**The role of microalgae in the bioeconomy**

F. Gabriel Acién Fernández1, Alberto Reis2, René H. Wijffels 3,4, Maria Barbosa3, Vitor Verdelho5, Bernardo Llamas6

1Department of Chemical Engineering, University of Almería, Almería, Spain

2National Laboratory of Energy and Geology - LNEG,I.P, Lisbon, Portugal

3Bioprocess Engineering, AlgaePARC, Wageningen University & Research, Wageningen, The Netherlands

4Faculty of Biosciences and Aquaculture, Nord University, Bodø, Norway

5A4F Alga 4 Future S.A., Estrada do Paço do Lumiar Campus do Lumiar, Ed. E – R/C

1649-038 Lisboa, Portugal

6Ppolytechnic university of Madrid. ETSI Mines and Energy. Alenza 4. 28003 Madrid. Spain

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**Abstract**

The bioeconomy is a new and essential paradigm for reducing our dependence on natural resources and responding to the environmental threats that the Earth is currently facing. In this regard, microalgae offer almost unlimited possibilities for developing a modern bioeconomy given their metabolic flexibility and high biomass output rates, even when produced under harsh conditions such as when treating wastewaters or using flue gases. In this article, the microalgal contribution to important economic activities such as the production of food and feed, cosmetics and health-related compounds is reviewed. Moreover, microalgae’s potential contribution to emerging sectors is discussed, for instance, in the production of biomaterials, agriculture-related products, biofuels, and providing services such as wastewater treatment and the clean-up of industrial gases. The different microalgal production technologies have also been analyzed to identify the main bottlenecks affecting microalgae use in different applications. Finally, the major challenges facing microalgae biotechnology in enlarging its contribution to the bioeconomy are evaluated, and future trends discussed.

# Introduction

Microalgae contribute to the planet’s sustainability, mainly by transforming CO2 into O2. They are the primary producers of biomass for aquatic systems, thus supporting life on Earth. Moreover, microalgal biotechnology is currently contributing to the global bioeconomy, producing valuable biomass for human-related applications such as pharmaceuticals, cosmetics, food and feed [1–3]. Nevertheless, microalgae can potentially contribute much more to the bioeconomy by increasing the current production capacity and developing new applications. They have been proposed as a source for biofuel, chemical and biofertilizer production, although they can also provide services such as wastewater treatment and clean-up of flue gases [4–6].

The term microalgae include both microalgae and cyanobacteria. Although they are different microorganisms (eukaryotic and prokaryotic, respectively), both perform oxygenic photosynthesis in the same way and are produced using the same fundamentals and technologies. Microalgae are produced in water and require adequately designed production systems. The design of these systems must be based on prior knowledge while also accommodating the requirements of target markets in terms of production capacity and quality among others. Microalgae are flexible microorganisms that can be cultivated under different conditions; indeed, they are produced in a wide variety of locations around the world [7]. Moreover, they can be cultivated without using valuable resources that are needed for other human-related applications, such as freshwater or arable land. Microalgae are (i) fast-growing microorganisms that double in less than a day, (ii) capable of achieving high biomass productivities above 100 t/ha·year (by dry weight) and (iii) mainly use sunlight as the energy source, with efficiencies as high as 10%. For these reasons, they are considered fundamental for the development of sustainable processes that contribute to the global bioeconomy [8]. However, these are optimistic values are really difficult to achieve at large scale: under real outdoor conditions the duplication time reduces up to two days, the biomass productivity decreases up to 40 t/ha·year, and the photosynthetic efficiency decreases up to 3%.

Here, the major factors determining the performance of microalgae-related processes are reviewed, followed by an analysis of the most relevant contributions made by microalgae to the bioeconomy. This review provides a critical overview of the microalgae biotechnology field to identify the main short-term challenges that need to be faced as this biotechnology contributes further to the global bioeconomy.

# Large-scale microalgal production

## *Heterotrophic versus autotrophic production*

Microalgae can be produced using two main strategies - autotrophically or heterotrophically. Autotrophic production is the most conventional method although, currently, heterotrophic production is rapidly growing. The heterotrophic production of microalgae has consistently improved growth performance and cell concentrations compared to photoautotrophic production[9]. Conversely, heterotrophic cultivation of microalgae can increase the production costs, due to the need of an organic carbon source, and lead to lower protein and pigment contents, which can decrease the biomass market value[9]. The heterotrophic production of biomass requires organic carbon sources such as sugars, which are already produced from agriculture. To produce 1 kg of microalgae biomass, up to 2 kg of glucose are required. Other carbon sources like glycerol or acetic acid can also be used. In this process, microalgae such as yeast or bacteria are manipulated to transform short chain molecules into valuable biomass or other molecules [10]. This strategy is mainly used to produce food-grade biomass from microalgae such as *Chlorella*, modifying the culture conditions and thus the colour and biochemical composition of the biomass; it is used specially to avoid the green colour that might be undesirable in some cases. Not all microalgal species are suitable for heterotrophic production; indeed, it is mainly only *Chlorella*-like genera that can cope with this production method. One exception is *Schizochytrium,* produced as a polyunsaturated fatty acid source for both human and aquaculture use [11]. However, heterotrophic production is unsustainable because large quantities of sugars are needed in addition to the inputs required to operate the reactors; furthermore, the sugar itself has to be produced, which greatly reduces the sustainability of the entire process.

