for handling and storing of the harvested biomass until processing. Macroalgae biomass quality varies from one location to another depending on latitude and climatic conditions, and distinct seasonal variation occurs (Forbord et al., 2020), so harvesting must be planned accordingly. Seasonal fouling of macroalgae by other organisms is also a quality and processing problem (Førde et al., 2016; Visch, Nylund, & Pavia, 2020), but sometimes also an opportunity such as the epiphytic *Vertebrata lanosa* which is considered a flavoring agent similar to truffles (Bjordal et al., 2020).

Microalgae biomass production in lab- and pilot scales is performed under strictly controlled conditions using optimized nutrient media and light/temperature control. Under such circumstances, the biomass qualities are stable over time and the biochemical profile can be modulated to some extent by varying the cultivation conditions (Wang et al., 2019). However, large-scale facilities are often outdoors in open systems, and the biomass quality may undergo seasonal variations. Microalgae produced in suspension cultures must be separated from the water, which in most production settings implies removal of >95% water. Large-scale water removal is often performed through biomass settling with or without clays or chemical aids to enhance settlement and decanting of water (Barros et al., 2015; Branyikova et al., 2018; Leite & Daniel, 2020). Emerging technologies using nanomaterials such as charged ion oxide ions (Fraga-García et al., 2018) are introduced as a nondamaging separation method at lab scale, but economics and lack of knowledge regarding health and nanoparticles are restricting the use at present. Settling or flocculation is applied (Branyikova et al., 2018) and separators, centrifuges, and membrane filtration are used to further remove cultivation water (Drexler & Yeh, 2014) and the resulting algae slurry or paste may have 15%–25% biomass concentration. Further removal of water implies a high energetic investment and higher costs (Fasaei et al., 2018), and drying methods vary from low-tech and low-cost sun-drying, to high-tech and more costly spin flash (Ljubic et al., 2019) and drum dryers or lyophilizers. The high energy demand of drying, however, can be balanced by applying other, more energy-efficient methods.

Both micro- and macroalgae cells have large amounts of intracellular water, with important effects regarding quality conservation (Figure 2). Cell metabolism and enzymatic activities continue after harvesting if the raw material is not stabilized, and degradation soon starts. Microbial activity in harvested biomass is also a challenge, and

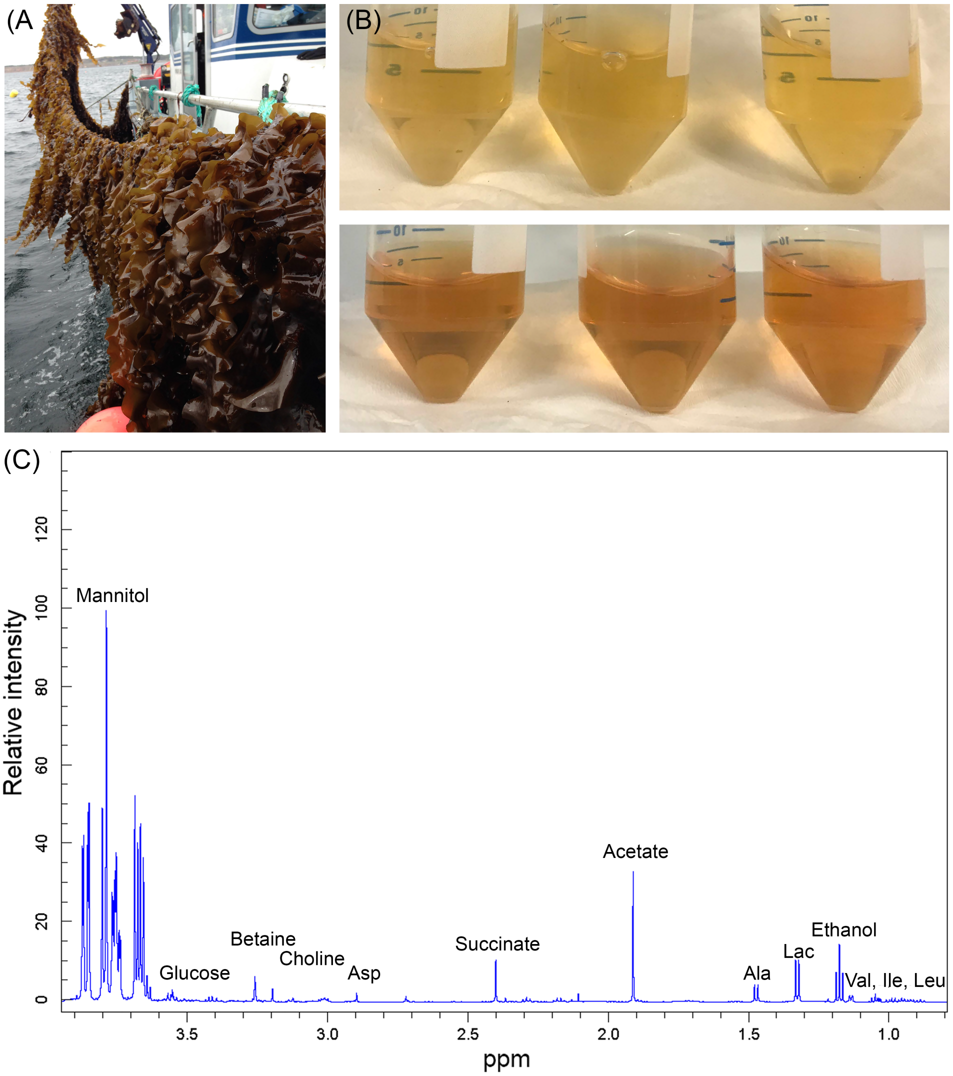

FIGURE 2 Stabilization of freshly harvested raw materials and quality optimization. (A) The macroalgae *Saccharina latissima* is harvested from ropes at the production site and brought to lab for experiments. (B) Leakage of cell constituents starts almost immediately after harvesting, and a test of storage conditions showed that substantial amounts of material is leaking out with water both at room temperature and under cold room storage. (C) ^{1}H NMR analysis of the leacheate showed that carbohydrates (especially mannitol), amino acids, and osmolytes are lost from the macroalgae biomass unless it is stabilized and stored properly as soon as possible after harvesting. Picture rights: Sintef

