

Modern Advancement in Biotechnological Applications for Wastewater Treatment through Microalgae: a Review

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Abstract Microalgae are microscopic organisms that have a broad range of applications, from wastewater treatment, CO_2 mitigation to therapeutic proteins, and pharmaceuticals. Recently, the combination of wastewater treatment-based microalgae and the use of the obtained biomass as biofertilizers/stimulants/pesticides have been highly emphasized for their use in the agriculture field. Biofertilizers are a need of today's agriculture practices due to the increasing demand for food to feed a hungry planet while avoiding chemical contamination by the over-application of synthetic fertilizers. There is a constant need for modern techniques for the use of microalgae in a sustainable manner to harness their products to their full extent. Various types of bioreactors are available on the market, each with its own advantages and disadvantages, which, based on their efficiency, can be used for microalgae cultivation. This review aims at reporting recent developments in microalgae biotechnology, especially related to CO_2 mitigation, wastewater purification, biofuel, feedstock, future food, therapeutic proteins, pharmaceuticals, and biofertilizers, highlighting some of the current research in this field and future development priorities.

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1 Introduction

Microscopic algae are generally photosynthetic eukaryotes that have the potential to be produced in mass with the least amount of investment (Banerjee et al., 2023). These microalgae have been utilized for the same reason as a tool for the removal of various contaminants from the environment (Dhanker & Tiwari, 2021; Dhanker et al., 2022; Mathew et al., 2022). The wastewater treatment by these microbes results in the decreased COD (chemical oxygen demand) (Paddock et al., 2020) of the treated sewage, and this effluent sewage later used for biogas production has shown a 25% increase in methane gas production (Vassalle et al., 2020; Srimongkol et al., 2022). These microbes are present in sewage treatment as they have the ability to metabolize and mobilize various organic compounds present in the sewage. They can also utilize CO_2 from the surroundings as their energy source to produce biomass in abundance. Sewage generally has a high concentration of heavy metals including cadmium, zinc, copper, and lead which are the major cause of eutrophication in the water bodies (Dhanker et al., 2021; Ansari et al., 2022; El-Mahdy et al., 2021).

The ability of eutrophic microalgae to consume CO_2 from the environment, one of the major contributors to environmental pollution, has been used

to resolve the aftermath of increasing population demands and industrial waste (Dhanker et al., 2021; Mathew et al., 2022). So, microalgae can be enhanced with the application of genetic engineering resulting in the formation of recombinant microalgal species which can help in phycoremediation of the pollutant from the environment, which can further be used to produce biomass having a large concentration of accumulated lipids, proteins, and carbohydrate in their cells (Sun et al., 2018). Henceforth, these eukaryotic autotrophs can be utilized as a tool for the betterment of the environment which in turn produces cell biomass having a rich concentration of lipids and other potential applications such as feed and food for living beings. Lipids produced from microalgae is suitable for the production of biofuel in the future and the residual portion further can be used as biofertilizers (Lucakova et al., 2022) as shown in Fig. 1.

In some types of microalgae, proteins can account for up to 70% of the dry weight of the biomass. Popular species of microalgae that are high in protein include *Arthrospira*, *Chlorella*, *Aphanizomenon*, and *Nostoc*. All of the essential amino acids (EAAs) are present in microalgae proteins, which typically have a balanced total amino acid (TAA) profile. The FAO and WHO state that the amino-acid profiles of proteins extracted from Arthrospira are compatible



Fig. 1 Sustainable use of microalgae with the production of high-value products

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with those that are advised for human consumption (Caporgno et al., 2018). As was already mentioned, these microalgae can also be used as strong fertilizers to boost crop yield and quality while avoiding the negative effects of synthetic fertilizers (El-Beltagi et al., 2022; Osorio-Reyes et al., 2023).

The continuous use of synthetic and chemicalbased fertilizers to increase the yield and quality of crops to meet the food demand of the increasing population has resulted in so many side effects leading to the destruction of the fertility of the soil (Ahmad et al., 2021). The excessive use of these fertilizers containing reactive forms of several ions including nitrogen in the form of nitrate and nitrates oxides causes groundwater pollution (Basit et al., 2021; Kang et al., 2021). Hence, as an alternative, the use of biofertilizers has been implied to counter most if not all the side effects of the modern-day chemical fertilizers. Biofertilizers include various kinds of microorganisms, such as prokaryotic cyanobacteria, eukaryotic microalgae, fungi, bacteria, or natural compounds, derived from those microorganisms (Haris et al., 2022). Microalgae/cyanobacteria have been widely recognized by their massive applications and their use as biofertilizer/biostimulant/biopesticide recently highlighted as the short-term top application (Ferreira et al., 2019, 2021; Navarro-López et al., 2020a, 2020b; Viegas et al., 2021a, 2021b; Sofy et al., 2021) as shown in Fig. 2.

The biofertilizers include microalgae and several other PGPB (plant growth-promoting bacteria) which help in mobilizing the reactive forms of these synthetic fertilizers and also promote the necessary nourishment to the developing crops to aid in



Fig. 2 Different applications of microalgae

growth (Jha & Mohamed, 2023). Several microalgae have shown a positive effect in improving and promoting the growth of PGPR (plant growth-promoting rhizobacteria) (Etesami & Adl, 2020; Kim et al., 2020). In addition to promoting the growth and development of crops directly, these natural biofertilizers also aid in the improvement of soil efficacy and health by maintaining an optimal balance between microbiota and the nutrient balance of the soil (De Mandal et al., 2021). Furthermore, several studies have suggested these living microalgae having a wide array of biostimulants that help in improving the enzyme activity of soil as well as crops which in turn improves the crop yield. Barone et al. (2019) have demonstrated that extract of different microalgae such as Chlorella vulgaris promoted the increased bioactivity of the soil and thereby improved the growth of tomato plants.

In this review, we highlighted the ability of microalgae to consume CO_2 from the environment and recycling of nutrients from wastewaters which can be used for higher microalgal biomass. Microalgal biomass can be further utilized for various applications such as biofuel, feedstock, future food, therapeutic proteins, and pharmaceuticals. The residual portion can be utilized as biofertilizer.

2 Role of Microalgae in CO₂ Mitigation and Wastewater Treatment

Microalgae are effective in reducing CO₂ emissions due to their significant ability to convert CO2 into biomass (Demirbas, 2011; Collotta et al., 2018). In major Indian cities, 38 million cubic meters of wastewater is generated daily and only about 35% is treated (Kaur et al., 2012). Wastewater (WW) contains many nutrients, such as N (nitrogen), P (phosphorus), K (potassium), and other micronutrients that microalgae need to grow. The use of WW to grow microalgae can substantially reduce the production cost and help in lowering water and carbon footprints (Chanakya et al., 2012; Ferreira et al., 2019). Different microalgae were used to remove nutrient rate in different wastewater sources as shown in Table 1. Microalgae have been successfully used in a variety of wastewaters such as urban WW (municipal, including the removal of pharmaceuticals), agro-industrial WW (food processing plants, breweries, etc.), and agriculture WW (e.g., wastes from farming — poultry, swine, cow, dairy, aquaculture) to sequester heavy metals and toxic compounds, as well as to sustain their growth using inorganic N and P (Kumar et al., 2022; Caporgno et al., 2015; Lv et al., 2017; Viegas et al., 2021a,

Table 1 Effects of microalgae on the effectiveness of nutrient removal in various types of wastewaters

Microalgae	Wastewater source	Nutrient removal efficiency (%)	References
Dunaliella salina	Municipal wastewater	NO3 – 88, NH4-N 70, TP 47.5	Liu and Yildiz (2018)
Parachlorella kessleri	Secondary effluent	TN 78.3, TP>97.7, COD 88.8	Chen et al. (2020a, 2020b, 2020c, 2020d)
Chlorella pyrenoidosa	Agricultural wastewater	TN: 88.7, TP: 67.6	Tan et al. (2021)
Spirulina sp. LEB	Aquaculture waste (1 L)	TN: 79.28, TP: 93.84	Cardoso et al. (2020)
C. sorokiniana	Dehydration of sludge	NH4-N 98-100	Srimongkol et al. (2019)
Mixed indigenous microalgae	Secondary settling tank	TN: 63.2, TP 70, NH4-N 63.2, COD 64.9, TN: 67.3, TP 30.8, NH4-N 67.5, COD 70.3, TN: 80.8, TP 50, NH4-N 71.1, COD 69.3, TN 98, TP 25	Aketo et al. (2020)
Chlorella sp. and Scenedesmus sp.	Municipal wastewater	NH4-N: 98, TN: 94, TP: 95	Silambarasan et al. (2021)
S. obliquus	Pre-treated municipal wastewater	TN: 99.8, TP 83.1	Han et al. (2021)
Picochlorum sp.	HTL-APL	TN: 95.4, TP: 97.2	Das et al. (2020a)
Tetraselmis sp.	HTL-APL	TN: 98.5, TP: 98.0	Das et al. (2020b)
Microalgal consortia	Industrial wastewater	TN: 74, TP: 92	Villar-Navarro et al. (2018)
Chlorella sp.	Industrial wastewater	NH4-N: 95.6, TP: 26.4	Vadiveloo et al. (2021)
C. vulgaris	Tertiary wastewater	N: 100, TP: 60–90	Filippino et al. (2015)

2021b). Scenedesmus obliquus, Chlorella vulgaris, Chlorella protothecoides, and Spirulina spp. are valuable species that have demonstrated their potential in the sequestration of heavy metals (Assunção et al., 2017; Batista et al., 2015; Ferreira et al., 2019, 2021; Rosa et al., 2015).

The activated sludge process used in traditional wastewater treatment (WWT) systems costs \$0.3 per cubic meter and consumes a lot of energy (0.6 kWh/ m³). In opposition, the use of microalgae allows for the removal of pollutants/nutrients and treatment of the effluents at low consumption of energy and cost (Acién Fernández et al., 2018; Arora et al., 2021). The robustness of microalgae and their great capacity to adapt to different cultivation conditions, such as pH and temperature, carbon/nitrogen and nitrogen/ phosphorus ratios, CO₂ supplementation, light (intensity and light/dark cycle), and cultivation modes, indicates their importance in the WW treatment (Tripathi & Hussain, 2022). Therefore, the WWT efficiency of microalgae and their productivity is dependent on cultivation conditions (Tripathi & Hussain, 2021; Umamaheswari & Shanthakumar, 2016). The efficient removal of pollutants/nutrients allows the water reuse with the benefit of using the produced biomass/compounds in markets with different applications, such as biofuels, biofertilizers, biostimulants, and high-value chemicals, turned the microalgae an important skill of circular economy (Shah et al., 2022).

WWT-based microalgae biomass used as biofertilizers/biostimulants also can accelerate seed germination. Tetradesmus obliquus (also known as Scenedesmus obliquus) cultivated on brewery WW at 0.1 g L⁻¹ concentration and without any pre-treatment, led to an increase by 40% in germination index of watercress seeds (Navarro-López et al., 2020). In addition, Ferreira et al. (2019) also showed a good efficiency of Tetradesmus obliguus to treat brewery WWT and have good biostimulant effect on different seeds mainly on barley, which is the main raw material for beer production (Ferreira et al., 2019). T. obliquus, C. vulgaris, and C. protothecoides showed 100% removal for total nitrogen, more than 80% for total phosphorus, and over 70% for COD of poultry WW (Viegas et al., 2021a). The average biomass productivities were about 94.9 mg/L for T. obliquus, 76.2 mg/L for C. vulgaris, and 72.0 mg/L for C. protothecoides over the course of 10 days, respectively. The addition of C. vulgaris microalgae resulted in a 147% rise in the wheat germination index. T. obliquus and C. protothecoides were able to treat WW obtained from cattle farm. From the produced biomasses, an increase of 177% in the germination index for wheat using C. protothecoides and 34% for watercress using T. obliquus (both for only 0.2 g/L biomass concentration) were observed (Viegas et al., 2021b). C. vulgaris and T. obliquus were capable of growing in aquaculture WW and bioremediation that had excellent rates for total nitrogen, total phosphorus, COD, and BOD₅ removals (100, 96.5, 96.2, and 99.7% for C. vulgaris and 100, 98.6, 97.7, and 99.7% for T. obliquus, respectively) (Viegas et al., 2021b). The obtained biomasses showed very promising results as a biostimulant in the germination index of wheat and watercress seeds (increments of 175% for C. vulgaris and 98% for T. obliquus) (Viegas et al., 2021b). A variety of plants (tomato, watercress, cucumber, soybean, wheat, and barley) were tested for germination and growth using T. obliquus, C. protothecoides, C. vulgaris, and the cyanobacterium Synechocystis sp. grown in swine WW. Because of the growth of long roots, it was found that seeds treated with microalgae generally had a higher germination index. Approximately 75–138% more cucumber seeds germinated after receiving the microalgae treatments (Ferreira et al., 2021).

Two strains of Chlorella sp. (YG01 and YG02) were tested by Rasoul-Amini et al. (2014) for the removal of nitrogen and phosphorus from municipal wastewater. The results demonstrated that Chlorella sp. (YG01) can be regarded as an effective nutrient remover in wastewaters of various origins, while the other strains only demonstrated marginal efficacy in the purification process. In sugar beet, Chlorella vulgaris and Tetradesmus quadricauda increased the expression of genes involved in nutrient availability (Barone et al., 2018) while Acutodesmus dimorphus improved nutrient uptake in tomato plants (Garcia-Gonzalez & Sommerfeld, 2016). AQUALIA, a wastewater treatment company based in Chiclana (Spain), is the largest demonstration facility and a real case of worldwide success, where WWT is based on microalgae use, and biomass generated from that can be used to generate biogas and biofertilizers (Arbib et al., 2014). According to the ALL-GAS project case study, it was possible to achieve up to 80 and 90% of the total efficiencies of N and P removal, respectively, at an energy consumption of 0.2 kWh/m³. The obtained clean water complies with national and European regulations, and each year, enough biogas is produced to propel seven cars and a bus 325,000 km. Additionally, 40–60 tons of biomass is produced for use as biofertilizers. At a hydraulic retention time of 2 days and required land of less than 3 m²/PE (person equivalent), an average biomass production capacity of up to 90 t/ha year (Arbib et al., 2014) is close to the theoretical values for autotrophic growth.

In two nutrient media with various nitrogen and phosphorus compounds, Zhu et al. (2018) investigated the removal of nitrogen and phosphorus during the growth of the Anabaena flosaquae biofilm. The results showed that the removal of nitrogen and phosphorus in the form of ammonium nitrogen reached 94.9 and 96.8%, respectively, while the removal of phosphorus in the form of orthophosphate phosphorous reached 97.7%. Four microalgae strains-Calothrix sp., Lyngbya sp., Chlorella sp., and Ulothrix sp.—were evaluated by Renuka et al. (2013) for their capacity for phycoremediation. The results noticed that the strains behaved differently, always removing a significant amount of NO₃-N (between 57 and 78%) and PO₄-P (between 44 and 91%). In order to produce biodiesel, Hena et al. (2018) assessed the removal capacity of Arthrospira platensis grown in dairy farm wastewater. The findings demonstrated A. platensis strong ability to eliminate the major pollutants.

3 Microalgae as Commercial Products Factories

3.1 Biofuel, Feedstock, and Future Food

Algae have advantages over first-generation biofuels made from sugar, starch, and vegetable oil due to their rapid growth and productivity, capacity to grow on non-arable land using wastewater, use of water contaminants, and capacity to generate a variety of high-value biological compounds (Cheng & Luo, 2022). The use of fossil fuels has resulted in the deterioration of environmental health as these fuels on combustion produce a lot of greenhouse gases including CO_2 which aids in global warming. Hence, various studies have been designed in finding the best possible alternative to reduce and replace fossil fuels by the employment of economically renewable energy sources such as biofuels. However, the production of biofuels from crops and plants is not advisable as this will result in food scarcity so the microalgae containing a high amount of lipids are being utilized for the production of biofuels as they do not utilize the arable land and are being produced in mass for very low cost (Sun et al., 2018; Dhanker et al., 2022; Wang et al., 2022). One of the major disadvantages associated with the use of microalgae for biofuel production was the low concentration of lipids in cell mass. Thus, the development of various methods has been employed and reported in successfully increasing the overall accumulation of lipids in cells. These methods include modification and modulation of several factors including light intensity, temperature, CO₂ concentration, inducting nutrients starvation, fluctuating stress, and use of genetic engineering to produce recombinants having a high concentration of accumulated lipids (Alishah Aratboni et al., 2019).

Both lipid extraction from microalgal cells and lipid transesterification using alcohol and a catalyst are required for the manufacture of biodiesel from microalgae (Mondal et al., 2017). Microalgae can generate and store a lot of carbohydrates that are helpful for the manufacture of bioethanol (Maia et al., 2020). The complex sugars in wastewatergrown microalgae typically need to be pre-treated in order for fermentative microorganisms to hydrolyze them into simple, easily metabolizable carbon sources (Pancha et al., 2019). According to a recent study by Bhuyar et al. (2021), C. vulgaris growing in wastewater effluent from a tilapia culture pond generated biomass of 94.21 mg/L after cultivation and the maximum ethanol concentration of 33.213 g/L after 96 h of fermentation. Microalgae can produce biohydrogen in a variety of ways, but the most common ones are photosynthesis and fermentation (e.g., direct biological photolysis and indirect biological photolysis biohydrogen production) (Wang et al., 2021). According to Batista et al. (2015), S. obliquus can grow in urban wastewater, and Enterobacter aerogenes can convert the biomass into biohydrogen through dark fermentation, yielding 56.8 ml H₂/gvs.

In addition to lipids, these "biological cell factories" also contain a wide range of nutrients including proteins, vitamins, fatty acids, antioxidants, and various other bioactive compounds. These biological cells contain a large amount of protein in their dry weight and hence can be used to fulfil the food scarcity of the never-ending increase in the world population (MU et al., 2019). Microalgae also contain a high amount of omega-3 and omega-6 LCFAs (long-chain fatty acids) which can be used as an alternative to the consumption of fish for its purity and can be considered a vegan option (Kusmayadi et al., 2021). The implementation of these microbial cell masses as feeds for the animal has resulted in increased growth and mass weight, a high level of immunity and efficient durability against common illnesses, antimicrobial activity, and bioactive compounds enriched livestock products (de Medeiros et al., 2021). However, producing this food and feeds from microalgae is quite challenging as harvesting these small cells to extract bioproducts is hard and includes a list of techniques (Liber et al., 2020). Though all of these advantages, microalgal foods are not easily available on market because of a lack of awareness and the fear associated with the consumption and production of microalgae food and feeds.

3.2 Therapeutic Proteins and Pharmaceuticals

Microalgae are phototropic microorganisms capable of producing various bioactive molecules including proteins, polysaccharides, lipids, and carotenoids which have several applications in human healthcare (Khavari et al., 2021). Some of the bioactive compounds produced by microalgae have been shown to have anti-cancerous, antiinflammatory, antioxidants, antimicrobial, and antiviral properties (Khavari et al., 2021) as shown in Table 2. These macro and micro cell factories can also be used to produce various recombinant proteins such as antibiotics, monoclonal antibodies, hormonal enzymes, and various other bioactive compounds which can be used in healthcare practices (Shi et al., 2021). Furthermore, microalgae

 Table 2
 The application of microalgae in industries

Microalgae	Applications	References
C. reinhardtii	HPV vaccine (E7 oncoprotein)	Ramos-Vega et al. (2021)
Phaeodactylum tricornutum	Monoclonal IgG antibody against the nucleoprotein of Marburg virus	Butler et al. (2020)
Haematococcus pluvialis	Antibacterial activity against E. coli and S. aureus	Rather et al. (2021)
Porphyridium cruentum	Stabilizers in the food industry, hydrating agents in cosmetics and pharmaceuticals, stimulate the human immune system	Wu et al. (2021)
Cyanobacteria, Dinophyta	Mycosporine-like amino acids for sunscreen	Rosic (2019)
Nannochloropsis sp.	Food supplements, infant formulae, pharmaceuticals, aquaculture	Hassan et al. (2022)
Chlorophyta, Phaeophyta, and Rhodophyta	Anti-cancer, antifungal, hepatoprotective, anti- helminthic, anti-protozoal, anti-inflammatory, anti-coagulant, immunomodulation, and enhanced skin tissue regeneration. Reducing coronary heart disease	de Grahl and Reumann (2021)
Chlamydomonas elipsoidea, Chla- mydomonas reinhardtii	Immunotoxins against B-cell lymphoma and increase resistance to UV-induced stress	Kiran and Venkata Mohan (2021)
Schizochytrium limacinum	Antioxidant properties	Moaveni et al. (2022)
Aphanothece sacrum	Anti-inflammatory, anti-allergic, adsorption of metal ions, liquid crystallization	Ngatu et al. (2012)
S. intermedius	Antibacterial activity	Davoodbasha et al. (2018)
Spirulina platensis	Anti-cancer, anti-diabetic, and anti-inflammatory	Prabakaran et al. (2020)
Synechococcus sp.	Antioxidant, anti-inflammatory, and anti-colon cancer	Suttisuwan et al. (2019a), (2019b)
C. vulgaris	Anti-diabetes (type 2)	Zhu et al. (2017)
C. ellipsoidea	Decrease blood pressure levels	Ko et al. (2012)
Chlamydomonas reinhardtii	Antioxidant properties	Bafana (2013)
H. pluvialis	Anti-inflammatory, anti-cancer, and disease-preven- tion abilities	Khoo et al. (2019)

have been reported to produce several carbs, lipids, and algae-based proteins showing significant anti-proliferating properties thereby can be studied to aid in the development of anti-tumor drugs (Skjånes et al., 2021). The use of standard chemo and radiotherapy procedures in cancer treatment has a vast array of side effects which can be reduced if not resolved with the application of a natural extract of microalgae having several bioactive compounds (Qamar et al., 2021). This natural product enhances the innate defence mechanism of the cell defence system in countering growth (Abolhasani et al., 2018). The microalgae extracts can induce the caspase cascade of signaling leading to the apoptosis of cancer cells with bare minimum side effects (Abolhasani et al., 2018; Sahin, 2021).

In addition to the use of these extracts from microalgae, diatoms, a class of brown algae having an exoskeleton of silica, can be used as a potential drug carrier in the form of natural nanoparticles (Guleri et al., 2020; Zhong et al., 2020; Dhanker et al., 2023). These silica nanoparticles can be modified with some functional amino groups and can be used for the delivery of therapeutic genes directly inside the cell nucleus (Maher et al., 2018; Zhong et al., 2020). Hence, these photosynthetic microorganisms have an immense application in the medicine and healthcare field; however, a bulk of massive information is still not available and needs a well-organized and thorough study before we can use these natural products at their optimum potential (Mathew et al., 2022). Microalgae have the ability to produce bioactive substances that are difficult to chemically synthesize, such as antibiotics, subunit vaccines, monoclonal antibodies, hepatotoxic and neurotoxic substances, hormones, enzymes, and other substances with pharmaceutical and therapeutic purposes (de Grahl & Reumann, 2021). Additionally, microalgae pigments have health advantages like the ability to prevent cancer, heart disease, neurological disorders, and eye diseases (Bratchkova & Kroumov, 2020). Microalgae are a perfect host for the synthesis of recombinant proteins due to their special characteristics, such as their quick growth rate and inexpensive, simple media, while also sharing more similarities with mammalian cells than with bacterial cells in terms of post-translational modifications (El-Beltagi et al., 2022).

3.3 Role of Microalgae in Control COVID-19

A novel coronavirus virus has been posing a hazard to humans and other animals since the end of 2019. The world is currently experiencing a lethal coronavirus outbreak for the third time in less than two decades, which raises concerns about the new corona or COVID-19 virus (Khaligh & Asoodeh, 2022). It has recently been looked at if synthetic microalgal products may be used to create serological test kits based on the immunoassay technique. Recombinant SARS-CoV-2 receptor-binding domain (RBD) has mostly been taken into account in serological assays. According to Chia et al. (2021), microalgae are now a highly promising platform for the synthesis of viral protein antigens.

For instance, Berndt et al. (2021) reported employing the green alga Chlamydomonas reinhardtii to produce the SARS-CoV-2 spike protein RBD. By adding several intracellular localization features to the transgene, including (a) a chloroplast-directed design with the psaE chloroplast sequence given in the N-terminus, they described three forms of the RBD; (b) a kind that is secreted, with the Pherophorin 2 (PHC2) signal peptide located in the N-terminus; and (c) a type that is retained in the ER-Golgi, with the PHC2 secretion peptide's C-terminal KDEL target motif added. According to the findings, among these three variations, the one intended for the ER-Golgi has the appropriate size, folding, and amino acid sequence in addition to having the capacity to bind the angiotensin-converting enzyme-2 (ACE2) receptor, which is the major target of the SARS-CoV-2 virus.

As a result, algae might be acknowledged as a unique strategy to vaccine antigen production and reagents to quickly and affordably find antibodies in patient's serum. Additionally, cutting-edge developments in gene editing technologies raise the possibility that algae will contribute to the synthesis of the proteins required to recognize or amplify SARS-CoV 2 proteins in order to address COVID-19-related health issues. Recent developments in the development of oral vaccines should not be overlooked in the production of injectable vaccinations (Gunasekaran & Gothandam, 2020).

For a long time, polysaccharides obtained from marine microorganisms have been recognized as antiviral agents. By reducing adhesion, reverse transcriptase activity, and protease activity, seaweed polysaccharides can sabotage different phases of the SARS-CoV-2 life cycle (Iravani & Varma, 2021). On the basis of nanotechnology, Chen et al. (2020a, 2020b, 2020c) have developed an intriguing concept for the therapy of COVID-19. They hypothesized that adding coronavirus S or N protein to carrageenan (CGN) oligosaccharides cap AuNPs would result in an immunological vaccination adjuvant and promote the release of antibodies. The effectiveness of a nasal spray containing Iota-Carrageenan (I-C) in avoiding SARS-Cov-2 has recently been assessed by hospital healthcare professionals who are involved with patients who have COVID-19. Three hundred ninetyfour volunteers were given four doses of I-C spray or a placebo four times per day for 21 days. The results revealed that the prevalence of COVID-19 was much lower in the I-C receiving group than in the placebo group (1.0% vs. 5.0%). Furthermore, there was no difference in the incidence of side effects between the two groups (17.3% in the I-C group and 15.2% in the placebo group; Figueroa et al., 2021).

Astaxanthin (ASX), a reddish pigment generated from microalgae, is a subclass of compounds known as terpenes. Its anti-inflammatory activity in cytokine release syndrome is highly significant, in addition to its antioxidant and oxidative stress reduction characteristics. As a result, administering ASX to SARS-CoV-2-infected lungs may reduce the overproduction of inflammatory substances as well as modulate oxidative stress by preventing the synthesis of oxidative enzymes and ROS (Talukdar et al., 2020).

Spirulina is a spiral-shaped, green–blue alga that is high in phenolic acids, essential fatty acids, amino acids, sulfated polysaccharides, and vitamin B12. It is 70% protein and also contains these nutrients. As a result, spirulina has long been thought of as a popular supplement. Spirulina's antiviral capabilities have been mentioned in a number of studies. *Spirulina* significantly contributes to the activation of the immune system against viruses by increasing the synthesis of interferon-gamma and activating immune cells (Daoud & Soliman, 2015).

4 Biofertilizers

Biofertilizers play a crucial part in organic agriculture by boosting the supply or availability of essential nutrients to the host plant. The use of biofertilizers is to increase the number of microorganisms that accelerate the microbial processes and boost the availability of nutrients used by the plants (Kristiansen et al., 2006; Mukherjee et al., 2022). Biofertilizers are of various types based on the use of natural ingredients such as animal manure, domestic sewage, agriculture leftovers, remains of organic matter, and microorganisms such as fungi, bacteria, and microalgae/cyanobacteria (Carvajal-Muñoz & Carmona-Garcia, 2012; Chirinos et al., 2006; Haris et al., 2023; Sneha et al., 2018).

The benefits of using biofertilizers are secretion of plant growth hormones, promoting plant growth, improving soil fertility, building soil organic matter, restoring the soil's natural nutrient cycle, and protection against pathogens and other environmental hazards. Biofertilizers can improve agricultural productivity by several mechanisms: by (1) producing phytohormones; (2) fixing atmospheric nitrogen; (3) increasing the bioavailability of soil organic compounds; (4) increasing mineral uptake by plants; (5) protection of crops under hostile conditions; and (6) protection against infection by plant pathogens. To enhance these traits, several practices can be applied, such as using new temperature and drought-resistant microbes or modifying the existing microbes through genetic engineering tools, increasing the proportion of cytoprotectants of the optimized biofertilizer formulation (Bailey-Serres et al., 2019).

Although biofertilizers offer numerous advantages over chemical fertilizers as shown in Table 3, there are certain drawbacks associated with their use. Biofertilizers tend to have shorter shelf life than chemical fertilizers since biofertilizers consist of living microbial strains or their extracts, which are difficult to store for longer periods without hampering their efficiency. In addition, the efficiency of biofertilizers is highly dependent on the type of the crop and physicochemical properties of the soil and depends on the bioactive components produced from the microbial strains. The activity of biofertilizer formulations requires sophisticated machinery and techniques for optimized production.

From the environmental point of view, biofertilizers are far better than chemical fertilizers, and since they are made from natural sources, there is no harmful effect on the environment, atmosphere, soil, or water. Furthermore, biofertilizers are costeffective compared to synthetic fertilizers since they are made from natural components which also helps

Biological activities	Examples
N_2 fixing biofertilizers	Azotobacter, Beijerinkia, Clostridium, Macrotermes natalensis, Odontotermes badius, Nostoc, Rhizobium, Frankia, Anabaena azollae, Azospirillum
	Bacillus megaterium, Bacillus subtilis, Bacillus circulans
P solubilizing biofertilizers	Pseudomonas striata, Aspergillus awamori, Penicillium bilaii, Aspergillus tubingensis, Calothrix braunii
	Glomus mosseae, Gigaspora sp., Acaulospora sp., Scutellospora sp., and Sclerocystis sp., Lac- caria sp.
P mobilizing biofertilizers	Pisolithus sp., Boletus sp., Amanita sp., Pezizella ericae, Rhizoctonia solani
Biofertilizers for micronutrients	Bacillus sp.
Plant growth-promoting bacteria	Pseudomonas fluorescens

 Table 3 Examples of different types of biofertilizers (Agarwal et al., 2018)

farmers with fewer resources (Singh et al., 2016). A summary of the comparison of biofertilizers and chemical fertilizers is shown in Fig. 3.

Microalgae biomass has widespread applications including high-value food and feed, natural colorants, omega-3 fatty acids, enzyme production, bioactive molecule extraction, medicinal and cosmetic products, bioplastic, biofuel, and biofertilizer production. All these applications make microalgae a valuable product from an economic point of view, but the product of biofertilizers is gaining increasing attention worldwide due to their advantages (Ronga et al., 2019):

- Microalgae grow very rapidly and have a high photosynthetic ability when compared to terrestrial plants (3–8% vs. 0.5% for terrestrial plants).
- (ii) Microalgal biomass can be cultivated in both freshwater and saltwater, as well as in waters with poor quality, like wastewaters, which aids in bioremediation.
- (iii) There is no competition from feeds and foods, or there is less risk of it.
- (iv) High absorption of greenhouse gases, superior CO_2 sequestration and capture, and increased oxygen release during growth.
- (v) Possibility of adjusting microalgae biomass composition based on culture conditions, such

Biofertilizer		Synthetic Fertilizer	
Microorganisms like bacteria, algae and fungi	Composition	Synthetic chemical	
Organic fertilizer	Fertilizer Type	Chemical fertilizer	
Generated by microorganism	Micronutrients	Defined, Synthetic Chemical	
Cost effective as low input cost	Cost	High input cost	
No	Health Hazard	Very High	
Improve soil quality by enriching the soil	Effect on soil	Deplete quality of soil by ove use of chemicals	
No impact, Environment Friendly	Effect on environment	Negative impact, Excess us leads to environment pollutio	

Fig. 3 Comparison of biofertilizers and synthetic fertilizers

as light (intensity and dark/light cycle), temperature, pH, and agitation, among others.

(vi) Abundant and inexpensive resources for the synthesis of some minerals, the production of biochemicals, sorbents, fertilizers, building materials, and the recovery of specific elements and compounds.

Microalgae can be used directly from the cultures (Ferreira et al., 2019, 2021; Navarro-López et al., 2020b) or as extracts (Michalak et al., 2016, 2017; Navarro-López et al., 2020). Both are known to protect plants against abiotic stress such as salinity, drought, and frost (abiotic stress) and pathogens and insects (biotic stress); therefore, they can be an alternative to chemical pesticides (Khan et al., 2019). Algae include a variety of classes of active substances, such as:

- Pigments, such as phycobilins (phycocyanin, phycoerythrin), carotenoids (carotene and xan-thophyll—fucoxanthin, astaxanthin, zeaxan-thin, lutein), and chlorophylls polysaccharides, e.g., alginate, fucoidan, laminarin, agar, carrageenan, mannan, porphyrin, and ulvan.
- (ii) Lipids, such as polyunsaturated fatty acids PUFAs (*e.g.*, EPA—eicosapentaenoic acid (C20:5, n-3), DHA—docosahexaenoic acid (C22:6, n-3), and GLA—gamma-linolenic acid (C18:3, n-6)).
- Polysaccharides such as alginate, fucoidan, laminarin, agar, carrageenan, mannan, porphyrin, and ulvan.
- (iv) Polyphones such as phlorotannin, catechin, and flavonoids.
- (v) Peptides, proteins, amino acids, and vitamins and minerals.
- (vi) Plant growth-promoting substances such as plant hormones (cytokinins, auxins, gibberellins, abscisic acid, and ethylene), betaines, polyamines, and sterols.

Some studies have already demonstrated the microalgae potential as a biofertilizer and summarized in Table 4. Dineshkumar et al. (2020) showed in their study that a mixture of *Spirulina platensis* and *Chlorella vulgaris* promoted onion's high growth, and production yield, together with high quantities of nutritional factors and mineral content (Dineshkumar et al., 2020). Similarly, on onion, El-Khawaga studied an *S. platensis* biofertilizer from 5 to 25 ml/tree/ year resulted in the major promotion of the leaf area and its content of N, P, and K, yield, and fruit quality when compared with lower than 50% of inorganic N (El-Khawaga, 2013). The use of *C. vulgaris* and *S. platensis* also revealed an evident increase in rice and maize's growth parameters, seed germination and quality, growth higher yield, and physical–chemical parameters. The effect of *C. vulgaris* as organic fertilizer on the growth and yield of grapevines, banana trees, and lettuce was witnessed earlier (Abdl el Moniem et al., 2008; Faheed & Fattah, 2008). The same authors also found an increase in metabolic activities of the lettuce plants.

The production cost of inorganic nitrogen fertilizers is extremely high (Hegde et al., 1999; Mahanty et al., 2017; Vaishampayan et al., 2001). However, the deficiency of nitrogen in crops could be fulfilled sustainably using biofertilizer by the few cyanobacteria and microalgae genera such as Arthrospira, Chlorella, Haematococcus, and Dunaliella that have been economically cultivated on a large scale (Rosenberg et al., 2008). Yearly approx. 10-30 kg/ha of nitrogen is fixed by dense mats of cyanobacteria (Aiyer et al., 1972; Jhala et al., 2017). Cyanobacteria which are also used as biofertilizers can fix less than 10 kg/ha of nitrogen. Anabaena and Nostoc survive on the surface of soil and rocks and fix up to 20-25 kg/ha of atmospheric nitrogen. Anabaena can fix 60 kg/ha/season of nitrogen and enriches the soil with organic matter. Cyanobacteria play a key role in the maintenance and buildup of soil fertility and enhance crop yield, acting as a natural biofertilizer (Moore, 1969; Song et al., 2005). The most efficient nitrogen-fixing cyanobacteria such as Nostoc linkia, Anabaena variabilis, Aulosira fertilisima, Calothrix sp., Tolypothrix sp., and Scytonema sp. are present in the cultivation area of rice (Kamrul Hasan et al., 2020; Prasad & Prasad, 2001). Applications of microalgae biofertilizers have been reported in barley, oats, tomato, radish, cotton, sugarcane, maize, chili, lettuce, wheat, barley, watercress, cucumber, and soya (Chatterjee et al., 2017; Chittora et al., 2020; Ferreira et al., 2021; Thajuddin & Subramanian, 2005).

The co-production of tomato (*Solanum lycopersicum* L.) and microalga (*Chlorella infusionum*) in a hydroponic system (Zhang et al., 2017) does not require any additional inputs because microalgae can

Microalgae	Plants	Effects	References
Chlorella pyrenoidosa	Rice, lettuce, cucumber, and eggplant	Increasing germination, and salinity tolerance, and boosting chlorophyll level	Elhafiz et al. (2015)
C. vulgaris	Rice	Enhancing the soil's biological activity, chemical composition, and macronutrient availability	Dineshkumar et al. (2018)
Nannochloropsis sp.	Tomato	Fruit quality improvement through enhanced sugar and carotenoid content	Coppens et al. (2016)
Spirulina platensis	Eruca sativa	Improvement of germination and	Wuang et al. (2016)
	Brassica rapa	growth of plants	
	Brassica oleracea		
Aphanothece sp.	Tomato	Improvement of chlorophyll	Mutale-joan et al. (2020)
C. ellipsoidea		content, nutrient absorption,	
Aphanothece sp.		germination, and dry weight	
Nannochloropsis gaditana			
Porphyridium sp.			
Dunaliella salina	Tomato	Increased germination and root dry weight	Rachidi et al. (2020)
Porphorydium sp.	Wheat		
	Pepper		
Ascophyllum sp.	Tomato	Increased morphological criteria	Mógor et al. (2018)
Acutodesmus dimorphus	Lettuce		
Chlorella			
Scenedesmus obliquus	Watercress	Increased germination and mor- phological criteria	Lopéz et al. (2020)
	Bean		
	Cucumber		
Chlamydomonas reinhardtii cc 124 and Chlorella sp. MACC- 360	Tomato	Boost leaf pigment and fruit weight	Gitau et al. (2022)
Chlorella vulgaris	<i>Brassica napus</i> var. Pabularia	Boost total contents of chlo- rophyll and carotenoid and total contents of phenol and flavonoids	Park et al. (2022)

add oxygen (O_2) to nutrient solutions that are necessary for crop root respiration and growth. Although microalgae typically develop on their own in hydroponic systems, they are regarded as a crucial component because they can lead to issues with pipeline clogging and nutritional deficiencies. Additionally, when Plaza et al. (2018) evaluated the phytohormone contents of *Arthrospira* spp. and *Scenedesmus* spp., they found that *Scenedesmus* spp. had a higher level of cytokinins, gibberellins, auxins, salicylic acid, and abscisic acid. As a result, the authors hypothesized that *Scenedesmus* spp. extract could be used to promote plant growth and development after discovering that petunias (*Petunia hybrida*) produced a sizable number of flowers, shoots, and leaves. By boosting the carotenoids that typically enhance the yellow and orange color of petals, *Scenedesmus* spp. also improved the quality of flowers (*Rosa* spp.) (Tripathi et al., 2008).

Some other study looked into how rice (*Oryza sativa* L.) growth was impacted by *Aulosira fertilis-sima* (Karthikeyan et al., 2007). The authors claimed that auxins, cytokinins, and gibberellic acid—root-promoting hormones—increased the growth of rice seedlings. Furthermore, Coppens et al. (2016) noted the elevated sugar and carotenoid levels in tomato

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fruits treated with the combination of dried biomass from *Nannochloropsis* spp., *Ulothrix* spp., and *Klebsormidium* spp., demonstrating their capacity to improve the quality and financial value of tomato fruits. However, there are some drawbacks to microalgae cultivation for biofertilizers. These drawbacks include the unpredictability of algae feedstock supply, regional and seasonal availability, and local energy supply; high production costs for cultivation, harvesting, transporting, storing, and pre-treating; variability in quality, low farmer awareness and assurance (Patra & Singh, 2019); and high initial capital investment. However, using wastewater and removing pollutants and nutrients is a win–win process that is more affordable and environmentally sustainable.

Microalgae are emerging as a business configuration industry in many nations such as the USA, Europe, Japan, Malaysia, China, and the Netherlands. It mainly includes microalgae products, to create joint business opportunities for companies in the European Union. Recently, the good results of biofertilizer/ biostimulant-based microalgae have led companies to initiate and develop products using microalgae in their formulations. Table 5 shows companies producing microalgae-based biofertilizers/biostimulants.

5 Conclusion and Future Perspectives

Microalgae biomass obtained after wastewater treatment can be used in animal feed to increase the production of food, milk, wool, and chickens, and to increase the source of aquatic income. Besides, the clean water could be used for crop irrigation fields or animal consumption after careful analysis. Cleaner renewable energy sources are necessary as people become more aware of the effects of climate change. Native biofuels could produce energy without releasing greenhouse gases or other air pollutants into the atmosphere. The government should work tirelessly to enhance social and economic conditions in rural India.

Rural development is very important and dependent on the agricultural sector. Systems for growing microalgae can help with rural development, connectivity with urban areas, and the production of new goods by giving farmers and landless rural residents jobs. Numerous economic sectors in India are climate-sensitive; in particular, 51% of the country's workforce is employed in agriculture and related fields. For the management of plant diseases, new plant protection-based products, such as liquid bio formulations and granule forms, can be developed at the state level and propagated in rural areas. At the same time, these products can be used to increase crop production and soil fertility with less consumption of synthetic fertilizers, improving the health of the living communities. Since 56% of the Indian population lives in rural areas, the government should promote entrepreneurship and innovation in these regions. These schemes aim to increase employment, reduce poverty, and improve innovation in rural India. The main idea is to clean wastewater while growing microalgae in it and utilize biomass for different applications and promote the agri-business industry and produce microalgae-based biofertilizers in a

Company	Location	Microalgae	Brand
BIORIZON	Spain	Spirulina	AlgaFert
			FlorAlgal
AlgaeEnergy	Spain	Microalgae	AgriAlgae Premium
BioFlora	Peru	Scenedesmus quadricauda	ISOGREEN®
		Bacillus amyloliquefaciens	
	USA	Bacillus subtilis	
SEANERGY	Spain	Spirulina platensis	KimitecAgro
		Ascophyllum nodosum	
NEOALGAE	Spain	Spirulina platensis	SpiraGrow
LABGAE	Colombia	Chlorella vulgaris	MICROCELL
ALLMICROALGAE—	Portugal	Chlorella vulgaris	AllFertis
Natural Products S.A		Spirulina	

 Table 5
 List of

 companies engaged
 in the manufacturing

 of microalgae-based
 biofertilizers/biostimulants

short-term and sustainable economic and environmental way. The latest achievements in controlling the COVID-19 pandemic were reported.

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SG, RD, TH, AF, LG, KK, HIM: conceptualization; data curation; formal analysis; funding acquisition; investigation; methodology.

SG, RD, TH, AF, LG, KK, HIM: roles/writing — original draft.

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References

- Abdl el Moniem, E. A., Abd-Allah, A. S. E., & Ahmed, M. A. (2008). The combined effect of some organic manures, mineral N fertilizers and algal cells extract on yield and fruit quality of Williams banana plants. *American-Eurasian Journal of Agricultural & Environmental Sciences*, 4, 417–426.
- Abolhasani, M. H., Safavi, M., Goodarzi, M. T., &, et al. (2018). Identification and anti-cancer activity in 2D and 3D cell culture evaluation of an Iranian isolated marine microalgae *Picochlorum* sp. RCC486. *DARU Journal of Pharmaceutical Sciences*, 26, 105–116. https://doi.org/ 10.1007/s40199-018-0213-5
- Acién Fernández, F. G., Gómez-Serrano, C., & Fernández-Sevilla, J. M. (2018). Recovery of nutrients from

wastewaters using microalgae. *Frontiers in Sustainable Food Systems*, 2, 1–13. https://doi.org/10.3389/fsufs. 2018.00059

- Agarwal, P., Gupta, R., & Gill, I. K. (2018). Importance of biofertilizers in agriculture biotechnology are human beings at risk for COVID-19 contamination with type 2 diabetes? View project importance of biofertilizers in agriculture biotechnology. *Annals of Biological Research*, 9, 1–3.
- Ahmad, G., Khan, A. A., & Mohamed, H. I. (2021). Impact of the low and high concentrations of fly ash amended soil on growth, physiological response, and yield of pumpkin (*Cucurbita moschata* Duch. Ex Poiret L.). *Environmental Science Pollution Research*, 28, 17068–17083. https:// doi.org/10.1007/s11356-020-12029-8
- Aiyer, R. S., Salahudeen, S., & Venkataraman, G. S. (1972). Long-term algalization field trial with high-yielding varieties of rice (*Oryza sativa* L.). *Indian Journal of Agricultural Sciences*, 42, 380–383.
- Aketo, T., Hoshikawa, Y., Nojima, D., Yabu, Y., Maeda, Y., Yoshino, T., et al. (2020). Selection and characterization of microalgae with potential for nutrient removal from municipal wastewater and simultaneous lipid production. *Journal of Bioscience and Bioengineering*, 129(5), 565– 572. https://doi.org/10.1016/j.jbiosc.2019.12.004
- AlishahAratboni, H., Rafiei, N., Garcia-Granados, R., et al. (2019). Biomass and lipid induction strategies in microalgae for biofuel production and other applications. *Microbial Cell Factories*, 18, 1–17. https://doi.org/10. 1186/s12934-019-1228-4
- Ansari, M. S., Tauseef, A., Haris, M., Khan, A., Hussain, T., Khan, AA. (2022). Effects of heavy metals present in sewage sludge, their impact on soil fertility, soil microbial activity, and environment. *Development in Waste Water Treatment Research and Processes. Treatment and Reuse of Sewage Sludge: An Innovative Approach for Wastewater Treatment.* pp. 197–214. https://doi.org/10. 1016/B978-0-323-85584-6.00013-3
- Arbib, Z., Ruiz, J., Álvarez-Díaz, P., Garrido-Pérez, C., & Perales, J. A. (2014). Capability of different microalgae species for phytoremediation processes: Wastewater tertiary treatment, CO₂ bio-fixation and low cost biofuels production. *Water Research*, 49, 465–474. https://doi. org/10.1016/J.WATRES.2013.10.036
- Arora, K., Kaur, P., Kumar, P., Singh, A., Patel, S. K. S., Li, X., Yang, Y. H., Bhatia, S. K., & Kulshrestha, S. (2021). Valorization of wastewater resources into biofuel and value-added products using microalgal system. *Frontiers Energy Research*, 9, 646571. https://doi.org/10.3389/ fenrg.2021.646571
- Assunção, J., Batista, A. P., Manoel, J., da Silva, T. L., Marques, P., Reis, A., & Gouveia, L. (2017). CO₂ utilization in the production of biomass and biocompounds by three different microalgae. *Engineering in Life Sciences*, 17, 1126–1135.
- Bafana, A. (2013). Characterization and optimization of production of exopolysaccharide from Chlamydomonas reinhardtii. *Carbohydrate Polymers*, 95(2), 746–752. https://doi.org/10.1016/j.carbpol.2013.02.01610.1002/ ELSC.201700075

- Bailey-Serres, J., Parker, J. E., Ainsworth, E. A., Oldroyd, G. E. D., & Schroeder, J. I. (2019). Genetic strategies for improving crop yields. *Nature*, 575, 109–118. https://doi. org/10.1038/s41586-019-1679-0
- Banerjee, S., Ghosh, D., Pandit, C., Saha, S., Mohapatra, A., Pandit, S., Sharma, M., Sridhar, K., Inbaraj, B. S., & Prasad, R. (2023). Microalgal pandora for potent bioenergy production: A way forward? *Fuel*, 333, 126253.
- Barone, V., Baglieri, A., Stevanato, P., Broccanello, C., Bertoldo, G., Bertaggia, M., Cagnin, M., Pizzeghello, D., Moliterni, V. M. C., Mandolino, G., Fornasier, F., Squartini, A., Nardi, S., & Concheri, G. (2018). Root morphological and molecular responses induced by microalgae extracts in sugar beet (*Beta vulgaris* L.). Journal Applied Phycology, 30, 1061–1071. https://doi.org/10.1007/ s10811-017-1283-3
- Barone, V., Puglisi, I., Fragalà, F., Stevanato, P., & Baglieri, A. (2019). Effect of living cells of microalgae or their extracts on soil enzyme activities. *Archives of Agronomy* and Soil Science, 65(5), 712–726. https://doi.org/10. 1080/03650340.2018.1521513
- Basit, A., Shah, S. T., Ullah, I., Muntha, S. T., & Mohamed, H. I. (2021). Microbe-assisted phytoremediation of environmental pollutants and energy recycling in sustainable agriculture. *Archives of Microbiology*, 203, 5859–5885. https://doi.org/10.1007/s00203-021-02576-0
- Batista, A. P., Ambrosano, L., Graça, S., Sousa, C., Marques, P. A. S. S., Ribeiro, B., Botrel, E. P., Neto, P. C., & Gouveia, L. (2015). Combining urban wastewater treatment with biohydrogen production — An integrated microalgae-based approach. *Bioresource Technology*, 184, 230– 235. https://doi.org/10.1016/j.biortech.2014.10.064
- Berndt, A. J., Smalley, T. N., Ren, B., Simkovsky, R., Badary, A., Sproles, A. E., Fields, F. J., Torres-Tiji, Y., Heredia, V., & Mayfield, S. P. (2021). Recombinant production of a functional SARS-CoV-2 spike receptor binding domain in the green algae *Chlamydomonas reinhardtii*. *PLoS One*, 16(11), e0257089. https://doi.org/10.1371/journal. pone.0257089
- Bhuyar, P., Trejo, M., Dussadee, N., Unpaprom, Y., Ramaraj, R., & Whangchai, K. (2021). Microalgae cultivation in wastewater effluent from tilapia culture pond for enhanced bioethanol production. *Water Science and Technology*, 84(10–11), 2686–2694. https://doi.org/10. 2166/wst.2021.194
- Bratchkova, A., & Kroumov, A. D. (2020). Microalgae as producers of biologically active compounds with antibacterial, antiviral, antifungal, antialgal, antiprotozoal, antiparasitic and anticancer activity. *Acta Microbiologica Bulgarica*, 36, 79–89.
- Butler, T., Kapoore, R. V., & Vaidyanathan, S. (2020). Phaeodactylum tricornutum: A diatom cell factory. *Trends in Biotechnology*, 38(6), 606–622. https://doi.org/10.1016/j. tibtech.2019.12.023
- Caporgno, M. P., Taleb, A., Olkiewicz, M., Font, J., Pruvost, J., Legrand, J., & Bengoa, C. (2015). Microalgae cultivation in urban wastewater: Nutrient removal and biomass production for biodiesel and methane. *Algal Research*, 10, 232–239. https://doi.org/10.1016/J.ALGAL.2015.05.011
- Caporgno, M. P., & Mathys, A. (2018). Trends in microalgae incorporation into innovative food products with

potential health benefits. *Frontiers in Nutrition*, 5. https://doi.org/10.3389/fnut.2018.00058

- Cardoso, L., Lombardi, A., de Jesus Silva, J., Lemos, P., Costa, J., de Souza, C., Druzian, J., & Chinalia, F. (2020). Scaling-up production of spirulina sp. leb18 grown in aquaculture wastewater. *Aquaculture*, 544, 737045. https:// doi.org/10.1016/j.aquaculture.2021.737045
- Carvajal-Muñoz, J. S., & Carmona-Garcia, C. E. (2012). Benefits and limitations of biofertilization in agricultural practices. *Livestock Research for Rural Development*, 24(3), 1–8.
- Chanakya, H. N., Mahapatra, D. M., Ravi, S., Chauhan, V. S., & Abitha, R. (2012). Sustainability of large-scale algal biofuel production in India. *Journal of the Indian Institute of Science*, 92(1), 63–98.
- Chatterjee, A., Singh, S., Agrawal, C., Yadav, S., Rai, R., & Rai, L.C. (2017). Algal green chemistry: Recent progress in biotechnology. In: Rastogi, R.P., Madamwar, D., Pandey, A. (Eds.), *Algal Green Chemistry*. Elsevier, pp. 189–200. https://doi.org/10.1016/B978-0-444-63784-0. 00010-2
- Chen, C. Y., Kuo, E. W., Nagarajan, D., Ho, S. H., Dong, C. D., Lee, D. J., &, et al. (2020a). Cultivating Chlorella sorokiniana AK-1 with swine wastewater for simultaneous wastewater treatment and algal biomass production. *Bioresource Technology*, 302, 122814. https://doi.org/10.1016/j.biortech.2020.122814
- Chen, H., Wang, X., & Wang, Q. (2020b). Microalgal biofuels in China: The past, progress and prospects. GCB Bioenergy, 12(12), 1044–1065.
- Chen, X., Han, W., Wang, G., & Zhao, X. (2020c). Application prospect of polysaccharides in the development of anti-novel coronavirus drugs and vaccines. *International Journal of Biological Macromolecules*, 164, 331–343.
- Chen, Z., Xiao, J., Liu, H., Yao, K., Hou, X., Cao, Y., et al. (2020d). Astaxanthin attenuates oxidative stress and immune impairment in d-galactose-induced aging in rats by activating the Nrf2/Keap1 pathway and suppressing the NF-κB pathway. *Food & Function*, 11(9), 8099–8111.
- Cheng, F., & Luo, H. (2022). Evaluating the minimum fuel selling price of algaederived biofuel from hydrothermal liquefaction. *Bioresource Technology Reports*, 17, 100901. https://doi.org/10.1016/j.biteb.2021.100901
- Chia, W. Y., Kok, H., Chew, K. W., Low, S. S., & Show, P. L. (2021). Can algae contribute to the war with COVID-19? *Bioengineered*, 12(1), 1226–1237.
- Chirinos, V., Leal, A. & Montilla, J. (2006). Uso de insumos biológicos como alternativa para la agricultura sostenible en la zona sur del Estado Anzoátegui. *CENIAP HOY* (*Venezuela*).
- Chittora, D., Meena, M., Barupal, T., & Swapnil, P. (2020). Cyanobacteria as a source of biofertilizers for sustainable agriculture. *Biochemistry and Biophysics Reports*, 22, 100737. https://doi.org/10.1016/J.BBREP.2020.100737
- Collotta, M., Champagne, P., Mabee, W., & Tomasoni, G. (2018). Wastewater and waste CO2 for sustainable biofuels from microalgae. *Algal Research*, 29, 12–21. https:// doi.org/10.1016/J.ALGAL.2017.11.013
- Coppens, J., Grunert, O., Van Den Hende, S., Vanhoutte, I., Boon, N., Haesaert, G., & De Gelder, L. (2016). The use

of microalgae as a high-value organic slow-release fertilizer results in tomatoes with increased carotenoid and sugar levels. *Journal Applied Phycology*, 28, 2367–2377. https://doi.org/10.1007/s10811-015-0775-2

- da Rosa, G. M., Moraes, L., Cardias, B. B., de Souza, M. da R. A. Z., & Costa, J. A. V. (2015). Chemical absorption and CO₂ biofixation via the cultivation of spirulina in semicontinuous mode with nutrient recycle. *Bioresourse Technology*, *192*, 321–327. https://doi.org/10.1016/J. BIORTECH.2015.05.020
- Daoud, H. M., & Soliman, E. M. (2015). Evaluation of Spirulina platensis extract as natural antivirus against foot and mouth disease virus strains (A, O, SAT2). Veterinary World, 8(10), 1260.
- Das, P., AbdulQuadir, M., Thaher, M., Khan, S., Chaudhary, A. K., & Al-Jabri, H. (2020). A feasibility study of utilizing hydrothermal liquefaction derived aqueous phase as nutrients for semi-continuous cultivation of *Tetraselmis* Sp. *Bioresource Technology*, 295, 122310. https://doi. org/10.1016/j.biortech.2019.122310
- Das, P., Khan, S., AbdulQuadir, M., Thaher, M., Waqas, M., Easa, A., et al. (2020). Energy recovery and nutrients recycling from municipal sewage sludge. *Science of Total Environment*, 715, 136775. https://doi.org/10.1016/j.scito tenv.2020b.136775
- Davoodbasha, M., Edachery, B., Nooruddin, T., Lee, S., & Kim, J. W. (2018). An evidence of C16 fatty acid methyl esters extracted from microalga for effective antimicrobial and antioxidant property. *Microbial Pathogenesis*, *115*, 233–238. https://doi.org/10.1016/j.micpath.2017.12. 049
- de Grahl, I., & Reumann, S. (2021). Stramenopile microalgae as "green biofactories" for recombinant protein production. World Journal of Microbiology and Biotechnology, 37(9), 1–9. https://doi.org/10.1007/s11274-021-03126-y
- De Mandal, S., Sonali, Singh, S., Hussain, K., Hussain, T. (2021). Plant-microbe association for mutual benefits for plant growth and soil health. In: A.N. Yadav, J. Singh, C. Singh, & N. Yadav (Eds.), *Current trends in microbial biotechnology for sustainable agriculture*. Environmental and Microbial Biotechnology. Springer, Singapore. https://doi.org/10.1007/978-981-15-6949-4_5
- de Medeiros, V. P. B., Pimentel, T. C., Sant'ana, A. S., & Magnani, M. (2021). Microalgae in the meat processing chain: Feed for animal production or source of technofunctional ingredients. *Current Opinion in Food Science*, 37, 125–134. https://doi.org/10.1016/j.cofs.2020.10.014
- Demirbas, M. F. (2011). Biofuels from algae for sustainable development. Applied Energy, 88, 3473–3480. https:// doi.org/10.1016/J.APENERGY.2011.01.059
- Dhanker, R., Hussain, T., Tyagi, P., Singh, K. J., & Kamble, S. S. (2021). The emerging trend of bio-engineering approaches for microbial nanomaterial synthesis and its applications. *Frontiers in Microbiology*, 12. https://doi. org/10.3389/fmicb.2021.638003
- Dhanker, R., Kumar, R., Tiwari, A., & Kumar, V. (2022). Diatoms as a biotechnological resource for the sustainable biofuel production: A state-of-the-art review. *Biotechnology and Genetic Engineering Reviews*, 38(1), 111–131. https://doi.org/10.1080/02648725.2022.2053319

- Dhanker, R., Singh, P., Sharma, D., Tyagi, P., Kumar, M., Singh, R., & Prakash, S. (2023). Diatom silica a potential tool as biosensors and for biomedical field. *Plant Life* and Environment Dynamics, 175–193. https://doi.org/10. 1007/978-981-19-5920-2_11
- Dhanker, R., & Tiwari, A. (2021). Bioprocess for algal biofuels production. Clean Energy Production Technologies, 81–94. https://doi.org/10.1007/978-981-15-7070-4_4
- Dineshkumar, R., Subramanian, J., Arumugam, A., Ahamed Rasheeq, A., & Sampathkumar, P. (2020). Exploring the microalgae biofertilizer effect on onion cultivation by field experiment. *Waste and Biomass Valorization*, 11, 77–87. https://doi.org/10.1007/s12649-018-0466-8
- Dineshkumar, R., Kumaravel, R., Gopalsamy, J., Sikder, M. N. A., & Sampathkumar, P. (2018). Microalgae as bio-fertilizers for rice growth and seed yield productivity. *Waste Biomass Valorization*, 9, 793–800.
- El-Beltagi, H. S., Mohamed, A. A., Mohamed, H. I., Ramadan, K. M. A., Barqawi, A. A., & Mansour, A. T. (2022). Phytochemical and potential properties of seaweeds and their recent applications: A review. *Marine Drugs*, 20, 342. https://doi.org/10.3390/md20060342
- Elhafiz, A. A., Gaur, A. E. S. S., Osman, N. H. M., & Lakshmi, T. R. (2015). *Chlorella vulgaris* and *Chlorella pyrenoidosa* cells appear to be promising sustainable to grow rice, lettuce, cucumber and eggplant in the UAE soils. *Recent Research in Science and Technology*, 7, 14–21.
- El-Khawaga, A. S. (2013). Effect of anti-salinity agents on growth and fruiting of different date palm cultivars. *Asian Journal of Crop Science*, 5, 65–80. https://doi.org/ 10.3923/ajcs.2013.65.80
- El-Mahdy, O. M., Mohamed, H. I., & Mogazy, A. M. (2021). Biosorption effect of Aspergillus niger and Penicillium chrysosporium for Cd-and Pb-contaminated soil and their physiological effects on Vicia faba L. Environmental Science and Pollution Research, 28(47), 67608– 67631. https://doi.org/10.1007/s11356-021-15382-4
- Etesami, H., & Adl, S. M. (2020). Plant growth-promoting rhizobacteria (PGPR) and their action mechanisms in availability of nutrients to plants. In: Manoj Kumar, Vivek Kumar, Ram Prasad (eds) *Phyto-Microbiome in stress regulation* (147–203). Springer. https://doi.org/10. 1007/978-981-15-2576-6_9.
- Faheed, F. A., & Fattah, Z. A. E. (2008). Effect of Chlorella vulgaris as bio-fertilizer on growth parameters and metabolic aspects of lettuce plant. *Journal of Agriculture and Social Science*, 4, 165–169.
- Ferreira, A., Melkonyan, L., Carapinha, S., Ribeiro, B., Figueiredo, D., Avetisova, G., & Gouveia, L. (2021). Biostimulant and biopesticide potential of microalgae growing in piggery wastewater. *Environmental Advances*, 4, 100062. https://doi.org/10.1016/j.envadv.2021.100062
- Ferreira, A., Ribeiro, B., Ferreira, A. F., Tavares, M. L. A., Vladic, J., Vidović, S., Cvetkovic, D., Melkonyan, L., Avetisova, G., Goginyan, V., & Gouveia, L. (2019). Scenedesmus obliquus microalga-based biorefinery – from brewery effluent to bioactive compounds, biofuels and biofertilizers – aiming at a circular bioeconomy. *Biofuels, Bioproducts and Biorefining, 13*, 1169–1186. https://doi.org/10.1002/bbb.2032

- Figueroa, J. M., Lombardo, M., Dogliotti, A., Flynn, L., Giugliano, R. P., Simonelli, G., et al. (2021). Efficacy of a nasal spray containing Iota-Carrageenan in the prophylaxis of COVID-19 in hospital personnel dedicated to patients care with COVID-19 disease. *International Journal of General Medicine*, 14, 6277–6286.
- Filippino, K. C., Mulholland, M. R., & Bott, C. B. (2015). Phycoremediation strategies for rapid tertiary nutrient removal in a waste stream. *Algal Research*, 11, 125–133. https://doi.org/10.1016/j.algal.2015.06.011
- Garcia-Gonzalez, J., & Sommerfeld, M. (2016). Biofertilizer and biostimulant properties of the microalga Acutodesmus dimorphus. Journal Applied Phycology, 28, 1051– 1061. https://doi.org/10.1007/s10811-015-0625-2
- Gitau, M. M., Farkas, A., Ördög, V., & Maróti, G. (2022). Evaluation of the biostimulant effects of two Chlorophyta microalgae on tomato (*Solanum lycopersicum*). *Journal* of Cleaner Production, 364, 132689. https://doi.org/10. 1016/j.jclepro.2022.132689
- Guleri, S., Singh, K., Kaushik, R., Dhankar, R., & Tiwari, A. (2020). Phycoremediation: A novel and synergistic approach in wastewater remediation. *Journal of Microbiology, Biotechnology and Food Sciences, 10*(1), 98–106. https://doi.org/10.15414/jmbfs.2020.10.1.98-106
- Gunasekaran, B., & Gothandam, K. M. (2020). A review on edible vaccines and their prospects. *Brazilian Journal of Medical and Biological Research*, 53(2), 1–10.
- Han, W., Jin, W., Li, Z., Wei, Y., He, Z., Chen, C., et al. (2021). Cultivation of microalgae for lipid production using municipal wastewater. *Process Safety and Environmental Protection*, 155, 155–165. https://doi.org/10.1016/j.psep. 2021.09.014
- Haris, M., Hussain, T., Mohamed, H. I., Khan, A., Ansari, M. S., Tauseef, A., & Akhtar, N. (2022). Nanotechnology– a new frontier of nano-farming in agricultural and food production and its development. *Science of The Total Environment*, 857, 159639. https://doi.org/10.1016/j.scito tenv.2022.159639
- Haris, M., Hussain, T., Tauseef, A., Khan, A., Khan, A. A., & Yasheshwar. (2023). Application of microbial inoculants as an alternative to chemical products for decomposition of organic wastes. *Microbial Inoculants, Recent Progress* and Applications Developments in Applied Microbiology and Biotechnology. pp. 29-52. https://doi.org/10.1016/ B978-0-323-99043-1.00006-2
- Hassan, S., Meenatchi, R., Pachillu, K., Bansal, S., Brindangnanam, P., Arockiaraj, J., et al. (2022). Identification and characterization of the novel bioactive compounds from microalgae and cyanobacteria for pharmaceutical and nutraceutical applications. *Journal of Basic Microbiol*ogy, 62, 999–1029. https://doi.org/10.1002/jobm.20210 0477
- Hegde, D., Dwivedi, B. S., & Babu, S. (1999). Biofertilizers for cereal production in India: A review. *Indian Journal Agriculture Science*, 69, 73–83.
- Hena, S., Znad, H., Heong, K. T., & Judd, S. (2018). Dairy farm wastewater treatment and lipid accumulation by *Arthrospira platensis*. *Water Research*, 128, 267–277.
- Iravani, S., & Varma, R. S. (2021). Important roles of oligo-and polysaccharides against SARS-CoV-2: Recent advances. *Applied Sciences*, 11(8), 3512.

- Jha, Y., & Mohamed, H. I. (2023). Inoculation with Lysinibacillus fusiformis strain YJ4 and Lysinibacillus sphaericus strain YJ5 alleviates the effects of cold stress in maize plants. Gesunde Pflanzen, 75, 77–95. https://doi.org/10. 1007/s10343-022-00666-7
- Jhala, Y.K., Panpatte, D.G., & Vyas, R. V. (2017). Cyanobacteria: Source of organic fertilizers for plant growth. In: D. G. Panpatte, Y. K. Jhala, R. V. Vyas, H. N. Shelat (eds) *Microorganisms for Green Revolution* (pp. 253–264). Springer. https://doi.org/10.1007/978-981-10-6241-4_13.
- Kamrul Hasan, M., Tanaka, T. T. S., MonjurulAlam, M., Rostom Ali, M., & KumerSaha, C. (2020). Reviews open access impact of modern rice harvesting practices over traditional ones. *Reviews in Agricultral Science*, 8, 89–108. https://doi.org/10.7831/ras.8.0_89
- Kang, Y., Kim, M., Shim, C., Bae, S., & Jang, S. (2021). Potential of algae–bacteria synergistic effects on vegetable production. *Frontiers in Plant Science*, 12, 556. https://doi. org/10.3389/fpls.2021.656662
- Karthikeyan, N., Prasanna, R., Nain, L., & Kaushik, B. D. (2007). Evaluating the potential of plant growth promoting cyanobacteria as inoculants for wheat. *European Journal of Soil Biology*, 43, 23–30. https://doi.org/10. 1016/j.ejsobi.2006.11.001
- Kaur, R., Wani, S.P., Singh, A.K. & Lal, K. (2012). May. Wastewater production, treatment and use in India. In National Report presented at the 2nd regional workshop on Safe Use of Wastewater in Agriculture (pp. 1–13).
- Khaligh, S. F., & Asoodeh, A. (2022). Recent advances in the bio-application of microalgae-derived biochemical metabolites and development trends of photobioreactorbased culture systems. *3 Biotech*, *12*, 260. https://doi.org/ 10.1007/s13205-022-03327-8
- Khan, S. A., Sharma, G. K., Malla, F. A., Kumar, A., & Rashmi, G. N. (2019). Microalgae based biofertilizers: A biorefinery approach to phycoremediate wastewater and harvest biodiesel and manure. *Journal Cleanear Production*, 211, 1412–1419. https://doi.org/10.1016/j.jclepro. 2018.11.281
- Khavari, F., Saidijam, M., Taheri, M., et al. (2021). Microalgae: Therapeutic potentials and applications. *Molecular Biology Reports*, 48(5), 4757–4765. https://doi.org/10. 1007/s11033-021-06422-w
- Khoo, K. S., Lee, S. Y., Ooi, C. W., Fu, X., Miao, X., Ling, T. C., &, et al. (2019). Recent advances in biorefinery of astaxanthin from *Haematococcus pluvialis*. *Bioresource Technology*, 288, 121606. https://doi.org/10.1016/j.biort ech.2019.121606
- Kim, M. J., Shim, C. K., Ko, B. G., & Kim, J. (2020). Effect of the microalga *Chlorella fusca* CHK0059 on strawberry PGPR and biological control of fusarium wilt disease in non-pesticide hydroponic strawberry cultivation. *Journal Microbiology Biotechnology*, 30, 708–716. https://doi. org/10.4014/jmb.2001.01015
- Kiran, B. R., & Venkata Mohan, S. (2021). Microalgal cell biofactory-therapeutic, nutraceutical and functional food applications. *Plants (basel, Switzerland), 10*(5), 836. https://doi.org/10.3390/plants10050836
- Ko, S. C., Kang, N., Kim, E. A., Kang, M. C., Lee, S. H., Kang, S. M., & et al. (2012). A novel angiotensin I-converting

enzyme (ACE) inhibitory peptide from a marine Chlorella ellipsoidea and its antihypertensive effect in spontaneously hypertensive rats. *Process Biochemistry*, 47(12), 2005–2011. https://doi.org/10.1016/j.procbio.2012.07. 015

- Kristiansen, P., Taji, A., & Reganold, J. (2006). Organic agriculture: Opportunities and challenges. In: P. Kristiansen, A. Taji, J. Reganold (Eds.), Organic agriculture: a global perspective (pp. 421–441). CABI https://doi.org/10. 1079/9781845931698.0421.
- Kumar, A., Chaurasia, U., Elshobary, M. E., Kumari, S., Hussain, T., Bharti, A. P., Maurya, D. K., Samanta, L., & El-Sheekh, M. (2022). Utilization of algae in crop improvement and crop protection for a better agricultural system. In: M. El-Sheekh, N. Abdullah, & I. Ahmad (Eds.), *Handbook of research on algae as a sustainable solution for food, energy, and the environment* (pp. 442-470). IGI Global. https://doi.org/10.4018/978-1-6684-2438-4. ch018
- Kusmayadi, A., Leong, Y. K., Yen, H. W., Huang, C. Y., & Chang, J. S. (2021). Microalgae as sustainable food and feed sources for animals and humans–biotechnological and environmental aspects. *Chemosphere*, 271, 129800. https://doi.org/10.1016/j.chemosphere.2021.129800
- Liber, J. A., Bryson, A. E., Bonito, G., & Du, Z. Y. (2020). Harvesting microalgae for food and energy products. *Small Methods*, 4(10), 2000349. https://doi.org/10.1002/ smtd.202000349
- Liu, Y., & Yildiz, I. (2018). The effect of salinity concentration on algal biomass production and nutrient removal from municipal wastewater by Dunaliella salina. *International Journal of Energy Research*, 42, 2997–3006. https://doi. org/10.1002/er.3967
- Lopéz, E., Ruiz, N. A., Ferreira, A., Acién, F. G., & Gouveia, L. (2020). Biostimulant potential of *Scenedesmus obliquus* grown in brewery wastewater. *Molecules*, 25, 664–669.
- Lucakova, S., Branyikova, I., & Hayes, M. (2022). Microalgal proteins and bioactives for food, feed, and other applications. *Applied Sciences*, 12(9), 4402. https://doi.org/10. 3390/app12094402
- Lv, J., Feng, J., Liu, Q., & Xie, S. (2017). Microalgal cultivation in secondary effluent: Recent developments and future work. *International Journal Molecular Science*, 18, 79. https://doi.org/10.3390/ijms18010079
- Mahanty, T., Bhattacharjee, S., & Goswami, M. (2017). Biofertilizers: A potential approach for sustainable agriculture development. *Environmental Science Pollutation Research*, 24(4), 3315–3335. https://doi.org/10.1007/ s11356-016-8104-0
- Maher, S., Kumeria, T., Aw, M. S., & Losic, D. (2018). Diatom silica for biomedical applications: Recent progress and advances. *Advanced Healthcare Materials*, 7(19), 1800552. https://doi/abs/https://doi.org/10.1002/adhm. 201800552
- Maia, J. L. D., Cardoso, J. S., Mastrantonio, D. J. D. S., Bierhals, C. K., Moreira, J. B., Costa, J. A. V., et al. (2020). Microalgae starch: A promising raw material for the bioethanol production. *International Journal Biological Macromolecules*, 165(2), 2739–2749. https://doi.org/10. 1016/j.ijbiomac.2020.10.159

- Mathew, M. M., Khatana, K., Vats, V., Dhanker, R., Kumar, R., Dahms, H.-U., & Hwang, J.-S. (2022). Biological approaches integrating algae and bacteria for the degradation of wastewater contaminants—a review. *Frontiers in Microbiology*, *12*. https://doi.org/10.3389/fmicb.2021. 801051
- Michalak, I., Chojnacka, K., Dmytryk, A., Wilk, R., Gramza, M., & Rój, E. (2016). Evaluation of supercritical extracts of algae as biostimulants of plant growth in field trials. *Frontiers Plant Science*, 7, 1–11. https://doi.org/10.3389/ fpls.2016.01591
- Mógor, Á. F., Ördög, V., Lima, G. P. P., Molnár, Z., & Mógor, G. (2018). Biostimulant properties of cyanobacterial hydrolysate related to polyamines. *Journal Applied Phycology*, 30, 453–460. https://doi.org/10.1007/ s10811-017-1242-z
- Moore, A. W. (1969). Azolla: Biology and agronomic significance. *Botanical Review*, 35, 17–34. https://doi.org/10. 1007/BF02859886
- Moaveni, S., Salami, M., Khodadadi, M., McDougall, M., & Emam- Djomeh, Z. (2022). Investigation of S. limacinum microalgae digestibility and production of antioxidant bioactive peptides. *LWT*, 154, 112468. doi:https://doi. org/10.1016/j.lwt.2021.112468.
- Mondal, M., Goswami, S., Ghosh, A., Oinam, G., Tiwari, O. N., Das, P., &, et al. (2017). Production of biodiesel from microalgae through biological carbon capture: A review. 3 Biotech., 7(2), 99. https://doi.org/10.1007/ s13205-017-0727-4
- Mu, N., Mehar, J. G., Mudliar, S. N., & Shekh, A. Y. (2019). Recent advances in microalgal bioactives for food, feed, and healthcare products: Commercial potential, market space, and sustainability. *Comprehensive Eeviews in Food Science and Food Safety*, 18(6), 1882–1897. https:// doi.org/10.1111/1541-4337.12500
- Mukherjee, S., Pandey, V., Parvez, A., Qi, X., Hussain, T. (2022). Bacillus as a versatile tool for Crop improvement and agro-industry. In: M. T. Islam, M. Rahman, P. Pandey (Eds.), *Bacilli in agrobiotechnology. Bacilli in climate resilient agriculture and bioprospecting.* Springer, Cham. https://doi.org/10.1007/978-3-030-85465-2_19
- Mutale-joan, C., Redouane, B., Najib, E., Yassine, K., Lyamlouli, K., Laila, S., Zeroual, Y., & Hicham, E. (2020). Screening of microalgae liquid extracts for their biostimulant properties on plant growth, nutrient uptake and metabolite profile of *Solanum lycopersicum* L. *Scientific Report*, 10, 2820. https://doi.org/10.1038/ s41598-020-59840-4
- Navarro-López, Elvira, Cerón-García, M. del C., López-Rodríguez, M., Acién-Fernández, F.G., & Molina-Grima, E. (2020a). Biostimulants obtained after pilot-scale highpressure homogenization of *Scenedesmus* sp. grown in pig manure. *Algal Research*, 52, 102123. https://doi.org/ 10.1016/j.algal.2020.102123.
- Navarro-López, E., Ruíz-Nieto, A., Ferreira, A., Gabriel Acién, F., & Gouveia, L. (2020). Biostimulant potential of Scenedesmus obliquus grown in brewery wastewater. *Molecules*, 25(3), 664. https://doi.org/10.3390/molec ules25030664
- Ngatu, N. R., Okajima, M. K., Yokogawa, M., Hirota, R., Eitoku, M., Muzembo, B. A., &, et al. (2012).

Anti-inflammatory effects of sacran, a novel polysaccharide from *Aphanothece sacrum*, on 2, 4, 6-trinitrochlorobenzene–induced allergic dermatitis in vivo. *Annals* of *Allergy, Asthma & Immunology, 108*(2), 117-122.e2. https://doi.org/10.1016/j.anai.2011.10.013

- Osorio-Reyes, J. G., Valenzuela-Amaro, H. M., Pizaña-Aranda, J. J., Ramírez-Gamboa, D., Meléndez-Sánchez, E. R., López-Arellanes, M. E., Castañeda-Antonio, M., Coronado-Apodaca, K. G., Gomes Araújo, R., Sosa-Hernández, J. E., & Melchor-Martínez, E. M. (2023). Microalgae-based biotechnology as alternative biofertilizers for soil enhancement and carbon footprint reduction: Advantages and implications. *Marine Drugs*, 21(2), 93. https:// doi.org/10.3390/md21020093
- Paddock, M. B., Fernández-Bayo, J. D., & VanderGheynst, J. S. (2020). The effect of the microalgae-bacteria microbiome on wastewater treatment and biomass production. *Applied Microbiology and Biotechnology*, 104(2), 893– 905. https://doi.org/10.1007/s00253-019-10246-x
- Pancha, I., Chokshi, K., & Mishra, S. (2019). Industrial wastewater-based microalgal biorefinery: A dual strategy to remediate waste and produce microalgal bioproducts. In S. Gupta & F. Bux (Eds.), *Application of Microalgae in Wastewater Treatment* (pp. 173–193). Springer.
- Park, Y. J., Park, J. E., Truong, T. Q., Koo, S. Y., Choi, J. H., & Kim, S. M. (2022). Effect of Chlorella vulgaris on the growth and phytochemical contents of "Red Russian" kale (*Brassica napus* var. Pabularia). Agronomy, 12, 2138. https://doi.org/10.3390/agronomy12092138
- Patra, B., & Singh, J. (2019). A review: Usage of biofertilizer in cereal crops. *Current Journal of Applied Science and Technology*, 36, 1–8. https://doi.org/10.9734/cjast/2019/ v36i330233
- Plaza, B. M., Gómez-Serrano, C., Acién-Fernández, F. G., & Jimenez-Becker, S. (2018). Effect of microalgae hydrolysate foliar application (*Arthrospira platensis* and *Scenedesmus* sp.) on Petunia x hybrida growth. *Journal Applied Phycology*, 30, 2359–2365. https://doi.org/10. 1007/s10811-018-1427-0
- Prabakaran, G., Sampathkumar, P., Kavisri, M., & Moovendhan, M. (2020). Extraction and characterization of phycocyanin from Spirulina platensis and evaluation of its anticancer, antidiabetic and antiinflammatory effect. *International Journal of Biological Macromolecules*, 153, 256–263. https://doi.org/10.1016/j.ijbiomac.2020. 03.009
- Prasad, R. C., & Prasad, B. N. (2001). Cyanobacteria as a source biofertilizer for sustainable agriculture in Nepal. *Journal Plant Science Botany Orientalis*, 1, 127–133.
- Qamar, H., Hussain, K., Soni, A., Khan, A., Hussain, T., Chénais, B. (2021). Cyanobacteria as natural therapeutics and pharmaceutical potential: Role in antitumor activity and as nanovectors. *Molecules*, 26(1), 247. https://doi. org/10.3390/molecules26010247
- Rachidi, F., Benhima, R., Sbabou, L., & El Arroussi, H. (2020). Microalgae polysaccharides bio-stimulating effect on tomato plants: Growth and metabolic distribution. *Biotechnology Reports*, 25, e00426. https://doi.org/ 10.1016/j.btre.2020.e00426
- Ramos-Vega, A., Angulo, C., Bañuelos-Hernández, B., & Monreal-Escalante, E. (2021). Microalgae-made

vaccines against infectious diseases. *Algal Research, 58*, 102408. https://doi.org/10.1016/j.algal.2021.102408

- Rasoul-Amini, S., Montazeri-Najafabady, N., Shaker, S., Safari, A., Kazemi, A., Mousavi, P., Mobasher, M. A., & Ghasemi, Y. (2014). Removal of nitrogen and phosphorus fromwastewater using microalgae free cells in bath culture system. *Biocatalysis Agricultural Biotechnology*, *3*, 126–131. https://doi.org/10.1016/j.bcab.2013.09.003
- Rather, A. H., Singh, S., & Choudhary, S. (2021). Antibacterial activity of Haematococcus pluvialis crude astaxanthin extract. *Journal of Drug Delivery and Therapeutics*, 11(2-S), 28–30. https://doi.org/10.22270/jddt. v11i2-S.4662
- Renuka, N., Sood, A., Ratha, S. K., Prasanna, R., & Ahluwalia, A. S. (2013). Nutrient sequestration, biomass production by microalgae and phytoremediation of sewage water. *International Journal Phytoremediation*, 15, 789–800. https://doi.org/10.1080/15226514.2012.736436
- Ronga, D., Biazzi, E., Parati, K., Carminati, D., Carminati, E., & Tava, A. (2019). Microalgal biostimulants and biofertilisers in crop productions. *Agronomy*, 9, 192. https:// doi.org/10.3390/agronomy9040192
- Rosenberg, J. N., Oyler, G. A., Wilkinson, L., & Betenbaugh, M. J. (2008). A green light for engineered algae: Redirecting metabolism to fuel a biotechnology revolution. *Current Opinion in Biotechnology*, 19, 430–436. https:// doi.org/10.1016/J.COPBIO.2008.07.008
- Rosic, N. N. (2019). Mycosporine-like amino acids: Making the foundation for organic personalised sunscreens. *Marine Drugs*, 17(11), 638. https://doi.org/10.3390/ md17110638
- Sahin, D. (2021). Effect of oil extract from microalgae (Schizochytrium sp.) on the viability and apoptosis of human osteosarcoma cells. *Current Pharmaceutical Biotechnol*ogy, 22(8), 1099–1105. https://doi.org/10.2174/13892 01021666200928101029
- Shah, K. J., Singh, A. V., Tripathi, S., Hussain, T., & You, Z. (2022). Environmental management system as sustainable tools in water environmental management: A review. *Current Chinese Science*, 2(1), 48-56(9). https:// doi.org/10.2174/2210298102999211228114721
- Shi, Q., Chen, C., Zhang, W., Wu, P., Sun, M., Wu, H., et al. (2021). Transgenic eukaryotic microalgae as green factories: Providing new ideas for the production of biologically active substances. *Journal of Applied Phycology*, 33(2), 705–728. https://doi.org/10.1007/ s10811-020-02350-7
- Silambarasan, S., Logeswari, P., Sivaramakrishnan, R., Incharoensakdi, A., Cornejo, P., Kamaraj, B., et al. (2021). Removal of nutrients from domestic wastewater by microalgae coupled to lipid augmentation for biodiesel production and influence of deoiled algal biomass as biofertilizer for *Solanum lycopersicum* cultivation. *Chemosphere*, 268, 129323. https://doi.org/10.1016/j.chemo sphere.2020.129323
- Singh, M., Dotaniya, M.L., Mishra, A., Dotaniya, C.K., Regar, K.L., & Lata, M. (2016). Role of biofertilizers in conservation agriculture. Conserv. Agric. An Approach to Combat Clim. Chang. Indian Himalaya, 113–134. https:// doi.org/10.1007/978-981-10-2558-7_4.

- Skjånes, K., Aesoy, R., Herfindal, L., & Skomedal, H. (2021). Bioactive peptides from microalgae: Focus on anti-cancer and immunomodulating activity. *Physiologia Plantarum*, 173(2), 612–623. https://doi.org/10.1111/ppl. 13472
- Sneha, S., Anitha, B., Sahair, R. A., Raghu, N., Gopenath, T. S., Chandrashekrappa, G. K., & Basalingappa, M. K. (2018). Biofertilizer for crop production and soil fertility. *Journal Agriculture Research*, *6*, 299–306.
- Sofy, M. R., Mohamed, H. I., Dawood, M. F. A., Abu-Elsaoud, A. M., & Soliman, M. H. (2021). Integrated usage of *Trichoderma harzianum* and biochar to ameliorate salt stress on spinach plants. *Archives of Agronomy and Soil Science.*, 68(14), 2005–2026. https://doi.org/10.1080/ 03650340.2021.1949709
- Song, T., Mårtensson, L., Eriksson, T., Zheng, W., & Rasmussen, U. (2005). Biodiversity and seasonal variation of the cyanobacterial assemblage in a rice paddy field in Fujian, China. *FEMS Microbiology Ecology*, 54, 131–140. https://doi.org/10.1016/J.FEMSEC.2005.03.008
- Srimongkol, P., Thongchul, N., Phunpruch, S., & Karnchanatat, A. (2019). Ability of marine cyanobacterium Synechococcus sp. VDW to remove ammonium from brackish aquaculture wastewater. *Agricultural Water Management*, 212, 155–161. https://doi.org/10.1016/j.agwat.2018.09. 006
- Srimongkol, P., Sangtanoo, P., Songserm, P., Watsuntorn, W., & Karnchanatat, A. (2022). Microalgae based wastewater treatment for developing economic and environmental sustainability: Current status and future prospects. *Frontiers in Bioengineering and Biotechnology*, 10, 904046. https://doi.org/10.3389/fbioe.2022.904046
- Sun, X. M., Ren, L. J., Zhao, Q. Y., Ji, X. J., & Huang, H. (2018). Microalgae for the production of lipid and carotenoids: A review with focus on stress regulation and adaptation. *Biotechnology for Biofuels*, 11(1), 1–16. https:// doi.org/10.1186/s13068-018-1275-9
- Suttisuwan, R., Phunpruch, S., Saisavoey, T., Sangtanoo, P., Thongchul, N., & Karnchanatat, A. (2019). Isolation and characterization of anti-inflammatory peptides derived from trypsin hydrolysis of microalgae protein *Synechococcus* sp. VDW). *Food Biotechnology*, 33(4), 303–324. https://doi.org/10.1080/08905436.2019.1673171
- Suttisuwan, R., Phunpruch, S., Saisavoey, T., Sangtanoo, P., Thongchul, N., & Karnchanatat, A. (2019). Free radical scavenging properties and induction of apoptotic effects of Fa fraction obtained after proteolysis of bioactive peptides from microalgae Synechococcus sp. VDW. Food Technology and Biotechnology, 57(3), 358–368. https:// doi.org/10.17113/ftb.57.03.19.6028
- Talukdar, J., Dasgupta, S., Nagle, V., & Bhadra, B. (2020). COVID19: Potential of microalgae derived natural astaxanthin as adjunctive supplement in alleviating cytokine storm. Available at SSRN 1–17.
- Tan, X. -B., Zhang, Y. -L., Zhao, X. -C., Yang, L. -B., Yangwang, S. -C., Zou, Y., & Lu, J. -M. (2021). Anaerobic digestates grown oleaginous microalgae for pollutants removal and lipids production. *Chemosphere*, 308, 136177. https://doi.org/10.1016/j.chemosphere.2022. 136177

- Thajuddin, N., & Subramanian, G. (2005). Cyanobacterial biodiversity and potential applications in biotechnology. *Current Science*, 89, 47–57. http://www.jstor.org/stable/ 24110431.
- Tripathi, R. D., Dwivedi, S., Shukla, M. K., Mishra, S., Srivastava, S., Singh, R., Rai, U. N., & Gupta, D. K. (2008). Role of blue green algae biofertilizer in ameliorating the nitrogen demand and fly-ash stress to the growth and yield of rice (*Oryza sativa* L.) plants. *Chemosphere*, 70, 1919–1929. https://doi.org/10.1016/j.chemosphere.2007. 07.038
- Tripathi, S., & Hussain, T. (2021). Treatment of industrial wastewater through new approaches using algae biomass. In: M. Shah (Ed.), *The future of effluent treatment plantsbiological treatment systems* (pp. 89–112). Elsevier. https://doi.org/10.1016/B978-0-12-822956-9.00006-4
- Tripathi, S., & Hussain, T. (2022). Water and wastewater treatment through ozone-based technologies. *Development* in wastewater treatment research and processes. Elsevier Inc. https://doi.org/10.1016/b978-0-323-85583-9. 00015-6
- Umamaheswari, J., & Shanthakumar, S. (2016). Efficacy of microalgae for industrial wastewater treatment: A review on operating conditions, treatment efficiency and biomass productivity. *Reviews in Environmental Science* and Biotechnology, 15, 265–284. https://doi.org/10.1007/ S11157-016-9397-7
- Vadiveloo, A., Foster, L., Kwambai, C., Bahri, P. A., & Moheimani, N. R. (2021). Microalgae cultivation for the treatment of anaerobically digested municipal centrate (ADMC) and anaerobically digested abattoir effluent (ADAE). Science Total Environment, 775, 145853. https://doi.org/10.1016/j.scitotenv.2021.145853
- Vaishampayan, A., Sinha, R. P., Häder, D.-P., Dey, T., Gupta, A. K., Bhan, U., & Rao, A. L. (2001). Cyanobacterial biofertilizers in rice agriculture. *Botanical Review*, 67, 453–516. https://doi.org/10.1007/BF02857893
- Vassalle, L., Díez-Montero, R., Machado, A. T. R., Moreira, C., Ferrer, I., Mota, C. R., & Passos, F. (2020). Upflow anaerobic sludge blanket in microalgae-based sewage treatment: Co-digestion for improving biogas production. *Bioresource Technology*, 300, 122677. https://doi.org/10. 1016/j.biortech.2019.122677
- Viegas, C., Gouveia, L., & Gonçalves, M. (2021). Evaluation of microalgae as bioremediation agent for poultry effluent and biostimulant for germination. *Environmental Technology and Innovation*, 24, 102048. https://doi.org/ 10.1016/J.ETI.2021.102048
- Viegas, C., Gouveia, L., & Gonçalves, M. (2021). Aquaculture wastewater treatment through microalgal. Biomass potential applications on animal feed, agriculture, and energy. *Journal Environmental Management*, 286, 112187. https://doi.org/10.1016/J.JENVMAN.2021. 112187
- Villar-Navarro, E., Baena-Nogueras, R. M., Paniw, M., Perales, J. A., & Lara-Martín, P. A. (2018). Removal of pharmaceuticals in urban wastewater: High rate algae pond (HRAP) based technologies as an alternative to activated sludge based processes. *Water Research*, 139, 19–29. https://doi.org/10.1016/j.watres.2018.03.072

- Wang, K., Khoo, S. K., Kit, W. C., Anurita, S., Wei-Hsin, C., Jo-Shu, C., et al. (2021). Microalgae: The future supply house of biohydrogen and biogas. *Frontiers Energy Research*, 9, 660399. https://doi.org/10.3389/fenrg.2021. 660399
- Wang, S., Mukhambet, Y., Esakkimuthu, S., & Abomohra, A. (2022). Integrated microalgal biorefinery—Routes, energy, economic and environmental perspectives. *Journal Cleanear Production*, 348, 131245. https://doi.org/ 10.1016/j.jclepro.2022.131245
- Wu, J., Gu, X., Yang, D., Xu, S., Wang, S., Chen, X., & Wang, Z. (2021). Bioactive substances and potentiality of marine microalgae. *Food Science & Nutrition*, 9(9), 5279–5292. https://doi.org/10.1002/fsn3.2471
- Wuang, S. C., Khin, M. C., Chua, P. Q., & Luo, Y. D. (2016). Use of spirulina biomass produced from treatment of aquaculture wastewater as agricultural fertilizers. *Algal Research*, 15, 59–64. https://doi.org/10.1016/j.algal. 2016.02.009
- Zhang, J., Wang, X., & Zhou, Q. (2017). Co-cultivation of Chlorella spp and tomato in a hydroponic system. *Biomass and Bioenergy*, 97, 132–138. https://doi.org/10. 1016/J.BIOMBIOE.2016.12.024
- Zhong, D., Zhang, D., Xie, T., & Zhou, M. (2020). Biodegradable microalgae-based carriers for targeted delivery and imaging guided therapy toward lung metastasis of breast

cancer. Small (Weinheim an Der Bergstrasse, Germany), 16(20), 2000819. https://doi.org/10.1002/smll.20200 0819

- Zhu, Q., Chen, X., Wu, J., Zhou, Y., Qian, Y., Fang, M., et al. (2017). Dipeptidyl peptidase IV inhibitory peptides from *Chlorella vulgaris*: In silico gastrointestinal hydrolysis and molecular mechanism. *European Food Research* and Technology, 243(10), 1739–1748. https://doi.org/10. 1007/s00217-017-2879-1
- Zhu, Y., Tu, X., Chai, X. S., Wei, Q., & Guo, L. (2018). Biological activities and nitrogen and phosphorus removal during the Anabaena flos-aquae biofilm growth using different nutrient form. *Bioresource Technology*, 251, 7–12. https://doi.org/10.1016/j.biortech.2017.12.003

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