Autotrophic microalgae production utilizes light as the energy source along with inorganic carbon and other nutrients (**Figure 1**). As the output, the microalgae produce biomass and oxygen in large amounts. Up to 2 tCO2, 0.1 tN, 0.010 tP and 0.015 tK are required for each ton of microalgal biomass, with up to 2 tO2 also released during the process. Biomass produced in this way has already proved useful in a range of applications, including wastewater treatment and bioenergy production. This strategy can be employed for any microalgal genus, the most common being *Spirulina (Arthrospira)*, *Chlorella*, *Dunaliella* and *Haematococcus*, which are already used for human-related applications [12]. However, many more microalgae – whether marine genera such as *Nannochloropsis*, *Tetraselmis*, T-ISO and *Phaeodactylum*, or freshwater ones such as *Scenedesmus* - are being produced for other applications including aquaculture, agriculture and bioenergy. To maximize the productivity of autotrophic systems, there needs to be an adequate supply of light and carbon. Up to 8-10 mol of photons are required to produce one mole of carbohydrates while up to 2 kg of CO2 is needed to produce one kg of biomass. Given that sunlight and CO2 from the atmosphere (or from flue gases) can be used to produce microalgae, biomass production is generally assumed to be sustainable. However, this depends on the technology and the inputs used for the overall production process, with only some systems and culture conditions proving to be sustainable [13]. Nonetheless, compared to other food sources, microalgae production is far more sustainable - the arable land and water requirements, along with the related CO2 emissions, are 40 times less when producing 1 kg of golden *Chlorella* protein than that required to produce 1 kg of beef protein [7].

To achieve sustainable microalgal production processes, two conditions are needed. First, to design highly efficient systems that maximize the sunlight utilized by the cells, while at the same time consuming the minimum energy for microalgal production and harvesting/processing. Secondly, to use low impact materials and nutrients, thus minimizing the use of metal or concrete to build the reactors, and to use pure CO2 or fertilizers as the nutrient source [4,5]. In any microalgal production system, the core of the process is the photobioreactor itself, where the biomass is produced. It must be optimized to intercept as large an amount of light as possible and to allow the cells to use it optimally. For this to occur, the culture conditions must be optimized to those required by the specific strain being produced. The main culture conditions that need to be controlled include temperature, pH, dissolved O2 and nutrient availability. Mixing is required to minimize the existence of gradients for properties such as temperature, pH and nutrient availability, but mainly to maximize the cells’ exposure to light. To avoid property gradients, it is sufficient to achieve mixing times in the range of minutes, whereas to achieve maximum light integration, mixing times or frequencies at which the cells must be exposed to light are in the range of milliseconds [14]; the former is possible by providing reasonable amounts of energy, whereas the latter is not possible without investing enormous amounts of energy [15,16]. Concerning nutrients, large amounts of carbon, nitrogen and phosphorus are required to produce microalgal biomass. Microalgae can recover these nutrients from effluents such as wastewater and manure, thus enhancing treatment processes at the same time as producing large amounts of biomass with minimum inputs [4].

## *Open versus closed production systems*

For microalgal production systems, two main reactor-types are considered - closed and open. In closed photobioreactors, the culture is separated from the atmosphere by a transparent material, whether plastic or glass; there are also different designs such as bubble-column, tubular or flat-panel. In these reactors, the culture is mixed both by aeration and pumping, both of which consume large amounts of energy (up to 400 W/m3). To maximize how much light is intercepted, large surface-to-volume ratios are used (up to 200 m2/m3); for this, large quantities of transparent material are needed. Given the substantial amounts of energy and materials required to build and operate these reactors, they are mainly utilized to produce high or medium-value biomass. As a result, the value of the biomass produced cannot be lower than 20 €/kg when using these technologies, even at the large scale [17,18]. Production costs such as these are only affordable for human-related applications that require high-quality nutrients such as pure CO2 and clean fertilizers, the utilization of wastes being not allowed. As the production of chemical fertilizers has already resulted in large related impacts, this type of system is not sustainable. However, in these reactors, the culture conditions can be quite accurately controlled, especially to avoid contamination problems; therefore, they can produce any microalgae species and achieve maximal productivity. This is important when considering the different microalgae-related applications.

