Microalgae Biodiversity: Sustainable Biofactories for Food, Fuel and Therapeutics

---

Libertine Rose S. Sanchez
University of the Philippines Diliman
lssanchez@up.edu.ph
Wilberto D. Monotilla
University of the Philippines Diliman
wdmonotilla@up.edu.ph

ABSTRACT

Microalgae refers to diverse range of microscopic algae that are of great economic, biomedical, environmental, industrial and agricultural resources for all life forms. Applied phycology is a promising field making use of the microalgae biodiversity as a response to the needs of times: food, green fuel and therapeutics resources. These photosynthetic prokaryotic cyanobacteria and eukaryotic microalgae are regarded as sustainable biofactories because of their great capability to convert dioxide and nutrients into biomass. The high composition and concentration of valuable metabolites in these microalgae mitigate our current demands for functional foods as needed by both animals and humans, nutrition and health therapeutics as well as bio-energy resources. Genomics and genetic engineering along with morphometric and biochemical characterization are being used to analyze their metabolic pathways in order to improve their lipid synthesis and biomass accumulation. *Arthrospira platensis*, *Haematococcus pluvialis*, *Porphyridium* sp., *Chlamydomonas reinhardtii* and *Nostoc* sp. dominate the biomass production in open and closed system photobioreactors. They are in high demand as food, feeds, nutraceuticals, bioactive metabolite sources for antimicrobial, antiviral and antitumor treatments, bio-oil and biodiesel sources. This mini-review paper might spur the interest of Asian industries to establish microalgae production since most photobioreactors are in European and American countries.

Keywords: biodiversity, biofactories, biofuel, microalgae, therapeutics

Introduction

Phycology is a discipline focusing on the morphological, environmental physiological and genetic studies of photosynthetic algae. This includes the prokaryotic cyanobacteria, microscopic algae and seaweed macroalgae (R. E. Lee, 2018). Microalgae have an enormous biodiversity due to their photosynthetic capability as prokaryotic or eukaryotic algae. Out of the 10 million strains, only about 5% were carefully identified to have vast morphological features, widely distributed in natural and extreme habitats, simple cellular organization but complex biochemical compositions. They are currently regarded as highly valuable microorganisms due to their widespread utilization in agriculture, environment, pharmaceutical and biomedical industries (Mutanda et al., 2020; Susanti & Taufikurahman, 2021b). A thorough knowledge on their biodiversity could readily provide information on their cultivation, conservation and optimization of biomass production for natural, synthetic and biofuel products.

This review provides an update on the microalgal biodiversity using polyphasic approaches such as molecular genomics, physicochemical, advanced morphometric and physiological characterization. A thorough understanding of their biodiversity provides information on the current list of identified microalgae and the newly established species (Athulya & Anitha, 2020). This can also be of great help to reveal their multipurpose significance in conservation efforts and long term investigation in the stability of ecosystem dynamics (Gao & Lin, 2018; Susanti & Taufikurahman, 2021a). Several approaches on nutrient modification and optimum growth conditions are also included in this review that can be used by the academe and research industries to produce a cost-efficient microalgal biomass production and increase market profitability. It also discusses their potentials in bioengineering methods as valuable biofuel and biofertilizers including their large-scale production in bioreactors. Remarkable compounds such as primary and secondary metabolites reported to have variable therapeutic and nutraceutical activities for human and animals were also included in this review. The potentiality of cyanobacterial pigments for biotechnological applications as colorant in food and textile industries were also mentioned (Assunção et al., 2022). These syntheses may serve as a springboard to choose interesting microalgae for future studies as potential markets and as exploited resources in a sustainable manner.

1. Biodiversity of Microalgae

Microalgae are unicellular, colonial or filamentous algae widely distributed in terrestrial, freshwater, marine or brackish environments. They possess unique metabolic plasticity that enables them to greatly adapt even to extreme environments (Forján et al., 2015). Some also serve as primary producers in the food chain of most aquatic habitats (Mehariya et al., 2021a; Molino et al., 2018). They also have diverse relationships with other organisms that generally serves as their hosts or they are mutually symbiotic (Susanti & Taufikurahman, 2021b). The so called aero-terrestrial or aerophil microalgae have interesting physiological features, desiccation tolerance and can be found thriving in soil, rock crevices, leaf surfaces, tree barks or in symbiosis with fungi. This includes the prokaryotic cyanobacteria from the orders Chroococcales, Oscillatoriales, Nostocales, Pseudanabaenales and the eukaryotic greens from the classes Trebouxiophyceae, Chlorophyceae, Ulvophyceaea (Büdel, 2011; Hoffmann, 1989), Chlorokybophyceae, Zygnematophyceae (Lewis & McCourt, 2004), Klebsormidiophyceae (Holzinger et al., 2014), Coleochaetophyceae (Cook & Graham, 2016). The other colored microalgae includes the Xanthophyta, Eustigmatophyta, Bacillariophyta (Lakatos & Strieth, 2017), and the cosmopolitan diatoms. They can withstand environmental conditions of extreme pH values, temperatures, conductivity, salinity, humidity, light exposure and interrelationships with other organisms (Manoylov, 2014; Susanti & Taufikurahman, 2021b). There are also terrestrial cryophiles found in the snow and in spaces between ice crystals (Gray et al., 2020).

On the other hand, majority of the aquatic microalgae are being used commercially *since* they are easier to cultivate in liquid cultures (Lakatos & Strieth, 2017). Their morphology is consistent with any season composed of diverse cellular features, plastid morphology, biochemical and genetic composition (Sahoo & Seckbach, 2015). They range in size from the smallest 1.3 µm *Braarudosphaera* µm (Kamennaya et al., 2018) up to a 100 µm *Spirulina* (Becker, 2013).

Prokaryotic Microalgae

The blue-green algae, collectively known as cyanobacteria are the only photosynthetic representative prokaryotic algae thriving in a wide range of marine, freshwater and terrestrial habitats. They possess a Gram-negative four-layered cell wall, free floating 70S ribosomes, DNA, and thylakoids (R. E. Lee, 2018; Samiee et al., 2019). Cyanobacteria resemble more of the prokaryotic bacteria in terms of cellular structures but they are regarded as algae due to the presence of chorophyll a, b d, phycobiliproteins and carotenoids (Assunção et al., 2022). They have the simplest morphology of unicellular to colonial or multicellular to filamentous free-living algae enclosed in a mucilaginous membrane. Their cell size range from <1 ìm in diameter for unicellular species up to 10 ìm for the filamentous strains (Mehdizadeh Allaf & Peerhossaini, 2022). Several cyanobacterial species possess a trichome surrounded by a sheath. They also possess akinetes that developed from vegetative cells with an increased cytoplasmic density due to protoplasm full of food reserves such as glycogen and cyanophycin. At the same time, there is also a tremendous decrease in photosynthesis and respiration activities as akinetes become dormant upon maturity (R. E. Lee, 2018). Their heavily thickened wall made them survive in extreme and starvation conditions. Heterocysts, on the other hand, also possess a thickened cell wall similar to akinetes but with less dense granular cytoplasm since they do not contain photosynthetic apparatus . They are usually found along the filament and are only produced when there is insufficient amount of nitrogen. *Anabaena* and *Nostoc*, for instance, are filamentous cyanobacteria with heterocycsts that activate their genes for nitrogen fixation and repressing genes for photosynthesis (Sukenik et al., 2019).

To date, there are 5749 identified cyanobacterial species found in AlgaeBase repository, with at least 140 genera and 273 species were newly described. The Phylum Cyanophyceae was categorized into seven Orders namely: Chroococcales, Gloeobacterales, Pleurocapsales, Synechococcales, Nostocales, Oscillatoriales, and Spirulinales (Guiry & Guiry, 2023; Strunecky et al., 2020). The unicellular coccoid to colonial forms of cyanobacteria generally belong to Chroococcales, Gloeobacterales and Pleurocapsales. Chroococcales cells are usually contained in a mucilaginous envelope. Its common representative is the algal bloom-forming *Microcystis*. On the other hand, *Gloeobacter* genus from a monophyletic family belonging to Gloeobacterales, is the only cyanobacteria that lacks thylakoid (Guiry & Guiry, 2023). Little studies has been conducted with Pleurocapsales since they are endoliths that are difficult to observe (Roush & Garcia-Pichel, 2020). The notable representative of this order include *Pleurocapsa*, *Stainiera* and *Xenococcus* that exists as coccoids or pseudo-filaments, which form a complex colony. Whereas the most abundant Synechococcales are composed of unicellular, colonial and filamentous cyanobacteria. Its representative *Synechocystis* is a model organism that can grow in autotrophic and heterotrophic conditions in the absence of light, hence, constantly used in photosynthetic researches and biotechnological applications (Zhao et al., 2023). In the case of filamentous species, Nostocales, Oscillatoriales and Spirulinales are the most identified cyanobacteria where the latter have screw-like coiled trichomes without sheaths (Dvoøák et al., 2017). *Nostoc*, *Anabaena* and *Fischerella* are the widely known Nostocales with heterocysts that fix nitrogen for their neighboring cells (Herrero et al., 2016; Zeng & Zhang, 2022). The most abundant linear filamentous cyanobacteria Oscillatoria, *Lyngbya*, *Phormidium* including those with complicated thylakoid arrangement belong to Oscillatoriales with the exception of a coccoid *Cyanothece* (Komarek et al., 2014; Kumari & Rai, 2022).

Eukaryotic Microalgae

The early eukaryotic microalgae were believed to have existed during the evolution of chloroplasts. Konstantin Mereschkowsky was the first biologist who proposed the endosymbiotic origin of chloroplast. A theory where a cyanobacterium was taken up by a phagocytic protozoan that was not consumed but only stored into food vesicle. This made the cyanobacterium an endosymbiont of the protozoan, giving the latter some of the photosynthates whereas the cyanobacterium benefited from having a stable environment. Through evolution, a mutation in the endosymbiont cyanobacterium resulted to its loss of cell wall probably to give way for easier transport of photosynthates and other compounds from the endosymbiont to the host protozoan. This in turn led to a theory that the plasma membrane of the endosymbiont became the inner membrane of the chloroplast while the membrane of the protozoan's food vesicle became the outer membrane of the chloroplast. In addition, the thylakoid membrane rearrangement and further evolution of polyhedral bodies giving rise into a pyrenoid completely described its transition into a true chloroplast, with such structures clearly evident in the present-day red and green algae (R. E. Lee, 2018).

All eukaryotic microalgae are photosynthetic with chloroplasts made up of multiple flattened thylakoids containing chlorophyll a, b , c1, c2, c3, d, f, carotenoids and phycobiliprotein pigments (Miazek et al., 2015). Most of them possess cellulose cell walls surrounded by an amorphous layer and laminated polysaccharides (Passos et al., 2015). Some microalgae have silica, calcium carbonate scales and highly ornamented scalesin their cell walls such as those in diatoms, coccoliths and Chrysophytes, repsectively (Fawley & Fawley, 2020).

There are about 15 taxonomic phyla of micro algae that differ in terms of plastid type and photosynthetic pigments (Raven & Giordano, 2014; Solymosi, 2012). This include Cyanobacteria (blue-green algae), Rhodophyta (red algae), Glaucophyta (blue algae), Prasinophyta (primitive green algae), Chlorophyta (green algae), Xanthophyta (yellow-green algae), Chrysophyta (golden brown algae), Phaeophyta (brown algae), Cryptophyta (cryptomonads), Haptophyta (haptophytes), Ochrophyta (Ochrophytes), Euglenophyta (euglenoids), Dinophyta (dinoflagellates), Raphidophyta (raphidophytes) and Bacillariophyta (diatoms) (John et al., 2011; Ruggiero et al., 2015). These groups exhibit variations in plastid anatomy, and pigment compositions (Susanti & Taufikurahman, 2021b).

2. Growth and Physiology of Microalgae

It is very important to understand the growth phases in microalgae, which includes its lag, exponential, declining relative growth, stationary and death/lysis phases. The lag phase is relatively short in liquid cultures. An increased biomass production is usually observed in the exponential growth phase where there is a moderate light intensity requirement (Farag & Price, 2013). The specific growth rates for aquatic and terrestrial microalgae ranges from 0.3 to 1.1 ì day $^{-1}$ (Nascimento et al., 2013) and 0.37 to 1.15 ì day $^{-1}$ (Lakatos & Strieth, 2017), respectively. Moreover, the production of secondary metabolites such as carotenoids and antioxidants relatively occur during the declining or retardment growth phase where light, carbon dioxide and nutrient factors becomes limited (Forján et al., 2015).

In terms of irradiance, microalgae have high adaptability to various light intensities depending on the environments they are exposed to. The photosynthetic active radiance (PAR) from 400nm to 700 nm is the requirement for its optimal growth. High irradiances induce the biosynthetic production of polyunsaturated fatty acids (PUFA), carotenoids and vitamins (Forján et al., 2015). Aquatic microalgae generally adapted to low and intermediate light intensities and alternating light-time/dark-time fluctuations while terrestrial microalgae are adapted to low light requirements. Light quality also greatly influences the microalgae's light adaptation processes. The photosystem (PS) light harvesting complex (LHC) of most microalgae is governed by chlorophyll (*chlor*) a, *chlor* b and carotenoids in blue and red light spectra (Lakatos & Strieth, 2017). Furthermore, there is an extremely LHC I in green algae that captures and transfers energy at a faster rate to the PS I core as reported in *Bryopsis corticulans* (Qin et al., 2019). Whereas cyanobacteria and red algae utilize only *chlor* a, carotenoids and their phycobilisomes protein complexes to enhance their photosynthetic capabilities. Phycobilisomes are granules found on the outer surface of thylakoids containing the light-harvesting phycobiliproteins (PBPs) namely, phycoerythrin, phycoerythrocyanin, phycocyanin and allophycocyanin differing in the orientation and number of attached phycobilin chromophore responsible for their color differences. These PBPs are accessory pigments that carry out PS II (Barsanti & Gualtieri, 2014; Lakatos & Strieth, 2017). In addition, recent evidence of a pigment-protein supermolecule composed of LHC and PS II has been identified in the red algae *Nannochloropsis granulate* (Umetani et al., 2018).

Major variables such as pH and temperature are also necessary for their growth conditions. The optimal pH range for microalgae are generally 7.0 to 10.0 (Filali et al., 2021), while the others thrive at acidic conditions below 3.0 (Acién et al., 2017). It greatly affects enzymatic activities and their entire metabolic processes Microalgae are classified as psychrophiles (growing optimally below 15°C), mesophiles (growing between15°C-50°C), thermophiles (growing at above 50°C), or hyperthermophiles (growing optimally above 80°C) (Lakatos & Strieth, 2017; Varshney et al., 2015) as shown in Table 1. The optimal temperature growth for cyanobacteria is 25°C–35°C while for chlorophytes is 27.5°C-35°C (Lürling et al., 2013). The upper temperature limit for cyanobacteria is 75°C while the threshold for eukaryotic algae is 62°C.

Table 1. Optimum growth temperatures for microalgae commonly used in biotechnology.

Classification	**Growth temperature**	**Genus**	**Biotechnological Application**
Mesophilic Cyanobacteria	45°C – 50°C	*Synechocystis, Gloeocapsa, Symploca, Plectonema, Lyngbya, Spirulina, Pleurocapsa, Calothriz* (Castenholz, 1981), *Chroocidiopsis thermalis* (Lakatos & Strieth, 2017)	Carotenoid production, heavy metal adsorption, H2 production, nutraceuticals (Antal & Lindblad, 2005; Hoseini et al., 2013; Melnic et al., 2011; Pokrovsky et al., 2008; Raungsomboon et al., 2008)
Thermophilic Cyanobacteria	52°C - 58°C	*Phormidium boryana, Thermosynechococcus elongatus, T. Vulcanus, Oscillatoria terebriformis* (Varshney et al., 2015)	CO2 mitigation from industrial flue gas and C-phycocyanin production (Leu et al., 2013)
	55°C – 70°C	*Synechococcus lividus* (Castenholz, 1981)	Hydrogen peroxide production (Sheridan, 1973)
	55°C, 60°C	*Phormidium laminosum, Oscillatoria, Mastigocladus* (Castenholz, 1981)	Biomass for bioethanol production, lipid production, thermostable restriction enzyme, treatment of dye-rich wastewater, biosorption of chromium (VI) and Remazol

Classification	Growth temperature	Genus	Biotechnological Application
			Black B reactive dye, antimicrobial, removal of nitrate and phosphate ions from water (Patel et al., 2019; Piechula et al., 2001)
	62°C	*Synechococcus elongatus* (Miyairi, 1995)	CO2 assimilation (Patel et al., 2019)
Psychrophilic Chlorophyte	15°C	*Chlamydomonas raudensis* (Lakatos & Strieth, 2017)	Biorememidation (Cervera-Carles et al., 2020)
Mesophilic Cholorophytes	8°C – 28°C	*Haematococcus pluvialis* (Borowitzka et al., 1991)	Carotenoid production, antioxidant (Kathiresan & Sarada, 2009)
	45°C – 50°C	*Desmodesmus, Chlorella sorokiniana, Chlorella kessleri, Scenedesmus obliquus,* (Lakatos & Strieth, 2017)	Biofuel, lipid production, CO2 assimilation, carotenoid production, antioxidant (Patel et al., 2019)
Thermophilic Rhodophyte	56°C	*Cyanidium caldarium, Cyanidioschizon merolae, Galdieria sulphuraria* (Doemel & F, 1971)	Blue pigment phycocyanin (PC) used as a fluorescent marker in histochemistry, wastewater treatment (Patel et al., 2019)
Ice algae Extremophile	> 80°C	*Chloromonas, Chlorosarcina antarctica, Chlamydomonas, Chlainomonas,*	2006; H. Ling & Seppelt, 1990; H. U. Ling, 1996, 2001, 2002) Glycerol, sucrose, glucose (Roser et al., 1992)

Classification	Growth temperature	Genus	Biotechnological Application
		Desmotetra aureospora, *Mesotaenium berggrennii* (Hoham, 1975; Hoham et al.,	

3. Plastids of Microalgae

One of the most essential structures during the growth of microalgae is the plastid development that contain various pigments, fatty acids, oils, starch and terpene metabolites (Choi et al., 2021). The plastid morphology and colors are highly diverse due to the abiotic factors exhibited by the various types of environment. Stress-inducing factors can also be applied in such as high temperature, salinity, pH or light intensity, nutrient deprivation of N, Ca, K, C, Si or addition of heavy metals (Susanti & Taufikurahman, 2021b) in order to produce the expected high valuable compounds (Markou & Nerantzis, 2013).

4. Genomes of Microalgae

Out of the 40,000 algal species reported (S. Khan et al., 2017), only 62 algal genomes have been sequenced and deposited at the National Center for Biotechnology Information (NCBI) repository (Nelson et al., 2019). The earliest microalgae that had been sequenced include the chlorophyte *Ostreococcus tauri*, haptophyte *Emiliana huxleyi* and dinophyte *Karenia brevis* with genome sizes of 12.6 Mbp, 168 Mbp and 10,000 Mbp, respectively. Post-genomic approaches such as transcriptomics, proteomics and other omics technology are being used to understand the various physiological, metabolic and signal transduction pathway in microalgae similar to the "Marine Microbial Transcriptome Project" (Keeling et al., 2014), Tara Oceans (Sunagawa et al., 2020), and Prometheus portal for interkingdom comparative genomic analysis (Ko et al., 2020). The transcriptomic data from these projects speeds up the development and production of microalgae-derived metabolites.

There is a need for microalgal sequencing since their genomes could be mined for agro-industrial, environmental and biomedical insights. As the cost of next generation sequencing technology are getting low, identification of gene functions at the transcriptomic, proteomic and metabolic levels are also rapidly developing. This progression in microalgal genomics led to faster exploitation of the biotechnological applications of microalgae. The collection of microalgal genomes will also help resolve the geographic distribution (Yun et al., 2019), differences in habitat alkalinity (Nelson et al., 2019), pigment compositions (Narang et al., 2021), viral load (Hunter, 2021; Jeanniard et al., 2013; Kimura & Tomaru, 2015; Sun & Ku, 2021) and biosynthetic metabolites of various microalgae species.

5. Biotechnological Applications of Microalgae

Microalgae are generally used as model organisms for genetic studies and gives a promising ingenious biotechnological solutions since they accumulate organic materials that enables to them to accumulate high biomass. On the average, their biomass doubles every 2 to 5 days, and a yield of 20 kg/m^2/year (Vaz et al., 2016). This in turn results to their numerous potentials in the production of bioactive metabolites and bioenergy chemicals (S. Khan et al., 2017; Kuo et al., 2021). This is also due to high demand for pharmaceuticals, renewable biomaterials, food supplements, nutraceuticals, additive, substitutes, feeds, textile dyes and mordants (Novoveská et al., 2019). Microalgae produced high valuable, carotenoids (Chagas et al., 2015; Hopkins et al., 2019; Hosseinzadeh Gharajeh et al., 2020), phycobilin (Solymosi, 2012; Tan et al., 2021), exopolysaccharides (EPS), eicosapentaenoic acid (EPA) (Adarme-Vega et al., 2012; Asgharpour, 2015; S. Khan et al., 2017) and docosahexaenoic acid (DHA) (Diao et al., 2018; Song et al., 2020).

The current product estimation of dry biomass from microalgae is 56,456 tonnes dominated by the cyanobacterium *Arthrospira* at 56,208 tonnes while the rest are the green microalgae *Haematococcus pluvialis*, *Dunaliella salina*, *Chlorella vulgaris* and *Tetraselmis* sp. at 248 tonnes (Cai et al., 2021). Table 2 summarizes the bioactive metabolites and pharmacological properties of the different strains of microalgae.

The production of algal biomass is increasing globally reaching about 32.67 Mt fresh weight in 2016, where 97% of which is based on aquaculture cultivation (Dos, 2019). There is a very high cultivation of microalgae in European countries dominated by France, Germany, Spain and Italy where they utilize photobioreactors with fermenters or open ponds for production (Araújo et al., 2021).

Microalgae are also widely used as bioindicators and bio-remediators (Sahoo & Seckbach, 2015) in bio-film photobioreactors and bioengineering (Lakatos & Strieth, 2017). The commonly used system in the large-scale production of algal biomass are open ponds as shown in Figure 1 (Acién et al., 2017; El-Baz & Baky, 2018; Narala et al., 2016) since it is less expensive when it comes to construction, maintenance and operation (Costa & de Morais, 2014; Lakatos & Strieth, 2017). Open systems are practically designed with shallow depth for a fast and efficient penetration of light energy. The culture mixing of algae that demands for a lesser energy requirement is the topmost benefit derived from an open raceway pond. However, since they are open systems, many organisms such as heterotrophic microbes, small and large predators can contaminate the culture. The weather seasons also greatly affects the algal growth which means different conditions and requirements must be applied for a specific season. Another issue as well for open commercial systems is poor mixing that results to lower biomass productivity (Dunford, 2015).

Figure 1. Open pond systems of microalgae cultivation (Acién et al., 2017; El-Baz & Baky, 2018; Narala et al., 2016).

On the other hand, many countries prefer to use the closed photobioreactors in order to reduce contamination and achieve higher productivity rate (Amaro et al., 2011) as shown in Figure 2 (Masojídek & Torzillo, 2008; Mohr, 2013; Schreiber et al., 2017). This photobioreactors can be operated and maintained at a highly-controlled environment. It also requires lesser space, which in turn, decreases contamination rates while increasing light availablility (Narala et al., 2016). There are several categories and classification of closed photobioreactors based on the vessel orientation and according to their geometrical configuration. Flat panel and tubular designs have been commonly used for large scale production of algal biomass that are sources for high value products (Dunford, 2015).

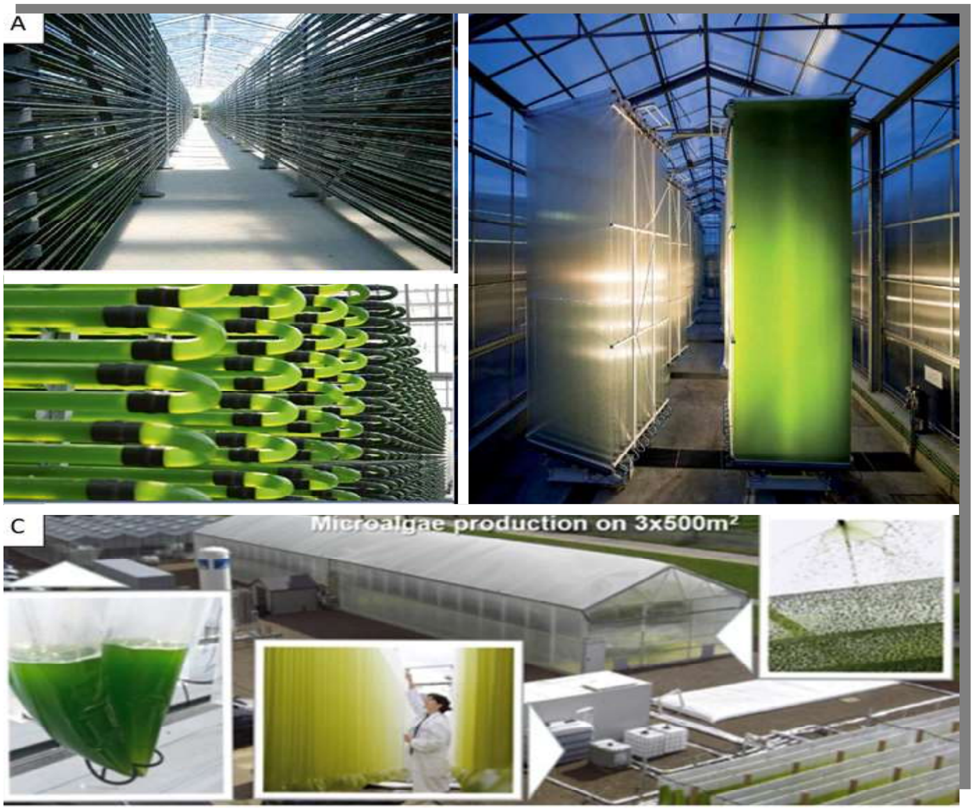

Figure 2. A closed-system type of photobioreactors. A. Tubular photobioreactor in Klötze, Germany Photo© Jörg Ullmann (Masojídek & Torzillo, 2008), B. Flat-plate photobioreactor known as "Hanging Gardens" developed by ecoduna-produktions GmbH in Bruck/Leitha, Austria Photo© ecoduna (Mohr, 2013), and C. Foil photobioreactor set-up by the NOVAgreen company in Bergheim-Neideraussem, Germany (Schreiber et al., 2017).

5.1 Microalgae-derived compounds as Functional FOOD

The chemical composition, antioxidant capacity, high protein concentration, volatile substances, fatty acid and carotenoid profiles of microalgae render them ideal source of nutraceuticals that gives tremendous benefits for both animal and human health (Ward & Singh, 2005).

In the study conducted by Nascimento and colleagues (2020) on the lipophilic, aqueous, carotenoid extracts of *Scenedesmus obliquus* and *Phormidium autumnal*e biomass showing its high polyunsaturated fatty acids (PUFA) content and higher antioxidant properties (Nascimento et al., 2013). Omega-3 fatty acids derived from microalgae have better organoleptic qualities compared to those derived from fish (Mendes et al., 2009). These lipid products will then be incorporated to most milk and dairy products. *Arthrospira,* on the other hand, has high protein content and good nutritional value of (Forján et al., 2015).

There are non-toxic microalgae that can be directly consumed just like in the case of people from the low-income countries utilizing *Spirulina* harvested from lakes that gave them sufficient nutritional value and health benefits (Habib et al., 2008; Piccolo, 2012). There are also several microalgae extracts that are being used as food additives or feeds in aquaculture and farm feeds industries. They are utilized for larvae nutrition and play an important role in fish, mollusks and crustaceans breeding process due to their high protein content and PUFA (Cai et al., 2021; Forján et al., 2015).

5.2 Microalgae-derived compounds as Biofuel

The addition of CO_2 to illuminated growing microalgae cultures enhances their biomass for oil production. There are several ongoing researches exploring the biosynthetic pathways of triglycerides in potential microalgae species (Forján et al., 2015) using genomic, transcriptomic, metabolomic as well as genetic manipulation to improve oil productivity (Cadoret et al., 2012). Researchers firmly believed that microalgae are appropriate sources for biofuel production due to their high lipid content, faster growth, photoautotrophs that fixes CO_2 from the air converting it into lipids and carbohydrates and some species are very capable of accumulating large amounts of triglycerides that is deemed appropriate for biodiesel production (Kumar et al., 2010; Scott et al., 2010). Thirty-eight percent biomass *Arthrospira platensis* has been used as a substrate for the production of bioethanol (Alfarisi, 2020; Markou & Nerantzis, 2013). On the other hand, biomethane is produced by microalgae species under anaerobic conditions. This is greatly possible due to the high lipid, protein and starch compounds in several microalgae species (Forján et al., 2015) usually done in a two-step process. This includes anaerobic digestion of microalgae biomass that enhances the biogas production using a mixture of methane and CO_2. This in turn is followed by enrichment of methane biogas with the aid of *Arthrospira* platensis that functions to remove CO_2 in the biogas compound (Converti et al., 2006; El-Kassas et al., 2015).

5.3 Microalgae-derived compounds as Therapeutics

Microalgae are known sources of Vitamins A, B1, B2, B3, B6, B9, B12, C, E, nicotinic acid, biotin, folic acid, pantothenic acid that are added to cosmetic products or improve the culinary qualities of fish like the improvement of coloring in salmonid flesh (Guerin et al., 2003). They also possess various bioactive metabolites such as carotenoids, alkaloids, terpenoids, phenols, PUFAs gamma-linolenic acid (GLA), arachidonic acid (AA), EPA and DHA that have antimicrobial, antiviral, antioxidant and antitumor activities (Das & Madhavi, 2011; Varfolomeev & Wasserman, 2011). This spurred the interest of the pharmaceutical industry to explore microalgae with biotherapeutics potential. Table 2 shows the summary of highly valuable biochemical metabolites derived from various microalgae.

Table 2. Microalgae-derived compounds and bioactive metabolites (Lakatos & Strieth, 2017; Raanan et al., 2016; Susanti & Taufikurahman, 2021).

Taxonomy	**Microalgae species**	**Biochemical Compounds/ Application**	**References**
Eustigmatophyceae	*Nannochloropsis oculata*	Biodiesel, Hydrocarbon (HC), Eicosapentaenoic Acid (EPA), Bio-oil	(Adarme-Vega et al., 2012; Asgharpour, 2015; Culaba et al., 2020; M. I. Khan et al., 2018; Raanan et al., 2016; Raja et al., 2014; Saad et al., 2019)
Euglenaceae	*Euglena viridis*	Organic Extract	(Das & Madhavi, 2011)

Taxonomy	**Microalgae species**	**Biochemical Compounds/ Application**	**References**
Bacillariophyceae	*Chaetoceros muelleri*	Fatty acids	(Mendiola et al., 2007)
	Navicula directa	Naviculan polysaccharide as antiviral	(J.-B. Lee et al., 2006)
	Phaeodactylum sp.	EPA, Bio-oil	(Adarme-Vega et al., 2012; Asgharpour, 2015; M. I. Khan et al., 2018; Raja et al., 2014)
	Phaeodactylum tricornutum	Organic extracts, EPA, PUFA as antimicrobial	(Desbois et al., 2009)
	Skeletonema costatum	Fatty acids	(Naviner et al., 1999)
	Thalassiosira pseudonana	EPA	(Forhan et al., 2015)
Rhodophyceae	Porphyridium cruentum *Porphyridium* sp.	Ethanol extracts, EPA, Sulfated polysaccharides as antiviral	(Adarme-Vega et al., 2012; Asgharpour, 2015; Huheihel et al., 2002; M. I. Khan et al., 2018; Raja et al., 2014; Rodriguez-Garcia & Guil-Guerrero, 2008)
Prymnesiphyceae	*Isochrysis galbanaIsochrysis* sp.	EPA	(Adarme-Vega et al., 2012; Asgharpour, 2015; Gouveia et al., 2008; M. I. Khan et al., 2018; Lazarus & Bhimba, 2008; Raja et al., 2014)

Taxonomy	Microalgae species	Biochemical Compounds/ Application	References
Chlorophyceae	*Botryococcus braunii*	Biodiesel, HC, antioxidant	(Culaba et al., 2020; M. I. Khan et al., 2018; Saad et al., 2019; Sathasivam et al., 2019)
	Chlamydomonas sp.	Vitamins	(M. I. Khan et al., 2018; Sathasivam et al., 2019)
	Chlamydomonas reinhardtii	Model organism, methanol and hexane extract	(Culaba et al., 2020; Ghasemi et al., 2007; Saad et al., 2019)
	Chlamydomonas nivalis	Antioxidant	(M. I. Khan et al., 2018; Sathasivam et al., 2019)
	Chlorella autotrohpica	Sulfated polysaccharides	(Fabregas et al., 1999)
	Chlorella pyrenoidosa	Polypeptides	(Wang & Zhang, 2013)
	Chlorella sorokiniana	Ethanol, extracts as antitumor	(Chung et al., 2012)
	Chlorella sp.	Biodiesel, HC, Bio-oil, Food product, Vitamins, antitumor compounds such as sterols, polypeptides, glycoproteins	(Chung et al., 2012; Culaba et al., 2020; M. I. Khan et al., 2018; Saad et al., 2019)
	Chlorella stigmatophora	Hydro and liposoluble extracts	(Guzmán et al., 2001)

Taxonomy	Microalgae species	Biochemical Compounds/ Application	References
	Chlorella keslerii	Biogas	(Culaba et al., 2020; Saad et al., 2019)
	Chlorella vulgaris	Feed, food additives, Carotenoid production, anti-hypertensive metabolites lutein and peptides	(Cha et al., 2008; Hozawa et al., 2007; Martins et al., 2021; Panahi et al., 2016)
	Desmodesmus sp.	Biodiesel, HC	(Culaba et al., 2020; M. I. Khan et al., 2018; Saad et al., 2019)
	Chlorococcum sp.	Astaxanthin, Bioethanol	(Culaba et al., 2020; Saad et al., 2019S.-J. Lee et al., 2003)
	Coccomyxa onubensis	Lutein as antioxidants	(Garbayo et al., 2012)
	Dunaliella salina	β-carotene as anti-inflammatory and astaxanthin production	(M. I. Khan et al., 2018; Lavy et al., 2003; Raja et al., 2014; Sathasivam et al., 2019)
	Dunaliella tertiolecta	EPA, Carotenoid and Lipid production	(Chagas et al., 2015; Hopkins et al., 2019; Hosseinzadeh Gharajeh et al., 2020)
	Haematococcus lacustris *Haematococcus* sp. *Haematococcus pluvialis*	Food product, Carotenoid production, Antioxidant, PUFA as antimicrobial	(Caporgno & Mathys, 2018; M. I. Khan et al., 2018; Niccolai et al., 2019; Raja et al., 2014;

Taxonomy	**Microalgae species**	**Biochemical Compounds/ Application**	**References**
			Rodríguez-Meizoso et al., 2010; Sathasivam et al., 2019)
	Muriellopsis sp.	Lutein as antioxidants	(Garbayo et al., 2012)
	Scenedesmus S. obliquus	Bio-oil, Vitamins, Carotenoid and Lipid production	(Culaba et al., 2020; M. I. Khan et al., 2018; Nascimento et al., 2013; Saad et al., 2019; Sathasivam et al., 2019)
	Tetraselmis sp.	EPA, Food product, Bio-oil	(Adarme-Vega et al., 2012; Asgharpour, 2015; Caporgno & Mathys, 2018; M. I. Khan et al., 2018; Niccolai et al., 2019; Raja et al., 2014; Sathasivam et al., 2019)
	Phormidium autumnale	Carotenoid and Lipid production	(Nascimento et al., 2013)
Ulvophyceaea	*Trentepohlia arborum*	Carotenoid production	(Chen et al., 2015)

Taxonomy	Microalgae species	Biochemical Compounds/ Application	References
Dinophyceae	*Crypthecodinium cohnii*	Docosahexaenoic acid (DHA)	(Diao et al., 2018; Song et al., 2020)
	Gymnodinium sp.	Extracellular Polysaccharide (EPS)	(Umemura et al., 2003)
Bangiophyceae	*Anabaena* sp.	Hydrosoluble extracts, Biogas	(Culaba et al., 2020; Najdenski et al., 2013; Saad et al., 2019)
	Aphanizomenon flos-aqua	Dietary supplement	(Cadoret et al., 2012; Jensen et al., 2000)
	Cyanidium sp.	phycocyanin production	(Eisele et al., 2000; Moon et al., 2014; Raja et al., 2014)
	Galdiera sp.	phycocyanin production	(Eisele et al., 2000; Moon et al., 2014; Raja et al., 2014)
Cyanophyceae	*Arthrospira platensis*	Food products/ additives, phycocyanin production, PUFA as antimicrobial, anti-hypertensive metabolites lutein and peptides	(Caporgno & Mathys, 2018; Colla et al., 2004; Eisele et al., 2000; Hozawa et al., 2007; Moon et al., 2014; Niccolai et al., 2019; Raja et al., 2014; Sathasivam et al., 2019)
	Gloeocapsa sp.	EPS	(Najdenski et al., 2013)

Taxonomy	Microalgae species	Biochemical Compounds/ Application	References
	Leptolyngbya sp.	Carotenoid production	(Kuhne et al., 2013)
	Nostoc sp.*Nostoc ellipsosporumNostoc linckiaNostoc spongiaforme*	Food products, Crytophycin and Cyanovirin as antiviral, Borophycin as antimicrobial and cytotoxic activities against colorectal cancer	(Burja et al., 2001; Caporgno & Mathys, 2018; Magarvey et al., 2006; Niccolai et al., 2019; O'Keefe et al., 2010; Sathasivam et al., 2019)
	Synechococcus PCC 7002	Metabolic model organism, Cyanovirin	(Hendry et al., 2016; Ludwig & Bryant, 2012; O'Keefe et al., 2010)
	Synechococcus PCC 6803	Model organism	(Ikeuchi & Tabata, 2001; Yu et al., 2013)
	Synechococcus elongatus	Saccharose as bioethanol	(Ducat et al., 2012)
	Synechocystis sp.	PUFA as antimicrobial	(Najdenski et al., 2013; Plaza et al., 2010)

Conclusion

This review carefully evaluated the current abundance, cultivation techniques, and biotechnological applications of prokaryotic and eukaryotic microalgae. It also pointed out the numerous microalgae natural products and metabolites such as PUFAs, carotenoids, EPAs, EPSs, DHA, and lutein among others produced from microalgal biorefinery.

The relatively easier and cost-effective means of culturing microalgae is most likely a probable alternative to harvesting traditional products from plants. Numerous cultivation techniques and strategies for large-scale biomass production can be applied in order to extract the chemical compounds and natural products that can contribute to food, biofuel, and biotherapeutics industries for farm and agriculture development, for human health benefits and for sustainable green resources.

However, there is still a vast diversity of microalgae with potential for biotechnological processes that are yet to be screened and validated for better cultivation. Gene editing and genetic manipulation tools are current breakthroughs, which can be developed for increasing the potentiality of microalgae as a natural, sustainable source in the biofuel, pharmaceutical and agricultural industries.

Libertine Rose S. Sanchez *is a Senior Lecturer from the Institute of Biology and National Institute of Molecular Biology and Biotechnology. At present, she is a full time PhD Graduate Fellow of the DOST-SEI with UPD-NIMBB as Host Institute working on the DNA barcoding and Metabarcoding of green microalgae. Together with other science enthusiasts, Sanchez started biobanking of green microalgae and cyanobacteria at the NIMBB and IB, respectively. She is also part of a team who started the genomics and metabolomics in green algae for carotenoid or astaxanthin extraction. She is currently part of a project at the Institute of Biology about the whole genome sequencing of local cyanobacteria with biotherapeutic potentials.*

Wilberto D. Monotilla *is presently an Associate Professor of Molecular Biology and Biotechnology (NIMBB) and Principal Investigator at the Aquatic Biotechnology Laboratory (ABL) in the National Institute of Molecular Biology and Biotechnology in UP Diliman. He received his MS and PhD. in Aquatic Biosciences, major in Applied Phycology in 2002 and 2005, respectively from Tokyo University of Marine Science and Technology, Japan under the Monbusho scholarship program. He had joined NIMBB in 2009 after some teaching stint at other universities in Metro Manila. He is also a recipient of several UP Centennial Professorial Chair for his contributions in scientific research, and for his several international and local publications. He is currently the president of Philippine Phycological Society, Inc (PPSI). Dr. Monotilla's research area is in the field of algal biotechnology and aquatic ecosystems. His current researches include understanding the molecular mechanisms involved in the production of microalga secondary carotenoid, algal metabolites, and occasionally on microalgal biofuels.*

REFERENCES

Acién, F. G., Molina, E., Reis, A., Torzillo, G., Zittelli, G. C., Sepúlveda, C., & Masojídek, J. (2017). 1—Photobioreactors for the production of microalgae. In C. Gonzalez-Fernandez & R. Muñoz (Eds.), *Microalgae-Based Biofuels and Bioproducts* (pp. 1–44). Woodhead Publishing. https://doi.org/10.1016/B978-0-08-101023-5.00001-7

Adarme-Vega, T. C., Lim, D. K. Y., Timmins, M., Vernen, F., Li, Y., & Schenk, P. M. (2012). Microalgal biofactories: A promising approach towards sustainable omega-3 fatty acid production. *Microbial Cell Factories*, *11*, 96. https://doi.org/10.1186/1475-2859-11-96

Alfarisi, M. S. (2020). Sustainable bioethanol production from microalgae through ionic liquid as a potential catalyst: Review. *AIP Conference Proceedings*, *2223*(1), 050003. https://doi.org/10.1063/5.0000952

Amaro, H. M., Guedes, A. C., & Malcata, F. X. (2011). Advances and perspectives in using microalgae to produce biodiesel. *Applied Energy*, *88*(10), 3402–3410. https://doi.org/10.1016/j.apenergy.2010.12.014

Antal, T. K., & Lindblad, P. (2005). Production of H2 by sulphur deprived cells of the unicellular cyanobacteria Gloeocapsa alpicola and Synechocystis sp. PCC 6803 during dark incubation with methane or at various extracellular pH. *Journal of Applied Microbiology*, *98*(1), 114–120. https://doi.org/10.1111/j.1365-2672.2004.02431.x

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. *Frontiers in Marine Science*, *7*. https://www.frontiersin.org/articles/10.3389/fmars.2020.626389

Asgharpour, M. (2015). Eicosapentaenoic Acid (EPA) from Porphyridium Cruentum: Increasing Growth and Productivity of the Microalgae for Pharmaceutical Products. *Graduate Theses and Dissertations*. https://scholarworks.uark.edu/etd/1438

Assunção, J., Amaro, H. M., Malcata, F. X., & Guedes, A. C. (2022). Chapter 8 - Cyanobacterial pigments: Photosynthetic function and biotechnological purposes. In G. Lopes, M. Silva, & V. Vasconcelos (Eds.), *The Pharmacological Potential of Cyanobacteria* (pp. 201–256). Academic Press. https://doi.org/10.1016/B978-0-12-821491-6.00008-9

Athulya, K., & Anitha, T. (2020). Algal Biodiversity along Southern Coasts of India: A Review. *INTERNATIONAL JOURNAL OF ADVANCED RESEARCH IN BIOLOGICAL SCIENCES*, *7*(10), 32–42. http://dx.doi.org/10.22192/ijarbs.2020.07.10.004

Barsanti, L., & Gualtieri, P. (2014). Algae: Anatomy, Biochemistry, and Biotechnology, Second Edition. *CRC Press Taylor & Francis Group*, 344.

Becker, E. W. (2013). *Becker, 2013. In: Richmond, A., Qiang Hu (Eds), 2013, Handbook of microalgal culture: Applied phycology and biotechnology, 2nd edition, Wiley-Blackwell: 671-691 | Feedipedia*. https://www.feedipedia.org/node/22544

Büdel, B. (2011). Eukaryotic Algae. In U. Lüttge, E. Beck, & D. Bartels (Eds.), *Plant Desiccation Tolerance* (pp. 45–63). Springer. https://doi.org/10.1007/978-3-642-19106-0_4

Burja, A. M., Banaigs, B., Abou-Mansour, E., Burgess, J. G., & Wright, P. C. (2001). Marine cyanobacteria—A prolific source of natural products. *Tetrahedron*, *57*(46), Article 46. https://doi.org/10.1016/S0040-4020(01)00931-0

Cadoret, J.-P., Garnier, M., & Saint-Jean, B. (2012). Microalgae, Functional Genomics and Biotechnology. In *Advances in Botanical Research* (Vol. 64, pp. 285–341). Elsevier. https://doi.org/10.1016/B978-0-12-391499-6.00008-6

Cai, J., Lovatelli, A., Agilar-Manjarrez, J., Cornish, L., Dabbadie, L., Desrochers, A., Diffey, S., Garrido Gamarro, E., Geehan, J., Hurtado, A., Lucente, D., Mair, G., Miao, W., Potin, P., Przbyla, C., Reantaso, M., Roubach, R., Tauati, M., & Yuan, X. (2021). *Seaweeds and microalgae: An overview for unlocking their potential in global aquaculture development*. FAO Fisheries and Aquaculture Circular No. 1229. Rome, FAO. https://doi.org/10.4060/cb5670en

Caporgno, M. P., & Mathys, A. (2018). Trends in Microalgae Incorporation Into Innovative Food Products With Potential Health Benefits. *Frontiers in Nutrition*, *5*. https://www.frontiersin.org/articles/10.3389/fnut.2018.00058

Cervera-Carles, L., Dols-Icardo, O., Molina-Porcel, L., Alcolea, D., Cervantes-Gonzalez, A., Muñoz-Llahuna, L., & Clarimon, J. (2020). Assessing circular RNAs in Alzheimer's disease and frontotemporal lobar degeneration. *Neurobiology of Aging*, *92*, 7–11. https://doi.org/10.1016/j.neurobiolaging.2020.03.017

Cha, K. H., Koo, S. Y., & Lee, D.-U. (2008). Antiproliferative effects of carotenoids extracted from Chlorella ellipsoidea and Chlorella vulgaris on human colon cancer cells. *Journal of Agricultural and Food Chemistry*, *56*(22), 10521–10526. https://doi.org/10.1021/jf802111x

Chagas, A. L., Rios, A. O., Jarenkow, A., Marcílio, N. R., Ayub, M. A. Z., & Rech, R. (2015). Production of carotenoids and lipids by Dunaliella tertiolecta using CO2 from beer fermentation. *Process Biochemistry*, *50*(6), 981–988. https://doi.org/10.1016/j.procbio.2015.03.012

Chen, L., Zhang, L., Zhang, W., & Liu, T. (2015). Comparative analysis of growth and carotenoid accumulation of Trentepohlia arborum in aerial, subaerial, and aquatic cultivation. *Journal of Applied Phycology*, *27*(3), 1079–1087. https://doi.org/10.1007/s10811-014-0436-x

Choi, H., Yi, T., & Ha, S.-H. (2021). Diversity of Plastid Types and Their Interconversions. *Frontiers in Plant Science*, *12*. https://www.frontiersin.org/articles/10.3389/fpls.2021.692024

Chung, J.-G., Peng, H.-Y., Chu, Y.-C., Hsieh, Y.-M., Wang, S.-D., & Chou, S.-T. (2012). Anti-invasion and apoptosis induction of chlorella (Chlorella sorokiniana) in Hep G2 human hepatocellular carcinoma cells. *Journal of Functional Foods*, *4*(1), 302–310. https://doi.org/10.1016/j.jff.2011.12.008

Colla, L. M., Bertolin, T. E., & Costa, J. A. V. (2004). Fatty acids profile of Spirulina platensis grown under different temperatures and nitrogen concentrations. *Zeitschrift Fur Naturforschung. C, Journal of Biosciences*, *59*(1–2), 55–59. https://doi.org/10.1515/znc-2004-1-212

Converti, A., Lodi, A., Del Borghi, A., & Solisio, C. (2006). Cultivation of Spirulina platensis in a combined airlift-tubular reactor system. *Biochemical Engineering Journal*, *32*(1), 13–18. https://doi.org/10.1016/j.bej.2006.08.013

Cook, M. E., & Graham, L. E. (2016). Chlorokybophyceae, Klebsormidiophyceae, Coleochaetophyceae. In J. M. Archibald, A. G. B. Simpson, C. H. Slamovits, L. Margulis, M. Melkonian, D. J. Chapman, & J. O. Corliss (Eds.), *Handbook of the Protists* (pp. 1–20). Springer International Publishing. https://doi.org/10.1007/978-3-319-32669-6_36-1

Costa, J. A. V., & de Morais, M. G. (2014). Chapter 1—An Open Pond System for Microalgal Cultivation. In A. Pandey, D.-J. Lee, Y. Chisti, & C. R. Soccol (Eds.), *Biofuels from Algae* (pp. 1–22). Elsevier. https://doi.org/10.1016/B978-0-444-59558-4.00001-2

Culaba, A. B., Ubando, A. T., Ching, P. M. L., Chen, W.-H., & Chang, J.-S. (2020). Biofuel from Microalgae: Sustainable Pathways. *Sustainability*, *12*(19), Article 19. https://doi.org/10.3390/su12198009

Das, U. N., & Madhavi, N. (2011). Effect of polyunsaturated fatty acids on drug-sensitive and resistant tumor cells in vitro. *Lipids in Health and Disease*, *10*(1), 159. https://doi.org/10.1186/1476-511X-10-159

Desbois, A. P., Mearns-Spragg, A., & Smith, V. J. (2009). A fatty acid from the diatom Phaeodactylum tricornutum is antibacterial against diverse bacteria including multi-resistant Staphylococcus aureus (MRSA). *Marine Biotechnology (New York, N.Y.)*, *11*(1), 45–52. https://doi.org/10.1007/s10126-008-9118-5

Diao, J., Song, X., Zhang, X., Chen, L., & Zhang, W. (2018). Genetic Engineering of Crypthecodinium cohnii to Increase Growth and Lipid Accumulation. *Frontiers in Microbiology*, *9*. https://www.frontiersin.org/articles/10.3389/fmicb.2018.00492

Dos, S. F. D. A. R. (2019, December 19). *Brief on algae biomass production*. JRC Publications Repository. https://doi.org/10.2760/402819

Ducat, D. C., Avelar-Rivas, J. A., Way, J. C., & Silver, P. A. (2012). Rerouting carbon flux to enhance photosynthetic productivity. *Applied and Environmental Microbiology*, *78*(8), 2660–2668. https://doi.org/10.1128/AEM.07901-11

Dunford, N. (2015, March 1). *Photobioreactor Design for Algal Biomass Production—Oklahoma State University*. https://extension.okstate.edu/fact-sheets/photobioreactor-design-for-algal-biomass-production.html

Dvoøák, P., Casamatta, D. A., Hašler, P., Jahodáøová, E., Norwich, A. R., & Poulíèková, A. (2017). Diversity of the Cyanobacteria. In P. C. Hallenbeck (Ed.), *Modern Topics in the Phototrophic Prokaryotes: Environmental and Applied Aspects* (pp. 3–46). Springer International Publishing. https://doi.org/10.1007/978-3-319-46261-5_1

Eisele, L. E., Bakhru, S. H., Liu, X., MacColl, R., & Edwards, M. R. (2000). Studies on C-phycocyanin from Cyanidium caldarium, a eukaryote at the extremes of habitat. *Biochimica Et Biophysica Acta*, *1456*(2–3), 99–107. https://doi.org/10.1016/s0005-2728(99)00110-3

El-Baz, F. K., & Baky, H. H. A. E. (2018). Pilot Scale of Microalgal Production Using Photobioreactor. In *Photosynthesis—From Its Evolution to Future Improvements in Photosynthetic Efficiency Using Nanomaterials*. IntechOpen. https://doi.org/10.5772/intechopen.78780

El-Kassas, H. Y., Heneash, A. M. M., & Hussein, N. R. (2015). Cultivation of Arthrospira (Spirulina) platensis using confectionary wastes for aquaculture feeding. *Journal of Genetic Engineering and Biotechnology*, *13*(2), 145–155. https:/ /doi.org/10.1016/j.jgeb.2015.08.003

Fabregas, J., Garcýìa, D., Fernandez-Alonso, M., Rocha, A. I., Gómez-Puertas, P., Escribano, J. M., Otero, A., & Coll, J. M. (1999). In vitro inhibition of the replication of haemorrhagic septicaemia virus (VHSV) and African swine fever virus (ASFV) by extracts from marine microalgae. *Antiviral Research*, *44*(1), 67–73. https://doi.org/10.1016/S0166-3542(99)00049-2

Farag, I., & Price, K. (2013). Resources Conservation in Microalgae Biodiesel Production. *“ International Journal of Engineering and Technical Research (IJETR*, *1*, 49–56.

Fawley, M. W., & Fawley, K. P. (2020). Identification of Eukaryotic Microalgal Strains. *Journal of Applied Phycology*, *32*(5), 2699–2709. https://doi.org/10.1007/s10811-020-02190-5

Filali, R., Tian, H., Michelis, E., & Taidi, B. (2021). Evaluation of the Growth Performance of Microalgae Based on Fine pH Changes. *Austin Journal of Biotechnology & Bioengineering*, *8*(1). https://doi.org/10.26420/austinjbiotechnolbioeng.2021.1109

Forján, E., Navarro, F., Cuaresma, M., Vaquero, I., Ruíz-Domínguez, M. C., Gojkovic, Ž., Vázquez, M., Márquez, M., Mogedas, B., Bermejo, E., Girlich, S., Domínguez, M. J., Vílchez, C., Vega, J. M., & Garbayo, I. (2015). Microalgae: Fast-Growth Sustainable Green Factories. *Critical Reviews in Environmental Science and Technology*, *45*(16), 1705–1755. https://doi.org/10.1080/10643389.2014.966426

Gao, Y., & Lin, G. (2018). Algal diversity and their importance in ecological processes in typical mangrove ecosystems. *Biodiversity Science*, *26*(11), 1223. https://doi.org/10.17520/biods.2018080

Garbayo, I., Torronteras, R., Forján, E., Cuaresma, M., Casal, C., Mogedas, B., Ruiz-Domínguez, M. C., Márquez, C., Vaquero, I., Fuentes-Cordero, J. L., Fuentes, R., González-Del-Valle, M., & Vílchez, C. (2012). IDENTIFICATION AND PHYSIOLOGICAL ASPECTS OF A NOVEL CAROTENOID-ENRICHED, METAL-RESISTANT MICROALGA ISOLATED FROM AN ACIDIC RIVER IN HUELVA (SPAIN)(1). *Journal of Phycology*, *48*(3), 607–614. https://doi.org/10.1111/j.1529-8817.2012.01160.x

Ghasemi, Y., Moradian, A., Mohagheghzadeh, A., Shokravi, S., & Morowvat, M. H. (2007). *Antifungal and Antibacterial Activity of the Microalgae Collected from Paddy Fields of Iran: Characterization of Antimicrobial Activity of Chroococcus dispersus*. Asian Network for Scientific Information, Pakistan. http://www.scialert.net/pdfs/jbs/2007/904-910.pdf

Gouveia, L., Coutinho, C., Mendonça, E., Batista, A. P., Sousa, I., Bandarra, N. M., & Raymundo, A. (2008). Functional biscuits with PUFA-ù3 fromIsochrysis galbana. *Journal of the Science of Food and Agriculture*, *88*(5), 891–896. https://doi.org/10.1002/jsfa.3166

Gray, A., Krolikowski, M., Fretwell, P., Convey, P., Peck, L. S., Mendelova, M., Smith, A. G., & Davey, M. P. (2020). Remote sensing reveals Antarctic green snow algae as important terrestrial carbon sink. *Nature Communications*, *11*(1), Article 1. https://doi.org/10.1038/s41467-020-16018-w

Guerin, M., Huntley, M. E., & Olaizola, M. (2003). Haematococcus astaxanthin: Applications for human health and nutrition. *Trends in Biotechnology*, *21*(5), 210–216. https://doi.org/10.1016/S0167-7799(03)00078-7

Guiry, M., & Guiry, G. (2023, September 7). *Algaebase: Listing the World's Algae*. AlgaeBase. World-Wide Electronic Publication. https://www.algaebase.org/browse/taxonomy/detail/?taxonid=4351

Guzmán, S., Gato, A., & Calleja, J. M. (2001). Antiinflammatory, analgesic and free radical scavenging activities of the marine microalgae Chlorella stigmatophora and Phaeodactylum tricornutum. *Phytotherapy Research: PTR*, *15*(3), 224–230. https://doi.org/10.1002/ptr.715

Habib, M. A. B., Parvin, M., Huntington, T. C., Hasan, M. R., & Fisheries and Aquaculture Management Division. (2008). *A review on culture, production and use of* *spirulina as food for humans and feeds for domestic animals*. FAO. https://www.fao.org/publications/card/en/c/bae29089-6c97-52e9-a00d-cf4420e644ac/

Hendry, J. I., Prasannan, C. B., Joshi, A., Dasgupta, S., & Wangikar, P. P. (2016). Metabolic model of Synechococcus sp. PCC 7002: Prediction of flux distribution and network modification for enhanced biofuel production. *Bioresource Technology*, *213*, 190–197. https://doi.org/10.1016/j.biortech.2016.02.128

Herrero, A., Stavans, J., & Flores, E. (2016). The multicellular nature of filamentous heterocyst-forming cyanobacteria. *FEMS Microbiology Reviews*, *40*(6), 831–854. https://doi.org/10.1093/femsre/fuw029

Hoffmann, L. (1989). Algae of terrestrial habitats. *The Botanical Review*, *55*(2), 77–105. https://doi.org/10.1007/BF02858529

Holzinger, A., Kaplan, F., Blaas, K., Zechmann, B., Komsic-Buchmann, K., & Becker, B. (2014). Transcriptomics of Desiccation Tolerance in the Streptophyte Green Alga Klebsormidium Reveal a Land Plant-Like Defense Reaction. *PLOS ONE*, *9*(10), e110630. https://doi.org/10.1371/journal.pone.0110630

Hopkins, T. C., Sullivan Graham, E. J., & Schuler, A. J. (2019). Biomass and lipid productivity of Dunaliella tertiolecta in a produced water-based medium over a range of salinities. *Journal of Applied Phycology*, *31*(6), 3349–3358. https://doi.org/10.1007/s10811-019-01836-3

Hoseini, S. M., Khosravi-Darani, K., & Mozafari, M. R. (2013). Nutritional and Medical Applications of Spirulina Microalgae. *Mini Reviews in Medicinal Chemistry*, *13*(8), 1231–1237.

Hosseinzadeh Gharajeh, N., Valizadeh, M., Dorani, E., & Hejazi, M. A. (2020). Biochemical profiling of three indigenous Dunaliella isolates with main focus on fatty acid composition towards potential biotechnological application. *Biotechnology Reports*, *26*, e00479. https://doi.org/10.1016/j.btre.2020.e00479

Hozawa, A., Jacobs, D. R., Steffes, M. W., Gross, M. D., Steffen, L. M., & Lee, D.-H. (2007). Relationships of circulating carotenoid concentrations with several markers of inflammation, oxidative stress, and endothelial dysfunction: The Coronary Artery Risk Development in Young Adults (CARDIA)/Young Adult Longitudinal Trends in Antioxidants (YALTA) study. *Clinical Chemistry*, *53*(3), 447–455. https://doi.org/10.1373/clinchem.2006.074930

Huheihel, M., Ishanu, V., Tal, J., & Arad, S. M. (2002). Activity of Porphyridium sp. Polysaccharide against herpes simplex viruses in vitro and in vivo. *Journal of Biochemical and Biophysical Methods*, *50*(2–3), 189–200. https://doi.org/10.1016/s0165-022x(01)00186-5

Hunter, P. (2021). A bag of genes and surprises: Giant viruses continue to fascinate researchers for their role in eukaryote evolution and ecology. *EMBO Reports*, *22*(8), e53464. https://doi.org/10.15252/embr.202153464

Ikeuchi, M., & Tabata, S. (2001). Synechocystis sp. PCC 6803—A useful tool in the study of the genetics of cyanobacteria. *Photosynthesis Research*, *70*(1), 73–83. https://doi.org/10.1023/A:1013887908680

Jeanniard, A., Dunigan, D. D., Gurnon, J. R., Agarkova, I. V., Kang, M., Vitek, J., Duncan, G., McClung, O. W., Larsen, M., Claverie, J.-M., Van Etten, J. L., & Blanc, G. (2013). Towards defining the chloroviruses: A genomic journey through a genus of large DNA viruses. *BMC Genomics*, *14*, 158. https://doi.org/10.1186/1471-2164-14-158

Jensen, G., Ginsberg, D., Huerta, P., Citton, M., & Drapeau, C. (2000). Consumption of Aphanizomenon flos-aquae Has Rapid Effects on the Circulation and Function of Immune Cells in Humans A novel approach to nutritional mobilization of the immune system. *JANA*, *2*.

John, D., Brooks, A. J., & Whitton, B. (2011). *The Freshwater Algal Flora of the British Isles. An Identification Guide to Freshwater and Terrestrial Algae*.

Kamennaya, N. A., Kennaway, G., Fuchs, B. M., & Zubkov, M. V. (2018). “Pomacytosis”—Semi-extracellular phagocytosis of cyanobacteria by the smallest marine algae. *PLOS Biology*, *16*(1), e2003502. https://doi.org/10.1371/journal.pbio.2003502

Kathiresan, S., & Sarada, R. (2009). Towards genetic improvement of commercially important microalga Haematococcus pluvialis for biotech applications. *Journal of Applied Phycology*, *21*(5), 553–558. https://doi.org/10.1007/s10811-009-9414-0

Keeling, P. J., Burki, F., Wilcox, H. M., Allam, B., Allen, E. E., Amaral-Zettler, L. A., Armbrust, E. V., Archibald, J. M., Bharti, A. K., Bell, C. J., Beszteri, B., Bidle, K. D., Cameron, C. T., Campbell, L., Caron, D. A., Cattolico, R. A., Collier, J. L., Coyne, K., Davy, S. K., … Worden, A. Z. (2014). The Marine Microbial Eukaryote Transcriptome Sequencing Project (MMETSP): Illuminating the Functional Diversity of Eukaryotic Life in the Oceans through Transcriptome Sequencing. *PLOS Biology*, *12*(6), e1001889. https://doi.org/10.1371/journal.pbio.1001889

Khan, M. I., Shin, J. H., & Kim, J. D. (2018). The promising future of microalgae: Current status, challenges, and optimization of a sustainable and renewable industry for biofuels, feed, and other products. *Microbial Cell Factories*, *17*(1), 36. https://doi.org/10.1186/s12934-018-0879-x

Khan, S., Siddique, R., Sajjad, W., Nabi, G., Hayat, K. M., Duan, P., & Yao, L. (2017). Biodiesel Production From Algae to Overcome the Energy Crisis. *HAYATI Journal of Biosciences*, *24*(4), Article 4. https://doi.org/10.1016/j.hjb.2017.10.003

Kim, J.-D., & Lee, C.-G. (2005). Systemic optimization of microalgae for bioactive compound production. *Biotechnology and Bioprocess Engineering*, *10*(5), 418–424. https://doi.org/10.1007/BF02989824

Kimura, K., & Tomaru, Y. (2015). Marine Viruses that infect Eukaryotic Microalgae. *Uirusu*, *65*(1), 37–46. https://doi.org/10.2222/jsv.65.37

Ko, G., Jang, I., Koo, N., Park, S.-J., Oh, S.-H., Kim, M.-S., Choi, J.-H., Kim, H., Sim, Y. M., Byeon, I., Kim, P.-G., Kim, K. Y., Yoon, J.-C., Mun, K.-L., Lee, B., Han, G., & Kim, Y.-M. (2020). Prometheus, an omics portal for interkingdom comparative genomic analyses. *PLoS ONE*, *15*(10), e0240191. https://doi.org/10.1371/journal.pone.0240191

Komarek, J., Katsovsky, J., Mareš, J., & Jonhansen, J. R. (2014). *(PDF) Taxonomic classification of cyanoprokaryotes (cyanobacterial genera) 2014, using a polyphasic approach*. Https://Www.Preslia.Cz/Article/Pdf?Id=103. https://www.researchgate.net/publication/269094990_Taxonomic_classification_of_cyanoprokaryotes_cyanobacterial_genera_2014_using_a_polyphasic_approach

Kuhne, S., Lakatos, M., Foltz, S., Muffler, K., & Ulber, R. (2013). Characterization of terrestrial cyanobacteria to increase process efficiency in low energy consuming production processes. *Sustainable Chemical Processes*, *1*(1), 6. https://doi.org/10.1186/2043-7129-1-6

Kumar, A., Ergas, S., Yuan, X., Sahu, A., Zhang, Q., Dewulf, J., Malcata, F. X., & van Langenhove, H. (2010). Enhanced CO2 fixation and biofuel production via microalgae: Recent developments and future directions. *Trends in Biotechnology*, *28*(7), 371–380. https://doi.org/10.1016/j.tibtech.2010.04.004

Kumari, N., & Rai, L. C. (2022). Chapter12—Molecular characterization of local cyanobacterial isolates using 16S rRNA, rpoB, and nif H biomarkers. In P. Singh, M. Fillat, & A. Kumar (Eds.), *Cyanobacterial Lifestyle and its Applications in Biotechnology* (pp. 307–334). Academic Press. https://doi.org/10.1016/B978-0-323-90634-0.00004-4

Kuo, C.-M., Sun, Y.-L., Lin, C.-H., Lin, C.-H., Wu, H.-T., & Lin, C.-S. (2021). Cultivation and Biorefinery of Microalgae (Chlorella sp.) for Producing Biofuels and Other Byproducts: A Review. *Sustainability*. https://doi.org/10.3390/su132313480

Lakatos, M., & Strieth, D. (2017). Terrestrial Microalgae: Novel Concepts for Biotechnology and Applications. In F. M. Cánovas, U. Lüttge, & R. Matyssek (Eds.), *Progress in Botany Vol. 79* (Vol. 79, pp. 269–312). Springer International Publishing. https://doi.org/10.1007/124_2017_10

Lavy, A., Naveh, Y., Coleman, R., Mokady, S., & Werman, M. J. (2003). Dietary Dunaliella bardawil, a â-Carotene–Rich Alga, Protects Against Acetic Acid–Induced Small Bowel Inflammation in Rats. *Inflammatory Bowel Diseases*, *9*(6), 372–379. https://doi.org/10.1097/00054725-200311000-00005

Lazarus, S., & Bhimba, V. (2008). Antibacterial Activity Of Marine Microalgae Against Multidrug Resistant Human Pathogens. *International Journal on Applied Bioengineering*, *2*. https://doi.org/10.18000/ijabeg.10020

Lee, J.-B., Hayashi, K., Hirata, M., Kuroda, E., Suzuki, E., Kubo, Y., & Hayashi, T. (2006). Antiviral sulfated polysaccharide from Navicula directa, a diatom collected from deep-sea water in Toyama Bay. *Biological & Pharmaceutical Bulletin*, *29*(10), 2135–2139. https://doi.org/10.1248/bpb.29.2135

Lee, R. E. (2018, March 1). *Phycology*. Higher Education from Cambridge University Press; Cambridge University Press. https://doi.org/10.1017/9781316407219

Leu, J.-Y., Lin, T.-H., Selvamani, M. J. P., Chen, H.-C., Liang, J.-Z., & Pan, K.-M. (2013). Characterization of a novel thermophilic cyanobacterial strain from Taian hot springs in Taiwan for high CO2 mitigation and C-phycocyanin extraction. *Process Biochemistry*, *48*(1), 41–48. https://doi.org/10.1016/j.procbio.2012.09.019

Lewis, L. A., & McCourt, R. M. (2004). Green algae and the origin of land plants. *American Journal of Botany*, *91*(10), 1535–1556. https://doi.org/10.3732/ajb.91.10.1535

Ludwig, M., & Bryant, D. A. (2012). Synechococcus sp. Strain PCC 7002 Transcriptome: Acclimation to Temperature, Salinity, Oxidative Stress, and Mixotrophic Growth Conditions. *Frontiers in Microbiology*, *3*, 354. https://doi.org/10.3389/fmicb.2012.00354

Lürling, M., Eshetu, F., Faassen, E. J., Kosten, S., & Huszar, V. L. M. (2013). Comparison of cyanobacterial and green algal growth rates at different temperatures. *Freshwater Biology*, *58*(3), 552–559. https://doi.org/10.1111/j.1365-2427.2012.02866.x

Magarvey, N. A., Beck, Z. Q., Golakoti, T., Ding, Y., Huber, U., Hemscheidt, T. K., Abelson, D., Moore, R. E., & Sherman, D. H. (2006). Biosynthetic characterization and chemoenzymatic assembly of the cryptophycins. Potent anticancer agents from cyanobionts. *ACS Chemical Biology*, *1*(12), 766–779. https://doi.org/10.1021/cb6004307

Manoylov, K. M. (2014). Taxonomic identification of algae (morphological and molecular): Species concepts, methodologies, and their implications for ecological bioassessment. *Journal of Phycology*, *50*(3), 409–424. https://doi.org/10.1111/jpy.12183

Markou, G., & Nerantzis, E. (2013). Microalgae for high-value compounds and biofuels production: A review with focus on cultivation under stress conditions. *Biotechnology Advances*, *31*(8), 1532–1542. https://doi.org/10.1016/j.biotechadv.2013.07.011

Martins, C. F., Pestana, J. M., Alfaia, C. M., Costa, M., Ribeiro, D. M., Coelho, D., Lopes, P. A., Almeida, A. M., Freire, J. P. B., & Prates, J. A. M. (2021).

Effects of Chlorella vulgaris as a Feed Ingredient on the Quality and Nutritional Value of Weaned Piglets' Meat. *Foods*, *10*(6), Article 6. https://doi.org/10.3390/foods10061155

Masojídek, J., & Torzillo, G. (2008). Mass Cultivation of Freshwater Microalgae. In *Encyclopedia of Ecology* (pp. 2226–2235). https://doi.org/10.1016/B978-008045405-4.00830-2

Mehdizadeh Allaf, M., & Peerhossaini, H. (2022). Cyanobacteria: Model Microorganisms and Beyond. *Microorganisms*, *10*(4), 696. https://doi.org/10.3390/microorganisms10040696

Melnic, S., Prodius, D., Simmons, C., Zosim, L., Chiriac, T., Bulimaga, V., Rudic, V., & Turta, C. (2011). Biotechnological application of homo- and heterotrinuclear iron(III) furoates for cultivation of iron-enriched Spirulina. *Inorganica Chimica Acta*, *373*(1), 167–172. https://doi.org/10.1016/j.ica.2011.04.011

Mendes, A., Reis, A., Vasconcelos, R., Guerra, P., & Lopes da Silva, T. (2009). Crypthecodinium cohnii with emphasis on DHA production: A review. *Journal of Applied Phycology*, *21*(2), 199–214. https://doi.org/10.1007/s10811-008-9351-3

Mendiola, J. A., Torres, C. F., Toré, A., Martín-Álvarez, P. J., Santoyo, S., Arredondo, B. O., Señoráns, F. J., Cifuentes, A., & Ibáñez, E. (2007). Use of supercritical CO2 to obtain extracts with antimicrobial activity from Chaetoceros muelleri microalga. A correlation with their lipidic content. *European Food Research and Technology*, *224*(4), 505–510. https://doi.org/10.1007/s00217-006-0353-6

Miazek, K., Iwanek, W., Remacle, C., Richel, A., & Goffin, D. (2015). Effect of Metals, Metalloids and Metallic Nanoparticles on Microalgae Growth and Industrial Product Biosynthesis: A Review. *International Journal of Molecular Sciences*, *16*, 23929–23969. https://doi.org/10.3390/ijms161023929

Mohr, M. (2013). *There are hydro-mechanical problems that we have to solve so that the liquid can circulate through the reactor with as little resistance as possible. To create the flowing organic forms that enable circulation, you need a software package like Autodesk Inventor that not only allows this type of prototyping, but is also specifically designed for this purpose.* 2. http://images.autodesk.com/adsk/files/ecoduna_Customer_Story.pdf

Moon, M., Mishra, S. K., Kim, C. W., Suh, W. I., Park, M. S., & Yang, J.-W. (2014). Isolation and characterization of thermostable phycocyanin from Galdieria sulphuraria. *Korean Journal of Chemical Engineering*, *31*(3), 490–495. https://doi.org/10.1007/s11814-013-0239-9

Mutanda, T., Naidoo, D., Bwapwa, J. K., & Anandraj, A. (2020). Biotechnological Applications of Microalgal Oleaginous Compounds: Current Trends on Microalgal Bioprocessing of Products. *Frontiers in Energy Research*, *8*. https://www.frontiersin.org/article/10.3389/fenrg.2020.598803

Najdenski, H. M., Gigova, L. G., Iliev, I. I., Pilarski, P. S., Lukavský, J., Tsvetkova, I. V., Ninova, M. S., & Kussovski, V. K. (2013). Antibacterial and antifungal activities of selected microalgae and cyanobacteria. *International Journal of Food Science & Technology*, *48*(7), 1533–1540. https://doi.org/10.1111/ijfs.12122

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. *Frontiers in Energy Research*, *4*. https://www.frontiersin.org/articles/10.3389/fenrg.2016.00029

Narang, P. K., Dey, J., Mahapatra, S. R., Roy, R., Kushwaha, G. S., Misra, N., Suar, M., & Raina, V. (2021). Genome-based identification and comparative analysis of enzymes for carotenoid biosynthesis in microalgae. *World Journal of Microbiology & Biotechnology*, *38*(1), 8. https://doi.org/10.1007/s11274-021-03188-y

Nascimento, I. A., Marques, S. S. I., Cabanelas, I. T. D., Pereira, S. A., Druzian, J. I., de Souza, C. O., Vich, D. V., de Carvalho, G. C., & Nascimento, M. A. (2013). Screening Microalgae Strains for Biodiesel Production: Lipid Productivity and Estimation of Fuel Quality Based on Fatty Acids Profiles as Selective Criteria. *BioEnergy Research*, *6*(1), 1–13. https://doi.org/10.1007/s12155-012-9222-2

Naviner, M., Bergé, J.-P., Durand, P., & Le Bris, H. (1999). Antibacterial activity of the marine diatom Skeletonema costatum against aquacultural pathogens. *Aquaculture*, *174*(1), 15–24. https://doi.org/10.1016/S0044-8486(98)00513-4

Nelson, J. M., Hauser, D. A., Gudiño, J. A., Guadalupe, Y. A., Meeks, J. C., Salazar Allen, N., Villarreal, J. C., & Li, F.-W. (2019). Complete Genomes of Symbiotic Cyanobacteria Clarify the Evolution of Vanadium-Nitrogenase. *Genome Biology and Evolution*, *11*(7), Article 7. https://doi.org/10.1093/gbe/evz137

Niccolai, A., Chini Zittelli, G., Rodolfi, L., Biondi, N., & Tredici, M. R. (2019). Microalgae of interest as food source: Biochemical composition and digestibility. *Algal Research*, *42*, 101617. https://doi.org/10.1016/j.algal.2019.101617

Novoveská, L., Ross, M. E., Stanley, M. S., Pradelles, R., Wasiolek, V., & Sassi, J.-F. (2019). Microalgal Carotenoids: A Review of Production, Current Markets, Regulations, and Future Direction. *Marine Drugs*, *17*(11), 640. https://doi.org/10.3390/md17110640

O'Keefe, B. R., Giomarelli, B., Barnard, D. L., Shenoy, S. R., Chan, P. K. S., McMahon, J. B., Palmer, K. E., Barnett, B. W., Meyerholz, D. K., Wohlford-Lenane, C. L., & McCray, P. B. (2010). Broad-spectrum in vitro activity and in vivo efficacy of the antiviral protein griffithsin against emerging viruses of the family Coronaviridae. *Journal of Virology*, *84*(5), Article 5. https://doi.org/10.1128/JVI.02322-09

Panahi, Y., Darvishi, B., Jowzi, N., Beiraghdar, F., & Sahebkar, A. (2016). Chlorella vulgaris: A Multifunctional Dietary Supplement with Diverse Medicinal Properties. *Current Pharmaceutical Design*, *22*(2), 164–173. https://doi.org/10.2174/1381612822666151112145226

Passos, F., Uggetti, E., Carrère, H., & Ferrer, I. (2015). Chapter 11 - Algal Biomass: Physical Pretreatments. In A. Pandey, S. Negi, P. Binod, & C. Larroche (Eds.), *Pretreatment of Biomass* (pp. 195–226). Elsevier. https://doi.org/10.1016/B978-0-12-800080-9.00011-6

Patel, A., Matsakas, L., Rova, U., & Christakopoulos, P. (2019). A perspective on biotechnological applications of thermophilic microalgae and cyanobacteria. *Bioresource Technology*, *278*, 424–434. https://doi.org/10.1016/j.biortech.2019.01.063

Piccolo, A. (2012). *SPIRULINA – A LIVELIHOOD AND A BUSINESS VENTURE*. Moam.Info. www.fao.org/3/az386e/az386e.pdf

Piechula, S., Waleron, K., Swiatek, W., Biedrzycka, I., & Podhajska, A. J. (2001). Mesophilic cyanobacteria producing thermophilic restriction endonucleases. *FEMS Microbiology Letters*, *198*(2), 135–140. https://doi.org/10.1111/j.1574-6968.2001.tb10632.x

Plaza, M., Santoyo, S., Jaime, L., García-Blairsy Reina, G., Herrero, M., Señoráns, F. J., & Ibáñez, E. (2010). Screening for bioactive compounds from algae. *Journal of Pharmaceutical and Biomedical Analysis*, *51*(2), 450–455. https://doi.org/10.1016/j.jpba.2009.03.016

Pokrovsky, O. S., Martinez, R. E., Golubev, S. V., Kompantseva, E. I., & Shirokova, L. S. (2008). Adsorption of metals and protons on Gloeocapsa sp. cyanobacteria: A surface speciation approach. *Applied Geochemistry*, *23*(9), 2574–2588. https://doi.org/10.1016/j.apgeochem.2008.05.007

Qin, X., Pi, X., Wang, W., Han, G., Zhu, L., Liu, M., Cheng, L., Shen, J.-R., Kuang, T., & Sui, S.-F. (2019). Structure of a green algal photosystem I in complex with a large number of light-harvesting complex I subunits. *Nature Plants*, *5*(3), 263–272. https://doi.org/10.1038/s41477-019-0379-y

Raanan, H., Oren, N., Treves, H., Keren, N., Ohad, I., Berkowicz, S. M., Hagemann, M., Koch, M., Shotland, Y., & Kaplan, A. (2016). Towards clarifying what distinguishes cyanobacteria able to resurrect after desiccation from those that cannot: The photosynthetic aspect. *Biochimica Et Biophysica Acta*, *1857*(6), 715–722. https://doi.org/10.1016/j.bbabio.2016.02.007

Raja, R., Shanmugam, H., Ganesan, & Carvalho, I. (2014). *Biomass from Microalgae: An Overview*. https://doi.org/10.4172/2332-2632.1000118

Raungsomboon, S., Chidthaisong, A., Bunnag, B., Inthorn, D., & Harvey, N. W. (2008). Removal of lead (Pb2+) by the Cyanobacterium Gloeocapsa sp. *Bioresource Technology*, *99*(13), 5650–5658. https://doi.org/10.1016/j.biortech.2007.10.056

Raven, J. A., & Giordano, M. (2014). Algae. *Current Biology*, *24*(13), R590–R595. https://doi.org/10.1016/j.cub.2014.05.039

Rodriguez-Garcia, I., & Guil-Guerrero, J. L. (2008). Evaluation of the antioxidant activity of three microalgal species for use as dietary supplements and in the preservation of foods. *Food Chemistry*, *108*(3), 1023–1026. https://doi.org/10.1016/j.foodchem.2007.11.059

Rodríguez-Meizoso, I., Jaime, L., Santoyo, S., Señoráns, F. J., Cifuentes, A., & Ibáñez, E. (2010). Subcritical water extraction and characterization of bioactive compounds from Haematococcus pluvialis microalga. *Journal of Pharmaceutical and Biomedical Analysis*, *51*(2), 456–463. https://doi.org/10.1016/j.jpba.2009.03.014

Roser, D. J., Melick, D. R., Ling, H. U., & Seppelt, R. D. (1992). Polyol and sugar content of terrestrial plants from continental Antarctica. *Antarctic Science*, *4*(4), 413–420. https://doi.org/10.1017/S0954102092000610

Roush, D., & Garcia-Pichel, F. (2020). Succession and Colonization Dynamics of Endolithic Phototrophs within Intertidal Carbonates. *Microorganisms*, *8*(2), Article 2. https://doi.org/10.3390/microorganisms8020214

Ruggiero, M. A., Gordon, D. P., Orrell, T. M., Bailly, N., Bourgoin, T., Brusca, R. C., Cavalier-Smith, T., Guiry, M. D., & Kirk, P. M. (2015). A Higher Level Classification of All Living Organisms. *PLOS ONE*, *10*(4), e0119248. https://doi.org/10.1371/journal.pone.0119248

Saad, M. G., Dosoky, N. S., Zoromba, M. S., & Shafik, H. M. (2019). Algal Biofuels: Current Status and Key Challenges. *Energies*, *12*(10), Article 10. https://doi.org/10.3390/en12101920

Sahoo, D., & Seckbach, J. (2015). *The Algae World*. https://doi.org/10.1007/978-94-017-7321-8

Samiee, S., Ahmad, H., Hossein, M., & Lyon, S. (2019). *Prokaryotic Microalgae—An overview | ScienceDirect Topics*. https://pdf.sciencedirectassets.com/321027/3-s2.0-C20180024366/3-s2.0-B9780128179413000176main.pdf?X-Amz-Security Token=IQoJb3JpZ2luX2VjEOP%2F%2F%2F%2F%2F%2F%2F%2F% 2F%2FwEaCXVzLWVhc3QtMSJHMEUCIB%2B3aRzvNb%2B9ZFaL%2F%2FXlMhAWMVF9q%2Fw2Gjclz8s8oQM2AiEArsVQ%2B0P6ukgwQ u9zE%2F6RNmbExQ3sXyCJQ1ehYYS0eAYqswUIOxAFGgwwNTkwMDM1NDY4NjUiD LMfVR2tWIYFmd8I4SqQBcA%2FPEsyKW7dB8%2FsD92ctMYNuPav2r1HbKkz%2BRAdlqiTsItwBg2ib7CQAgdPJLJhqI13%2FZnnvpu6sj9s2iRnde2Jz60LyIzCHkBdimT568891tUImTIXtx%2BswnxRmurIQ7CWka%2B%2BkTdUkqsdHwGqwRGObiEllqSlH%2FRS38GxT10S3KFJs6iKxA2LtNzYqh0oHLHexSCL9UdiGJpXShoI2AKAdQX9y4zbcsNQP3dI2pUNk6jfuyoGQq%2BY2FYQ%2B4X5ht6uZM9q%2F5UMixPIsQ8iL291g7JPeIOK17UZOBXmZvbhX%2F9b1LmjvsCH6VQ0WgFnuolaVY7JXrp45lUg0%2B%2FQ8V87nK%2BwodXmhdiy5dLWfygaCL5LG6dU7MYdDeWOuE85FZvPtzCzZPWSnMyema01WxKsDhge7U

I2oT4I10L97zvZtW%2BwVNnQAiHFpgvEbCozbbUuaXPsVv%2FqNhA8pCNyzTT9%2FMJ4G5A3rB3cj0W8iYP7f6GIUI%2BFTifn1Au5sPb9TfYmNM8o3gudGOcX8N7PSueIMTu8KtGAkrYeF%2F7Md2q1U iBNPtSzLInf6UQJdg%2FABoUoznAmC6SIGd0ThC2s1xAh19%2F%2FLrj8%2BdNCXDwrwz8Hbq563PMi6DsNshiEnX3I7boWW4XEZ7B7YwHWx7BeBjgZK2oEhm%2BgKNcDcdXqcPNyyOn5Ox3%2F2%2F4yhMZtJGSsUITOvEtfyB6P%2Bfj8fDwrZcxD2R91FX%2FHzmFc0Io2Vk6v3iawriZx7xuvThxHjDWfyeMBg8M8WiqWrAqIKkumFR0CRatm5wMAnzwinpK4T00XLw7Ej9pFfxWfjFoOUsGOpdmfjKky51ME%2FLdmWJA0%2FOJJBBYEIz1a7kkMeqjl8YrlMLrm%2BqoGOrEBb7mb206jxNryyexP5Ghl0Be1s%2Fv7gd4y729WScmASBdBFAzIb8JUGxh9bQqtF0MmAO8IFrZqiwT1F42jWt41BQ8e2dqp%2BfJuMbZkKjtNZXnKDjL514oh8V%2FBvsdt8ZMTZeAQ5qWwvKSLdsWkx2jm28%2Ft2p2%2FZvVtp%2Bcdi52Zxed0KqZmDhOQMWMO7XJRRUPDOdmDcpC%2FC%2B4uhUKKdS0vRSSqRjNoplYgnOn9RgVq37hm&X-Amz-Algorithm=AWS4-HMAC-SHA256&X-Amz-Date=20231123T030003Z&X-Amz-SignedHeaders=host&X-Amz-Expires=300&X-Amz-Credential=ASIAQ3PHCVTY3V66NC4T%2F20231123%2Fus-east-1%2Fs3%2Faws4_request&X-Amz-Signature=2108f14b73853c9c8f9e3a12e883715ac25ece24dc7198359329118f1d86ac07&hash=3644bfc6cee648eb6b776f1bceebaf9eddb7231faa1b9bd2 b44d57f2f1775210&host=68042c943591013ac2b2430a89b270f6af2c76d8dfd086a07176afe7c76c2c61&pii=B9780128179413000176&tid=spdf-674a3e25-c16b-4916-bf50-c4f6bca9c282&sid=bcbde75734680344908b3fd86e845208b496gxrqa&type=client&tsoh=d3d3LnNjaWVuY2VkaXlY3QuY29t&ua=0a085c5507565c5a0707&rr=82a628dd8e7304db&cc=ph

Sathasivam, R., Radhakrishnan, R., Hashem, A., & Abd_Allah, E. F. (2019). Microalgae metabolites: A rich source for food and medicine. *Saudi Journal of Biological Sciences*, *26*(4), Article 4. https://doi.org/10.1016/j.sjbs.2017.11.003

Schreiber, C., Behrendt, D., Huber, G., Pfaff, C., Widzgowski, J., Ackermann, B., Müller, A., Zachleder, V., Moudøíková, Š., Mojzeš, P., Schurr, U., Grobbelaar, J., & Nedbal, L. (2017). Growth of algal biomass in laboratory and in large-scale algal photobioreactors in the temperate climate of western Germany. *Bioresource Technology*, *234*, 140–149. https://doi.org/10.1016/j.biortech.2017.03.028

Scott, S. A., Davey, M. P., Dennis, J. S., Horst, I., Howe, C. J., Lea-Smith, D. J., & Smith, A. G. (2010). Biodiesel from algae: Challenges and prospects. *Current Opinion in Biotechnology*, *21*(3), 277–286. https://doi.org/10.1016/j.copbio.2010.03.005

Sheridan, R. P. (1973). HYDROGEN SULFIDE PRODUCTION BY SYNECHOCOCCUS LIVIDUS Y52-s1. *Journal of Phycology*, *9*(4), 437–445. https://doi.org/10.1111/j.1529-8817.1973.tb04118.x

Solymosi, K. (2012). Plastid Structure, Diversification and Interconversions I. Algae. *Current Chemical Biology*, *6*, 167–186. https://doi.org/10.2174/2212796811206030002

Song, P., Kuryatov, A., & Axelsen, P. H. (2020). A new synthetic medium for the optimization of docosahexaenoic acid production in Crypthecodinium cohnii. *PLOS ONE*, *15*(3), e0229556. https://doi.org/10.1371/journal.pone.0229556

Souffreau, C., Vanormelingen, P., Van de Vijver, B., Isheva, T., Verleyen, E., Sabbe, K., & Vyverman, W. (2013). Molecular evidence for distinct Antarctic lineages in the cosmopolitan terrestrial diatoms Pinnularia borealis and Hantzschia amphioxys. *Protist*, *164*(1), 101–115. https://doi.org/10.1016/j.protis.2012.04.001

Strunecky, O., Raabova, L., Bernardova, A., Ivanova, A. P., Semanova, A., Crossley, J., & Kaftan, D. (2020). Diversity of cyanobacteria at the Alaska North Slope with description of two new genera: Gibliniella and Shackletoniella. *FEMS Microbiology Ecology*, *96*(3), fiz189. https://doi.org/10.1093/femsec/fiz189

Sukenik, A., Rücker, J., & Maldener, I. (2019). Chapter 4—Dormant Cells (Akinetes) of Filamentous Cyanobacteria Demonstrate a Great Variability in Morphology, Physiology, and Ecological Function. In A. K. Mishra, D. N. Tiwari, & A. N. Rai (Eds.), *Cyanobacteria* (pp. 65–77). Academic Press. https://doi.org/10.1016/B978-0-12-814667-5.00004-0

Sun, T.-W., & Ku, C. (2021). Unraveling gene content variation across eukaryotic giant viruses based on network analyses and host associations. *Virus Evolution*, *7*(2), veab081. https://doi.org/10.1093/ve/veab081

Sunagawa, S., Acinas, S. G., Bork, P., Bowler, C., Tara Oceans Coordinators, Acinas, S. G., Babin, M., Bork, P., Boss, E., Bowler, C., Cochrane, G., de Vargas, C., Follows, M., Gorsky, G., Grimsley, N., Guidi, L., Hingamp, P., Iudicone, D., Jaillon, O., … de Vargas, C. (2020). Tara Oceans: Towards global ocean ecosystems biology. *Nature Reviews Microbiology*, *18*(8), 428–445. https://doi.org/10.1038/s41579-020-0364-5

Susanti, H., & Taufikurahman, T. (2021a). *Microalgae Biodiversity and Applications*.

Susanti, H., & Taufikurahman, T. (2021b, May 2). *Microalgae Biodiversity and Applications*.

Tan, H. T., Yusoff, F. M., Khaw, Y. S., Ahmad, S. A., & Shaharuddin, N. A. (2021). Uncovering Research Trends of Phycobiliproteins Using Bibliometric Approach. *Plants*, *10*(11), Article 11. https://doi.org/10.3390/plants10112358

Umemura, K., Yanase, K., Suzuki, M., Okutani, K., Yamori, T., & Andoh, T. (2003). Inhibition of DNA topoisomerases I and II, and growth inhibition of human cancer cell lines by a marine microalgal polysaccharide. *Biochemical Pharmacology*, *66*(3), 481–487. https://doi.org/10.1016/s0006-2952(03)00281-8

Umetani, I., Kunugi, M., Yokono, M., Takabayashi, A., & Tanaka, A. (2018). Evidence of the supercomplex organization of photosystem II and light-harvesting complexes in Nannochloropsis granulata. *Photosynthesis Research*, *136*(1), 49–61. https://doi.org/10.1007/s11120-017-0438-z

Varfolomeev, S. D., & Wasserman, L. A. (2011). Microalgae as source of biofuel, food, fodder, and medicines. *Applied Biochemistry and Microbiology*. https://doi.org/10.1134/S0003683811090079

Varshney, P., Mikulic, P., Vonshak, A., Beardall, J., & Wangikar, P. P. (2015). Extremophilic micro-algae and their potential contribution in biotechnology. *Bioresource Technology*, *184*, 363–372. https://doi.org/10.1016/j.biortech.2014.11.040

Vaz, B. da S., Moreira, J. B., Morais, M. G. de, & Costa, J. A. V. (2016). Microalgae as a new source of bioactive compounds in food supplements. *Current Opinion in Food Science*, *7*, 73–77. https://doi.org/10.1016/j.cofs.2015.12.006

Wang, X., & Zhang, X. (2013). Separation, antitumor activities, and encapsulation of polypeptide from Chlorella pyrenoidosa. *Biotechnology Progress*, *29*(3), 681–687. https://doi.org/10.1002/btpr.1725

Ward, O. P., & Singh, A. (2005). Omega-3/6 fatty acids: Alternative sources of production. *Process Biochemistry*, *40*(12), 3627–3652. https://doi.org/10.1016/j.procbio.2005.02.020

Yu, Y., You, L., Liu, D., Hollinshead, W., Tang, Y. J., & Zhang, F. (2013). Development of Synechocystis sp. PCC 6803 as a Phototrophic Cell Factory. *Marine Drugs*, *11*(8), 2894–2916. https://doi.org/10.3390/md11082894

Yun, H.-S., Kim, Y.-S., & Yoon, H.-S. (2019). Illumina MiSeq Analysis and Comparison of Freshwater Microalgal Communities on Ulleungdo and Dokdo Islands. *Polish Journal of Microbiology*, *68*(4), Article 4. https://doi.org/10.33073/pjm-2019-053

Zeng, X., & Zhang, C.-C. (2022). The Making of a Heterocyst in Cyanobacteria. *Annual Review of Microbiology*, *76*, 597–618. https://doi.org/10.1146/annurev-micro-041320-093442

Zhao, C., Xu, Y., Wang, B., & Johnson, C. H. (2023). Synechocystis: A model system for expanding the study of cyanobacterial circadian rhythms. *Frontiers in Physiology*, *13*. https://www.frontiersin.org/articles/10.3389/fphys.2022.1085959