appropriate preservation techniques are required to ensure supply of high-quality products or processing. Blanching is used as preservation method for macroalgae to human consumption, and a recent study on the edible kelp *S. latissima* indicated that microbial activity can be suppressed, and salt/iodine content reduced by soaking the algae in hot water (Nielsen et al., 2020). Freezing or drying are known and applied technologies for seaweed stabilization, and comparison of convective air-drying (at 25°C, 40°C, and 70°C) and freeze-drying on the quality of *S. latissima* indicated that carbohydrate and amino acid profiles, polyphenol, and fucoxanthin content, ash, aroma, and flavor intensity were not significantly affected by the different drying methods within this range of temperatures. Furthermore, swelling capacity of air-dried samples was significantly lower compared to freeze-dried ones, indicating changes of the physico-chemical properties in air-dried seaweed leading to reduced capacity of the final product to rehydrate (Stévant et al., 2018). Raw material stability and conservation of valuable properties during storage of microalgae were investigated in freeze-dried samples of *Nannochloropsis salina* with different temperatures and with or without air (vacuum storage). The results showed lower yields and oxidative effects on carotenoids and other lipids (Safafar et al., 2017). Ensiling is currently being investigated as a promising and simple conservation method for both micro- (Wahlen et al., 2020) and macroalgae (Gallagher et al., 2017; Wu et al., 2018). Ensiling is a commonly used method for the preservation of biomass for feed purposes, both from terrestrial (e.g., hay and grass) and marine origin (e.g., fish by-products). The main principle is to minimize the activity of deteriorating microorganisms using either added acid or natural acidification from lactic acid bacteria to lower the pH.

2.4 | Case story: Year-round supplies of macroalgae raw material and optimal conservation of the biomass

Year-round availability of stable raw material for further processing is important to facilitate growth in the macroalgae product sector. Some studies describe ensiling and fermentation of seaweeds for the production of biofuels (Herrmann et al., 2015; Sandbakken et al., 2018), food (Bruhn et al., 2019), or feeds (Campbell et al., 2020; Novoa-Garrido et al., 2020), but effects on valuable ingredients such as proteins, carotenoids, or phenols are generally not evaluated in such studies. Ensiling of *S. latissima* was therefore tested in the NordAqua project to evaluate this process to ensure supply of year-round availability of stable raw material for further processing and the effects of the treatment on the biochemical profile. During ensiling, lactic acid bacteria (LAB) ferment available carbohydrates, such as mannitol or glucose, into organic acids, mainly lactic acid. This leads to pH reduction, and microbial spoilage by other degrading bacteria is hindered (Chades et al., 2018; Wu et al., 2018). The outcome of ensiling depends on parameters such as temperature, time, type of acid, absence of oxygen, and the amount of LAB. It also depends on the physical integrity of the biomass (whole versus minced fronds) and contents of soluble carbohydrates (Milledge & Harvey, 2016).

Changes in quality of whole and cut *S. latissima* stored at different temperatures (4°C and 20°C), pressure (ambient and vacuum-packed), pH-adjustment, and added LAB were studied to better understand the chemical changes taking place in seaweed at different storage conditions. The quality was evaluated based on microbial analysis, protein content and composition, and content of carotenoids (such as fucoxanthin). In addition, NMR metabolomics on water extracts/drip loss was applied for a nontargeted analysis of changes taking place during the different storage conditions. ^{1}H NMR may give quantitative results on a wide range of metabolites in algae, such as carbohydrates, free amino acids, alcohols, osmolytes, and organic acids (Chauton et al., 2003). In this work, the drip loss samples were dominated by mannitol in early samplings and also in acidified samples where pH was adjusted to 4 (Figure 2). Based on the project results, ensiling of *S. latissima* is a promising technology for preservation of proteins, probably because mannitol is easily available for the fermentation activity resulting in pH decrease and further conservation of the biomass (Chades et al., 2018). LABs are not naturally present in high numbers in the harvested macroalgae, but addition of LAB inoculum ensures an efficient silage process where lactate is the dominating fermentation product. The results also showed that fucoxanthin and proteins did not leak out in significant amounts during the storage, while the protein content (expressed on a dry weight basis of algae) increased due to leakage of other compounds. Degradation of fucoxanthin, however, was apparent and the content was reduced to ca 50% of the initial content after six weeks of storage, even with pH adjustments.

2.5 | Processing and biorefinery preparations

Biomass processing is an important step in the value chain and the degree of processing span from almost nonprocessed "raw food" (i.e., microalgae paste or fresh seaweeds) via semi-processed (dried meal, dried nori) to highly processed and refined ingredients such as alginates or bioactives such as extracted carotenoids, LC-PUFA-rich oils, or hydrolyzed proteins (Afonso et al., 2019; Niccolai et al., 2019; Silva et al., 2020; Wells et al., 2017). Potential anti-nutritious compounds are also investigated, such as heavy metals or high iodine contents (Duinker et al., 2016). Depending on the starting material and the desired product, we can choose from a long list of biomass extraction protocols and very often they start from a known procedure such as e.g., the Bligh & Dyer protocol for lipid extraction which has been in use for more than half a century. This and other chemical extraction methods are often adapted to very small samples obtained from experimental lab work where the application of chemicals is limited and easily controlled (Fiset et al., 2017; Gorgich et al., 2020; Ryckebosch et al., 2012). Such protocols are not suitable for extraction of lipids for feed or food purposes due to the use of solvents such as methanol and chloroform, and for large-scale extraction we need alternatives which are both environmentally and economically sustainable.

With applications in the food and feed areas, we look for "green extraction" alternatives to avoid unhealthy chemicals (Dixon &

Wilken, 2018; Santoro et al., 2019) and instead use high temperature or pressure to increase the extraction yield. Supercritical fluid extraction using CO_2 has been investigated with micro- and macroalgae and may work well to extract nonpolar or low-polarity compounds (Gallego et al., 2018; Silva et al., 2020). Liquid extraction in combination with high pressure is being adapted for extraction of algae components, and can be used to extract, for example, carotenoids, phenols, and fatty acids (Esquivel-Hernández et al., 2017). This method can be targeted by using solvents with different polarity, and temperature/pressure changes, and the solvent efficiency also depends on the pretreatment with, for example, increased lutein-recovery from freeze-dried microalgae *Muriellopsis* sp. compared to spray-dried material subjected to supercritical extraction (Ruiz-Domínguez et al., 2020). SWE is an interesting option for recovering functional fractions from various biobased raw materials. Subcritical water is defined as the water that maintains its liquid state under adequate pressure at temperature between the boiling point 100°C and critical point 374°C. Water has a high polarity under regular conditions, but under subcritical conditions (high temperature and pressure) the dielectric constant of water is reduced, resulting in modification of the solvent properties. Depending on the temperature and pressure applied, SWE can extract both polar and nonpolar analytes. As a clean and green process with nonflammable and nontoxic solvents, short reaction time, and wide extraction capacity, SWE is a favorable technique for the extraction of valuable products from various biomasses, including algae (Saravana et al., 2016; Shitu et al., 2015; Zakaria & Kamal, 2016).

2.6 | Case: Processing and refining: Recovery of functional compounds from algae biomass by SWE

SWE has been used to recover functional compounds with various chemical properties from both micro- and macroalgae biomass. For example, antioxidant compounds such as polyphenols (Plaza et al., 2010; Vo Dinh et al., 2018; Zakaria & Kamal, 2016), functional polysaccharides including fucoidan (Saravana et al., 2016; Zhang et al., 2019), lipids such as eicosapentaenoic acid (EPA; Ho et al., 2018), as well as amino acids and sugars (Saravana et al., 2016) have been extracted using the SWE process. In addition, SWE has been applied in combination with ionic liquids to recover polyphenols, for example, from the brown macroalga *Saccharina japonica* (Vo Dinh et al., 2018). SWE has shown potential also for fractioning algae biomass into bio-oil, aqueous, and solid fractions for biofuel production (Thiruvenkadam et al., 2015).

Processing parameters, including temperature, pressure, reaction time, and solid to liquid ratio. Potential additives such as ethanol or methanol can affect significantly on the yield of the target compounds and functional properties of the extracts produced with SWE (Zakaria & Kamal, 2016). Among the processing parameters, temperature is regarded as the most important factor inducing significant differentiation in the extraction efficiency of water. For recovering polyphenols from algae biomass, temperatures between 110°C and 250°C with varying extraction times typically from 5 to 20 min have been applied (Plaza et al., 2010; Vo Dinh et al., 2018; Zakaria & Kamal, 2016). For example, high recoveries of ferulic, p-coumaric, and caffeic acid have been obtained by SWE of *Chlorella* sp. at 175°C with an extraction time of 5 min. The recoveries were higher in comparison to soxhlet extraction using methanol (Zakaria & Kamal, 2016). In general, the yield of polyphenols has been observed to increase with the increasing extraction temperature up to approximately 160°C–180°C, but temperatures higher than that may cause heat-induced degradation of sensitive compounds. On the other hand, it has been suggested, that SWE treatment of brown seaweed at temperatures over 180°C can result in the formation of antioxidant compounds due to Maillard caramelization and thermo-oxidation reactions (Plaza et al., 2010).

Extraction of lipids such as EPA with SWE, requires higher extraction temperatures compared to the recovery of polyphenols. SWE was optimized for the microalgae *Nannochloropsis gaditana* to maximize the lipid yield and EPA content (Ho et al., 2018) and the optimal parameters for recovering the lipid fraction with high EPA content were 236.54°C and 13.95 min. Optimal SWE conditions for extracting crude fucoidan with good functional properties from *S. japonica* has been found to be 127°C and 11.98 min (Saravana et al., 2016). High yields of amino acids and saccharides such as glucose, mannitol, and fructose from *S. japonica* has been reported at extraction temperature of 180°C with 5 min extraction time. In conclusion, SWE provides an interesting potential for the development of cascade extraction of several valuable fractions by modifying the solvent properties of water by temperature and pressure.

2.7 | Bioactive compounds in algae

Algal carotenoids have been extensively demonstrated to contain both antioxidant, anti-inflammatory, and anticancer activities (the latter perhaps as a result of the former two). Among them, fucoxanthin and astaxanthin have been shown to reduce oxidative stress and inflammation, limit metastatic potential, and kill cancer cells both in vitro and using animal models (Sathasivam & Ki, 2018). Phlorotannins are polyphenols with strong antioxidant and radical scavenging properties. They have been shown to have classical bioactive effects, such as antioxidant, anticancer, and anti-inflammatory activities (Cotas et al., 2020). Furthermore, they can be used as industrial antioxidants for food preservation as a safer and more ecological replacement for synthetic antioxidants (Freile-Pelegrín & Robledo, 2013; Michalak & Chojnacka, 2015).

Bioactive peptides underscore the untapped potential of algal and cyanobacterial metabolites as therapeutics. Several peptides have been used directly, modified, or conjugated to antibodies to treat cancer. For example, brentuximab vedotin is an antibody-conjugated version of the cytotoxic peptide dolastatin 10 from cyanobacteria. It has been approved to treat several hematological malignancies (Giordano et al., 2018). Defensins are antibacterial peptides that can supplement or potentially replace antibiotics, and they were efficiently produced in the green microalga *Chlorella ellipsoidea* (Bai et al., 2013). Similarly, Mycosporine-like amino acids are secondary metabolites found in a variety of algae with high UV-absorption capacities (Chrapusta et al., 2017). They can be used to produce safe, eco-friendly sun care products (Lawrence et al., 2018; Oren & Gunde-Cimerman, 2007).

The sulfonated polysaccharide fucoidan, which is derived from the cell walls of brown seaweeds, has a unique chemical structure and a range of bioactive properties. In addition to classical bioactivities, fucoidan has been shown to alleviate metabolic syndrome, protect the gastrointestinal tract, and benefit bone health (Wang et al., 2019). However, the specific bioactivities and the magnitudes thereof are likely a function of the exact chemical makeup of the molecule (i.e., the length and fucose/sulfate content), so reductive studies to elucidate its mechanisms of action are difficult to perform (Hu et al., 2010).

2.8 | Future prospects in cultivation and harvesting of algae in the Nordic areas

The present focus on natural resources and sustainable production of ingredients and bioactives from micro- and macroalgae has revitalized research and technology development for upscaled production and industrialization of biomass processing. The Nordic region has some advantages which should be exploited, such as access to state-of-the-art research infrastructure platforms and close collaboration with emerging industries, clean, and abundant water and exploitable resources from other industries.

Upscaled production of microalgae is progressing slowly in the Nordic countries, and seasonal climate challenges like cold and dark winters are handled using greenhouse infrastructure and novel light sources like LEDs. On the biology side, we can exploit the already adapted local strains and utilize them as starting points for optimized production of interesting bioactives. The most important bottleneck to solve regarding the macroalgae production in Norway and other Western countries is the market segment which is not yet mature enough to handle the biomass delivered from the upcoming large-scale cultivation. Without the market, the upscaling of production and development of automated equipment in association with this is challenging. Presently, this is difficult due to the strong correlation between biochemical content and variable environmental conditions during the cultivation period at sea. Site selection is thus crucial, and the optimal site is dependent on the desired end-product.

Both at Nordic and European level there is an increasing research focus on the composition, stability, and quality of different algae, as well as ingredients from this valuable biomass, from whole meal to refined compounds. Suitable post-harvesting preservation methods for the biomass should be chosen and in parallel with the market development, cost- and energy-efficient technology for producing sustainable end products is needed. "Green" biorefinery approaches using, for example, SWE for extraction of high-value and bulk products are important for future commercialization of algae products. In conclusion, there is a clear potential in compounds from both micro- and macroalgae for feed, food, or even human therapeutic use. However, despite the wide array of compounds with promising bioactivities, few products have made it to clinical trials, let alone commercial use. There is therefore a need to more systematic compound screening and bioprospecting studies to identify the most promising candidate compounds to develop into high-value ingredients or pharmaceutical and personal care products. This should be integrated into other applications (e.g. biofuel production) to streamline production, reduce costs, and waste and improve competitiveness in biorefinery.

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AUTHOR CONTRIBUTIONS

Matilde Skogen Chauton, Silje Forbord and Jorunn Skjermo planned and drafted the manuscript, Matilde Skogen Chauton and Silje Forbord wrote the main sections and Silje Forbord, Sari Mäkinen, Antonio Sarno, Rasa Slizyte, Revilija Mozuraityte, and Inger Beate Standal wrote corresponding sections of case studies and contributed to the main text. All authors read and consented to the submitted version of the manuscript.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

Afonso, N.C., Catarino, M.D., Silva, A.M.S. & Cardoso, S.M. (2019) Brown macroalgae as valuable food ingredients. *Antioxidants*, 8, 365.

Agregán, R., Munekata, P.E.S., Franco, D., Carballo, J., Barba, F.J. & Lorenzo, J.M. (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. *Medicine*, 5, 33.

Andreotti, V., Solimeno, A., Rossi, S., Ficara, E., Marazzi, F., Mezzanotte, V. et al. (2020) Bioremediation of aquaculture wastewater with the microalgae *Tetraselmis suecica*: semi-continuous experiments, simulation and photo-respirometric tests. *Science of The Total Environment*, 738, 139859.

Ariede, M., Candido, T., Morocho-Jácome, A., Velasco, M., Carvalho, J. & Baby, A. (2017) Cosmetic attributes of algae—A review. *Algal Research*, 25, 483–487.

Bai, L.L., Yin, W.B., Chen, Y.H., Niu, L.L., Sun, Y.R., Zhao, S.M. et al. (2013) A new strategy to produce a defensin: stable production of mutated NP-1 in nitrate reductase-deficient *Chlorella ellipsoidea*. *PLoS ONE*, 8, e54966.

Bak, U., 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 Research*, 33, 36–47.

Barbosa, M., Valentão, P. & Andrade, P.B. (2014) Bioactive compounds from macroalgae in the new millennium: implications for neurodegenerative diseases. *Marine Drugs*, 12, 4934–4972.

Barros, A.I., Gonçalves, A.L., Simões, M. & Pires, J.C.M. (2015) Harvesting techniques applied to microalgae: A review. *Renewable & Sustainable Energy Reviews*, 41, 1489–1500.

Barsanti, L. & Gualtieri, P. (2018) Is exploitation of microalgae economically and energetically sustainable? *Algal Research*, 31, 107–115.

Bjordal, M.V., Jensen, K.H. & Sjøtun, K. (2020) A field study of the edible red alga *Vertebrata lanosa* (Rhodophyta). *Journal of Applied Phycology*, 32, 671–681.

Branyikova, I., Prochazkova, G., Potocar, T., Jezkova, Z. & Branyik, T. (2018) Harvesting of microalgae by flocculation. *Fermentation*, 4, 93.

Broch, O.J., Alver, M.O., Bekkby, T., Gundersen, H., Forbord, S., Handå, A. et al. (2019) The kelp cultivation potential in coastal and offshore regions of Norway. *Frontiers in Marine Science*, 5, 529.

Bruhn, A., Brynning, G., Johansen, A., Lindegaard, M.S., Sveigaard, H.H., Aarup, B. et al. (2019) Fermentation of sugar kelp (*Saccharina latissima*)—effects on sensory properties, and content of minerals and metals. *Journal of Applied Phycology*, 31, 3175–3187.

Bruhn, A., Tørring, D.B., Thomsen, M., Canal-Vergés, P., Nielsen, M., Rasmussen, M. et al. (2016) Impact of environmental conditions on biomass yield, quality, and bio-mitigation of *Saccharina latissima*. *Aquaculture Environment Interactions*, 8, 619–636.

Buck, B.H., Troell, M.F., Krause, G., Angel, D.L., Grote, B. & Chopin, T. (2018) State of the art and challenges for offshore integrated multi-trophic aquaculture (IMTA). *Frontiers in Marine Science*, 5, 165.

Buschmann, A., Camus, C., Infante Rosselot, J., Neori, A., Israel, A., Hernández-González, M. et al. (2017) Seaweed production: overview of the global state of exploitation, farming and emerging research activity. *European Journal of Phycology*, 52, 391–406.

Campbell, M., Ortuño, J., Ford, L., Davies, D.R., Koidis, A., Walsh, P.J. et al. (2020) The effect of ensiling on the nutritional composition and fermentation characteristics of brown seaweeds as a ruminant feed ingredient. *Animals*, 10(6), 1019.

Chades, T., Scully, S.M., Ingvadottir, E.M. & Orlygsson, J. (2018) Fermentation of mannitol extracts from brown macroalgae by thermophilic *Clostridia*. *Frontiers in Microbiology*, 9, 1931.

Chauton, M.S., Optun, O.I., Bathen, F.T., Volent, Z., Gribbestad, I.S. & Johnsen, G. (2003) HR MAS 1H NMR spectroscopy analysis of whole cells of marine microalgae. *Marine Ecology Progress Series*, 256, 57–62.

Chauton, M.S., Reitan, K.I., Norsker, N.H., Tveteras, R. & Kleivdal, H.T. (2015) A techno-economic analysis of industrial production of marine microalgae as a source of EPA and DHA-rich raw material for aquafeed: research challenges and possibilities. *Aquaculture*, 436, 95–103.

Cheregi, O., Ekendahl, S., Engelbrektsson, J., Strömberg, N., Godhe, A. & Spetea, C. (2019) Microalgae biotechnology in Nordic countries—the potential of local strains. *Physiologia Plantarum*, 166, 438–450.

Chrapusta, E., Kaminski, A., Duchnik, K., Bober, B., Adamski, M. & Bialczyk, J. (2017) Mycosporine-like amino acids: potential health and beauty ingredients. *Marine Drugs*, 15(10), 326–355.

Clark, J.S., Poore, A.G.B., Coleman, M.A. & Doblin, M.A. (2020) Local scale thermal environment and limited gene flow indicates vulnerability of warm edge populations in a habitat forming macroalga. *Frontiers in Marine Science*, 7, 711.

Cotas, J., Leandro, A., Pacheco, D., Gonçalves, A.M.M. & Pereira, P. (2020) A comprehensive review of the nutraceutical and therapeutic applications of red seaweeds (Rhodophyta). *Life*, 10, 19.

de Jesus Raposo, M.F., de Morais, A.M.M.B. & de Morais, R.M.S.C. (2016) Emergent sources of prebiotics: seaweeds and microalgae. *Marine Drugs*, 14(2), 27.

Dixon, C. & Wilken, L.R. (2018) Green microalgae biomolecule separations and recovery. *Biores Bioprocess*, 5, 14.

Drexler, I.L.C. & Yeh, D.H. (2014) Membrane applications for microalgae cultivation and harvesting: a review. *Reviews in Environmental Science and Bio/Technology*, 13, 487–504.

Duffy, J.E., Benedetti-Cecchi, L., Trinanes, J., Muller-Karger, F.E., Ambo-Rappe, R., Boström, C. et al. (2019) Toward a coordinated global observing system for seagrasses and marine macroalgae. *Frontiers in Marine Science*, 6, 317.

Duinker, A., Roiha, I., Amlund, H., Dahl, L., Kögel, T., Maage, A. et al. (2016) Potential risks posed by macroalgae for application as feed and food - a Norwegian perspective. *National Institute of Nutrition and Seafood Research (NIFES) report* 24 p.

Esquivel-Hernández, D.A., Ibarra-Garza, I.P., Rodríguez-Rodríguez, J., Cuéllar-Bermúdez, S.P., Rostro-Alanis, M.J., Alemán-Nava, G.S. et al. (2017) Green extraction technologies for high-value metabolites from algae: a review. *Biofuels, Bioproducts & Biorefining*, 11, 215–231.

EU (2018) The 2018 annual economic report on EU blue economy. DOI https://doi.org/10.2771/305342.

FAO (2020) The state of world fisheries and aquaculture. 10.4060/ca9229en.

Fasaei, F., Bitter, J.H., Slegers, P.M. & van Boxtel, A.J.B. (2018) Techno-economic evaluation of microalgae harvesting and dewatering systems. *Algal Research*, 31, 347–362.

Fiset, C., Liefer, J., Irwin, A.J. & Finkel, Z.V. (2017) Methodological biases in estimates of macroalgal macromolecular composition. *Limnology and Oceanography: Methods*, 15, 618–630.

Fiskeridirektoratet (2020) Akvakulturstatistikk (tidsserier)-Alger (in Norwegian). 2020. http://www.fiskeridir.no/Akvakultur/Statistikk-akvakultur/Akvakulturstatistikktidsserier/

Forbord, S., Matsson, S., Bluhm, B., Broch, O., Handå, A., Metaxas, A. et al. (2020) Latitudinal, seasonal and depth-dependent variation in growth, chemical composition and biofouling of cultivated *Saccharina latissima* (Phaeophyceae) along the Norwegian coast. *Journal of Applied Phycology*, 32, 2215–2232.

Forbord, S., Skjermo, S., Arff, J., Handå, A., Reitan, K. & Bjerregaard, L. (2012) Development of *Saccharina latissima* (Phaeophyceae) kelp hatcheries with year-round production of zoospores and juvenile sporophytes on culture ropes for kelp aquaculture. *Journal of Applied Phycology*, 24, 393–399.

Forbord, S., Steinhovden, K., Rød, K., Handå, A. & Skjermo, J. (2018) Cultivation protocol for *Saccharina latissima*. In: Charrier, B.W.T. & Reddy, C.R.K. (Eds.) *Protocols for macroalgae research*. Taylor & Francis Group, USA: CRC Press, pp. 37–59.

Forbord, S., Steinhovden, K.B., Solvang, T., Handå, A. & Skjermo, J. (2020) Effect of seeding methods and hatchery periods on sea cultivation of *Saccharina latissima* (Phaeophyceae): a Norwegian case study. *Journal of Applied Phycology*, 32, 2201–2212.

Førde, H., Forbord, S., Handå, A., Fossberg, J., Arff, J., Johnsen, G. et al. (2016) Development of bryozoan fouling on cultivated kelp (*Saccharina latissima*) in Norway. *Journal of Applied Phycology*, 28, 1225–1234.

Fossberg, J., Forbord, S., Broch, O.J., Malzahn, A.M., Jansen, H., Handå, A. et al. (2018) The potential for upscaling kelp (*Saccharina latissima*) cultivation in salmon-driven integrated multi-trophic aquaculture (IMTA). *Frontiers in Marine Science*, 5, 418.

Fraga-García, P., Kubbutat, P., Brammen, M., Schwaminger, S. & Berensmeier, S. (2018) Bare iron oxide nanoparticles for magnetic harvesting of microalgae: from interaction behavior to process realization. *Nanomaterials*, 8, 292.

Freile-Pelegrín, Y. & Robledo, D. (2013) Bioactive phenolic compounds from algae. In: Hernández-Ledesma, B. & Herrero, M. (Eds.) *Bioactive Compounds from Marine Foods*, pp. New Jersey, NJ: John Wiley & Sons, Ltd, 113–129.

Galasso, C., Gentile, A., Orefice, I., Ianora, A., Bruno, A., Noonan, D.M. et al. (2019) Microalgal derivatives as potential nutraceutical and food supplements for human health: A focus on cancer prevention and interception. *Nutrients*, 11, 1226.

Gallagher, J.A., Turner, L.B., Adams, J.M.M., Dyer, P.W. & Theodorou, M.K. (2017) Dewatering treatments to increase dry matter content of the brown seaweed, kelp (*Laminaria digitata* ([Hudson] JV Lamouroux)). *Bioresource Technology*, 224, 662–669.

Gallego, R., Montero, L., Cifuentes, A., Ibáñez, E. & Herrero, M. (2018) Green extraction of bioactive compounds from microalgae. *Journal of Analysis and Testing*, 2, 109–123.

García, J.L., de Vicente, M. & Galán, B. (2017) Microalgae, old sustainable food and fashion nutraceuticals. *Microbial Biotechnology*, 10, 1017–1024.

Garrido-Cardenas, J.A., Manzano-Agugliaro, F., Acien-Fernandez, F.G. & Molina-Grima, E. (2018) Microalgae research worldwide. *Algal Research*, 35, 50–60.

Giordano, D., Costantini, M., Coppola, D., Lauritano, C., Núñez Pons, L., Ruocco, N. et al. (2018) Biotechnological applications of bioactive peptides from marine sources. *Adv Microb Physiol*. pp. 73, 171–220. https://dx.doi.org/10.1016/bs.ampbs.2018.05.002.

Goecke, F., Klemetsdal, G. & Ergon, Å. (2020) Cultivar development of kelps for commercial cultivation—past lessons and future prospects. *Frontiers Marine Sciences*, 7, 110.

Gorgich, M., Mata, T.M., Martins, A.A., Branco-Vieira, M. & Caetano, N.S. (2020) Comparison of different lipid extraction procedures applied to three microalgal species. *Energy Reports*, 6, 477–482.

Hafting, J.T., Craigie, J.S., Stengel, D.B., Loureiro, R.R., Buschmann, A.H., Yarish, C. et al. (2015) Prospects and challenges for industrial production of seaweed bioactives. *Journal of Phycology*, 51, 821–837.

Han, P., Lu, Q., Fan, L. & Zhou, W. (2019) A review on the use of microalgae for sustainable aquaculture. *Applied Sciences*, 9, 2377.

Hanssen-Bauer I, Førland E, Haddeland I, Hisdal H, Lawrence D, Mayer S, Nesje A, Nilsen JE, Sandven S, Sandø A, Sorteberg A, Ådlandsvik B (2017) Climate in Norway 2100– a knowledge base for climate adaptation. NCCS report no. 2/2015, 204 p.

Hasselström, L., Visch, W., Gröndahl, F., Nylund, G.M. & Pavia, H. (2018) The impact of seaweed cultivation on ecosystem services - a case study from the west coast of Sweden. *Marine Pollution Bulletin*, 133, 53–64.

Herrmann, C., FitzGerald, J., O'Shea, R., Xia, A., O'Kiely, P. & Murphy, J.D. (2015) Ensiling of seaweed for a seaweed biofuel industry. *Bioresource Technology*, 196, 301–313.

Ho, B.C.H., Kamal, S.M.M., Danquah, M.K. & Harun, R. (2018) Optimization of subcritical water extraction (SWE) of lipid and eicosapentaenoic acid (EPA) from *Nannochloropsis gaditana*. *BioMed Research International*, 8273581, 2018.

Hu, T., Liu, D., Chen, Y., Wu, J. & Wang, S. (2010) Antioxidant activity of sulfated polysaccharide fractions extracted from *Undaria pinnitafida* in vitro. *International Journal of Biological Macromolecules*, 46, 193–198.

Jevne, L.S., Forbord, S. & Olsen, Y. (2020) The effect of nutrient availability and light conditions on the growth and intracellular nitrogen components of land-based cultivated *Saccharina latissima* (Phaeophyta). *Frontiers in Marine Science*, 7, 914.

Ji, M.K., Kim, H.C., Sapireddy, V.R., Yun, H.S., Abou-Shanab, R.A., Choi, J. et al. (2013) Simultaneous nutrient removal and lipid production from pretreated piggery wastewater by *Chlorella vulgaris* YSW-04. *Applied Microbiology and Biotechnology*, 97, 2701–2710.

Kanazawa, K., Ozaki, Y., Hashimoto, T., Das, S., Matsushita, S., Hirano, M. et al. (2008) Commercial-scale preparation of biofunctional fucoxanthin from waste parts of brown sea algae *Laminaria japonica*. *Food Science and Technology Research*, 14, 573–582.

Khan, A.H., Levac, E., Van Guelphen, L., Pohle, G. & Chmura, G.L. (2018) The effect of global climate change on the future distribution of economically important macroalgae (seaweeds) in the Northwest Atlantic. *FACETS*, 3, 275–286.

Knowler, D., Chopin, T., Martinez-Espineira, R., Neori, A., Nobre, A., Noce, A. et al. (2020) The economics of integrated multi-trophic aquaculture: where are we now and where do we need to go? *Reviews in Aquaculture*, 12, 1579–1594. https://dx.doi.org/10.1111/raq.12399.

Kotzen, B., Emerenciano, M.G.C., Moheimani, N. & Burnell, G.M. (2019) Aquaponics: alternative types and approaches. In: Goddek, S., Joyce, A., Kotzen, B. & Burnell, G.M. (Eds.) *Aquaponics food production systems: combined aquaculture and hydroponic production Technologies for the Future*. Cham: Springer International Publishing, pp. 301–330.

Lähteenmäki-Uutela, A., Rahikainen, M., Camarena-Gómez, M.T., Piiparinen, J., Spilling, K. & Yang, B. (2021) European Union legislation on macroalgae products. *Aquaculture International*. https://doi.org/10.1007/s10499-020-00633-x.

Laurens, L.M.L., Lane, M. & Nelson, R.S. (2020) Sustainable seaweed biotechnology solutions for carbon capture, composition, and deconstruction. *Trends in Biotechnology*, 38, 1232–1244.

Lawrence, K.P., Long, P.F. & Young, A.R. (2018) Mycosporine-like amino acids for skin photoprotection. *Current Medicinal Chemistry*, 25, 5512–5527.

Leite, L.S. & Daniel, L.A. (2020) Optimization of microalgae harvesting by sedimentation induced by high pH. *Water Science and Technology*, 82, 1227–1236.

Lin, H. & Qin, S. (2014) Tipping points in seaweed genetic engineering: scaling up opportunities in the next decade. *Marine Drugs*, 12, 3025–3045.

Ljubic, A., Safafar, H. & Jacobsen, C. (2019) Recovery of microalgal biomass and metabolites from homogenized, swirl flash-dried microalgae. *Journal of Applied Phycology*, 31, 2355–2363.

Llewellyn, C.A. & Airs, R.L. (2010) Distribution and abundance of MAAs in 33 species of microalgae across 13 classes. *Marine Drugs*, 8, 1273–1291.

Loureiro, R., Gachon, C.M.M. & Rebours, C. (2015) Seaweed cultivation: potential and challenges of crop domestication at an unprecedented pace. *New Phytologist*, 206, 489–492.

Marbà, N., Krause-Jensen, D., Olesen, B., Christensen, P.B., Merzouk, A., Rodrigues, J. et al. (2017) Climate change stimulates the growth of the intertidal macroalgae *Ascophyllum nodosum* near the northern distribution limit. *Ambio*, 46, 119–131.

Marinho-Soriano, E., Sdena, N., Carneiro, M. & Pereira, D.C. (2009) Nutrients' removal from aquaculture wastewater using the macroalgae *Gracilaria birdiae*. *Biomass and Bioenergy*, 33, 327–331.

Michalak, I. & Chojnacka, K. (2015) Algae as production systems of bioactive compounds. *Engineering in Life Sciences*, 15, 160–176.

Mikami, K. (2014) A technical breakthrough close at hand: feasible approaches toward establishing a gene-targeting genetic transformation system in seaweeds. *Frontiers in Plant Science*, 5, 498–498.

Milledge, J.J. & Harvey, P.J. (2016) Ensilage and anaerobic digestion of *Sargassum muticum*. *Journal of Applied Phycology*, 28, 3021–3030.

Navarro-López, E., Ruíz-Nieto, A., Ferreira, A., Acién, F.G. & Gouveia, L. (2020) Biostimulant potential of *Scenedesmus obliquus* grown in brewery wastewater. *Molecules and Cells*, 25, 664.

Neveux, N., Magnusson, M., Mata, L., Whelan, A., de Nys, R. & Paul, N.A. (2016) The treatment of municipal wastewater by the macroalga *Oedogonium* sp. and its potential for the production of biocrude. *Algal Research*, 13, 284–292.

Niccolai, A., Chini Zittelli, G., Rodolfi, L., Biondi, N. & Tredici, M.R. (2019) Microalgae of interest as food source: biochemical composition and digestibility. *Algal Research*, 42, 101617.

Nielsen, C.W., Holdt, S.L., Sloth, J.J., Marinho, G.S., Saether, M., Funderud, J. et al. (2020) Reducing the high iodine content of *Saccharina latissima* and improving the profile of other valuable compounds by water blanching. *Food*, 9, 569.

Novoa-Garrido, M., Marcos, C.N., Travieso, M.D., Alcaide, E.M., Larsen, M. & Weisbjerg, M.R. (2020) Preserving *Porphyra umbilicalis* and *Saccharina latissima* as silages for ruminant feeding. *Animals*, 10, 1957.

Novoveská, L., Ross, M.E., Stanley, M.S., Pradelles, R., Wasiolek, V. & Sassi, J.F. (2019) Microalgal carotenoids: A review of production, current markets, regulations, and future direction. *Marine Drugs*, 17, 640.

Nymark, M., Sharma, A.K., Sparstad, T., Bones, A.M. & Winge, P. (2016) A CRISPR/Cas9 system adapted for gene editing in marine algae. *Scientific Reports*, 6, 24951.

Oren, A. & Gunde-Cimerman, N. (2007) Mycosporines and mycosporine-like amino acids: UV protectants or multipurpose secondary metabolites? *FEMS Microbiology Letters*, 269, 1–10.

Orfanoudaki, M., Hartmann, A., Karsten, U. & Ganzera, M. (2019) Chemical profiling of mycosporine-like amino acids in twenty-three red algal species. *Journal of Phycology*, 55, 393–403.

Øverland, M., Mydland, L.T. & Skrede, A. (2019) Marine macroalgae as sources of protein and bioactive compounds in feed for monogastric animals. *Journal of the Science of Food and Agriculture*, 99, 13–24.

Pankratz, S., Oyedun, A.O. & Kumar, A. (2019) Development of cost models of algae production in a cold climate using different production systems. *Biofuels, Bioproducts & Biorefining*, 13, 1246–1260.

Park, J. (2017) Implications of rising temperatures for gametophyte performance of two kelp species from Arctic waters. *Botanica Marina*, 60, 39–48.

Peng, J., Yuan, J.-P., Wu, C.-F. & Wang, J.-H. (2011) Fucoxanthin, a marine marotenoid present in brown seaweeds and diatoms: metabolism and bioactivities relevant to human health. *Marine Drugs*, 9, 1806–1828.

Plaza, M., Amigo-Benavent, M., del Castillo, M.D., Ibáñez, E. & Herrero, M. (2010) Facts about the formation of new antioxidants in natural samples after subcritical water extraction. *Food Research International*, 43, 2341–2348.

Ritala, A., Häkkinen, S.T., Toivari, M. & Wiebe, M.G. (2017) Single cell protein—state-of-the-art, industrial landscape and patents 2001–2016. *Frontiers in Microbiology*, 8, 2009.

Roesijadi G, Jones S, Snowden-Swan L, Zhu Y (2010) Macroalgae as a Biomass Feedstock: A Preliminary Analysis (Technical Report) | OSTI. GOV. Analysis, US Department of Energy Report PNNL—19944, 51 p.

Roleda, M.Y., Skjermo, J., Marfaing, H., Jónsdóttir, R., Rebours, C., Gietl, A. et al. (2018) Iodine content in bulk biomass of wild-harvested and cultivated edible seaweeds: inherent variations determine species-specific daily allowable consumption. *Food Chemistry*, 254, 333–339.

Ruiz-Domínguez, M.C., Marticorena, P., Sepúlveda, C., Salinas, F., Cerezal, P. & Riquelme, C. (2020) Effect of drying methods on lutein content and recovery by supercritical extraction from the microalga *Muriellopsis* sp. (MCH35) cultivated in the arid north of Chile. *Marine Drugs*, 18, 528.

Ryckebosch, E., Muylaert, K. & Foubert, I. (2012) Optimization of an analytical procedure for extraction of lipids from microalgae. *Journal of the American Oil Chemists' Society*, 89, 189–198.

Safafar, H., Langvad, S., Møller, P. & Jacobsen, C. (2017) Storage conditions affect oxidative stability and nutritional composition of freeze-dried *Nannochloropsis salina*: oxidation of dried *Nannochloropsis salina* during storage. *European Journal of Lipid Science and Technology*, 1600477. 119

Sandbakken, I.S., Sæther, M., Funderud, J. & Aasen, I.M. (2018) Acid preservation of *Saccharina latissima* for application as a carbon source for fermentation to biofuels and chemicals. *Journal of Applied Phycology*, 30, 3581–3588.

Santoro, I., Nardi, M., Benincasa, C., Costanzo, P., Giordano, G., Procopio, A. et al. (2019) Sustainable and selective extraction of lipids and bioactive compounds from microalgae. *Molecules*, 24, 4347.

Santos, F.M., Lopes, A.P., Vilar, V.J.P. & Pires, J.C.M. (2020) Microalgal growth and nutrient uptake in heavy metal polluted environments. In: *Encyclopedia of Marine Biotechnology*, pp. New Jersey, NJ: Wiley-Blackwell, 497–514.

Saravana, P.S., Choi, J.H., Park, Y.B., Woo, H.C. & Chun, B.S. (2016) Evaluation of the chemical composition of brown seaweed (*Saccharina japonica*) hydrolysate by pressurized hot water extraction. *Algal Research*, 13, 246–254.

Sathasivam, R. & Ki, J.S. (2018) A review of the biological activities of microalgal carotenoids and their potential use in healthcare and cosmetic industries. *Marine Drugs*, 16, 26.

Sebök, S. & Hanelt, D. (2020) Examining the capacity for cultivating marine macroalgae using process liquids from biogas digestate as nutrient source and cultivation medium. *Biomass and Bioenergy*, 142, 105762.

Seghetta, M., Tørring, D., Bruhn, A. & Thomsen, M. (2016) Bioextraction potential of seaweed in Denmark—an instrument for circular nutrient management. *Sci enceTotal Environment*, 563-564, 513–529.

Shannon, E. & Abu-Ghannam, N. (2019) Seaweeds as nutraceuticals for health and nutrition. *Phycologia*, 58, 563–577.

Sheehan, J., Dunahay, T., Benemann, J. & Roessler, P. (2009) *A look back at the U.S. department of energy's aquatic species program: biodiesel from Algae*, Vol. 580. Washington, DC: US Department of Energy

Shitu, A., Izhar, S. & Tahir, T. (2015) Sub-critical water as a green solvent for production of valuable materials from agricultural waste biomass: A review of recent work. *Global Journal of Environmental Science and Management*, 1, 255–264.

Silva, A., Silva, S.A., Carpena, M., Garcia-Oliveira, P., Gullón, P., Barroso, M. F. et al. (2020) Macroalgae as a source of valuable antimicrobial compounds: extraction and applications. *Antibiotics*, 9, 642.

Stévant, P., Indergård, E., Ólafsdóttir, A., Marfaing, H., Larssen, W.E., Fleurence, J. et al. (2018) Effects of drying on the nutrient content, physico-chemical and sensory characteristics of the edible kelp *Saccharina latissima*. *Journal of Applied Phycology*, 30, 2587–2599.

Su, L., Pang, S., Shan, T.F. & Li, X. (2017) Large-scale hatchery of the kelp *Saccharina japonica*: a case study experience at Lvshun in northern China. *Journal of Applied Phycology*, 29, 3003–3013.

Thiruvenkadam, S., Izhar, S., Yoshida, H., Danquah, M.K. & Harun, R. (2015) Process application of subcritical water extraction (SWE) for algal bio-products and biofuels production. *Applied Energy*, 154, 815–828.

Van Den Hende, S., Beyls, J., De Buyck, P.-J. & Rousseau, D.P.L. (2016) Food-industry-effluent-grown microalgal bacterial flocs as a bioresource for high-value phycochemicals and biogas. *Algal Research*, 18, 25–32.

Vassilev, S. & Vassileva, C. (2016) Composition, properties and challenges of algae biomass for biofuel application: an overview. *Fuel*, 181, 1–33.

Vigani, M., Parisi, C., Rodriguez-Cerezo, E., Barbosa, M.J., Sijtsma, L., Ploeg, M. et al. (2015) Food and feed products from micro-algae: market opportunities and challenges for the EU. *Trends in Food Science and Technology*, 42, 81–92.

Visch, W., Kononets, M., Hall, P.O.J., Nylund, G.M. & Pavia, H. (2020) Environmental impact of kelp (*Saccharina latissima*) aquaculture. *Marine Pollution Bulletin*, 155, 110962.

Visch, W., Nylund, G.M. & Pavia, H. (2020) Growth and biofouling in kelp aquaculture (*Saccharina latissima*): the effect of location and wave exposure. *Journal of Applied Phycology*, 32, 3199–3209.

Vo Dinh, T., Saravana, P.S., Woo, H.C. & Chun, B.S. (2018) Ionic liquid-assisted subcritical water enhances the extraction of phenolics from brown seaweed and its antioxidant activity. *Separation and Purification Technology*, 196, 287–299.

Wade, R., Augyte, S., Harden, M., Nuzhdin, S., Yarish, C. & Alberto, F. (2020) Macroalgal germplasm banking for conservation, food security and industry. *PLoS Biol*, 18, e3000641.

Wahlen, B.D., Wendt, L.M., Murphy, A., Thompson, V.S., Hartley, D.S., Dempster, T. et al. (2020) Preservation of microalgae, lignocellulosic biomass blends by ensiling to enable consistent year-round feedstock supply for thermochemical conversion to biofuels. *Frontiers in Bioengineering and Biotechnology*, 8, 316.

Wan, A.H.L., Davies, S.J., Soler-Vila, A., Fitzgerald, R. & Johnson, M.P. (2019) Macroalgae as a sustainable aquafeed ingredient. *Reviews in Aquaculture*, 11, 458–492.

Wang, H., C-f, L., Qin, C., Cao, S.-Q. & Ding, J. (2007) Using a macroalgae *Ulva pertusa* biofilter in a recirculating system for production of juvenile sea cucumber *Apostichopus japonicus*. *Aquacultural Engineering*, 36, 217–224.

Wang, J.H., Zhang, T.Y., Dao, G.H., Xu, X.Q., Wang, X.X. & Hu, H. (2017) Microalgae-based advanced municipal wastewater treatment for reuse in water bodies. *Applied Microbiology and Biotechnology*, 101, 2659–2675.

Wang, X., Fosse, H.K., Li, K., Chauton, M.S., Vadstein, O. & Reitan, K.I. (2019) Influence of nitrogen limitation on lipid accumulation and EPA and DHA content in four marine microalgae for possible use in aquafeed. *Frontiers in Marine Science*, 6, 95.

Wang, Y., Xing, M., Cao, Q., Ji, A., Liang, H. & Song, S. (2019) Biological activities of fucoidan and the factors mediating its therapeutic effects: A review of recent studies. *Marine Drugs*, 17, 183.

Wells, M.L., Potin, P., Craigie, J.S., Raven, J.A., Merchant, S.S., Helliwell, K. E. et al. (2017) Algae as nutritional and functional food sources: revisiting our understanding. *Journal of Applied Phycology*, 29, 949–982.

Wu, Z.-Z., Li, D.-Y. & Cheng, Y.-S. (2018) Application of ensilage as a green approach for simultaneous preservation and pretreatment of macroalgae *Ulva lactuca* for fermentable sugar production. *Clean Technologies and Environmental Policy*, 20, 2057–2065.

Xing, R., Ma, W.-w., Y-w, S., Cao X-b, S.C., Song H-x, S.Q. & G-f, Z. (2018) Growth and potential purification ability of *Nitzschia* sp. benthic diatoms in sea cucumber aquaculture wastewater. *Aquaculture Research*, 49, 2644–2652.

Yu, H., Kim, J. & Lee, C. (2019) Nutrient removal and microalgal biomass production from different anaerobic digestion effluents with chlorella species. *Scientific Reports*, 9, 6123.

Zakaria, S.M. & Kamal, S.M.M. (2016) Subcritical water extraction of bioactive compounds from plants and algae: applications in pharmaceutical and food ingredients. *Food Engineering Reviews*, 8, 23–34.

Zhang, J., Wen, C., Chen, M., Gu, J., Zhou, J., Duan, Y. et al. (2019) Antioxidant activities of *Sagittaria sagittifolia* L. polysaccharides with subcritical water extraction. *International Journal of Biological Macromolecules*, 134, 172–179.

Zolotareva, E.K., Mokrosnop, V.M. & Stepanov, S.S. (2019) Polyphenol compounds of macroscopic and microscopic algae. *International Journal on Algae*, 21, 5–24.

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