In open reactors, the culture is not separated from the atmosphere, thus it is directly exposed to sunlight and to any atmospheric contaminants, making the adequate control of the culture conditions far more difficult. The most traditional design is the raceway reactor although thin-layer cascade and other designs have also been proposed. Nonetheless, only raceway reactors are used at the industrial scale, with more than 90% of autotrophic microalgal production worldwide being produced using this technology. In raceways, the culture is recirculated around the reactor using a paddlewheel system; this has an energy requirement of less than 10 W/m3 . To maximize raceway reactor productivity, the culture depth must be as low as possible. However, due to hydraulic bottlenecks, the culture depth cannot be lower than 0.2 m at large scale; for this reason, surface-to-volume ratios up to 5 m2/m3 are normally used. The only material required to build these reactors is the liner that separates the culture from the ground, low thickness polymers such as PVC or polyethylene. Using this technology, a biomass production cost below 10 €/kg is possible, with more than 70% of this cost corresponding to the nutrients required [18]. If effluents are used, such as flue gases containing CO2 and wastewaters containing N and P, the biomass production cost can be reduced below 2 €/kg [18]. At this cost, the microalgae biomass can be used for non-human-related applications such as feed, biofertilizers, and even bioenergy.

Due to the minimal amounts of energy and materials required to produce microalgal biomass in open reactors, this option is the most sustainable. Using waste streams such as flue gases and wastewater as the nutrient source further increases the sustainability of microalgal production in open systems. Moreover deployment of microalgae cultivation in wastewater systems can lead to reduced or even neutral impact of wastewater treatment regarding energy consumption and GHG release to the environment and can often simplify the treatment process (at the cost of significantly higher area requirements)[4].

## *Industrial facilities*

Microalgal production is still a small-scale industrial activity compared to other large sectors such as soy or fish-related products. Global microalgal production is over 20 kt/year; this is mainly being used for food applications and as a premix for feed, with typical biomass values ranging from 15 to 25 €/kg (**Table 1**). In comparison, the fish products sector produces more than 7,000 kt/year of fish oil and meal, mainly used as feed, with a regular value of 1.5 €/kg. The soy oil and meal sector is much larger, producing more than 200,000 kt/year; this forms the basis for feed production worldwide, with regular value below 0.5 €/kg.

In order to enlarge the microalgal contribution to the bioeconomy, the overall production capacity must be greatly increased. Today, most of the existing facilities in the world are small or medium scale; these range between 1 and 50 ha for open systems and from 10 to 500 m3 in the case of closed photobioreactors (**Figure 2**). Currently, facilities based on open systems are more common because they are able to produce biomass of sufficient quality for human-related applications, using strains such as *Spirulina*, *Chlorella,* *Dunaliella* and *Haematococcus*. There are more than 500 small-scale facilities (<5 ha), and up to 300 medium-scale facilities (5-50 ha). The number of large facilities (50-100 ha) is quite low, and these are mostly dedicated to *Spirulina* production. There are no facilities larger than 100 ha, so none can produce more than 5,000 t/year. Concerning closed photobioreactors, the facilities using these technologies are much smaller, most based on tubular systems – there are at present more than 100 facilities with an overall volume of less than 10 m3 worldwide. Medium-scale facilities with volumes up to 500 m3 are quite abundant, with as many as 50 around the world, whereas there are very few facilities that have a large volume (up to 2,000 m3). As yet, there are no production facilities producing volumes over 2,000 m3.

The total market volume for microalgae is difficult to estimate. Only a few microalgal products are produced in large quantities, and this is done by a limited number of companies. Larger facilities, like the BASF production plant in Australia, produce thousands of tons of dry biomass per year[19]. Recently, however, most of the companies in this field have produced less than 1t per year. Many, such as aquaculture hatcheries, just produce for their own use and do not bring the product to market; consequently, microalgae produced in aquaculture hatcheries cannot be included in the market volume estimation. Globally, production is estimated to be 25,000 t, of which more than half is produced in China. The total market volume is estimated to be 50 M€ and this is set to grow to 70 M€ by 2025 [20].

In Europe alone there are 480 companies in this sector, 170 of which are micro farmers with less than 5 employees; 280 companies have 5-10 employees, while only 30 companies employ more than 10 people. The total number working in this sector in Europe is 10,000, comprising 4,600 in industry and 5,400 in academia. The total amount of biomass produced in Europe is 500 t dry biomass per year [7].

The value of the biomass produced varies enormously depending on the scale of production. In Europe, the scale of production is relatively small; the value of the biomass produced for aquaculture hatcheries can be higher than 500 €/kg for quantities of 100s-kg per year per production facility. In larger-scale facilities, the biomass is produced at the 1000s-kg scale and the market price for this biomass is approximately 50 €/kg. *Spirulina* is produced in China at the 1000s-tons scale per year, with prices as low as 20 €/kg biomass [21]. It has been estimated that if production is near the 10,000 tons of biomass per year level, the cost price could be below 5 €/kg [22,23], and yet further industrialization could yield cost prices below 1 €/kg [23].

# Current microalgae applications

Current microalgae applications include food, feed, health-related and cosmetic applications (**Figure 3**). For these, the microalgae biomass price ranges from 5 to 500 €/kg, with a market size of up to 100 kt/year. In addition, there is a wide range of emerging applications such as biofuels, biofertilizers, wastewater treatment and chemicals, for which the biomass price is much lower (from less than 5 €/kg) but the market size is enormous.

## *Health foods*

Food applications for microalgae include food ingredients and health foods. Microalgae contribute to these fields because they possess a high nutritional value, containing (i) high protein concentrations with all the essential amino acids, (ii) lipids with a highly valuable profile and rich in polyunsaturated fatty acids, and (iii) bioactive carbohydrates such as polysaccharides. Microalgae are especially valuable for (iv) their high content of omega-3 fatty acids, such as eicosapentaenoic (EPA) and docosahexaenoic (DHA) acids, which are essential for human health, and (v) antioxidants, including pigments such as carotenes, chlorophylls, and phycobiliproteins. Microalgae have been (and still are) mostly used in health foods such as nutraceuticals, which are marketed in powder, tablet and capsule form. However, these applications are now expanding to other products and sectors, such as feed and (aqua)feed. Moreover, they have the potential to make these markets more sustainable, which is a prerequisite for them to attain an impact on the bioeconomy.

The most consumed microalgae in the world include *Spirulina*, *Chlorella,* *Dunaliella* and *Haematococcus;* thesehave mainly been exploited in the food industry, especially in the form of tablets and capsules (**Table 2**). *Spirulina* has been used as a traditional food for a long time, and is produced all around the world [24,25]. It is rich in proteins and vitamins but can only be grown phototrophically. Given its capacity to grow under very high pH conditions, it can be easily cultivated in open systems. *Spirulina* is produced by hundreds of companies, including 150 micro-farms in France (*Spiruliniers*). Global production is estimated to be 15,000 t dry biomass per year, of which 10,000 t is produced in China. In addition to the protein-rich biomass produced (up to 75% of DW biomass), phycocyanin extract is also produced. Worldwide, it is estimated that 200 t phycocyanin is produced annually.

Industrial production of *Chlorella* began in the early 1960s. Currently, *Chlorella* is grown industrially in light (phototrophically), on sugars (heterotrophically) or a combination of the two, where the inoculum is produced heterotrophically and the final growth stage is carried out phototrophically [26]. Industrial production became large-scale in Japan and Taiwan, initially in open, phototrophic systems, but later by fermentation, for the higher productivity and production capacity in heterotrophic mode. The annual production of *Chlorella* is about 5000 t dry biomass, half of which is produced in China. The main application for *Chlorella* is using the whole biomass as a health food or to produce peptides. Recently, the Corbion company took over Terravia and is now marketing a *Chlorella* and oil protein mix, used both for food and personal-care products[27].

Since the 1980s, *Dunaliella* has been cultivated commercially to produce beta-carotene. There are large-scale plants in Australia (BASF) and Israel (NBT). *Dunaliella* accumulates beta-carotene in oil bodies, reaching beta-carotene concentrations in the biomass of over 10%; these occur under stress conditions such as a high salt concentration and/or light conditions [28]. Global *Dunaliella* production each year amounts to 2,000 tons of dry biomass.

As with beta-carotene production from *Dunaliella*, *Haematococcus* produce astaxanthin under oxidative stress. In commercial production, the astaxanthin concentration is 4-5%. The production scale of *Haematococcus* is lower than that for *Dunaliella* [29]. Worldwide, it is estimated that 1,000 tons of astaxanthin-rich biomass is produced annually.

## *Aquaculture and animal feed*

Microalgal biomass contains relevant amounts of highly nutritional proteins (40%) and lipids (30%), which are of great value for aquaculture. Moreover, it contains additional compounds such as antioxidants, peptides and fatty acids, which can be incorporated into fish diets (1-5%) to improve the health and growth of individuals, especially in early stages (**Figure 4**). Microalgae also provide additional prebiotic benefits, improving digestive and immunity systems that increase fish tolerance to stress conditions and reduce the need for pharmaceuticals [30]. Proteins and polyunsaturated fatty acids are important components in feed for all aquatic organisms. Omega-3 long chain polyunsaturated fatty acids (n3-LC-PUFA), namely eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are essential fatty acids in aquaculture.

Photosynthetic marine microalgae are the primary producers of n3-LC-PUFAs. These fatty acids are present at small concentrations in the cells, up to 5.5% EPA on a dry weight basis [31] and even less DHA. DHA can be produced heterotrophically by *Thraustochytrid*, *Schizochytrium*, *Ulkenia* and *Crypthecodimium,* with a biomass DHA content of 20% (w/w) [32]. The estimated yearly DHA production is about 1,000 tons. Very little EPA is produced commercially although *Nannochloropsis* is being produced as a promising source of this fatty acid. This strain is of great importance in aquaculture because of its high EPA content. Many small-scale companies produce *Nannochloropsis*. The total market volume is, however, still small, estimated as being a few 10s of tons of dry biomass per year.

Besides aquafeed, potential microalgal applications in the feed industry are being considered for pets, horses, broilers and cows. Given the health properties of microalgae biomass, it has been recommended that low percentages are included in feed for young animals [33]. Microalgae provide benefits for animals such as pigs, cows, sheep, chicken and other domestic animals [34]. Including algae in feed benefits animals by improving their immune systems, lipid metabolism, gut function and stress resistance as well as increasing appetite, weight, number of eggs and reproductive performance; it can even reduce cholesterol levels [34]. Algae can be incorporated into poultry feed to replace up to 5-10% of conventional proteins [35], whereas in pigs, one can incorporate up to 33% without causing negative effects [2]. However, ruminants are the most suitable animals to feed algae because they are even able to digest unprocessed algal biomass [2]. Adding microalgae biomass to feed has been demonstrated to improve the quality of meat and eggs [36].

Despite the wide range of microalgal applications for animal feed, limitations exist regarding the present production scale and costs. Comparing the production volume values with those for soy oil and meal, and fish oil and meal, which are commonly used in feeds, clearly illustrates this. Total soy oil & meal production exceeds 200 million t/year, with a current price below 0.5 €/Kg. Fish oil & meal production is higher than 7 million t/year with a current price below 2 €/Kg. In contrast, current microalgae production (oil & meal) is estimated at around 25,000 t/year with a market price of 20-50 €/kg. It has been estimated that if production rose nearer to 10,000 t of biomass per year, the cost price would fall below 5 €/kg [23,37], and further industrialization could reduce this below 1 €/kg [23]. Regardless, the economic feasibility of incorporating microalgae biomass into diets has already been proven [38].

The market for feed premix products has a significant impact on the animal nutrition industry. This market is segmented based on the livestock. Feed premix products provide wholesome nutrition, metabolic efficiency, effective growth and development, and livestock health protection.

## ***Health and cosmetics***

Microalgae and Cyanobacteria contain valuable compounds for health and cosmetic applications; these include mainly bioactive carbohydrates, antioxidants, pigments and fatty acids, among others.

Carotenoids produced from microalgae are important in health protection. Beta-carotene from *Dunaliella salina* has proven efficient at preventing angiogenesis in laboratory studies, thus helping to prevent the irregular formation of new blood vessels in pathologies such as cancer [39]. Astaxanthin from *Haematococcus pluvialis* has been reported to lower blood pressure; it was shown to act as an anti-hypertensive in spontaneously hypertensive rats (SHRs) at a dosage of 50 mg/kg over 14 days [40]. Carotenoids have also been reported for their anti-cancer activity, especially contributing to the prevention of cancers such as breast, hepatic, intestinal and prostate cancer as well as leukaemia. Likewise, carotenoids have been reported for treating and controlling diabetes, with beta-carotene concentrations in the blood being inversely associated with fasting blood glucose levels and insulin resistance, respectively [41]. In addition, carotenoids such as lycopene, lutein, and zeaxanthin protect against diabetic retinopathy [42]. With regard to anti-obesity activity, the chemical structures of carotenoids are important for suppressing adipocyte differentiation, with fucoxanthin and neoxanthin exhibiting significant anti-obesity functions [43]. Among the different carotenoids, fucoxanthin is considered a promising food supplement and weight-loss drug for preventing and managing obesity [44]. Another carotenoid that exhibits strong antioxidant activity is astaxanthin, which shows higher levels of antioxidant activity than other carotenoids. In older people, age-related macular degeneration (ARMD) is one of the leading causes of visual impairment. As carotenoids absorb UV light and other forms of solar radiation that can damage our eyes, these molecules could help in preserving healthy eye cells by reducing oxidative damage and vision loss [45]. Microalgae strains such as *Scenedesmus* and *Muriellopsis* have been proposed as potential lutein producers to prevent ARMD [46].

Skin protection is one of the most extensively applied microalgae-related applications, with the use of some microalgal genera, especially *Arthrospira* and *Chlorella*, being well established and widely reported in the skin care market [47]. Microalgal-based extracts are currently found in anti-aging, refreshing and regenerating care products, in peelers as an anti-irritant and in sun-protection and haircare products [48,49]. Certain compounds present in cyanobacteria have photo-protective, moisturizing, antioxidant, anti-inflammatory and regenerative properties, which are useful in health and wellness treatments such as thalassotherapy [50]. Positive effects have been reported from metabolite contents such as flavonoids, β-carotene, phycobiliproteins, phenols, saponins, steroids, tannins, terpenes and vitamins [51]. Cyanobacteria are capable of producing compounds with photo-protective properties such as mycosporine-like amino acids (MAAs) and scytonemin (SCY).

Concerning microalgal-based fatty acids, polyunsaturated fatty acids (PUFA), especially those belonging to the omega-3 and omega-6 families, are most commonly used as nutrition supplements to provide a cardioprotective effect and prevent neurological disorders [49,52]. Microalgae belonging to the *Nannochloropsis*, *Tetraselmis*, *Crypthecodinium*, *Isochrysis*, *Thalassiosira*, *Phaeodactylum*, *Schizochytrium* and *Chaetoceros* genera, among others, have been reported as being good PUFA producers, especially for docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). These PUFAs are found as nutritional supplements in baby foods, infant formula, dairy and bakery products, eggs, poultry meat and a wide range of non-alcoholic beverages.

Finally, one should point out the secondary metabolites from microalgae (besides exopolysaccharides and vitamins). Microalgae and cyanobacteria produce other valuable compounds such as biologically active compounds that have antiviral, antiseptic, antifungal and anticancer properties, among other things [53].

# Emerging applications of microalgae

Emerging applications include the production of biomaterials, as an alternative to fossil-based materials, of agriculture-related products such as biofertilizers, biostimulants and biopesticides making food cultivation more sustainable, and of biofuels as an alternative to petroleum-based fuels. Moreover, they can be used in service-providing processes such as wastewater treatment and the clean-up of industrial gases, especially flue gases. Such applications are not yet commercial due to the large gap that still exists between the size of the facilities required and the currently available microalgal production technology. However, there is no doubt that this gap will lessen in the coming years making microalgae utilization possible in highly relevant applications.

## *Microalgal bio-based materials*

Biomaterials serve to reduce the consumption of conventional fossil-fuel-based materials; they also provide additional or improved properties for new applications. Algae-based compounds, whether pure or blended with other materials, can be used in a wide range of applications. Nonetheless, relevant challenges remain in commercializing these biomaterials, such as their production cost and capacity. Considering the current competitiveness regarding polysaccharides coming from well-established sources such as terrestrial plants, seaweed, fungi, animals and bacteria, it would appear that producing exopolysaccharides from microalgae for certain low-value, high-volume markets still requires time to mature. In any case, there are niche markets and specific applications where microalgal-based polysaccharides could play an important role in the near future. The vast improvement in technologies for mass producing microalgal biomass, and downstream processing using the biorefinery concept, has significantly decreased the cost of commercial microalgae products and paved the way for the cultivation of still unexploited microalgae species [54].

Similarly, microalgal bioplastics could soon become indispensable given their more environmentally friendly and biodegradable properties compared to ordinary fossil-based plastics. Indeed, microalgae produce a diverse range of intermediate ingredients for bioplastic (bio-derived and biodegradable plastics) synthesis, for instance, polyhydroxybutyrate (PHB), which is a polymer belonging to the polyester class [55]. Improved PHB production efficiency using microalgal biomass from high-rate algal ponds (HRAPs) is expected to trim the operational costs, making it an interesting and sustainable feedstock for bioplastic production in the near future. However, microalgal-based bioplastic production is still in the research and development stage, and thus far from commercialization.

## *Agriculture-related products*

Agriculture-related microalgae applications are well known and many microalgae-related products has been developed over recent years. Usually, they are sold as biofertilizers but considering their low nutrient content (<5% N, <1%P) and the low dosage used (5-10 L/ha), the net amount of nutrients provided is insignificant. Use of biostimulants allows reduction in the amount of fertilizers required by the crops, and therefore indirectly enhances agricultural sustainability - applying these products at a rate of 2 l/ha reduces the need for chemical fertilizers by more than 10%.

Microalgal biomass is rich in amino acids providing beneficial effects to the plants [56]. Amino acids act as biostimulants, so even low concentrations are advantageous for the plants, promoting root and fruit development, amongst others [56]. To maximize the positive effect of these amino acids, they must be adequately supplied, making the utilization of hydrolysed extracts recommendable. Furthermore, the degree of hydrolysis required is not excessive, so peptides and polypeptides remain following partial hydrolysis, and these are also beneficial to the crops [57]. In addition to amino acids, microalgae contain phytohormones such as auxins-like and cytokinins-like compounds, which act as plant growth promoters. Auxins greatly improve root development, thus they increase the plant’s capacity to take up water and nutrients from the soil and make them more tolerant to adverse stress conditions [58]. Cytokinins increase plant growth and also stimulate fruit enlargement [58]. Microalgae biomass contains relevant concentrations of these molecules, especially the fast growing strains such as *Chlorella* [58].

Microalgae also possess molecules that can act as biopesticides, thus protecting the plant against pathogens, mainly fungi or bacteria. Marine algae have been shown to engage in bactericidal [59,60], antifungal [61,62] and insecticidal activities [63,64]. Green microalgae genera such as *Nannochloropsis*, *Chlorella*, and *Scenedesmus* can produce phytohormones including indoleacetic acid (IAA), cytokinins, gibberellins, abscisic acid (ABA) and/or jasmonic acid [65]. In addition, the production of antibiotics and siderophores from *Chlorella* and *Scenedesmus* has been previously described. While cyanobacteria like *Arthrospira* (*Spirulina*), *Oscillatoria*, *Chlorogloea*, *Arthronema* and *Calothrix* are able to produce IAA, cytokinins and/or jasmonic acid [66], *Nostoc*, *Anabaena*, *Oscillatoria* and *Tolypothrix* cyanobacteria are very effective “biopesticide” agents.

The biofertilizer market is a prime focus of the agriculture industry. Biofertilizers improve the availability of nutrients and enhance their consumption by the plants. They also act as a barrier against pathogens and protect plants from pests, decompose organic residues and stimulate the plant’s overall growth and development. The biostimulant market is driven by increased customer attention to enhancing the premium value of crops. Among the types of plant growth regulators, which include auxins, cytokinins, gibberellins, and others, gibberellins account for the largest market share, followed by cytokinins and auxins. With respect to biopesticides, the increased awareness regarding occupational hazards caused by chemical pesticides is one of the main factors driving this market. Biopesticides are used primarily as preventative measures for plant disease. They are made from naturally occurring substances that control pests using nontoxic mechanisms and in an eco-friendly way.

## *Wastewater treatment and CO2 biofixation*

Microalgae have been widely reported as useful in wastewater treatment, producing oxygen required by the bacteria to remove the organic matter, allowing the recovery of nutrients already contained in wastewaters and transforming them into valuable biomass that is suitable for producing biofuels and other applications [67].Microalgae have also been described as an adequate carbon capture method for removing CO2 from flue gases, thus avoiding their release into the atmosphere; however, this process has not yet been commercialized [68]. Both microalgae and cyanobacteria have been widely reported to treat wastewaters (agro-industrial, urban/domestic and others) regardless of their origin [53,69]. These organisms are able to remove nutrients from the wastewater (which acts as a cost-effective culture medium) and convert them into valuable biomass that is suitable for various purposes such as bioenergy, bio-based products and materials falling within the bioeconomy framework.

Microalgae-related wastewater treatment is performed by microalgae and bacteria consortia in which the bacteria degrade the organic matter into inorganic compounds, which are then consumed by the microalgae cells to produce oxygen and microalgae biomass. Naturally occurring populations are dominated by microalgae biomass, with strains from the *Scenedesmus* and *Chlorella* genera predominating [70]. Regarding the operational conditions, the hydraulic retention time must be reduced as much as possible while ensuring adequate contaminant removal. Hydraulic retention times of up to 10 days have generally been reported, but these can be reduced to 3 days under optimal conditions [4]. Concerning pH control, this is necessary to ensure the stability of the biological system. It is usually performed by injecting CO2-rich gases, which at the same time provide carbon that avoids carbon limitation in the process [71]. With regard to the water depth, this must be reduced to facilitate microalgal growth; however, this also reduces the overall reactor volume and the amount of water that can be treated. The recommended water depth ranges from 0.2 to 0.4 m [72]. In any case, up to 1 kg of microalgae biomass can be produced per m3 of sewage treated. In addition to sewage, other wastewaters can be recycled using microalgae, such as manure, centrate or digestate, with the same principles being applied to these systems. Such effluents are richer in nutrients so they must be provided in lower amounts to avoid overloading the capacity of the systems. Given the higher nutrient concentration in these effluents, more microalgae biomass is produced, from 10 to 100 kg of microalgae biomass per m3 of effluent.

Several carbon capture and storage (CCS) technologies have been developed for flue gases, for example, absorption, adsorption, cryogenic, and membrane separation. However, the most efficient CO2 bio-capture process is carried out by microalgae and cyanobacteria. The process involves collecting flue gases containing CO2 from facilities where it is generated, such as fossil-fuel power plants, which are currently surpassing atmospheric CO2 levels. Microalgae and cyanobacteria should tolerate elevated CO2 levels in the gas phase (typically 15% v/v) together with high temperatures and other toxic substances such as NOx and SOx. Although most microalgae and cyanobacteria cannot withstand such selective conditions, exceptions have been reported [53]. For instance, *Chlorella sorokiniana* previously isolated in Japan performed well when exposed to a gaseous mixture containing 10% CO2 at 40 °C (Morita et al., 2000), even in the presence of NO (100 ppm) and SO2 (25 ppm). On the other hand, the marine microalga *Chlorococcum littorale* was reported to tolerate and perform carbon biofixation at CO2 concentrations up to 40% into the gas [73]. This field of application opens up excellent possibilities for either thermophilic or thermotolerant microalgae and cyanobacteria.

## *Bioenergy*

Microalgae appear to be a sustainable feedstock for 3rd generation bioenergy and biofuels. Therefore, given the various advantages that they offer, it is expected that in the near future they will become an important carbon-neutral biofuel feedstock. Microalgal biomass can be used to produce biofuels such as biodiesel [74], bioethanol, biobutanol, biogas and biohydrogen, among others [75,76]. Advanced biofuels can be made from microalgae through different conversion pathways (biochemical, chemical and thermochemical; independently or sequentially) [77]. Conversion technologies such as transesterification [74], pyrolysis [78], anaerobic digestion, hydro-treatment, fermentation and direct combustion for microalgal biofuel and bioenergy production have been widely reported. However, the development of cost-effective microalgal-based biofuel production is taking longer than expected. Significant cost reductions may be achieved if the CO2, nutrients and water can be obtained at low cost. A major R&D initiative is required to enhance the production yield while also reducing the overall operating cost [77]. Anaerobic digestion for biogas, and eventually biomethane and hydrothermal liquefaction [79], have been increasingly studied because there is no need to dewater the feedstock, thus saving on drying costs.

As previously stated, microalgae have a huge potential for use as a feedstock in biorefineries since a wide range of valuable products can be produced from them. However, the “only-biofuel” production approach hasn’t become commercially viable yet and the economics of alternative options will play a pivotal role [77]. Rather than the conventional option of a single product line, a matrix approach resulting in numerous alternatives is preferred for the successful operation of algal biorefineries. For instance, microalgal biodiesel production was reported to be 2.5-times as energy intensive as conventional diesel, but when considering co-production and the decarbonisation of the electricity used in the whole production process, this biofuel could become a financially and environmentally viable option [77]. Substantial cost reductions may be expected if the CO2, nutrients and water can be obtained at low cost [80].

A techno-economic assessment of direct bioethanol production using a genetically-modified cyanobacteria (*Synechocystis* sp.) has been carried out [81]. The process modelling design was based on two main scenarios: i) a bioenergy-driven microalgal biorefinery for the production of fuel-grade ethanol and biogas for CHP and ii) a biobased-driven microalgal biorefinery for the production of added-value bioproducts, such as zeaxanthin and phycocyanin, together with ethanol and CHP production. The functional size of the facility was a small-scale demo plant capable of producing 1000 L ethanol/day, which was then extrapolated for larger production capacities. Despite the innovation apparent in the direct bioethanol production scenario, it was not economically feasible. In contrast, producing bioethanol as a co-product alongside high added value products from the bio-based product biorefinery was economically feasible, even with payback periods longer than 10 years. Finally, if only high added value products are considered in the whole process, either the NPV or the payback period are more attractive (104.8 M€ and ca. 5 years, respectively) [81].

# Conclusions and future trends

A microalgae-based circular bioeconomy should involve the reincorporation of production side-streams and residues as secondary raw materials i.e. as a way of finding another use for waste products in microalgae-based production systems (microalgae biorefineries). The implementation of next-generation technologies is required for the targeted reduction of process waste, and energy and water consumption, across the entire microalgae value chain. Special attention should be given to developing new microalgae manufacturing processes with quality standards and guidelines focusing on zero-waste, diversifying the use of input feedstock, reducing contamination, infestation, predation and competition risk, as well as engaging producers so that they enhance recycling and reduce microalgae process waste. The new processes must include the approved uses of the biomass and derived products according to current regulations, for example avoiding the utilization of microalgae obtained when coupling biomass production with wastewater treatment processes in food related applications. Driving circular excellence requires the full exploitation and integration of new efficient and innovative technologies for the extraction, fractionation, conversion and purification of a wide range of bio-based microalgal fractions. This should include the valorisation of waste and side-streams into marketable value chains to create commercially successful products. Increasing market penetration for microalgae-based products as sustainable alternatives to the currently available options in the market will be crucial for the success of a bioeconomy based on microalgae.

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Table 1.- Comparison of the algae sector with other relevant sectors, such as soy and fish [7].

Table 2.- Most important autotrophic microalgae in the market.

Figure 1.- Summary of the major figures related to microalgae production [7].

Figure 2.- Comparison of industrial production facilities based on the technology and size.

Figure 3.- Current and emerging microalgae applications.

Figure 4.- Image of carotenoid extract obtained from microalgae for use as a feed additive and as aquafeed, prepared by incorporating up to 5% microalgae biomass with regular aquafeed, based on vegetables, fish meal and fish oil.