



# Cyanobacteria (BGA), A Boom Of Multiple Resources

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## Abstract

The ongoing rise in human population resulted in the depletion of energy resources which pose a threat to the environment's demands, food security, global warming as well as to the sustainable production of food and energy. The prokaryotic creature that has evolved and persisted the longest is the Cyanobacterium, often called as blue green algae. They are regarded as one of the earliest living organisms on Earth. They effectively convert radiative energy into chemical energy. As a by-product, this biological system creates oxygen. BGA are able to fix molecular nitrogen in to assimilable forms of nitrogen. These forms can be easily then absorbed by the plants for their growth and development. Thus BGA makes the soil more fertile. So they are used as biofertilizer. For the manufacturing of biofertilizer, "green technology," the most environmentally friendly method, has been used. Cyanobacteria also have the potential to be employed in a number of industries, including bioenergy, biotechnology, natural products, medicine, agriculture, and the environment, due to their remarkable pace of development. We have outlined the prospective uses of cyanobacteria in this review's several scientific and technological fields, with a focus on how they might be used to create biofuels and other useful by products.

**Key words:** BGA, green technology, biofuel, biotechnology, antibacterial, biofertilizer

## 1. Introduction:

Cyanobacteria are an ancient class of algae. Cyan, which refers to the colour "turquoise blue," is how cyanobacteria got their name. They are also known to be blue green algae. Prokaryotic life forms include cyanobacteria. They are autotrophic, especially found in marine and fresh water. They prefer diverse environment to grow. Marine water is found to be richest source of nutrients for the cultivation of blue green algae [1-4]. BGA typically grow in vast colonies and are filamentous, unicellular, and tiny in size. Up to this point, 150 genera of BGA have been recognized. As they contribute to the current oxygen-rich atmosphere on the surface of the earth, they also have evolutionary significance. Their earliest fossil evidence is thought to be about 3.5 billion years ago. In 1985, a classification of BGA was presented, with three phyla—Chroococcales, Gloeobaterales, and Pleurocapsales—and four orders: Chroococcales, Nostocales, Oscillatoriales, and Stigonematales. They have a significant potential for fixing nitrogen in the atmosphere. For the production of commercially significant agricultural plants like rice and beans, they could therefore be utilized as biofertilizer.

One of the main groups that contribute to the biomass in paddy fields that fixes nitrogen is BGA. BGA's ability to fix nitrogen is closely tied to its agricultural significance in rice farming. Fertilizers are used to compensate for nitrogen deficiency, which is the second element that limits plant development in many regions. [5]. The overuse of chemical fertilizers contributes to a number of environmental issues, including the greenhouse effect, ozone layer thinning, soil and water salinity, and changes in other physico-chemical aspects of soil. Such problems can be minimized by biofertilizers [6]. Biofertilizers are natural in origin. So they are beneficial. They provide nutrients and maintain soil texture and structure [7]. BGA play an important role in maintenance and buildup of soil fertility increasing rice cultivation [8].

BGA are composed of three different types of layers, including an inner plasma membrane, a cell wall, and an outermost mucilaginous sheath. The color-rich lamellae occupies the position in the cytoplasm which are not organized into plastid. Chlorophylls, carotenes, xanthophylls, c-phycoerythrin and c-phycoerythrin pigments are present in BGA. [9-10].

## **2. Role of organic inclusion bodies associated with BGA**

BGA consists of many organic inclusion bodies which have different specific functions. These bodies include the phycobilisomes [11-12] which act as light harvesting antennae, polyphosphate bodies [13], cyanophycean granules [14] store more nitrogen in the form of polypeptides, polyhydroxyalkanoate (PHA) granules [9,15,16], carboxysomes [17] which acts as reserve of RuBisCo ( Ribulose 1-5 bisphosphate carboxylase ), lipid bodies [14,18], thylakoid centers [19], DNA containing regions [20] present in the center of the cell showing fibrillar structure, ribosomes [21,22] and gas vacuoles which help BGA to float over the surface. In BGA, the nucleus is disorganized. BGA is made up of two crucial cells: a heterocyst that fixes nitrogen and a vegetative cell that performs photosynthesis and reproduction.

## **3. BGA as a tool for biological nitrogen fixation in paddy/rice fields.**

The world's population is more than 50% dependent on rice. About 75% of land under rice cultivation, are wetlands. The traditional wetland rice cultivation is found to be extremely successful. Stable yield at moderate level has been maintained for thousands of years without causing any harmful effects to the soil [23]. This is due to wetland conditions which establish an environment suitable to maintain soil nitrogen. So that all the nitrogen fixing microorganisms' can able to flourish well in wetland rice fields.

India is a populous country with a strong agricultural economy. A growing population calls for more food to be available. Given their financial situation, the majority of Indian farmers find it challenging to employ expensive chemical fertilizers that are also naturally problematic. There is only one solution to the problem of rising food demand: improving crop output at low production costs. This is made feasible by employing biofertilizers in the form of BGA. BGA serve as biofertilizer because of their capacity to fix nitrogen. By fixing 20–30 kg N/ha, BGA can boost crop output by 10%–15%.

Biological nitrogen fixation in rice fields and its uses have been reviewed by Watanabe and Roger [24] and Roger and Watanabe [25]. Specific reviews associated with BGA [26], biological nitrogen fixation associated with Straw [27], rice genotypic differences in stimulating biological nitrogen fixation [28], *Azolla* [29] and leguminous green manures [30]. BGA are directly related with their ability to fix atmospheric nitrogen and improve soil fertility, consequently increasing rice growth and yield as natural biofertilizer [31].

The BGA also converts CO<sub>2</sub> to O<sub>2</sub> and thus contribute in minimizing environmental pollution. BGA enhance the soil aeration resulting in considerable increase in amount of O<sub>2</sub> rhizosphere. BGA excrete growth promoting substances such as Auxins, gibberellins, vitamins and amino acids [32]. BGA increase water holding capacity of soil due to their jelly structure and also increase soil biomass after their death and decomposition. BGA reduce soil salinity and prevent weed growth. They increase soil phosphate by excreting organic acids [33]. Thus BGA ensure ecofriendly environment to agriculture, increasing soil fertility, decreasing chemical fertilizer's utilization and also production cost.

#### 4. Role of BGA as functional food

The food which supplies necessary amount of essential nutrients in the form of carbohydrates, proteins, fats, vitamins and minerals, is called functional food [34]. The food may contain bioactive compounds, which are organic substances that are good for human health and come from plants, animals, and even microorganisms. There are many characters associated with BGA which make them to use as functional food viz. they are globally distributed, high nutrient contents, ability to grow in small water contents, require small area for cultivation, food is easily digestible [35,36]. Now a days, BGA are available as food supplements in the market in various forms such as capsules, tablets and liquids [37, 38]. They are said to boost the nutritional content of drinks, pasta, candies, and snack items. They may be also used as food colorants [39-44]. The most frequently used BGA strain for the human food supplement is *Spirulina* (*Arthrospira*) as it contains large amount of proteins and has significant nutritive value [45,46,47]. One kilograms of *Spirulina* can replace 1,000 kilograms of various fruits and vegetables, according to some statistical statistics. In a number of nations, including Mexico, Chile, Peru, and the Philippines, some BGA are eaten as food. Commercially grown *Spirulina* plantensis is offered as powder, pills, flakes and capsules in the market. It has a protein content of about 60%, along with minerals, vitamin B-complex, thiamine, riboflavin, and alpha-carotene [47, 48, 49]. *Spirulina's* lipids are cholesterol-free and helpful in lowering blood cholesterol, obesity, and diabetes. Vitamins and minerals that are excellent for bones, teeth, and blood can be found in plenty in BGA.

They also produce secondary metabolites which act as source of bioactive molecules including anti-tumor, anti-viral, anti-bacterial, cytotoxic, anti-malarial, anti-mycotic agents [50-51]. There are some examples of BGA like *Oscillatoria tenuis*, *Lyngbya cryptovaginata*, *Tolipothrix tenuis* [51], *Spirulina platensis* [52], *Calothrix fusca* and *Gloeocapsa livida* [53], *Lyngbya limnetica*, *Scytonema bohneri*, *Oscillatoria acuminata*, *Oscillatoria calcuttensis*, *Oscillatoria foreau*, *Spirulina pacifica* [54], are good source of carbohydrates and proteins. At present time, there are 70 countries in the world which commercialized the products of nutritive value obtained from the BGA. The critical phases in producing nutritious items produced from BGA include cultivation, harvesting, processing (drying), and packaging. The table 1 lists a number of commercial businesses that produce BGA as functional food supplements. The need for large-scale cyanobacterial product manufacturing is growing, yet there are production challenges that need to be addressed (Figure 1.).

Companies	Country
Earthrise Farms, Cyanotech Corporation, Bio Earth Spirulina, Kalmath Valley Botanicals LLC	USA
Hainan DIC Microalgae, Nan Pao Resins, Fuqing King Dnarmsa Spirulina Co. Ltd, Hainan Simai Pharmacy Co. Ltd, Jiangsu Cibainian Nutrition Food Co. Ltd, Jiangxi Boyuan Spirulina Co. Ltd, Nanjing General Spirulina Developing Corporation, Blue bio Bio-Pharmaceutical Co. Ltd	China
Green Valley Spirulina, Blue Biotech, Sanatur Spirulina	Germany
Myanmar Microalgae Biotechnology Project, Myanmar Spirulina Factory	Myanmar
Bio Earth Spirulina	Italy
Ballarpur Industries, EID Parry, Zydus Cadila, Ahmedabad; Mapra Laboratories Pvt. Ltd, Mumbai; Cosmic Nutracos Solutions Pvt. Ltd, New Delhi; Hash Biotech Limited, Chandigarh; Sanat Products Ltd, New Delhi; Parry Neutraceuticals, Onnaiyur; Hydrolina Biotech Pvt Ltd, Chennai; Ecotech Technologies India Pvt Ltd, Mumbai; Essar Biotech, Hindupur; Miraculous Mushroom, Pune; Admark, Vijayawada; Care	India
Neotech Food, Siam Algae, Boonsom Spirulina Farm	Thailand
All Seasons Health	UK
Nan Pao Resins, Far East Bio-Tec Co. Ltd; Far East Microalgae Ind Co. Ltd	Taiwan
Natésis Spirulina	France
NaturKraftWerke Spirulina	Switzerland
Marcus Rohrer Spirulina	Netherlands
EXsymol S.A.M	Monacco
Solarium Biotechnology	Chile
Spirulina Mexicana	Mexico
Panmol	Australia
Inner Mongolia Biomedical Engineering	Mongolia
GeniX	Cuba

Ocean Nutrition	Canada
Koor Foods	Israel

**Production methods:**

- Natural environment.
- Open ponds with controlled cultivation process.
- Photo-FERMENTERS

**Provisionary explications:**

- Development of high throughput screening methods.
- Valuable germplasm Conservation.
- Genetical modification of strains.
- Optimization of production process.
- Food products safety by improving production technologies.
- Maintaining pure culture of efficient strains.

Fig 1: shows a diagrammatic representation of the production processes, uses, restrictions, and provisional explanations connected to the manufacture of cyanobacterial food items.

In India, to fulfil the nutritive demand of ever increasing population, BGA may have wide scope as an alternative source for sustainable food production.

**Limitations:**

- Less effective screening procedures.
- High nucleic acid content.
- Microorganisms and weed algae contamination.
- A significant amount of water is needed.

**Applications:**

- To manufacture Feed additives.
- To manufacture Pro-vitamin A.
- To manufacture Food pigment reagents.
- To manufacture Dietary supplements.
- To manufacture bioactive compounds like carotenoids, flavonoids, phytosterols, phytoestrogens.

## 5. BGA as a Resource for Biofuel Production

The word "biofuel" refers to the type of energy that is converted into chemical energy in the molecules that autotrophic organisms at the base of the food chain create through photosynthesis.

A variety of fuels known as "biofuels" are made in some way using biomass. Since the majority of the world's existing fuel supply is made up of fossil fuels, we urgently need new energy fuel sources. Although the idea of using micro algal biomass as a potential source of biofuel is not new, it is now being seriously considered in light of the rising cost of oil and, more significantly, the growing concern over climate change and global warming, which are more strongly linked to the burning of fossil fuels [55, 56, 57]. About 85% of all energy demand is met by these fossil fuels [58]. There is a significant demand to meet energy needs because fossil fuels are used so extensively. The necessity to investigate alternative energy sources has grown [59]. The most difficult challenges are finding clean, sustainable energy sources for future supplies. In the end, it is related to a higher level of living, economic prosperity, and stability. BGA have been designed to create a variety of various molecules linked to biofuels. Because of their genetic tractability, quick growth, and

capacity to repair carbon dioxide. *Synechococcus elongatus* sp. strain PCC 7942 (*S. elongatus*), which was successfully designed to create ethanol with the addition of a pyruvate decarboxylase and an alcohol dehydrogenase, redirecting carbon from pyruvate, is one of the first examples of biofuel production in cyanobacteria [60]. Since then, the ability to produce ethanol from BGA has substantially increased [61]. But because of its hygroscopicity and low energy density, ethanol makes a pretty poor alternative for gasoline. These factors have led to a shift in focus on fuels with longer carbon chains. *S. elongatus* effectively synthesised isobutyraldehyde, a crucial chemical feedstock for hydrocarbons typically sourced from petroleum. Chemical conversion makes it simple to create isobutyraldehyde, a viable substitute for gasoline. Direct biological production of Isobutanol from *S. elongatus* was achieved with the addition of an alcohol dehydrogenase reaching 450 mg/L in 6 days [62]. There are three heterologous enzymes, acetolactate synthase, 2-acetolactate decarboxylase, and a secondary alcohol dehydrogenase, introduced into *S. elongatus* which catalysed the conversion of carbon flux from pyruvate to the production of the 2,3-butanediol reaching 2.4 g/L in 21 days [63]. Other chemicals produced with heterologous biosynthetic pathways from cyanobacteria include 1-butanol (29.9 mg/L) [64], 2-methyl-1-butanol (200 mg/L) [65], ethylene (~171 mg/L·day) [66, 67], isoprene (0.05 mg/g dry cell day) [68], and fatty acids (197 mg/L) [69]. BGA also possess significant potential for lipid production, which can be used as biofuel feedstock [70].

As a result, BGA can produce biofuel in a more efficient, sustainable, and safe manner for the environment. They might replace the majority of the use of fossil fuels.

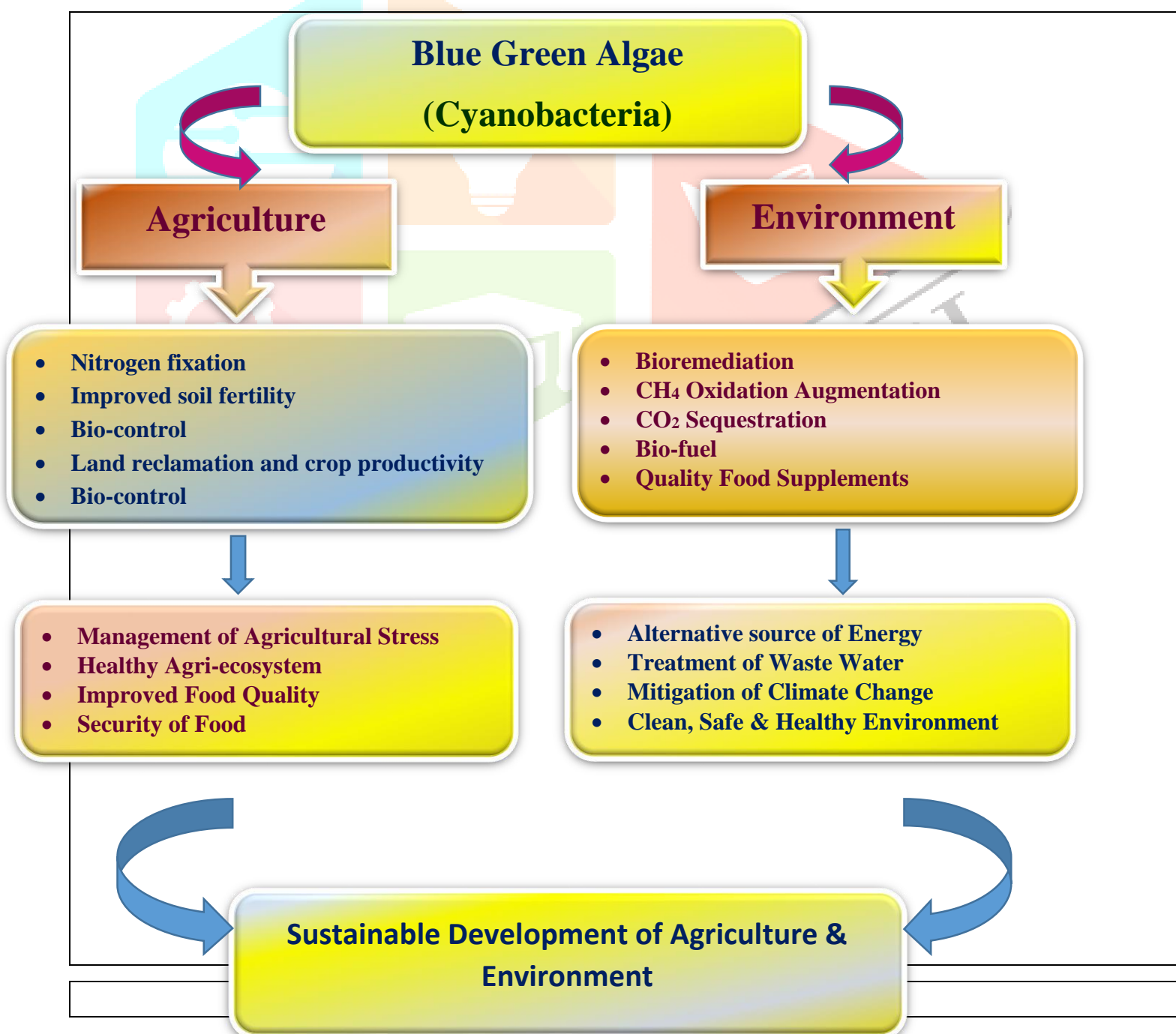


Figure 2: A fictitious example of how cyanobacteria might be used in environmentally friendly and sustainable agriculture.

## 6. Environmental management of blooms of BGA

BGA develop very quickly and produce large blooms on the water's surface when given enough phosphorus (P) and nitrogen (N), as well as water, air, sunlight, and other nutrients.

These BGA blooms have the potential to release toxins into the water and reduce its oxygen content. The development of other aquatic species can be adversely affected. The growth and reproduction of BGA depend heavily on phosphorus. Some cyanobacteria species are also capable of producing toxins or poisons. When exposed in excessive doses, these poisons can harm the liver or nerves in both humans and animals. When large amounts of the toxins are ingested, it can kill animals. Thus these BGA blooms act as a major agent of water quality deterioration and water pollution [71-72]. A few experimental studies on manipulating BBGA have been conducted. For the effective long-term control and management of damaging BGA blooms, the dual N and P input reductions are typically necessary [71, 73]. The prevention of BGA blooms has been the subject of some experimental experiments. It has been discovered that balancing the amounts of nitrogen and phosphate in water can help control BGA blooms. In general, nitrogen was thought to be the main ingredient that restricted the growth of phytoplankton biomass. [74, 75, 76].

There are two methods i.e. 1. Reducing the inputs of Nitrogen and Phosphorus. 2. Reducing the input of Phosphorus. So that the ratio of N and P differ greatly from the equilibrium [77-78]. The deficiency of 'P' can affect cell division which in turn reduce the growth. BGA require a high concentration of "N," which can't be supplied exclusively through nitrogen fixation. Therefore, the ban on importing nitrogen can still be utilised to limit BGA growth.

The growth rate of the BGA population can be slowed down and BGA blooms can be prevented if two environmental elements, P and N, are managed to some extent. As a result, it may be a method of reducing water quality pollution.

## 7. Cyanobacteria: A Potential Source of Bioactive compounds of pharmaceutical importance

The marine BGA are rich source of secondary metabolites [78]. Secondary metabolites of BGA contain various bioactive molecules which include 41% cytotoxic, 13% antitumor, 4% antiviral, 12% antimicrobial, and 18% other compounds including antimalarial, antimycotics, multidrug resistance reversers, herbicides, insecticides, algacides, and immuno-suppressive agents [79]. Both medications and prototypes for the creation of new drugs are made from these natural substances. Therefore, BGA metabolites continue to be explored for their application in many biological areas and can be an exceptional source of compounds for drug discovery [80, 81, 82].

### Anticancer activity

Moore (Oregon State University) and Gerwick (University of Hawaii) started screening cyanobacterial extracts for novel anticancer chemicals in the 1990s. Numerous cyanobacterial bioactive chemicals target tubulin or actin filaments in eukaryotic cells, making them an effective source of anticancer medicines [83]. Dolastatin 10 and 12 are two tiny anticancer peptides that were isolated from *Symploca* species and *Leptolyngbya* species, respectively. [84, 85]. Curacin A showed antiproliferative property that has been isolated from *Lyngbya majuscula* [86]. Curacin A was also artificially synthesized because of its pharmacological importance [87].

### Antibacterial Activity

Scientists are testing cyanobacterial extracts for their antibacterial activity in an effort to create novel antibiotics [88 89 90] and have discovered that they may be active against a variety of bacteria. Noscomin from *Nostoc commune* exhibited antibacterial activity against *Bacillus cereus*, *Staphylococcus epidermidis*, and *Escherichia coli* [91].

Nostocarboline from *Nostoc* was found to inhibit the growth of other cyanobacteria and green alga [92]. Nostocine A isolated from *Nostoc spongiaeforme* inhibited the growth of green algae more strongly than cyanobacteria [93]. Hapalindole (alkaloids) from *Nostoc* CCC537 and *Fischerella* sp. showed antimicrobial activity against *Mycobacterium tuberculosis* H37Rv, *Staphylococcus aureus* ATCC25923, *Salmonella typhi* MTCC3216, *Pseudomonas aeruginosa* ATCC27853, *E. coli* ATCC25992, and *Enterobacter aerogenes* MTCC2822 [94]. Cyanobacteria will be potentially viable candidates because of the urgent need to find novel active compounds with antibacterial activity due to the rise in bacterial resistance to antibiotics.

### Antiviral Activity

HIV, AIDS, dengue, and avian influenza (H5N1 virus) are lethal viral diseases spread all over the world and has had serious consequences. The anti-HIV highly active antiretroviral therapy (HAART) is found to be effective in controlling the development of HIV infections but it is toxic [95]. Therefore, new medications are required to combat these deadly diseases. By preventing viral absorption or penetration and slowing the multiplication phases of progeny viruses after penetration into host cells, antiviral substances derived from cyanobacteria shown bioactivity against these viruses. Protection of human lymphoblastoid T-cells from the cytopathic effect of HIV infection was reported with an extract of *Lyngbya lagerheimii* and *Phormidium tenue* [96]. Sulfonic acids, a new class of HIV inhibitors that contain glycolipid and were derived from an extract of cyanobacteria, were discovered to have anti-HIV activity. Cyanovirin-N (CVN), a peptide isolated from cyanobacteria, inactivates strains of HIV virus and inhibits cell-to-cell and virus-to-cell fusion [97].

### Antiprotozoal Activity

As per the data given by WHO, more than 1 billion people throughout the world are suffering from tropical diseases caused by *Plasmodium*, *Trypanosoma*, *Leishmania*, *Schistosoma*, and others [98]. Failures in the treatment of these diseases, especially in cases of malaria [99] and leishmaniasis [100], are due to development of resistance by these protozoa. On the other hand, progress in the advancement of drug discovery programs against these diseases is very slow [101]. To advance the creation of efficient and affordable medicines for a variety of ailments, the Panamanian International Cooperative Biodiversity Group is evaluating extracts from terrestrial and marine sources. In addition, the protease inhibitor nostocarboline [102], an alkaloid isolated from *Nostoc* sp., was found to be active against *Trypanosoma brucei*, *Trypanosoma cruzi*, *Leishmania donovani*, and *Plasmodium falciparum*. Aerucyclamide [103] isolated from *Microcystis aeruginosa* PCC 7806 was also found to be active against *T. brucei*, and the already known aerucyclamide B against *Plasmodium falciparum*. There are six new acyl proline derivatives tumonoic acids D–I, isolated from the marine cyanobacterium, *Blennothrix cantharidosmum*, among which tumonoic acid I displayed moderate activity in an antimalarial assay [104]. Microorganisms used for the production of nanoparticles and they are in use for food preservation [105] and showing antiprotozoal activity.

### Conclusion

BGA have a great potential as biofertilizer. BGA turn solar energy into biomass by using CO<sub>2</sub>, water, and nutrients. The thorough study found that BGA can be used in a variety of ways to improve human health, including enhancing food quality, balancing soil physicochemical properties, preventing soil-borne illnesses, amending the soil with organic matter, releasing phytohormones crucial for crop growth, solubilizing insoluble phosphates, and their use as nutraceuticals. BGA serve as a promising resource in pharmaceuticals. Well-structured applications of BGA in agriculture have been found to be minimize global warming as they utilize the atmospheric CO<sub>2</sub>. Algal biofuels appear to be the only current renewable energy source that could meet the global demand for transport fuels. Thus BGA are economical and eco-friendly natural resources. Role of BGA in all these fields needs to be further explored.

### Author's contribution

SPP came up with the concept for the manuscript, contributed the overall idea and inputs for each individual section, and partially wrote the manuscript. The review was written by VVC and MRN after they read the literature. The manuscript was edited, put together, and finalized by authors SPP and VVC. After reading and approving it for publishing, all authors signed off.

## Declaration of competing interest

The authors affirm that there were no business or financial ties that might be seen as a potential conflict of interest when the work was done.

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## References:

- [1] Pisciotta J.M, Zou Y, Baskakov I.V. Light-dependent electrogenic activity of cyanobacteria, PloS One 2010; 5:5 e10821, <https://doi.org/10.1371/journal.pone.0010821>.
- [2] Williams, P.J.B, Laurens, L.M.L. Microalgae as biodiesel and biomass feedstock: review and analysis of the biochemistry, energetic and economics, Energy Environ. Sci. 2010; 3 (5) 554–590, <https://doi.org/10.1039/b924978h>.
- [3] J.J. Milledge, Commercial application of microalgae other than as biofuels: a brief review, Rev. Environ. Sci. Biotechnol. 10 (1) (2011) 31–41, <https://doi.org/10.1007/s11157-010-9214-7>.
- [4] S.K. Hoekman, A. Broch, C. Robbins, E. Cenicerros, M. Natarajan, Review of bio- diesel composition, properties, and specifications, Renew. Sustain. Energy Rev. 16 (1) (2012) 143–169, <https://doi.org/10.1016/j.rser.2011.07.143>.
- [5] F. R. Malik, S. Ahmed and Y. M. Rizki, Utilization of lignocellulosic waste for the preparation of nitrogenous biofertilizer. Pakistan Journal of Biological Sciences. (4) (2001) 1217-1220.
- [6] A. T. M. A. Choudhary and I. R. Kennedy, Nitrogen Biofertilizer losses from rice soils and control of environmental pollution problems. Communications in Soil Science and Plant Analysis, (36) (2005) 1625–1639.
- [7] N. Board, The Complete Technology Book on Biofertilizer and Organic Farming, New Delhi. (2004).
- [8] T. Song, L. Martensson, T. Eriksson, W. Zheng and U. Rasmussen, Biodiversity and seasonal variation of the cyanobacterial assemblage in a rice paddy field in Fujian, China. The Federation of European Materials Societies Microbiology Ecology, (54) (2005) 131–140.
- [9] M. Koller, Cyanobacterial polyhydroxyalkanoate production: status quo and quo vadis? Curr. Biotechnol. 4 (4) (2015) 464–480. M. Meena, K. Divyanshu, S. Kumar, P. Swapnil, A. Zehra, V. Shukla, M. Yadav, R.S. Upadhyay, Regulation of L-proline biosynthesis, signal transduction, trans- port, accumulation and its vital role in plants during variable environmental conditions, Heliyon 5 (12) (2019) e02951, <https://doi.org/10.1016/j.heliyon.2019.e02952>.
- [10] M. Meena, P. Swapnil, T. Barupal, K. Sharma, A review on infectious pathogens and mode of transmission, J. Plant Pathol. Microbiol. 10 (2019) 472, <https://doi.org/10.4172/2157-7471.1000472>.
- [11] D.A. Bryant, G. Guiglielmi, N. Tandeau de Marsac, A. Castets, G. Cohen-Bazire, The structure of cyanobacterial phycobilisomes: a model, Arch. Microbiol. 123 (1979) 113–127.
- [12] S.A. El-Sohaimy, Functional foods and nutraceuticals – modern approach to food science, World Appl. Sci. J. 20 (5) (2012) 691–708.
- [13] T.E. Jensen, Electron microscopy of polyphosphate bodies in a blue-green alga, *Nostoc pruniforme*, Arch. Microbiol. 62 (1968) 144–152.
- [14] H.S. Pankratz, C.C. Bowen, Cytology of blue-green algae. I. The cells of *Symploca muscorum*, Int. J. Bot. 50 (1963) 387–399.



- [15] T.E. Jensen, L.M. Sicko, Fine structure of poly- $\beta$ -hydroxybutyric acid granules in a blue-green alga, *Chlorogloea fritschii*, J. Bacteriol. 106 (2) (1971) 683–686.
- [16] B. Drog, I. Fritz, F. Gattermayr, L. Silvestrini, Photo-autotrophic production of poly (hydroxyalkanoates) in cyanobacteria, Chem. Biochem. Eng. Q. 29 (2) (2015) 145–156.
- [17] T.E. Jensen, C.C. Bowen, Organization of the centropiasm in *Nostoc pruniforme*, Proc. Iowa Acad. Sci. 68 (1961) 86–89.
- [18] S.A. Nierzwickibauer, D.L. Balkwill, S.E. Stevens, 3-Dimensional ultrastructure of a unicellular cyanobacterium, J. Cell Biol. 97 (1983) 713–722.
- [19] D.D. Kunkel, Thylakoid centers: structures associated with the cyanobacterial photosynthetic membrane system, Arch. Microbiol. 133 (1982) 97–99, [https:// doi.org/10.1007/BF00413518](https://doi.org/10.1007/BF00413518).
- [20] T.M. Roberts, K.E. Koths, The blue-green alga *Agmenellum quadruplicatum* contains covalently closed DNA circles, Cell 9 (1976) 551–557.
- [21] H. Ris, R.N. Singh, Electron microscope studies on blue-green algae, J. Biophys. Biochem. Cytol. 9 (1961) 63–80.
- [22] G.W. Fuhs, Cytochemisch-elektronen mikroskopische Lokalisierung der Ribonucleinsäure und des Assimilats in Cyanophycean, Protoplasma 56 (1963) 178–187.
- [23] F. Bray, The Rice Economies, Technology and Development in Asian Societies. Basil Blackwell. 254 p. (1986).
- [24] I. Watanabe, P. A. Roger, Nitrogen fixation in wetland rice fields. In Current Development in Biological Nitrogen Fixation. Ed. N S Subba Rao. (1984) pp 237-276. Oxford and IBH Pub Co., New Delhi.
- [25] P. A. Roger, I. Watanabe, Technologies for utilizing biological nitrogen fixation in wetland rice: Potentialities, current usage, and limiting factors. Fert. Res. 9, (1986) 39-77.
- [26] P. A. Roger, Blue-green algae in agriculture. In Microorganisms that Promote Plant Productivity. Eds. J O Dawson and P J Dart. Kluwer Academic Publishers, Dordrecht, The Netherlands. (1991)
- [27] J. K. Ladha, N. Boonkerd, Biological nitrogen fixation by heterotrophic and phototrophic bacteria in association with straw. In Proceedings of the First International Symposium on Paddy Soil Fertility, Chiangmai, Thailand, (6-13 December 1988). pp 173-187. ISSS, Paddy Soil Fertility Group.
- [28] J. K. Ladha, A. T. Padre, G. C. Punzalan, I. Watanabe, S. K. De Datta, Ability of wetland rice to stimulate biological nitrogen fixation and utilize soil nitrogen. In Nitrogen Fixation: Hundred Years After. Eds. H Bothe, F J de Bruijn and W E Newton, (1988) pp 747-752. Gustav Fischer, Stuttgart, New York.
- [29] I. Watanabe, Azolla-Anabaena symbiosis - its physiology and use in tropical agriculture. In Microbiology of Tropical Soil and Plant Productivity. Eds. Y Dommergues and H S Diem. (1982) pp 169-185. Martinus Nijhoff Publishers, The Hague, The Netherlands.
- [30] J. K. Ladha, I. Watanabe, S. Saono, Nitrogen fixation by leguminous green manure and practices for its enhancement in tropical lowland rice. In Sustainable Agriculture: Green Manure in Rice Farming. (1988) pp 165-183. The International Rice Research Institute, Los Baños, Philippines.
- [31] T. Song, L. Martensson, T. Eriksson, W. Zheng, U. Rasmussen, Biodiversity and seasonal variation of the cyanobacterial assemblage in a rice paddy field in Fujian, China. The Federation of European Materials Societies Microbiology Ecology, (54) (2005) 131–140.
- [32] P. A. Roger, P. A. Reynaud, Free-living Blue-green Algae in Tropical Soils. Martinus Nijhoff Publisher, La Hague. (1982) A. A. Rodriguez, A. A. Stella, M. M. Storni, G. Zulpa, M. C. Zaccaro, Effects of cyanobacterial extracellular products and gibberellic acid on salinity tolerance in *Oryza sativa* L. Saline System, 2 (2006) 7.
- [33] L. T. Wilson, Cyanobacteria: A Potential Nitrogen Source in Rice Fields. Texas Rice, 6 (2006) 9–10.

- [34] S.A. El-Sohaimy, Functional foods and nutraceuticals – modern approach to food science, World Appl. Sci. J. 20 (5) (2012) 691–708.
- [35] M. Meena, M. Aamir, K. Vikas, P. Swapnil, R.S. Upadhyay, Evaluation of morpho-Physiological growth parameters of tomato in response to Cd induced toxicity and characterization of metal sensitive NRAMP3 transporter protein, Environ. Exp. Bot. 148 (2018) 144–167, <https://doi.org/10.1016/j.envexpbot.2018.01.007>.
- [36] M. Meena, P. Swapnil, A. Zehra, M.K. Dubey, M. Aamir, C.B. Patel, R.S. Upadhyay, Virulence factors and their associated genes in microbes, in: H.B. Singh, V.K. Gupta, S. Jogaiah (Eds.), New and Future Developments in Microbial Biotechnology and Bioengineering, Elsevier, 2018, pp. 181–208, <https://doi.org/10.1016/B978-0-444-63503-7.00011-5>.
- [37] R.J. Radmer, Algal diversity and commercial algal products, Bioscience 46 (1996) 263–270, <https://doi.org/10.2307/1312833>.
- [38] J.S. Singh, A. Kumar, A.N. Rai, D. P. Singh, Cyanobacteria: a precious bio-resource in agriculture, ecosystem, and environmental sustainability, Front. Microbiol. 7(2016) 529, <https://doi.org/10.3389/fmicb.2016.00529>.
- [39] C.O. Rangel-Yagui, E.D. Godoy Danesi, J.C.M. Carvalho, S. and Sato, Chlorophyll production from *Spirulina platensis*: cultivation with urea addition by fed-batch process, Bioresour. Technol. 92 (2004) 133–141, <https://doi.org/10.1016/j.biortech.2003.09.002>.
- [40] S.U. Bhaskar, G. Gopalswamy, R. Raghu, A simple method for efficient extraction and purification of C-phycoyanin from *Spirulina platensis* Geitler, Indian J. Exp. Biol. 43 (2005) 277–279.
- [41] D. Soletto, L. Binaghi, A. Lodi, J.C.M. Carvalho, A. Converti, Batch and fed-batch cultivations of *Spirulina platensis* using ammonium sulphate and urea as nitrogen sources, Aquaculture 243 (2005) 217–224, <https://doi.org/10.1016/j.aquaculture.2004.10.005>.
- [42] M. Meena, V. Prasad, R.S. Upadhyay, Assessment of the bio-weedicidal effects of *Alternaria alternata* metabolites against *Parthenium* species, Bull. Environ. Sci. Res. 5 (1) (2016) 1–7.
- [43] M. Meena, A. Zehra, M.K. Dubey, M. Aamir, V.K. Gupta, R.S. Upadhyay, Comparative evaluation of biochemical changes in tomato (*Lycopersicon esculentum* Mill.) infected by *Alternaria alternata* and its toxic metabolites (TeA, AOH, and AME), Front. Plant Sci. 7 (2016) 1408, <https://doi.org/10.3389/fpls.2016.01408>.
- [44] M. Meena, A. Zehra, M.K. Dubey, R.S. Upadhyay, Mannitol and proline accumulation in *Lycopersicon esculentum* during infection of *Alternaria alternata* and its toxins, Int. J. Biomed. Sci. Bioinform. 3 (2016) 64–68.
- [45] ] D. Soletto, L. Binaghi, A. Lodi, J.C.M. Carvalho, A. Converti, Batch and fed-batch cultivations of *Spirulina platensis* using ammonium sulphate and urea as nitrogen sources, Aquaculture 243 (2005) 217–224, <https://doi.org/10.1016/j.aquaculture.2004.10.005>.
- [46] H. Desmorieux, N. Decaen, Convective drying of *Spirulina* in thin layer, J. Food Eng. 66 (2005) 497–503, <https://doi.org/10.1016/j.jfoodeng.2004.04.021>.
- [47] M. Meena, V. Prasad, A. Zehra, V.K. Gupta, R.S. Upadhyay, Mannitol metabolism during pathogenic fungal–host interactions under stressed conditions, Front. Microbiol. 6 (2015) 1019–1026, <https://doi.org/10.3389/fmicb.2015.01019>.
- [48] L. Kedar, Y. Kashman, A. Oren, Mycosprine-2-glycine is the major mycosprine-like amino acid in a unicellular cyanobacterium (*Euhalothece* sp.) isolated from a gypsum crust in a hypersaline saltern pond, FEMS Microbiol. Lett. 208 (2002) 233–237, <https://doi.org/10.1111/j.1574-6968.2002.tb11087.x>.

- [49] ] S. Benedetti, F. Benvenuti, S. Pagliarani, S. Francogli, S. Scoglio, F. Canestrari, Antioxidant properties of a novel phycocyanin extract from the blue green alga *Aphanizomenon flos-aquae*, *Life Sci.* 75 (2004) 2353–2362, <https://doi.org/10.1016/j.lfs.2004.06.004>.
- [50] Gademann, K.; Portmann, C. Secondary metabolites from cyanobacteria: Complex structures and powerful bioactivities. *Curr. Org. Chem.* 2008, 12, 326–341. [CrossRef].
- [51] G. Subramanian, M.B. Anusha, A.L.G. Bai, R. Latha, J. Sasikala, R. Chandrasakaran, Carbohydrate and protein content of five species of marine cyanobacteria from Pamban and Vadakadu (Rameswaram) coastal regions, Tamil Nadu, India, *Int. J. Adv. Interdiscip. Res.* 1 (6) (2014) 18–20.
- [52] ] L.M. Moreira, A.C. Ribeiro, F.A. Duarte, M.G. Morais, L.A.S. Soares, *Spirulina platensis* biomass cultivated in Southern Brazil as a source of essential minerals and other nutrients, *Afr. J. Food Sci.* 7 (12) (2013) 451–455.
- [53] ] K.R. Rajeshwari, M. Rajashekhar, Biochemical composition of seven species of cyanobacteria isolated from different aquatic habitats of western ghats, southern India, *Braz. Arch. Biol. Technol.* 54 (5) (2011) 849–857.
- [54] L. Misurcova, S. Kracmar, B. Klejdus, J. Vacek, Nitrogen content, dietary fiber, and digestibility in algal food products, *Czech J. Food Sci.* 28 (1) (2010) 27–35.
- [55] N. Nagle, P. Lemke, Production of methyl-ester fuel from microalgae. *Appl Biochem Biotechnol* 24(5) (1990) 355–361.
- [56] S. Sawayama, S. Inoue, Y. Dote, S.Y. Yokoyama, CO<sub>2</sub> fixation and oil production through microalga. *Energy Convers Manag.* 36 (1995) 729–731.
- [57] M. Gavrilescu, Y. Chisti, Biotechnology—a sustainable alternative for chemical industry. *Biotechnol Adv.* 23(2005) 471–4.
- [58] P. Farrokh, M. Sheikhpour, A. Kasaeian, H. Asadi, R. Bavandi, Cyanobacteria as an eco-friendly resource for biofuel production: A critical review. *Biotechnol. Prog.* 35, e2835. [CrossRef] [PubMed] (2019)
- [59] N. Misra, P.K. Panda, B.K. Parida, Agrigenomics for microalgal biofuel production: An overview of various bioinformatics resources and recent studies to link omics to bioenergy and bio economy. *Omi. A J. Integr. Biol.* 17 (2013) 537–549. [CrossRef]
- [60] I. M. Machado, S. Atsumi, Cyanobacterial biofuel production. *J. Biotechnol.* 162, 50–56. Doi: 10.1016/j.jbiotec. (2012).03.005
- [61] M.D. Deng, J. R. Coleman, Ethanol synthesis by genetic engineering in cyanobacteria. *Appl. Environ. Microbiol.* 65, (1999). 523–528 [PMC free article] [PubMed] [Google Scholar].
- [62] J. Dexter, P. Fu, Metabolic engineering of cyanobacteria for ethanol production. *Energy Environ. Sci.* 2, (2009). 857. 10.1039/b811937f [CrossRef] [Google Scholar]
- [63] S. Atsumi, W. Higashide, J. Liao, Direct photosynthetic recycling of carbon dioxide to isobutyraldehyde. *Nat Biotechnol* 27, 1177–1180 (2009). <https://doi.org/10.1038/nbt.1586>.
- [64] J. Oliver, W. K., Machado, I. M. P., H. Yoneda, S. Atsumi, Cyanobacterial conversion of carbon dioxide to 2,3-butanediol. *Proc. Natl. Acad. Sci. U.S.A.* 110 (2013) 1249–1254. doi:10.1073/pnas.1213024110. PubMed Abstract | PubMed Full Text | CrossRef Full Text
- [65] E. I. Lan, J. C. Liao, ATP drives direct photosynthetic production of 1-butanol in cyanobacteria. *Proc. Natl. Acad. Sci. U.S.A.* 109 (2012). 6018–6023. doi:10.1073/pnas.1200074109. PubMed Abstract | Pubmed Full Text | CrossRef Full Text
- [66] C. R. Shen, J. C. Liao, Photosynthetic production of 2-methyl-1-butanol from CO<sub>2</sub> in cyanobacterium *Synechococcus elongatus* PCC7942 and characterization of the native acetohydroxy acid synthase. *Energy Environ. Sci.* 5, (2012). 9574–9583. Doi: 10.1039/c2ee23148d. CrossRef Full Text

- [67] K. Takahama, M. Matsuoka, K. Nagahama, T. Ogawa, Construction and analysis of a recombinant cyanobacterium expressing a chromosomally inserted gene for an ethylene-forming enzyme at the *psbAI* locus. *J. Biosci. Bioeng.* 95 (2003)302–305. doi:10.1263/jbb.95.302. Pubmed Abstract | Pubmed Full Text | CrossRef Full Text
- [68] J. Ungerer, L. Tao, M. Davis, M. Ghirardi, P. