Bioresource Technology xxx (xxxx) xxx

Contents lists available at ScienceDirect

Bioresource Technology

journal homepage: www.elsevier.com/locate/biortech

Review

Nutraceutical productions from microalgal derived compounds via circular bioeconomy perspective

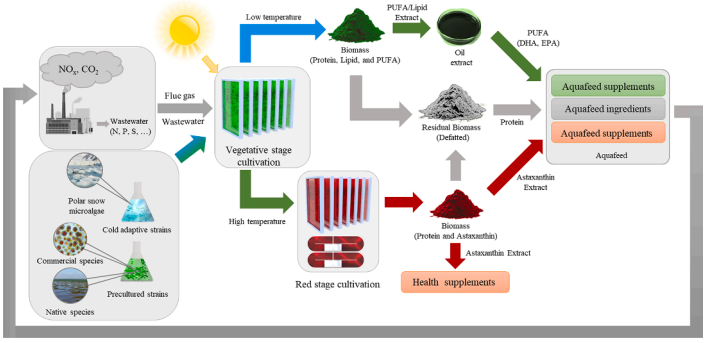
Menghour Huy, Ann Kristin Vatland, Gopalakrishnan Kumar *

Department of Chemistry, Bioscience, and Environmental Engineering, Faculty of Science and Technology, University of Stavanger, Box 8600 Forus, 4036 Stavanger, Norway

HIGHLIGHTS

- Algal cultivation during critical Scandinavian conditions is discussed.
- Nutraceuticals application of microalgae in Scandinavian perspective is presented.
- Microalga potential in aquafeed industries is noteworthy in circular economy context.

GRAPHICAL ABSTRACT



ARTICLE INFO

Keywords:
Indigenous strains
Astaxanthin
Polyunsaturated fatty acid
Protein
Microalgae

ABSTRACT

Circular bioeconomy has become a sustainable business model for commercial production that promises to reuse, recycle & recover while considering less environmental footprints in nutraceutical industries. Microalgae biotechnology has the synergy to bioremediate waste stream while generating high-value-added compounds such as astaxanthin, protein and polyunsaturated fatty acids that are potential compounds used in various industries, thus, the integration of this approach provides economic advantages. However, since the industrial production of these compounds is costly and affected by unstable climate in the Nordic regions such as low temperature, light intensity, and polar circle, the focus of biosynthesis has shifted from less tolerant commercial strains towards indigenous strains. Nutraceutical productions such as polyunsaturated fatty acids and protein can now be synthesized at low temperatures which significantly improve the industry's economy. In this review, the above-mentioned compounds with potential strains were discussed based on a Nordic region's perspective.

1. Introduction

In the COVID-19 era, most countries around the world are facing economic crises not excluding Scandinavian countries. Scandinavian countries' known economies today are based on petroleum drilling from the ocean, electronic devices, seafood exports, etc. Seafood exports are one of the traditional Scandinavian industries, especially Norway is still one of the largest salmon exporters until today (Marine Harvest, 2018).

* Corresponding author at: University of Stavanger, Norway.
E-mail address: gopalakrishnan.kumar@uis.no (G. Kumar).

https://doi.org/10.1016/j.biortech.2021.126575
Received 2 November 2021; Received in revised form 10 December 2021; Accepted 11 December 2021
Available online 16 December 2021

Recently, it has been reported that worldwide salmon production has increased and 73% of salmon production accounts as "farmed salmon". It is noteworthy to mention that nearly 43% of the production cost is related to feed (Marine Harvest, 2018). Therefore, part of the used feed is low-quality fish, which are directly used to feed the farmed salmon (Kim et al., 2019). The concern of these salmon's meat quality leads the Norwegian government to foresee microalgae biomass as one of the alternative solutions. Lead by example, Folvengaard AS, one Norwegian company has been given an agricultural innovation award 2020 by culturing microalgae from livestock manure for animal feed production (algae2future.no, 2020).

However, microalgae-based nutraceutical products are not cost-effective in the Nordic regions due to the outdoor climate requiring the microalgae to be cultivated in costly indoor photobioreactors instead of using cheaper technology such as open raceway pond cultivation or hybrid cultivation. The hybrid system is superior in the production of high-value added compound in which two-stage cultivation is required, however it's highly relied on climate (Narala et al., 2016). For instance, microalgae-based astaxanthin production in tropical countries could produce cheaper products by operating upstream processing outdoor where Nordic regions required massive energy supply for lighting and temperature control in order to reach a comparable production. However, in regard to product quality reliability, the indoor closed photobioreactor outmatch the outdoor facility due to the full parameter controlled in the system (Narala et al., 2016). In addition, these indoor closed photoreactors are also implemented by the other microalgae-based nutraceutical producers such as the Folvengaard AS, pilot-scale photobioreactor of CO2BIO in Norway (co2bio.no).

Most available commercial strains are generally not suitable for large-scale biomass cultivation in northern regions as optimal cultivation of those commercial strains needs artificial climate to satisfy industrial needs, which normally lead to a massive energy input throughout the process. As such addressed issues, researchers in Nordic countries believe that exploration of the potential of local strains will be beneficial to reduce the upstream processing cost in microalgae biotechnology; for instance, polyunsaturated fatty acid (PUFA) production can be obtained by cultivating local microalgae species at low temperature as well as biomass production with valuable lipid can also be generated via culturing in wastewater (Cheregi et al., 2019; Ferro et al., 2018; Hulatt et al., 2017a). In search of microalgae promising strain, microalgae consortia were sampled throughout these multiple northern parts of Scandinavian regions (Cheregi et al., 2019). Some microalgae strains were isolated from a different source from snowfield habitats (Hulatt et al., 2017a) and various northern Sweden water habitats (fresh water and wastewater) (Ferro et al., 2018) in the belief that local climate-adapted strains will benefit in the upstream of microalgae biotechnology.

2. Microalgae cultivation and challenges in Nordic regions

2.1. Parameters affecting biomass cultivation in the Nordic regions

In the Nordic regions, main challenges need to be overcome are the seasonal fluctuations of sunlight and temperature. Another important factor is the high amount of rain that affects the levels of salinity, nutrients, and pH when using outdoor ponds. Light intensity and day lengths are gradually decreasing when approaching northern areas. In regions of the Polar circle, there are midnight sun in the summer and long periods without daylight during the winter, with snow and ice covering the surfaces (Borowitzka and Vonshak, 2017). As a result, some arctic species such as *Chlorella* sp. have been suggested as a suitable species for biofuel in arctic regions due to the production of lipids at lower temperatures (Ahn et al., 2012). In northern areas, the freshwaters may contain low oxygen during winter (Leppi et al., 2016). The presence of microorganisms and various biological reactions further affects the dissolved gases such as oxygen and carbon dioxide (Guilini et al., 2012, Boetius and Wenzhöfer 2013). Cases of increased dissolved oxygen contributes to the removal of nitrogen and carbon dioxide by cyanobacteria and other organisms, fixing nitrogen gas into ammonium for use in amino acids and proteins. In addition, these organisms utilize compounds like sulphur, iron and phosphor, hence create organic source for other heterotrophic organisms (Falkowski, 2012). In a study on *Crypthecodinium cohnii*, triacylglycerol pathway was increasing at high oxygen levels (Diao et al., 2018). Investigation of well adapted microalgae strains could lead to other novel or improved sources of products with potential of creating new sustainable revenues.

2.2. Promising strains

There are eleven categories of most widely used strains, but *Spirulina* sp., *Chlorella* sp., *Haematococcus pluvialis,* and *Nannochloropsis* sp. are regarded as the most cultivated microalgae strains in terms of tonnes produced by shared companies in Europe (Araújo et al., 2021). Typically, cost-effectively producing biomass of these strains required high constant temperature via open cultivation (Béchet et al., 2014; De-Luca et al., 2019) in which climate is not suitable for largescale production in the Nordic regions. Alternatively, two cost-reduction scenarios of microalgae-based technology are foreseen as searching for local cold adaptive strains to reduce the temperature control cost or relying on light-independent heterotroph microalgae strains that produce denser biomass. In the belief that local adaptive strains would solve these challenges, researchers from Sweden isolated and tested microalgae strains from several areas of Northern Sweden including fresh and wastewater for the purpose of biomass production from wastewater. In the conclusion of the study, out of sixty-two strains, *Desmodesmus* sp., *Coelastrella* sp., and *Chlorella vulgaris* were the most representative species in the regions of which *Desmodesmus* sp. achieved the highest growth rate, also containing high amount of lipid (up to 36.7% of dried cell weight), which foresee as the most suitable strain for biomass generation from wastewater (Ferro et al., 2018).

On the other hand, with a different perspective and purposes, researchers in Norway sampled microalgae strains from many different habitats in the North regions aiming to obtain the robust cold adaptive strains to withstand the harsh climate. Species such as *Chlamydomonas pulsatilla, Chlamydomonas klinobasis, Chlamydomonas platystigma, Chlamydomonas malina*, *Tetraselmis chui, Koliella antarctica, Nannocloropsis gaditana, Nannochloropsis gaditana* were obtained and examined to produce high value-added compounds especially lipid and PUFA for fish feed oil supplements (Hulatt et al., 2017a). *Chlamydomonas* sp. isolated from this region has the capability of growing at a temperature as low as 6 °C (Hulatt et al., 2017a). This can be beneficial to cut down the necessary energy to heat the operating process if compared with the use of other commercial strains mentioned above. Therefore, *Chlamydomonas* sp. is one of the few strains that can be also explored for the production in heterotrophic metabolism (Zhang et al., 2019c) if it's more profitable.

Due to the unstable climate, it is not feasible to rely on a single strain for the whole year production; one strain can't withstand two extreme climate conditions in a year (Cheregi et al., 2019). Alternatively, two optimal strains culturing in two different periods of the year should be utilized to yield promising energy-efficient results (Cheregi et al., 2019).

2.3. Cultivation technologies

Open raceway cultivation and closed photobioreactors cultivation have served their benefits to different sectors (Narala et al., 2016). A large amount of biomass generation of open cultivation is cheaper than closed photobioreactors, which are the most seen technologies operating today (Singh and Sharma, 2012; Ye et al., 2018). Therefore, this technology has also been explored on large-scale CO_2 fixation in this recent carbon capture technology trench (Zhu et al., 2020). However, due to the open nature of these technologies, contamination of biomass can

hardly be controlled and therefore may affect the biomass quality (Narala et al., 2016; Singh and Sharma, 2012). The closed photobioreactor on the other hand has the advantages of contamination control and higher biomass density (Narala et al., 2016). Since critical parameters for product optimization are easier manipulated and controlled (Wang et al., 2012), it is the promising photobioreactor in the Nordic regions; One of the high-quality natural astaxanthin suppliers (Astareal) is also using the fully closed photobioreactor for the production in Sweden. A hybrid cultivation technology takes the advantage of both closed and open cultivation and operates as two-stage cultivation (Narala et al., 2016). Usually, different strategies for optimizing lipid and value-added production lead to two-stage cultivation; Sensitive parameters for biomass production are controlled in the first stage where desired compounds are induced at the second stage (Panis and Carreon, 2016; Todd Lorenz and Cysewsk, 2000). Several studies were also stated that this technology is superior and cost-effective compared to the other two cultivation systems (Narala et al., 2016; Panis and Carreon, 2016).

The case study showed that astaxanthin production in the Nordic region is using an energy-intensive process and is expensive when it comes to supplying high light illumination and high temperature required for the red stage (astaxanthin accumulation stage) of the facility. Whereas the cost-satisfying aim of this facility in the other region had led this technology to be able to utilize sunlight as the source for this red stage (Todd Lorenz and Cysewsk, 2000). For instance, astaxanthin production facilities in tropical countries are normally hybrid systems. The open nature of the second stage of the facility is compromised in parameters such as temperature- and light stability, a high risk of contamination, and high cost in the dewatering process (Béchet et al., 2014; De-Luca et al., 2019; Narala et al., 2016). Because of these drawbacks, Fuji chemical industry co., a natural astaxanthin company decided to move their production from a hybrid cultivation facility to a fully closed cultivation in Sweden to reach higher quality reliability (Starling, 2011). A similar scenario was found based on a techno-economic study (Panis and Carreon, 2016) where only 2.5% of astaxanthin was expected and up to around 4% of astaxanthin were promised by large-scale outdoor closed photoreactors (Hong et al., 2016). In addition to this, another large production of natural astaxanthin in China was also found to be operated in an outdoor fully closed cultivation system in 2013 (Algaeworldnews, 2015).

2.4. Circular bioeconomy perspective

Nutrients for microalgae cultivation in this region are normally chemical-based growth mediums. Wastewater used as a growth medium for microalgae cultivation is getting interesting since wastewater from fish is a growing challenge in Nordic countries as aquaculture is increasing also regarding new species (Paisley et al., 2010). Wastewater from aquaculture however is containing nutrients suitable for microalgae, such as phosphorous and nitrogen in addition to solid waste (Ackefors and Enell, 1994). Several techniques such as *Chlorella* sp. have been used, also together with solids, e.g., Moringa seeds to treat wastewater for nutrients (Hamid et al., 2014). The recent development in an increased awareness of circular economy makes the use of wastewater for microalgae an even more suitable alternative in order to reach economic values for the industry. Since wastewater is coming from both agriculture, municipal wastewater, and fisheries- these effluents are promising sources of nutrients to be utilized. Especially in the North and Norway, there are challenges due to the aquacultural water systems and a MIT based systems including microalgae as biofilters (Li et al., 2019) might be an interesting method to include, especially due to the current increased focus on bioeconomic and circular economic integrations (Nair and Paulose, 2014, Simas-Rodrigues et al. 2015, Thoré et al., 2021). The use of multitrophic systems might be an alternative method for the cost-efficient production of microalgae, lowering the energy cost and at the same time increasing the product price, enabling the development of sustainable business models.

Therefore, fish processing industry generates fish sludge is likely rich in nutrients (organic nitrogen source) and to be treated (Brod et al., 2017) could be a viable source of algal cultivation. Currently available technologies mostly refer to this fish sludges to be processed into fertilizer. Bioretur; a Norwegian company with expertise in sludge treatment is currently working on converting these waste streams into powder fertilizer (bioretur.no). Thus, a high nutrient source can also integrate into microalgae-based technology to produce high-value added products. One other Norwegian company, AlgaePro developed a circular business model, culturing microalgae via photoautotrophic conditions by utilizing agricultural sludge waste, CO_2 gas, and warm spilled water from industry to produce fish feed which is rich in omega-3 and proteins (algaepro.no). Another Norwegian fish feed company, Lerøy also formulate the enriched omega-3 (DHA and EPA) adapted microalgae strains in the feed to replace fish meal (leroyseafood.com) which is forecast to be decreased in the near future. With the pointed waste streams as well as the addressed industrial companies, integration of microalgae biotechnology in these waste stream bioremediations will close the loop of circular economy. The overall concept of circular bioeconomy of microalgae biorefinery in the Nordic regions can be seen in Fig. 1.

3. Nutraceutical application from microalgae biomass

3.1. Antioxidant

Astaxanthin is an antioxidant and therefore is widely used in the market as a supplement in products such as cosmetics, nutraceutical, and pharmaceutical industry and as a food and feed additive. Antioxidant activity of astaxanthin has been reported to be much higher in comparison to astaxanthin vitamin C, β-carotene, canthaxanthin, zeaxanthin, lutein, and α-tocopherol (Nagata et al., 2006, Borowitzka 2013, Koller et al., 2014, Pérez-López et al., 2014, Shah et al., 2016). Over 95 % of the astaxanthin available is produced synthetically, however synthetically produced astaxanthin has the lower antioxidant capacity and the safety of use has been discussed (Koller et al., 2014, Shah et al., 2016). Therefore, naturally produced, and isolated astaxanthin e.g from *Haematococcus pluvialis* is preferred for sales in high-end markets (Li et al., 2011, Shah et al., 2016). Astaxanthin biosynthesis starts from terpenoid precursors, isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), synthesized in the mevalonate pathway and non-mevalonate or 1-deoxy-D-xylulose 5-phosphate pathway, and includes several steps with main intermediates geranylgeranyl pyrophosphate and β-carotene before finalization by two hydroxylation and two ketolation reactions (Kirby and Keasling 2009, Zhang et al., 2013, Zhang et al., 2018).

3.2. Food or feed supplement

Animals and humans need essential amino acids added in their foods and feed respectively. (Becker 2013). Since protein is regarded as an expensive feed nutrient it can be applicable for the industry to develop alternative sources of feed (Craig et al., 2017). Several benefits have been reported from microalgae in feed, in regard to protein content, better growth, quality and flavor (Nagarajan et al., 2021). Further microalgal protein content is higher than ordinary sources of protein such as meat and dairy products and is considered a valuable and more sustainable source of protein and amino acids for both food and feed (Koyande et al., 2019, Chaves et al., 2021). *Chlorella* and *Spirulina* spp. are reported to contain approximately 70% protein (Wells et al., 2017) and according to WHO/FAO/UNU recommendations sufficient essential amino acids are required for a human balanced diet (Chronakis and Madsen 2011, Koyande et al., 2019). For example, the quantity of the amino acids' isoleucine, valine, lysine, tryptophan, methionine, threonine, and histidine was similar or higher in comparison to high-protein

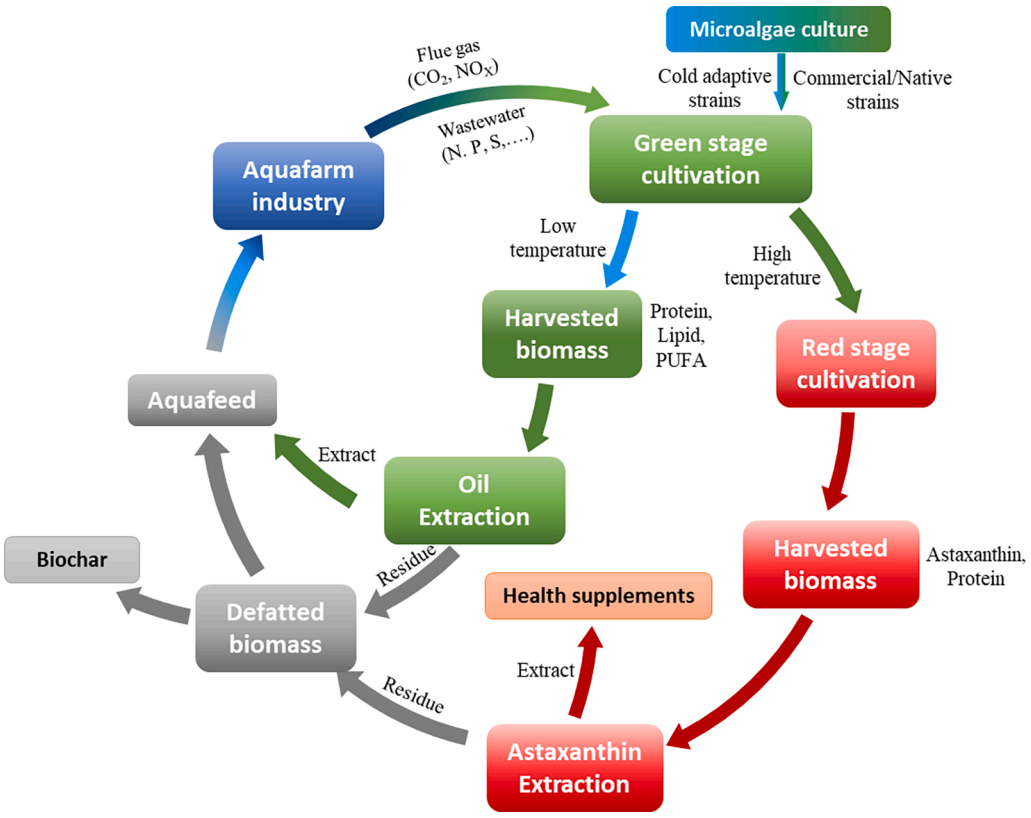


Fig. 1. Schematic chart of circular bioeconomy of microalgae biorefinery in the Nordic regions.

foods such as eggs and soybean (Koyande et al., 2019).

3.3. Long chain polyunsaturated fatty acids

Since human and animal biosynthesis rate of Long-Chain Polyunsaturated Fatty Acids (LC-PUFA) Eicosapentaenoic (EPA) and Docosahexaenoic (DHA) is low, these components must be added to the diet (Tocher 2015, Castro et al., 2016, van der Wurff et al., 2020). The majority of PUFA is produced in marine ecosystems and aquaculture. Although aquaculture is the largest supply of PUFA, at the same time there is an increasing demand in feed in the respective industry due to additives in feed (Jackson 2009). Microalgae is a potential new source that requires research in order to fill the gap of PUFA requirements versus the reported lacking available market supply and also more research is required regarding specific sources from microalgal species (Tocher et al., 2019).

The influence of PUFA has been linked to a high variety of health-related areas such as cardiovascular disease, depression, attention deficit disorder, autism, pregnancy, and cognitive development (Tocher et al., 2019). The LC-PUFA such as DHA and arachidonic acid are important constituents of the brain and have been related to beneficial effects on the nervous system (Innis 2007, Campoy et al., 2012). DHA, arachidonic acid, and EPA are involved in neurite growth, membrane fluidity, blood brain barrier and inflammation response (van der Wurff et al., 2020). By addition in animal feed, there is a direct increase of PUFA in the produced meat, in addition to health benefits for the animals such as improved cholesterol (Waszkiewicz-Robak et al., 2015) and increased fertility of pigs (Murphy et al., 2017) increased performance in lambs (Valença et al., 2021) and other benefits as reviewed by Nagarajan et al. (2021).

4. Desirable components from microalgae biomass

4.1. Protein production

Most majority of cultivated microalgae biomass is aimed towards bioenergy sectors until recent years, the research has shifted towards protein composition which is believed to be the sustainable animal feed ingredient (Kim et al., 2019; Nagappan et al., 2021; Priyadarshani and Rath, 2012; Tacon and Metian, 2015). Microalgae can synthesize protein in a response to the inorganic nitrogen source (NO_3^-, NO_2^-, NO, NH_4^+) and/or organic source (Urea and amino acids) in the aqua medium or assimilate N_2 to NH_4^+ using nitrogenase enzyme in some cases (Markou et al., 2014). Through this synthesis, they have been foreseen in the treatment of wastewater as well as flue gas emission (NO_x), which then transform into sustainable feeds (Munoz and Guieysse, 2006; Qie et al., 2019). The recent protein induction strategy is to use low flashing light frequency treatment shortly to maximize production before harvesting (Lima et al., 2021). Common species such as *Dunaliella* sp., Spi*rulina* sp., *Chlorella* sp., *Scendesmus* sp., *Desmosdesmus* sp., *Tetradesmus, Nannochloropsis,* have been studied for protein production.

Dunaliella sp. is one of the strains that does not have a cell wall which is one of the promised strains as protein-based production (Sui and Vlaeminck, 2020). Therefore, it can tolerate a high salinity level in which require less water footprint if ever to mass produce this strain (Sui and Vlaeminck, 2019). Under the specific condition, *Dunaliella* sp. can accumulate protein up to 80% protein biomass (64.8% ash-free biomass) (Sui and Vlaeminck, 2020, 2019). Due to the lack of cell wall, the non-protein nitrogen content is less than those with cell wall (nitrogen in cell wall affect the reported protein content) (Becker, 2007; Safi et al., 2013).

Spirulina sp. is one of the strains which superior in protein source and its nutritional value is also considered as a superfood. The protein content of this strain can be expected above 60% of dried weight (Becker, 2007; Ye et al., 2018), and mucopeptides in its cell wall can be

easily digested by fish (Nagappan et al., 2021). The LCA of the complete industrial process to produce *Spirulina* tablets concluded to be limited to the high nutrients used in the cultivation process (Ye et al., 2018). A recent study reported that the biomass produced by fish waste hydrolysate was almost identical to control in protein content and digestibility (Shanthi et al., 2021). Hence, this can solve the issue addressed by Ye et al., 2018.

Chlorella sp. is one of the popular strains which is known to be rich in protein above 60% (Chen et al., 2021; Madhubalaji et al., 2020). Therefore, full strength piggery wastewater grown *Chlorella sorokinna* can produce high biomass productivity with protein content of 61.1% (Chen et al., 2021). Highest reported protein content was reported at 69.68% with *Chlorella vulgaris* with the optimized airlift photobioreactor (Madhubalaji et al., 2020). However, similar to *Haematococcus* sp., they are also known to be tough in downstream processing as well (Carvalho et al., 2020). The series process of solvent treatment and lyophilization are needed to process all the protein fractions from *Chlorella* sp. which resulted in those different protein-rich fine powder 46.3 and 67.2 g.100 g^{-1} for soluble powder and insoluble powder, respectively (Grossmann et al., 2018a; Grossmann et al., 2018b).

Scenedesmus sp. on the other hand, is popular genera that consist of high protein content (up to 56%) (Becker, 2007), the lipid fraction (especially *Scenedesmus obliquus*) of this species is also well explored as a promising source for biodiesel production (Kaewkannetra et al., 2012). Therefore, the sequential utilization of this strain as aquafeed, biodiesel, and bioethanol has been studied in the lab-scale (Patnaik et al., 2019) but the upper-scale feasibility study is still unknown.

Desmodesmus sp. is one of the commercial strains which therefore native species can be easily isolated from their regions (Ferraro et al., 2021; Ferro et al., 2018). The native strain of Sweden shown the best growth rate in wastewater compared other native isolated strains including *Chlorella* sp. and *Scendesmus* sp. (Ferro et al., 2018). This can be seen as a promising strain for biomass production from wastewater in this region. In addition to this, extracting protein from wastewater grown *Desmodesmus* sp. can expect above 97% recovery (González-Balderas et al., 2020). Hence, 41% and 39% of protein content can be expect from full-fatted and defatted *Desmodesmus* sp., respectively (Sun et al., 2021).

Haematococcus sp. is one of the strains that can accumulate high protein. Apart from its known synthesis of astaxanthin, *Haematococcus* sp. can accumulate up to 45% protein content in the vegetative stage and 25% in the red stage (Shah et al., 2016). This decrease in protein content is the response to the stress of the nutrient depletion and strong light which regulate its composition towards secondary metabolite astaxanthin (Shah et al., 2016; Tran et al., 2009). Since this strain is known to be the best natural astaxanthin producer, commercialization of these strains tends to move in the astaxanthin direction. However, the protein fraction of this strain was studied in feed production to support its economy as well; here the dried defatted *Haematococcus pluvialis* biomass after astaxanthin extraction contained 40.3% crude protein (Ju et al., 2012).

4.2. Antioxidant - astaxanthin

Natural astaxanthin is predominant by *Haematococcus pluvialis* due to its GRAS status approval by FDA. Therefore, this particular strain has been explored for astaxanthin production for decades. In addition, methods of the astaxanthin production were optimized in many aspects such as its choice of growth metabolisms, strategies of optimizing chemical growth mediums, stress environment manipulation, and various operational parameters (Han et al., 2013; Novoveská et al., 2019). One major challenge of this strain is the rigidity of the cell wall (usually the result of the encystment process), which is costly to disrupt (Carvalho et al., 2020). In the attempt to solve this challenge, *Chlamydomonas reinhardtii* was genetically modified to produce astaxanthin by Perozeni et al., 2020 where astaxanthin productivity was also stated to be comparable to the commercial stain if it is to be optimized. However, since this genetically modified strain is going to be used in the food industry, it will take time to make this strain available (need approval from FDA) at the market. Other strains such as *Neochloris wimmeri*, *Protosiphon botryoides*, *Scotiellopsis oocystiformis*, was reported within the range of 1.1 to 1.9% astaxanthin content (Han et al., 2013), but only *Chlorella zonfingiensis*, *Chromochloris zofingiensis* was extensively studied attempted as astaxanthin producer. These strains are seen as potential candidates to produce natural astaxanthin but commercial availability of astaxanthin from these candidates are yet to be seen in the market. The summary table of astaxanthin production could be seen in Table 1.

Up to date, *Haematococcus pluvialis* still takes the lead as a commercial astaxanthin producer which can accumulate up to 98 mg.g^{-1} at the highest reported contents (Domínguez-Bocanegra et al., 2004). Known parameters inducing the astaxanthin content of *Haematococcus* sp. are nitrogen starvation medium, high-light intensity, high temperature, and high salinity (Kang et al., 2005). The astaxanthin induction by heterotrophic cultivation was also compared with photoautotrophic cultivation at the second stage (attempted to cut down light supplement cost) and but the production yielded 3.4 less than the production via photoautotrophic induction (Kang et al., 2005), which is why the commercial natural astaxanthin production is dominated by photoautotrophic cultivation. Domínguez-Bocanegra et al. (2004) examined this strain with four different growth mediums (BBM, BG-11, FAB, and BAR) which were reported that the growth of the cell was favorable to BBM where BAR induced the highest astaxanthin contents. Similar to this, Zhao et al. (2019) proposed two-stage cultivation where the green stage was cultured in BMM, where astaxanthin content was induced nitrogen starvation medium BG-11. The lower reported astaxanthin content of Zhao et al. (2019) was due to the higher nitrogen source in BG-11 medium (compared to BAR) at the second stage as well as the experiment was conducted at lower light intensity. On the other hand, one other study reported that an external sodium acetate supplement enhances astaxanthin accumulation (Zhang et al., 2019a). Large-scale indoor production was reported to produce astaxanthin up to 6.76% by using BBM medium supplemented with acetate to *Haematococcus lacutris* (formerly *Haematococcus pluvialis*) (Ashokkumar et al., 2021). Regarding outdoor production, large-scale cultivation in an open raceway pond yielded 2.71 to 2.75% of astaxanthin content (Wen et al., 2020) whereas closed cultivation in a fully closed thin-film (polypropylene-based cast polypropylene) photobioreactor yielded 3.73% and 4.05% in spring and summer, respectively (Hong et al., 2016).

Chlorella zonfingiensis on the other hand was also the proposed strain for astaxanthin production. It was found to synthesis β-carotene with an identical route as *Haemaococcus pluvialis* but takes a different path to make astaxanthin (Han et al., 2013). Most reported studies on this strain as an astaxanthin producer tend to explore more on heterotrophic cultivation. In heterotrophic cultivation, the astaxanthin productivity of this strain even outperforms the industrial strain (*Haematococcus pluvialis)* according to the table of Morales-Sánchez et al. (2017). Normally, astaxanthin based cultivation in heterotrophic mode tends to give good productivity as comparable but astaxanthin content per mass dried cell weight tends to be much lower than photoautotrophic cultivation (as shown in Table 1), thus, stress in the later production chain, e.g. higher biomass loading in the extraction process in order to produce the same amount of astaxanthin. For instance, *Chlorella zonfingiensis* cultured in pure glucose yielded astaxanthin content up to 1.23 mg.g^{-1} (2.27 mg.L^{-1}.d^{-1} astaxanthin productivity) (Liu et al., 2013), where via phototrophic yielded 3.7 mg.g^{-1} astaxanthin content (2.8 mg.L^{-1}.d^{-1} astaxanthin productivity) (Liu et al., 2014). This clearly shows that in order to extract a similar amount of astaxanthin from this strain, about 3 times higher biomass is needed to be processed in downstream. Several enhancement strategies such as two-stages cultivation (heterotrophic + phototrophic), heterotrophy-photoinduction, two-steps (heterotrophy-photoinduction + glucose without nitrate) (Sun et al., 2019; Zhang et al., 2017) where significant improvement of this strain was achieved

Table 1
Various type of cultivation techniques for astaxanthin production.

Strains	Cultivation mode	Medium/ substrate	Light intensity	Temp. °C	CO_2%	Biomass $g.L^{-1}$ ($g.L^{-1}.d^{-1}$)	Astaxanthin content ($mg.L^{-1}.d^{-1}$)	Lipid %	Protein %	Carbohydrate %	Reference
Haematococcus lacustris	M. – Batch	BBM + acetate supplement	45 μE. $m^{-2}.s^{-1}$ [a]	25	–	3.05 (0.145)	6.76% (8.26)	23.5	18.3	30.12	Ashokkumar et al., 2021
Haematococcus pluvialis	P. – Batch	BBM (green) BAR medium (Red)	177 μmol P. $m^{-2}.s^{-1}$ [a]345 μmol P. $m^{-2}.s^{-1}$ [a]	28	1.5	–	98 $mg.g^{-1}$	–	–	–	Domínguez-Bocanegra et al., 2004
Haematococcus pluvialis	P. – Batch	BBM (Green) BG-11 (Red)	30 μmol. $m^{-2}.s^{-1}$ [a]100 μmol. $m^{-2}.s^{-1}$ [a]	25 ± 1	–	1.38	21.5 $mg.g^{-1}$	–	–	–	Zhao et al., 2019
Haematococcus pluvialis	M. – Batch (racewaypond)	Modified BG-11 + acetate supplement	Solar: 40 – 43 μmol. $m^{-2}.s^{-1}$	25	1	- (4.54 – 5.08 g. $m^{-2}.d^{-1}$)	2.71 – 2.75% (0.12 – 0.14 $g.m^{-2}.d^{-1}$)	–	–	–	Wen et al., 2020
Haematococcus pluvialis	P. – Batch (racewaypond)	Modified BG-11	Solar: 40 – 43 μmol. $m^{-2}.s^{-1}$	25	1	- (3.61 – 3.98 g. $m^{-2}.d^{-1}$)	2.73 – 2.74% (0.10 – 0.11 $g.m^{-2}.d^{-1}$)	–	–	–	Wen et al., 2020
Haematococcus pluvialis	P. – Batch	NIES-C (green) NIES-N (Red)	Solar: 305 – 360 μE. $m^{-2}.s^{-1}$[c]	Spring	3.5	3.41 (0.045)	3.73% (2.235)	~47	~15	~30	Hong et al., 2016
Haematococcus pluvialis	P. – Batch	NIES-C (green) NIES-N (Red)	Solar: 315 – 380μE. $m^{-2}.s^{-1}$[c]	Summer	3.5	3.683 (0.113)	4.05% (5.531)	~40	~12	~41	Hong et al., 2016
Chromochloris zofingiensis	M – microplates	Modified Bristol medium +Glucose 10 g/L	> 300 μmol. $m^{-2}.s^{-1}$	26	–	5.98 (0.50)	6.51 $mg.g^{-1}$	–	–	–	Chen et al., 2017
Chromochloris zofingiensis	P – batch (High light + Salinity stress)	Khul medium + Glucose (5 g/L)	80 μE. $m^{-2}.s^{-1}$ [a] 400 μE. $m^{-2}.s^{-1}$ [a]	–	1.5	7.2 (1.11)	6.0 $mg.g^{-1}$ (7.0)	–	–	–	Kou et al., 2020
Chromochloris zofingiensis	M - Fed-batch	Khul medium + Glucose 5 g/ L	300 μE. $m^{-2}.s^{-1}$	25	–	7.8 (1.0843)	(2.0)	45.71	–	–	Sun et al., 2020
Chromochloris zofingiensis	M. – Batch	Khul medium + Glucose 30 g/L	30 μE. $m^{-2}.s^{-1}$	25	–	~11	0.6 $mg.g^{-1}$	–	–	–	Ye and Huang, 2020
Chlorella zofingensis	H.- Batch	Dilluted raw molasses (5 g/L)	–	–	–	45.6 (1.33)	1.23 (0.83)	–	–	–	Liu et al., 2013
Chlorella Zofingiensis	H.– Fed-Batch	Kul medium + Glucose 20 g/L	–	25	–	71.1 (5.8)	0.68 $mg.g^{-1}$ (4.0)	–	–	–	Sun et al., 2019
Chlorella Zofingiensis	H. + Photoinduction – Batch (Two-stage)	Kul medium + Glucose 20 g/L	50 μE. $m^{-2}.s^{-1}$	25	–	73.7 (4.8)	2.69 $mg.g^{-1}$ (9.9)	–	–	–	Sun et al., 2019
Chlorella Zofingiensis	H. + P. – Fed-Batch (two-step)	Kul medium + Glucose 20 g/L	Solar: 200 – 1500 μmol. $m^{-2}.s^{-1}$ [d]	25	–	98.4 (7.03)	0.074% (5.26)	–	–	–	Zhang et al., 2017

P = Photoautotrophic.
H = Heterotrophic.
M = Mixotrophic.
a. Continuous illumination.
b. 16:8 h light:dark.
c. 12:12 h light:dark.
d. 8:16 h light:dark.

and reported by Sun et al. (2019) which promised 4-fold the production increment by using low-intensity photoinduction on ultrahigh-density heterotrophic cultured biomass (Sun et al., 2019). Yet still, the astaxanthin production of this strain is incomparable to the commercial strain (*Haematococcus pluvialis*). In addition to this, unlike *Haematococcus* sp., *Chlorella zofingiensis* hasn't been fully explored on astaxanthin optimizing strategy via photoautotrophic as well as its downstream processing, which might be the reason why commercial astaxanthin product

of strain is yet to be seen in the market. Hence, *Chlorella zofingiensis* is one of the rapid nutrient consumption strains that has been well explored in wastewater for decades (Cheng et al., 2020; Zhao et al., 2018). Examination of this strain with wastewater as well as the astaxanthin optimizing strategy will be crucial to support the resource management via circular economy for astaxanthin production.

Further *Chromochloris zofingiensis* is examined to produce astaxanthin; the biomass of this strain cultured in mixotrophic produces higher biomass productivity yield lower in astaxanthin content and productivity compared to the commercial strains (*Haematococcus. pluvialis*) (Chen et al., 2017). Producing astaxanthin from *Chromochloris zofingiensis* in low light condition only yeild 0.6 $mg.g^{-1}$ with biomass about 11 $g.L^{-1}$ (Ye and Huang, 2020). It was shown that the presence of glucose induction degrade chloroplast and decrease the chlorophyll content of *Chromochloris zofingiensis* in which astaxanthin is induced (Zhang et al., 2019b; Zhang et al., 2020). Different glucose induction strategies with the high light condition were also done on this strain where the highest astaxanthin yield was up to 13.1 mg.g-1 with a biomass concentration of 8.3 $g.L^{-1}$ (Chen et al., 2020, 2017; Sun et al., 2020). Most optimizing strategies were done on heterotrophic and mixotrophic cultivation where on the other hand Kou et al., 2020 examined three different strategies (high light, salinity stress, high light, and salinity stress) aiming to optimize astaxanthin production via photoautotrophic concluded that high light with salinity stress yielded the highest astaxanthin productivity. The highest astaxanthin content of this strain via photoautotrophic was reported at around 7.0 $mg.g^{-1}$ (approximated data from the graph) (Fernando et al., 2021). Therefore, regarding wastewater as a growth medium to produce astaxanthin, it was found to be similar to Chen et al., 2017 as biomass production and productivity were quite similar to *Haematococcus pluvialis*, however accumulated lesser astaxanthin (Fernando et al., 2021).

4.3. Poly-Unsaturated Fatty-Acid

PUFA can be accumulated by microalgae in their lipid which has chains longer than C_{20} (López et al., 2019). Lipids produced by microalgae typically have chains longer than C_{20} which can expect to be Omega-3 and Omega-6. DHA and EPA (long-chain Omega-3 polyunsaturated fatty acids) are mostly the targeted compounds from microalgae biomass (Priyadarshani and Rath, 2012; Wang et al., 2019). For mass cultivation in Nordic regions, heterotrophic cultivation or in other terms algal fermentation is preferable due to its energy-efficient and light-independent technology, overcoming the unstable climate of the Nordic region on photoautotrophic cultivation which normally led to unreliable product quality if to commercially produce by open cultivation. Heterotrophic cultivation of microalgae promised higher DHA (essential PUFA) where 55% of the total fatty acids can be expected where autotrophic cultivation can only accumulate from 15 to 30% EPA of total biomass (Kleivdal et al., 2013). Following the microalgae-based technology in that period, commercial strains are limited to the high temperature which was favorable of heterotrophic cultivation (no required energy for light) (Kleivdal et al., 2013). Research questions were more focused on higher production yield with high value-added compounds compared with those commercialized heterotrophic strains. In terms of operation cost, heterotrophic cultivation can be upscale cost-effectively but needed to supply a huge amount of organic carbon source which is the known drawback of this technology (Lage et al., 2019). The typical industrial carbon substrate for the fermenter such as pure glucose can go up to 120 $g.L^{-1}$ in order to reach optimal biomass production and lipid content (Patel et al., 2020). However, these substrates are not cost-effective, which lead to a focus more on glycerol as an alternative since it's a waste source of biodiesel production (Kleivdal et al., 2013). Thus, increase in the cost of material is why this pure organic carbon source for fermenters are needed to be exchanged by another cost-effective source such as abandoned organic waste. Various types of waste such as organoslov-pretreated spruce hydrolysate (Patel et al., 2020), birchwood hydrolysate, and dairy effluent (Lage et al., 2019), were used to study to replace those expensive pure substrates. However, most of them normally target the bioenergy sector. Hence, these abandoned wastes might also be worth examining to produce PUFA and other value-added compounds. In a recent report, Patel et al., 2020 used organosolv-pretreated spruce hydrolysate intended to replace pure glucose to produce DHA cost-effectively. The results were stated to be feasible as DHA productivity and content were almost identical to pure glucose.

On the other hand, PUFA production via photoautotrophic cultivation is costly limited to light and temperature control in the system. To overcome this, in these past recent years, researchers in the Nordic regions believe that the potential of local strains which have been exposed to harsh conditions will benefit in producing PUFA cost-effectively at a lower temperature than the commercial strains (Cheregi et al., 2019). Hulatt et al. (2017a) isolated five polar snow microalgae strains (*Chlamydomonas klinobasis*, *Chlamydomonas pulsatilla*, *Chloromonas platystigma*, *Raphidonema sempervirens*, and *Macrochloris rubreoleum*) and found to be capable of cultivating down to 6 °C which achieved maximum productivity (*Chlamydomonas pulsatilla*) of 0.63 $g.L^{-1}.d^{-1}$ with lipid content of 39%. Referring to the other article, Morales-Sánchez et al. (2020a) reported that cultivated *Chlamydomonas malina* at 8 °C can yield up to 0.527 $g.L^{-1}.d^{-1}$ biomass productivity with 32.5% of lipid. In later investigation of the same strain, the temperature-dependent lipid/PUFA biosynthesis was found to be in favor at even lower temperature, where its highest biomass productivity and lipid productive were found at the lowest tested temperature (4 °C). Further at temperature higher than 8 °C the strain was stressed and redirected its metabolism to another compound (Morales-Sánchez et al., 2020b). By today's technology PUFA can be synthesized at colder temperatures, which improve the cost of biosynthesis of this compound significantly in the Nordic region. The summary of PUFA production via photoautotrophic cultivation could be seen in Table 2. As shown in Table 2, these isolated local strains even outperform those strains culturing at a higher temperature. This indicates that high lipid content and PUFA content with high biomass productivity can be achieved in a colder condition which is beneficial to the techno-economic of the photoautotrophic cultivation of this compound in the Nordic region. However, since all of the reported production was pure chemical growth based, research of those strains with wastewater could be beneficial to improve the material cost as well.

5. Biomass processing into nutraceutical productions or feed

Microalgae can have a higher composition of targeted components than most terrestrial biomass (Nagappan et al., 2021). However, since stress condition is normally applied in the upstream process, bioavailability of components such as nutrients can be limited due to the microalgae cell wall composition. Thickness and rigidity of microalgae strains can rank from naked strains (*Dunaliella salina*) to robust strains (*Haematococcus* sp. cyst) (Carvalho et al., 2020), which is why biomass utilization/processing should be considered and evaluated in three diffident forms; as whole-, disrupted-, and defatted biomass. Usually, the purpose of the preprocess on microalgae biomass is to provide more bioavailability of components to the consumers (Verspreet et al., 2021). Microalgae biomass as potential feed production, fish feed ingredients, and nutrient profile was precisely discussed in the extensive published review by Nagappan et al., (2021). The utilization of whole-cell biomass directly as feed should be strongly considered as it will cut down most of the production cost. Further the digestibility of the selected strain should be investigated before commercializing the product, as some microalgae may not be suitable for direct uses. High nutritional strains such as cell wall less *Dunaliella* sp. and digestible cell-wall compound like *Spirulina* sp. could be the promising candidates to be used as whole cell (Nagappan et al., 2021; Sui and Vlaeminck, 2020, 2019).

Disrupted biomass can be used from robust strains such as *Haematococcus* sp., *Chlorella* sp., *Scenedusmus* sp., *Nannochloropsis* sp., *and*

Table 2
Photoautotrophic cultivation for PUFA and lipid production in the Nordic regions.

Strains	Cultivation mode	Medium	Temperature °C	Light intensity $\mu mol.m^{-2}.s^{-1}$	CO_2 aeration	Biomass productivity (Biomass concentration)	PUFA $mg.L^{-1}.d^{-1}$	Lipid %	Protein %	Carbohydrate %	Reference
Chlamydomonas pulsatilla	Semi continuous	Bolds Basal Medium	6	230	2.5% v/v	0.63 $g.L^{-1}.d^{-1}$	–	39.4	–	–	Hulatt et al., 2017a
Chlamydomonas klinobasis	Semi continuous	Bolds Basal Medium	6	230	2.5% v/v	0.36 $g.L^{-1}.d^{-1}$	–	34.4	–	–	Hulatt et al., 2017a
Chlamydomonas platystigma	Batch	Bolds Basal Medium	6	135	1% v/v	0.25 $g.L^{-1}.d^{-1}$	–	31.4	–	–	Hulatt et al., 2017a
Chlamydomonas malina	Batch	f/2 medium	8	120 – 250[a]	1% v/v	0.527 $g.L^{-1}.d^{-1*}$	85.4	32.5 (161.3 mg. $L^{-1}.d^{-1}$)	26.1 – 27.6	49.5	Morales-Sánchez et al., 2020a
Chlamydomonas malina	Batch	f/2 medium (+N, -N)	8 – 15	120	ambient level	0.701 $g.L^{-1}.d^{-1*}$	79.7 – 122	44	41	32 – 44	Morales-Sánchez et al., 2020b
Tetraselmis chui	Batch	Modified F-medium	15	300[a]	1% v/v (100 $mL.min^{-1}$)	0.255 $g_{DW}.L^{-1}.d^{-1}$	–	8 – 17	6 – 30	–	Lima et al., 2021
Koliella antarctica	Batch	Modified F-medium	15	300[a]	1% v/v (100 $mL.min^{-1}$)	0.117 $g_{DW}.L^{-1}.d^{-1}$	–	11 – 23	8 – 47	–	Lima et al., 2021
Nannocloropsis gaditana	Batch	Modified F-medium	20	300[a]	1% v/v (100 $mL.min^{-1}$)	0.361 $g_{DW}.L^{-1}.d^{-1}$	–	23 – 43	12 – 49	–	Lima et al., 2021
Nannochloropsis gaditana	Batch	–	25	90 – 180[b]	1% v/v	0.51 $g.L^{-1}.d^{-1}$	–	37	4.2 – 4.9	–	Hulatt et al., 2017b
Nannochloropsis gaditana	Batch	–	26	63[b] to 636[b]	2 %	–	–	~40%	–	–	Janssen et al., 2018
Coelastrella sp.	Bath	Municipal wastewater	22	100[c]	–	(1.46 $g.L^{-1}$)	–	30.8%	–	–	Ferro et al., 2018
Desmodesmus sp.	Bath	Municipal wastewater	22	100[c]	–	(0.87 – 0.99 $g.L^{-1}$)	–	29.8–36.7%	–	–	Ferro et al., 2018
Chlorella vulgaris	Bath	Municipal wastewater	22	100[c]	–	(1.15 $g.L^{-1}$)	–	34.2%	–	–	Ferro et al., 2018

a. Continuous illumination.
b. 16:8 h light:dark.
c. 18:6 h light:dark.
* calculated from $mg.L^{-1}.d^{-1}$ to $g.L.^{-1}.d^{-1}$.
+N. nitrogen replete.
-N. nitrogen deplete.

Desmodesmus sp. (Nagappan et al., 2021). Understanding their cell wall composition might have a great influence on the overall disruption technology. Both cell walls and cell membrane can be disrupted by freeze-thawing and alkaline pretreatment. Cell wall disruption is more applicable by sonication, high-pressure homogenization, impingement, microfluidization, microbead wet milling, colloidal mills, rotor–stator homogenizers, grinding (microbead, ball or jet mills), autolysis, enzymatic hydrolysis, alkaline treatment, and enzymatic hydrolysis, where cell membrane is well suited by osmotic shock, thermolysis, detergent solubilization, and pulsed electric fields treatment (Carvalho et al., 2020). Cell disruption technologies should apply to the targeted cell wall or cell membrane of the specific strain in order to obtain the best result (Carvalho et al., 2020). For instance, different strains in the same genera will need different process parameters; *Chlorella protothecoides* need 6 passes with 150 MPa, where *Chlorella vulgaris* need only 1 pass with 138 MPa to get above 97% disruption in high-pressure homogenization (Cha et al., 2011; Grossmann et al., 2018b). The other process such as fermentation and enzyme treatment were highlighted to improve the nutrient value of *Chlorella* sp. and *Scenedemus sp*. (Moheimani et al., 2018). In regard to digestibility, protein, and fat of *Nannochloropsis gaditana* were significantly improved by bead milling treatment before processing it as feed (Teuling et al., 2019), therefore the evidence suggested that *Nannochloropsis gaditana* and *Scenedesmus* sp. must be disrupted, otherwise the most majority of the nutrient will not be digested (Verspreet et al., 2021). Bead milling, enzyme hydrolysis treatments, or the combination of both treatments are the most effective processes and widely used for the protein faction application due to the milder condition, short residence time without addition of harsh chemical solvent contaminated the final production (Alavijeh et al., 2020).

Defatted biomass gains popularity due to the increased interest in algal bioenergy production served as a coproduct to improve the algal bioenergy towards economy sustainable approaches, e.g. after lipid fraction is extracted and processed into biodiesel production, protein fraction in the residual biomass can be utilized as aquafeed production (El-Baz et al., 2021). In addition to improving the algal bioenergy economy, some defatted biomass used as a supplementary ingredient has been shown to enhance fed shrimp meat quality (Ju et al., 2012, Ju et al. (2011)) and give high digestibility of amino acids (Manor et al., 2017). This high digestibility may happen since defatted biomass is normally pretreated before going into the lipid extraction process. However, depending on the lipid extraction technologies, residual solvents may need to be washed to be used as feed (El-Baz et al., 2021). Typically, defatted biomass as feed ingredients is prepared by drying out all residual solvents until the biomass reaches constant weight (El-Baz et al., 2021; González-Balderas et al., 2020) or obtained as dried biomass from industrial supercritical CO_2 extraction processes (Ju et al., 2012). Commonly used defatted strains for animal feed are *Scenedemus obliquus* (El-Baz et al., 2021), *Desmodesmus* sp. (Kiron et al., 2016; Sun et al., 2021), *Nanochloropsis oceania* (Manor et al., 2017), *Haematococcus pluvialis* (Jiang et al., 2019; Ju et al., 2012) and *Tetraselmis* sp. (Pereira et al., 2020). The highest amount of defatted biomass tested to replace fishmeal protein (shrimp feed ingredient) was up to 50% of dried microalgae weight corresponding to 12% inclusion amounts of dry microalgae meal as a feed ingredient, which shows no adverse effect on the nutritional composition of the fed shrimp (Ju et al., 2012).

6. Perspective and future directions

In upstream processing, open cultivation is typically cost-efficient in tropical countries but less effective and very challenging due to the Nordic weather conditions. Closed-photobioreactor is generally the first prior consideration in terms of upscaling the technology as most of the parameters can be easily controlled by its compact design. Since rapid biomass generation with high protein and PUFA production can be produced at colder temperatures (local isolated such as *Chlamydomonas pulsatilla* and *Chlamydomonas malina)*, this could tremendously reduce the operational cost in the upstream in the Nordic regions. To support microalgal circular bioeconomy with regards of treating wastewater, native isolated *Desmodesmus* sp. is the most potential candidate with high biomass productivity and lipid content but needed temperature up to 22 °C. Hence, examining the cold strain with wastewater will gain both cost-reduction benefits for temperature control and nutrient supply to satisfy microalgal circular bioeconomy. In addition, optimizing production such as applying low-frequency flashing light shortly before harvesting will also be beneficial. Regarding astaxanthin production, the process can only be relying on *Haematococcus* sp. since it is still the strain with the highest content by far. Open and hybrid cultivation has shown to be the most economically feasible technology. However, astaxanthin can only be expected up to 2.75% in outdoor large-scale cultivation where closed cultivated can yield up to 4% via photoautotrophic cultivation. On the other hand, with the acetate supplement, mixotrophic cultivation can yield up to 6.76% which is the highest reported content for large-scale so far. Heterotrophic cultivation can be more selectable and would give the promise of low-cost production since it is a light-independent process if the astaxanthin contents can yield as comparable to photoautotrophic cultivation. Heterotrophic cultivation has significantly improved over these past years in regard to astaxanthin content with the recent enhancement strategy such as the photoinduction on ultrahigh density. This strategy would give an alternative to produce astaxanthin cost-effectively since the light is only used on the highly-dense biomass as well as its astaxanthin productivity even outperform the productivity via photoautotrophic cultivation in some cases. However, astaxanthin content in the optimized condition is still relatively low (2.69 $mg.g^{-1}$). This thus stresses the later processes with higher biomass loading (if compare to astaxanthin content in biomass via photoautotrophic above) since it normally carries out in series processes such as beading milling, spray drying, the extraction process; alternatively, if the production is only aimed for aquafeed production alone where the astaxanthin extraction process is not required, this reported astaxanthin content is enough to improve the fed shrimp quality considering the tested inclusion by Ju et al. (2012), and astaxanthin diet by Ju et al. (2011). Concise study on energy balance in the process and their economy between these two promised studies for fish feed production would provide intensively direction on the feasible large-scale astaxanthin production; still continue with the photoautotrophic or change to the heterotrophy-photoinduction process.

High value-added compound processing from microalgae biomass is still costly challenging due to series processes from cell disruption, dehydration/drying, and extraction. The attempt to remove the dry process from astaxanthin extraction has been made by Irshad et al., 2019, to combine bead milling and astaxanthin extraction in one process. This idea can also be implemented in the other value-added compounds such as chlorophylls, other pigments such as β-carotene, lutein, etc. In addition to this, to support its economy, co-products can be obtained through the process of residual biomass as biochar, animal feed, etc (Ashokkumar et al., 2021; Ju et al., 2012). Therefore, more research on the efficient utilization of defatted biomass should be given more focus in order to improve its economy as well. Interestingly, the astaxanthin residue in the defatted *Haematococcus* biomass improved the pigmentation of shrimp which improve its value significantly. Since there is yet to effect on growth and performance, given higher doses in the feed should be relevant for future study.

In summary, effective microalgae-based technologies for nutraceutical applications in Nordic regions can be seen as:

- To be unitized for aquafeed production alone: strains such as *Dunaliella* sp. and *Spirulina* sp. should first be considered as they hold the potential of whole-cell utilization. And regarding astaxanthin compound for aquafeed, heterotrophic cultivation with photoinduction on ultra-high density is the technique worth considering for the production.

- The cultivation process for PUFA and protein can be done by the use of cold adaptive strains since it requires less energy for the temperature control compared to the commercial strains.
- Astaxanthin production can only rely on *Haematococcus* sp. with closed cultivation system.
- Extraction of high value-added compounds such as PUFA, astaxanthin, lipid for feed/health supplements: The cell disruption process should be applied to the specific strain with primary targets (cell wall or cell membrane) to obtain an energy-efficient process.
- The residue after the extraction should be extensively studied as coproducts to improve the overall economy and the environmental footprint of the industry.

7. Conclusion

Overall, using microalgae biomass can be an alternative to many feed ingredients such as oil supplements, protein supplements and antioxidant additives. Microalgae-based technology is cost limited due to the known climate fluctuation of Nordic regions. Native isolated strains have shown high potential of biomass generation from wastewater as well as production of protein, lipid, and polyunsaturated fatty acid compounds. Updated studies reported here provide information regard the challenges and remedies towards effectively produce those compounds in Nordic regions.

Declaration of Competing Interest

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

References

Ackefors, H., Enell, M., 1994. The release of nutrients and organic matter from aquaculture systems in Nordic countries. J. Appl. Ichthyol. 10 (4), 225–241. https://doi.org/10.1111/j.1439-0426.1994.tb00163.x.

Ahn, J.-W., Hwangbo, K., Lee, S.Y., Choi, H.-G., Park, Y.-I., Liu, J.R., Jeong, W.-J., 2012. A new Arctic *Chlorella* species for biodiesel production. Bioresour. Technol. 125, 340–343. https://doi.org/10.1016/j.biortech.2012.09.026.

Alavijeh, R.S., Karimi, K., Wijffels, R.H., van den Berg, C., Eppink, M., 2020. Combined bead milling and enzymatic hydrolysis for efficient fractionation of lipids, proteins, and carbohydrates of *Chlorella vulgaris* microalgae. Bioresour. Technol. 309, 123321 https://doi.org/10.1016/j.biortech.2020.123321.

Araújo, R., Vázquez Calderón, F., Sánchez López, J., Azevedo, I.C., Bruhn, A., Fluch, S., Garcia Tasende, M., Ghaderiardakani, F., Ilmjärv, T., Laurans, M., Mac Monagail, M., Mangini, S., Peteiro, C., Rebours, C., Stefansson, T., Ullmann, J., 2021. Current status of the algae production industry in europe: an emerging sector of the blue bioeconomy. Front. Mar. Sci. 7, 1–24. https://doi.org/10.3389/fmars.2020.626389.

Ashokkumar, V., Chen, W.H., Kumar, G., Satjarak, A., Chanthapatchot, W., Ngamcharussrivichai, C., 2021. A biorefinery approach for high value-added bioproduct (astaxanthin) from alga *Haematococcus sp.* and residue pyrolysis for biochar synthesis and metallic iron production from hematite (Fe2O3). Fuel 304, 121150. https://doi.org/10.1016/j.fuel.2021.121150.

Béchet, Q., Shilton, A., Guieysse, B., 2014. Full-scale validation of a model of algal productivity. Environ. Sci. Technol. 48, 13826–13833. https://doi.org/10.1021/es503204e.

Becker, E.W., 2013. Microalgae for human and animal nutrition. Handbook of Microalgal Culture, second ed. 461–503 https://doi.org/10.1002/9781118567166.ch25.

Becker, E.W., 2007. Micro-algae as a source of protein. Biotechnol. Adv. 25, 207–210. https://doi.org/10.1016/j.biotechadv.2006.11.002.

Boetius, A., Wenzhöfer, F., 2013. Seafloor oxygen consumption fuelled by methane from cold seeps. Nat. Geosci. 6 (9), 725–734.

Borowitzka, M.A., 2013. High-value products from microalgae—their development and commercialisation. J. Appl. Phycol. 25 (3), 743–756. https://doi.org/10.1007/s10811-013-9983-9.

Borowitzka, M.A., Vonshak, A., 2017. Scaling up microalgal cultures to commercial scale. Eur. J. Phycol. 52 (4), 407–418. https://doi.org/10.1080/09670262.2017.1365177.

Brod, E., Oppen, J., Kristoffersen, A.Ø., Haraldsen, T.K., Krogstad, T., 2017. Drying or anaerobic digestion of fish sludge: nitrogen fertilisation effects and logistics. Ambio 46, 852–864. https://doi.org/10.1007/s13280-017-0927-5.

Campoy, C., Escolano-Margarit, M.V., Anjos, T., Szajewska, H., Uauy, R., 2012. Omega 3 fatty acids on child growth, visual acuity and neurodevelopment. Br. J. Nutr. 107 (S2), S85–S106. https://doi.org/10.1017/S0007114512001493.

Carvalho, J.C., Magalhães, A.I., de Melo Pereira, G.V., Medeiros, A.B.P., Sydney, E.B., Rodrigues, C., Aulestia, D.T.M., de Souza Vandenberghe, L.P., Soccol, V.T., Soccol, C. R., 2020. Microalgal biomass pretreatment for integrated processing into biofuels, food, and feed. Bioresour. Technol. 300, 122719 https://doi.org/10.1016/j.biortech.2019.122719.

Castro, L.F.C., Tocher, D.R., Monroig, O., 2016. Long-chain polyunsaturated fatty acid biosynthesis in chordates: Insights into the evolution of Fads and Elovl gene repertoire. Prog. Lipid Res. 62, 25–40. https://doi.org/10.1016/j.plipres.2016.01.001.

Cha, K.H., Lee, J.Y., Song, D.G., Kim, S.M., Lee, D.U., Jeon, J.Y., Pan, C.H., 2011. Effect of microfluidization on in vitro micellization and intestinal cell uptake of lutein from *Chlorella vulgaris*. J. Agric. Food Chem. 59, 8670–8674. https://doi.org/10.1021/jf2019243.

Chaves, A.A.M., Martins, C.F., Carvalho, D.F.P., Ribeiro, D.M., Lordelo, M., Freire, J.P.B., de Almeida, A.M., 2021. A viewpoint on the use of microalgae as an alternative feedstuff in the context of pig and poultry feeding—a special emphasis on tropical regions. Trop. Anim. Health Prod. 53 (3), 396. https://doi.org/10.1007/s11250-021-02800-5.

Chen, J. hui, Liu, L., Wei, D., 2017. Enhanced production of astaxanthin by *Chromochloris zofingiensis* in a microplate-based culture system under high light irradiation. Bioresour. Technol. 245, 518–529. https://doi.org/10.1016/j.biortech.2017.08.102.

Chen, J. hui, Wei, D., Lim, P.E., 2020. Enhanced coproduction of astaxanthin and lipids by the green microalga *Chromochloris zofingiensis*: Selected phytohormones as positive stimulators. Bioresour. Technol. 295, 122242. https://doi.org/10.1016/j.biortech.2019.122242.

Chen, C.Y., Kuo, E.W., Nagarajan, D., Dong, C.D., Lee, D.J., Varjani, S., Lam, S.S., Chang, J.S., 2021. Semi-batch cultivation of *Chlorella sorokiniana AK-1* with dual carriers for the effective treatment of full-strength piggery wastewater treatment. Bioresour. Technol. 326, 124773 https://doi.org/10.1016/j.biortech.2021.124773.

Cheng, P., Cheng, J.J., Cobb, K., Zhou, C., Zhou, N., Addy, M., Chen, P., Yan, X., Ruan, R., 2020. *Tribonema sp.* and *Chlorella zofingiensis* co-culture to treat swine wastewater diluted with fishery wastewater to facilitate harvest. Bioresour. Technol. 297, 122516 https://doi.org/10.1016/j.biortech.2019.122516.

Cheregi, O., Ekendahl, S., Engelbrektsson, J., Strömberg, N., Godhe, A., Spetea, C., 2019. Microalgae biotechnology in Nordic countries – the potential of local strains. Physiol. Plant. 166, 438–450. https://doi.org/10.1111/ppl.12951.

Chronakis, I.S., Madsen, M., 2011. Algal proteins. Elsevier, Handbook of food proteins, pp. 353–394.

Craig, S., L. A. Helfrich, D. Kuhn and M. H. Schwarz 2017. Understanding fish nutrition, feeds, and feeding. Va. Tech, 420-256.

De-Luca, R., Bezzo, F., Béchet, Q., Bernard, O., 2019. Meteorological data-based optimal control strategy for microalgae cultivation in open pond systems. Complex. 4363895 https://doi.org/10.1155/2019/4363895.

Diao, J., Li, X., Pei, G., Liu, L., Chen, L., 2018. Comparative metabolomic analysis of *Crypthecodinium cohnii* in response to different dissolved oxygen levels during docosahexaenoic acid fermentation. Biochem. Biophys. Res. Commun. 499 (4), 941–947. https://doi.org/10.1016/j.bbrc.2018.04.024.

Domínguez-Bocanegra, A.R., Guerrero Legarreta, I., Martinez Jeronimo, F., Tomasini Campocosio, A., 2004. Influence of environmental and nutritional factors in the production of astaxanthin from *Haematococcus pluvialis*. Bioresour. Technol. 92, 209–214. https://doi.org/10.1016/j.biortech.2003.04.001.

El-Baz, F.K., Abdoon, S.M., El-Sayed, D.A.A., Mostafa, M.A., Elsherif, H.M.R., Safaa, H. M., Abdon, A.S., 2021. Application of defatted *Scenedesmus obliquus* biomass for broilers' nutrition. Rev. Bras. Cienc. Avic. 23 https://doi.org/10.1590/1806-9061-2020-1366.

Falkowski, P., 2012. Ocean science: the power of plankton. Nat. 483 (7387), S17–S20.

Fernando, J.S.R., Premaratne, M., Dinalankara, D.M.S.D., Perera, G.L.N.J., Ariyadasa, T. U., 2021. Cultivation of microalgae in palm oil mill effluent (POME) for astaxanthin production and simultaneous phycoremediation. J. Environ. Chem. Eng. 9, 105375 https://doi.org/10.1016/j.jece.2021.105375.

Ferraro, G., Toranzo, R.M., Bagnato, C., Gómez Jousse, M., Areco, M.M., Bohé, A., Bagnarol, D., Pasquevich, D.M., Curutchet, G., 2021. Native *Desmodesmus sp.* and *Chlorella sp.* isolated from the Reconquista River display a different binding preference for Cu(II) and Zn(II). J. Environ. Manage. 293, 112835 https://doi.org/10.1016/j.jenvman.2021.112835.

Ferro, L., Gentili, F.G., Funk, C., 2018. Isolation and characterization of microalgal strains for biomass production and wastewater reclamation in Northern Sweden. Algal Res. 32, 44–53. https://doi.org/10.1016/j.algal.2018.03.006.

González-Balderas, R.M., Velásquez-Orta, S.B., Valdez-Vazquez, I., Orta Ledesma, M.T., 2020. Intensified recovery of lipids, proteins, and carbohydrates from wastewater-grown microalgae *Desmodesmus sp.* by using ultrasound or ozone. Ultrason. Sonochem. 62, 104852 https://doi.org/10.1016/j.ultsonch.2019.104852.

Grossmann, L., Ebert, S., Hinrichs, J., Weiss, J., 2018a. Production of protein-rich extracts from disrupted microalgae cells: Impact of solvent treatment and lyophilization. Algal Res. 36, 67–76. https://doi.org/10.1016/j.algal.2018.09.011.

Grossmann, L., Ebert, S., Hinrichs, J., Weiss, J., 2018b. Effect of precipitation, lyophilization, and organic solvent extraction on preparation of protein-rich powders from the microalgae *Chlorella protothecoides*. Algal Res. 29, 266–276. https://doi.org/10.1016/j.algal.2017.11.019.

Guilini, K., Levin, L.A., Vanreusel, A., 2012. Cold seep and oxygen minimum zone associated sources of margin heterogeneity affect benthic assemblages, diversity and nutrition at the Cascadian margin (NE Pacific Ocean). Prog. Oceanogr. 96 (1), 77–92. https://doi.org/10.1016/j.pocean.2011.10.003.

Hamid, S.H.A., Lananan, F., Din, W.N.S., Lam, S.S., Khatoon, H., Endut, A., Jusoh, A., 2014. Harvesting microalgae, Chlorella sp. by bio-flocculation of *Moringa oleifera* seed derivatives from aquaculture wastewater phytoremediation. Int. Biodeterior. Biodegradation 95, 270–275. https://doi.org/10.1016/j.ibiod.2014.06.021.

Han, D., Li, Y., Hu, Q., 2013. Astaxanthin in microalgae: Pathways, functions and biotechnological implications. Algae 28, 131–147. https://doi.org/10.4490/algae.2013.28.2.131.

Hong, M.E., Choi, Y.Y., Sim, S.J., 2016. Effect of red cyst cell inoculation and iron(II) supplementation on autotrophic astaxanthin production by *Haematococcus pluvialis* under outdoor summer conditions. J. Biotechnol. 218, 25–33. https://doi.org/10.1016/j.jbiotec.2015.11.019.

Hulatt, C.J., Berecz, O., Egeland, E.S., Wijffels, R.H., Kiron, V., 2017a. Polar snow algae as a valuable source of lipids? Bioresour. Technol. 235, 338–347. https://doi.org/10.1016/j.biortech.2017.03.130.

Hulatt, C.J., Wijffels, R.H., Bolla, S., Kiron, V., 2017b. Production of fatty acids and protein by *Nannochloropsis* in flat-plate photobioreactors. PLoS One 12, 1–17. https://doi.org/10.1371/journal.pone.0170440.

Innis, S.M., 2007. Dietary (n-3) fatty acids and brain development. J. Nutr. 137 (4), 855–859. https://doi.org/10.1093/jn/137.4.855.

Irshad, M., Myint, A.A., Hong, M.E., Kim, J., Sim, S.J., 2019. One-pot, simultaneous cell wall disruption and complete extraction of astaxanthin from *Haematococcus pluvialis* at room temperature. ACS Sustain. Chem. Eng. 7, 13898–13910. https://doi.org/10.1021/acssuschemeng.9b02089.

Jackson, A., 2009. The continuing demand for sustainable fishmeal and fish oil in aquaculture diets. Int. Aquafeed 12 (5), 32–36.

Janssen, J.H., Kastenhofer, J., de Hoop, J.A., Lamers, P.P., Wijffels, R.H., Barbosa, M.J., 2018. Effect of nitrogen addition on lipid productivity of nitrogen starved *Nannochloropsis gaditana*. Algal Res. 33, 125–132. https://doi.org/10.1016/j.algal.2018.05.009.

Jiang, M., Zhao, H.H., Zai, S.W., Shepherd, B., Wen, H., Deng, D.F., 2019. A defatted microalgae meal (*Haematococcus pluvialis*) as a partial protein source to replace fishmeal for feeding juvenile yellow perch *Perca flavescens*. J. Appl. Phycol. 31, 1197–1205. https://doi.org/10.1007/s10811-018-1610-3.

Ju, Z.Y., Deng, D.F., Dominy, W., 2012. A defatted microalgae (*Haematococcus pluvialis*) meal as a protein ingredient to partially replace fishmeal in diets of Pacific white shrimp (*Litopenaeus vannamei*, Boone, 1931). Aquaculture 354–355, 50–55. https://doi.org/10.1016/j.aquaculture.2012.04.028.

Ju, Z.Y., Deng, D.F., Dominy, W.G., Forster, I.P., 2011. Pigmentation of Pacific White Shrimp, *Litopenaeus vannamei*, by Dietary Astaxanthin Extracted from *Haematococcus pluvialis*. J. World Aquac. Soc. 42, 633–644. https://doi.org/10.1111/j.1749-7345.2011.00511.x.

Kaewkannetra, P., Enmak, P., Chiu, T., 2012. The effect of CO2 and salinity on the cultivation of Scenedesmus obliquus for biodiesel production. Biotechnol. Bioprocess Eng. 17, 591–597. https://doi.org/10.1007/s12257-011-0533-5.

Kang, C.D., Lee, J.S., Park, T.H., Sim, S.J., 2005. Comparison of heterotrophic and photoautotrophic induction on astaxanthin production by *Haematococcus pluvialis*. Appl. Microbiol. Biotechnol. 68, 237–241. https://doi.org/10.1007/s00253-005-1889-2.

Kim, S.W., Less, J.F., Wang, L., Yan, T., Kiron, V., Kaushik, S.J., Lei, X.G., 2019. Meeting global feed protein demand: challenge, opportunity, and strategy. Annu. Rev. Anim. Biosci. 7, 221–243. https://doi.org/10.1146/annurev-animal-030117-014838.

Kirby, J., Keasling, J.D., 2009. Biosynthesis of plant isoprenoids: perspectives for microbial engineering. Annu. Rev. Plant Biol. 60 (1), 335–355. https://doi.org/10.1146/annurev.arplant.043008.091955.

Kiron, V., Sørensen, M., Huntley, M., Vasanth, G.K., Gong, Y., Dahle, D., Palihawadana, A.M., 2016. Defatted biomass of the microalga, *Desmodesmus sp.*, can replace fishmeal in the feeds for atlantic salmon. Front. Mar. Sci. 3, 1–12. https://doi.org/10.3389/fmars.2016.00067.

Kleivdal, H., Chauton, M.S., Reitan, I., 2013. Industrial production of marine microalgae as a source of EPA and DHA rich raw material in fish feed - Basis. Knowledge status and possibilities 1–88.

Koller, M., Muhr, A., Braunegg, G., 2014. Microalgae as versatile cellular factories for valued products. Algal Res. 6, 52–63. https://doi.org/10.1016/j.algal.2014.09.002.

Kou, Y., Liu, M., Sun, P., Dong, Z., Liu, J., 2020. High light boosts salinity stress-induced biosynthesis of astaxanthin and lipids in the green alga *Chromochloris zofingiensis*. Algal Res. 50, 101976 https://doi.org/10.1016/j.algal.2020.101976.

Koyande, A.K., Chew, K.W., Rambabu, K., Tao, Y., Chu, D.-T., Show, P.-L., 2019. Microalgae: a potential alternative to health supplementation for humans. Food Sci. Hum. Wellness 8 (1), 16–24. https://doi.org/10.1016/j.fshw.2019.03.001.

Lage, S., Kudahettige, N.P., Ferro, L., Matsakas, L., Funk, C., Rova, U., Gentili, F.G., 2019. Microalgae cultivation for the biotransformation of birch wood hydrolysate and dairy effluent. Catalysts 9, 1–14. https://doi.org/10.3390/catal9020150.

Leppi, J.C., Arp, C.D., Whitman, M.S., 2016. Predicting late winter dissolved oxygen levels in Arctic lakes using morphology and landscape metrics. Environ. Manag. 57 (2), 463–473. https://doi.org/10.1007/s00267-015-0622-x.

Li, M., Callier, M.D., Blancheton, J.-P., Galès, A., Nahon, S., Triplet, S., Geoffroy, T., Menniti, C., Fouilland, E., Roque D'Orbcastel, E., 2019. Bioremediation of fishpond effluent and production of microalgae for an oyster farm in an innovative recirculating integrated multi-trophic aquaculture system. Aquaculture 504, 314–325. https://doi.org/10.1016/j.aquaculture.2019.02.013.

Li, J., Zhu, D., Niu, J., Shen, S., Wang, G., 2011. An economic assessment of astaxanthin production by large scale cultivation of *Haematococcus pluvialis*. Biotechnology Advances 29 (6), 568–574. https://doi.org/10.1016/j.biotechadv.2011.04.001.

Lima, S., Schulze, P.S.C., Schüler, L.M., Rautenberger, R., Morales-Sánchez, D., Santos, T. F., Pereira, H., Varela, J.C.S., Scargiali, F., Wijffels, R.H., Kiron, V., 2021. Flashing light emitting diodes (LEDs) induce proteins, polyunsaturated fatty acids and pigments in three microalgae. J. Biotechnol. 325, 15–24. https://doi.org/10.1016/j.jbiotec.2020.11.019.

Liu, J., Sun, Z., Gerken, H., Liu, Z., Jiang, Y., Chen, F., 2014. *Chlorella zofingiensis* as an alternative microalgal producer of astaxanthin: Biology and industrial potential. Mar. Drugs 12, 3487–3515. https://doi.org/10.3390/md12063487.

Liu, J., Sun, Z., Zhong, Y., Gerken, H., Huang, J., Chen, F., 2013. Utilization of cane molasses towards cost-saving astaxanthin production by a *Chlorella zofingiensis* mutant. J. Appl. Phycol. 25, 1447–1456. https://doi.org/10.1007/s10811-013-9974-x.

López, G., Yate, C., Ramos, F.A., Cala, M.P., Restrepo, S., Baena, S., 2019. Production of polyunsaturated fatty acids and lipids from autotrophic, mixotrophic and heterotrophic cultivation of *Galdieria* sp. strain USBA-GBX-832. Sci. Rep. 9, 1–13. https://doi.org/10.1038/s41598-019-46645-3.

Madhubalaji, C.K., Sarat Chandra, T., Chauhan, V.S., Sarada, R., Mudliar, S.N., 2020. *Chlorella vulgaris* cultivation in airlift photobioreactor with transparent draft tube: effect of hydrodynamics, light and carbon dioxide on biochemical profile particularly ω-6/ω-3 fatty acid ratio. J. Food Sci. Technol. 57, 866–876. https://doi.org/10.1007/s13197-019-04118-5.

Manor, M.L., Kim, J., Derksen, T.J., Schwartz, R.L., Roneker, C.A., Bhatnagar, R.S., Lei, X.G., 2017. Defatted microalgae serve as a dual dietary source of highly bioavailable iron and protein in an anemic pig model. Algal Res. 26, 409–414. https://doi.org/10.1016/j.algal.2017.07.018.

Markou, G., Vandamme, D., Muylaert, K., 2014. Microalgal and cyanobacterial cultivation: The supply of nutrients. Water Res. 65, 186–202. https://doi.org/10.1016/j.watres.2014.07.025.

Moheimani, N.R., Vadiveloo, A., Ayre, J.M., Pluske, J.R., 2018. Nutritional profile and in vitro digestibility of microalgae grown in anaerobically digested piggery effluent. Algal Res. 35, 362–369. https://doi.org/10.1016/j.algal.2018.09.007.

Morales-Sánchez, D., Martinez-Rodriguez, O.A., Martinez, A., 2017. Heterotrophic cultivation of microalgae: production of metabolites of commercial interest. J. Chem. Technol. Biotechnol. 92, 925–936. https://doi.org/10.1002/jctb.5115.

Morales-Sánchez, D., Schulze, P.S.C., Kiron, V., Wijffels, R.H., 2020a. Production of carbohydrates, lipids and polyunsaturated fatty acids (PUFA) by the polar marine microalga *Chlamydomonas malina* RCC2488. Algal Res. 50, 102016 https://doi.org/10.1016/j.algal.2020.102016.

Morales-Sánchez, D., Schulze, P.S.C., Kiron, V., Wijffels, R.H., 2020b. Temperature-Dependent Lipid Accumulation in the Polar Marine Microalga *Chlamydomonas malina* RCC2488. Front. Plant Sci. 11, 1–10. https://doi.org/10.3389/fpls.2020.619064.

Munoz, R., Guieysse, B., 2006. Algal-bacterial processes for the treatment of hazardous contaminants: A review. Water Res. 40, 2799–2815. https://doi.org/10.1016/j.watres.2006.06.011.

Murphy, E., Stanton, C., Brien, C., Murphy, C., Holden, S., Murphy, R., Varley, P., Boland, M., Fair, S., 2017. The effect of dietary supplementation of algae rich in docosahexaenoic acid on boar fertility. Theriogenology. 90, 78–87. https://doi.org/10.1016/j.theriogenology.2016.11.008.

Nagappan, S., Das, P., AbdulQuadir, M., Thaher, M., Khan, S., Mahata, C., Al-Jabri, H., Vatland, A.K., Kumar, G., 2021. Potential of microalgae as a sustainable feed ingredient for aquaculture. J. Biotechnol. 341, 1–20. https://doi.org/10.1016/j.jbiotec.2021.09.003.

Nagarajan, D., Varjani, S., Lee, D., Chang, J., 2021. Sustainable aquaculture and animal feed from microalgae – Nutritive value and techno-functional components. Renew. Sust. Energ. Rev. 150, 111549 https://doi.org/10.1016/j.rser.2021.111549.

Nagata, A., Tajima, T., Takahashi, J., 2006. Effect of astaxanthin 5 mg on anti fatigue and task performance of human. Carotenoid Sci. 10, 102–106. https://doi.org/10.3390/nu10030281.

Nair, S., Paulose, H., 2014. Emergence of green business models: The case of algae biofuel for aviation. Energy Policy 65, 175–184. https://doi.org/10.1016/j.enpol.2013.10.034.

Narala, R.R., Garg, S., Sharma, K.K., Thomas-Hall, S.R., Deme, M., Li, Y., Schenk, P.M., 2016. Comparison of microalgae cultivation in photobioreactor, open raceway pond, and a two-stage hybrid system. Front. Energy Res. 4, 1–10. https://doi.org/10.3389/fenrg.2016.00029.

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. Mar. Drugs 17, 1–21. https://doi.org/10.3390/md17110640.

Paisley, L.G., Ariel, E., Lyngstad, T., Jónsson, G., Vennerström, P., Hellström, A., Østergaard, P., 2010. An overview of aquaculture in the Nordic countries. J. World Aquac. Soc. 41 (1), 1–17. https://doi.org/10.1111/j.1749-7345.2009.00309.x.

Panis, G., Carreon, J.R., 2016. Commercial astaxanthin production derived by green alga *Haematococcus pluvialis*: A microalgae process model and a techno-economic assessment all through production line. Algal Res. 18, 175–190. https://doi.org/10.1016/j.algal.2016.06.007.

Patel, A., Liefeldt, S., Rova, U., Christakopoulos, P., Matsakas, L., 2020. Co-production of DHA and squalene by thraustochytrid from forest biomass. Sci. Rep. 10 https://doi.org/10.1038/s41598-020-58728-7.

Patnaik, R., Singh, N.K., Bagchi, S.K., Rao, P.S., Mallick, N., 2019. Utilization of *Scenedesmus obliquus* Protein as a Replacement of the Commercially Available Fish Meal Under an Algal Refinery Approach. Front. Microbiol. 10, 1–15. https://doi.org/10.3389/fmicb.2019.02114.

Pereira, H., Sardinha, M., Santos, T., Gouveia, L., Barreira, L., Dias, J., Varela, J., 2020. Incorporation of defatted microalgal biomass (*Tetraselmis sp.* CTP4) at the expense of soybean meal as a feed ingredient for juvenile gilthead seabream (*Sparus aurata*). Algal Res. 47, 101869 https://doi.org/10.1016/j.algal.2020.101869.

Pérez-López, P., González-García, S., Jeffryes, C., Agathos, S.N., McHugh, E., Walsh, D., Murray, P., Moane, S., Feijoo, G., Moreira, M.T., 2014. Life cycle assessment of the production of the red antioxidant carotenoid astaxanthin by microalgae: from lab to

pilot scale. J. Clean. Prod. 64, 332–344. https://doi.org/10.1016/j.jclepro.2013.07.011.

Perozeni, F., Cazzaniga, S., Baier, T., Zanoni, F., Zoccatelli, G., Lauersen, K.J., Wobbe, L., Ballottari, M., 2020. Turning a green alga red: engineering astaxanthin biosynthesis by intragenic pseudogene revival in *Chlamydomonas reinhardtii*. Plant Biotechnol. J. 18, 2053–2067. https://doi.org/10.1111/pbi.13364.

Priyadarshani, I., Rath, B., 2012. Commercial and industrial applications of micro algae – A review. J. Algal Biomass Util. 3, 89–100. https://doi.org/10.1016/j. (73).

Qie, F., Zhu, J., Rong, J., Zong, B., 2019. Biological removal of nitrogen oxides by microalgae, a promising strategy from nitrogen oxides to protein production. Bioresour. Technol. 292, 122037 https://doi.org/10.1016/j.biortech.2019.122037.

Todd Lorenz, R., Cysewsk, G.R., 2000. Commercial potential for *Haematococcus*. Trends Biotechnol. 18 (4), 160–167.

Safi, C., Charton, M., Pignolet, O., Silvestre, F., Vaca-Garcia, C., Pontalier, P.Y., 2013. Influence of microalgae cell wall characteristics on protein extractability and determination of nitrogen-to-protein conversion factors. J. Appl. Phycol. 25, 523–529. https://doi.org/10.1007/s10811-012-9886-1.

Shah, M.M.R., Liang, Y., Cheng, J.J., Daroch, M., 2016. Astaxanthin-producing green microalga *Haematococcus pluvialis*: From single cell to high value commercial products. Front. Plant Sci. 7 https://doi.org/10.3389/fpls.2016.00531.

Shanthi, G., Premalatha, M., Anantharaman, N., 2021. Potential utilization of fish waste for the sustainable production of microalgae rich in renewable protein and phycocyanin-*Arthrospira platensis/Spirulina*. J. Clean. Prod. 294, 126106 https://doi.org/10.1016/j.jclepro.2021.126106.

Simas-Rodrigues, C., Villela, H. D., Martins, A. P., Marques, L. G., Colepicolo, P., Tonon, A. P., 2015. Microalgae for economic applications: advantages and perspectives for bioethanol. J. Exp. Bot. 66(14), 4097-4108. Plantarum. https://doi.org/10.1093/jxb/erv130.

Singh, R.N., Sharma, S., 2012. Development of suitable photobioreactor for algae production - A review. Renew. Sustain. Energy Rev. 16, 2347–2353. https://doi.org/10.1016/j.rser.2012.01.026.

Sui, Y., Vlaeminck, S.E., 2019. Effects of salinity, pH and growth phase on the protein productivity by *Dunaliella salina*. J. Chem. Technol. Biotechnol. 94, 1032–1040. https://doi.org/10.1002/jctb.5850.

Sui, Y., Vlaeminck, S.E., 2020. *Dunaliella* Microalgae for Nutritional Protein: An Undervalued Asset. Trends Biotechnol. 38, 10–12. https://doi.org/10.1016/j.tibtech.2019.07.011.

Sun, H., Ren, Y., Lao, Y., Li, X., Chen, F., 2020. A novel fed-batch strategy enhances lipid and astaxanthin productivity without compromising biomass of *Chromochloris zofingiensis*. Bioresour. Technol. 308, 123306 https://doi.org/10.1016/j.biortech.2020.123306.

Sun, T., Wang, K., Wyman, B., Sudibyo, H., Liu, G., Beal, C., Manning, S., Johnson, Z.I., Aydemir, T.B., Tester, J.W., Lei, X.G., 2021. Supplemental dietary full-fatted and defatted *Desmodesmus sp.* exerted similar effects on growth performance, gut health, and excreta hydrothermal liquefaction of broiler chicks. Algal Res. 54, 102205 https://doi.org/10.1016/j.algal.2021.102205.

Sun, Z., Zhang, Y., Sun, L.P., Liu, J., 2019. Light Elicits Astaxanthin Biosynthesis and Accumulation in the Fermented Ultrahigh-Density *Chlorella zofinginesis*. J. Agric. Food Chem. 67, 5579–5586. https://doi.org/10.1021/acs.jafc.9b01176.

Tacon, A.G.J., Metian, M., 2015. Feed matters: Satisfying the feed demand of aquaculture. Rev. Fish. Sci. Aquac. 23, 1–10. https://doi.org/10.1080/23308249.2014.987209.

Teuling, E., Wierenga, P.A., Agboola, J.O., Gruppen, H., Schrama, J.W., 2019. Cell wall disruption increases bioavailability of *Nannochloropsis gaditana* nutrients for juvenile Nile tilapia (*Oreochromis niloticus*). Aquaculture 499, 269–282. https://doi.org/10.1016/j.aquaculture.2018.09.047.

Thoré, E.S.J., Schoeters, F., De Cuyper, A., Vleugels, R., Noyens, I., Bleyen, P., Van Miert, S., 2021. Waste Is the New Wealth – Recovering Resources From Poultry Wastewater for Multifunctional Microalgae Feedstock. Front. environ. sci. 9 (253) https://doi.org/10.3389/fenvs.2021.679917.

Tocher, D.R., 2015. Omega-3 long-chain polyunsaturated fatty acids and aquaculture in perspective. Aquaculture 449, 94–107. https://doi.org/10.1016/j.aquaculture.2015.01.010.

Tocher, D.R., Betancor, M.B., Sprague, M., Olsen, R.E., Napier, J.A., 2019. Omega-3 Long-Chain Polyunsaturated Fatty Acids, EPA and DHA: Bridging the Gap between Supply and Demand. Nutrients 11 (1), 89. https://doi.org/10.3390/nu11010089.

Tran, N.P., Park, J.K., Lee, C.G., 2009. Proteomics analysis of proteins in green alga *Haematococcus lacustris* (Chlorophyceae) expressed under combined stress of nitrogen starvation and high irradiance. Enzyme Microb. Technol. 45, 241–246. https://doi.org/10.1016/j.enzmictec.2009.07.006.

Valença, R. d. L., Silva Sobrinho, A. G. d., Borghi, T. H., Meza, D. A. R., Andrade, N. d., Silva, L. G., Bezerra, L. R., 2021. Performance, carcass traits, physicochemical properties and fatty acids composition of lamb's meat fed diets with marine microalgae meal (*Schizochytrium sp.*). Livest. Sci. 243, 104387. https://doi.org/10.1016/j.livsci.2020.104387.

van der Wurff, I.S.M., Meyer, B.J., de Groot, R.H.M., 2020. Effect of Omega-3 Long Chain Polyunsaturated Fatty Acids (n-3 LCPUFA) Supplementation on Cognition in Children and Adolescents: A Systematic Literature Review with a Focus on n-3 LCPUFA Blood Values and Dose of DHA and EPA. Nutrients 12 (10), 3115. https://doi.org/10.3390/nu9121305.

Verspreet, J., Soetemans, L., Gargan, C., Hayes, M., Bastiaens, L., 2021. Nutritional profiling and preliminary bioactivity screening of five micro-algae strains cultivated in northwest europe. Foods 10, 1–17. https://doi.org/10.3390/foods10071516.

Wang, B., Lan, C.Q., Horsman, M., 2012. Closed photobioreactors for production of microalgal biomasses. Biotechnol. Adv. 30, 904–912. https://doi.org/10.1016/j.biotechadv.2012.01.019.

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. Front. Mar. Sci. 6, 1–10. https://doi.org/10.3389/fmars.2019.00095.

Waszkiewicz-Robak, B., Szterk, A., Rogalski, M., Rambuszek, M., Kruk, M., Rokowska, E., 2015. Nutritional value of raw pork depending on the fat type contents in pigs feed. Acta. Sci. Pol. Technol. Aliment 14 (2), 153–163. https://doi.org/10.17306/J.AFS.2015.2.17.

Wells, M.L., Potin, P., Craigie, J.S., Raven, J.A., Merchant, S.S., Helliwell, K.E., Smith, A. G., Camire, M.E., Brawley, S.H., 2017. Algae as nutritional and functional food sources: revisiting our understanding. J. Appl. Phycol. 29 (2), 949–982. https://doi.org/10.1007/s10811-016-0974-5.

Wen, X., Wang, Z., Ding, Y., Geng, Y., Li, Y., 2020. Enhancing the production of astaxanthin by mixotrophic cultivation of *Haematococcus pluvialis* in open raceway ponds. Aquac. Int. 28, 625–638. https://doi.org/10.1007/s10499-019-00483-2.

Ye, C., Mu, D., Horowitz, N., Xue, Z., Chen, J., Xue, M., Zhou, Y., Klutts, M., Zhou, W., 2018. Life cycle assessment of industrial scale production of spirulina tablets. Algal Res. 34, 154–163. https://doi.org/10.1016/j.algal.2018.07.013.

Ye, Y., Huang, J.C., 2020. Defining the biosynthesis of ketocarotenoids in *Chromochloris zofingiensis*. Plant Divers. 42, 61–66. https://doi.org/10.1016/j.pld.2019.11.001.

Zhang, C., Chen, X., Zou, R., Zhou, K., Stephanopoulos, G., Too, H.-P., 2013. Combining Genotype Improvement and Statistical Media Optimization for Isoprenoid Production in E. coli. PLOS ONE 8 (10), e75164. https://doi.org/10.1371/journal.pone.0075164.

Zhang, C., Zhang, L., Liu, J., 2019a. Exogenous sodium acetate enhances astaxanthin accumulation and photoprotection in *Haematococcus pluvialis* at the non-motile stage. J. Appl. Phycol. 31, 1001–1008. https://doi.org/10.1007/s10811-018-1622-z.

Zhang, F., Liu, W., Xia, J., Zeng, J., Xiang, L., Zhu, S., Zheng, Q., Xie, H., Yang, C., Chen, M., Liao, Z., 2018. Molecular Characterization of the 1-Deoxy-D-Xylulose 5-Phosphate Synthase Gene Family in Artemisia annua. Front. Plant Sci. 9 (952) https://doi.org/10.3389/fpls.2018.00952.

Zhang, Z., Huang, J.J., Sun, D., Lee, Y., Chen, F., 2017. Two-step cultivation for production of astaxanthin in *Chlorella zofingiensis* using a patented energy-free rotating floating photobioreactor (RFP). Bioresour. Technol. 224, 515–522. https://doi.org/10.1016/j.biortech.2016.10.081.

Zhang, Z., Sun, D., Zhang, Y., Chen, F., 2020. Chloroplast morphogenesis in *Chromochloris zofingiensis* in the dark. Algal Res. 45, 101742 https://doi.org/10.1016/j.algal.2019.101742.

Zhang, Z., Sun, D., Zhang, Y., Chen, F., 2019b. Glucose triggers cell structure changes and regulates astaxanthin biosynthesis in *Chromochloris zofingiensis*. Algal Res. 39, 101455 https://doi.org/10.1016/j.algal.2019.101455.

Zhang, Z., Tan, Y., Wang, W., Bai, W., Fan, J., Huang, J., Wan, M., Li, Y., 2019c. Efficient heterotrophic cultivation of *Chlamydomonas reinhardtii*. J. Appl. Phycol. 31, 1545–1554. https://doi.org/10.1007/s10811-018-1666-0.

Zhao, W., Sun, H., Ren, Y., Wu, T., He, Y., Chen, F., 2018. *Chlorella zofingiensis* as a promising strain in wastewater treatment. Bioresour. Technol. 268, 286–291. https://doi.org/10.1016/j.biortech.2018.07.144.

Zhao, Y., Yue, C., Geng, S., Ning, D., Ma, T., Yu, X., 2019. Role of media composition in biomass and astaxanthin production of *Haematococcus pluvialis* under two-stage cultivation. Bioprocess Biosyst. Eng. 42, 593–602. https://doi.org/10.1007/s00449-018-02064-8.

Zhu, B., Shen, H., Li, Y., Liu, Q., Jin, G., Han, J., Zhao, Y., Pan, K., 2020. Large-Scale Cultivation Spirulina for Biological CO2 Mitigation in Open Raceway Ponds Using Purified CO2 From a Co. Front. Bioeng. Biotechnol. 7, 1–8. https://doi.org/10.3389/fbioe.2019.00441.

Algaeworldnews, 2015.07.17 (online) The world's largest *Haematococcus* farm built in china. URL: https://news.algaeworld.org/2015/07/the-worlds-largest-haematococcus-farm-in-china/.

Algae2future.no, 2020.12.01 (online) Folvengaard AS won the Agricultural Innovation Award 2020. URL: https://algae2future.no/articles/folvengaard-as-vann-landbrukets-innovasjonspris-2020.

Marine Harvest ASA, 2018 (online) Salmon Farming Industry Handbook. URL: https://mowi.com/wp-content/uploads/2019/04/2018-salmon-industry-handbook-1.pdf.

Starling, Shane, 2011.01.11 (online) Sweden takes over Fuji's astaxanthin production. Nutraingredients.com URL: https://www.nutraingredients.com/Article/2011/01/12/Sweden-takes-over-Fuji-s-astaxanthin-production?utm_source=copyright&utm_medium=OnSite&utm_campaign=copyright.