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 (ww 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 latisima 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 (Overland 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 (Seghetti 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 CO₂ 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 (Lewellyn & 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, antibacterial, and anti-malarial 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
et al., 2018). 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.

FIGURE 1 Morphological diversity and size variations in micro- and macroalgae. (A) Green macroalgae 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 Triplofus cf. longipes (scale bar 100 μm), (F) brown macroalgae Saccharina latissima cultivated on ropes at location in mid-Norway. Picture rights: Sintef

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 Bothnian 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; Hasselstrøm 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 CO₂, 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 macroalgae, 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](https://example.com/figure2.jpg)

**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 suppressed, and salt/iodine content reduced by soaking the algae in contents of soluble carbohydrates (Milledge & Harvey, 2016).

Physical integrity of the biomass (whole versus minced fronds) and absence of oxygen, and the amount of LAB. It also depends on parameters such as temperature, time, type of acid, 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. 1H 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; Nicolai 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 CO₂ 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 biomass, 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 macroalgae 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.

### ACKNOWLEDGMENTS

This work was funded by Nordforsk, project no. 82845 (NordAqua). The authors declare no conflict of interests.

### 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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How to cite this article: Chauton MS, Forbord S, Mäkinen S, et al. Sustainable resource production for manufacturing bioactives from micro- and macroalgae: Examples from harvesting and cultivation in the Nordic region. Physiologia Plantarum. 2021:1–12. https://doi.org/10.1111/ppl.13391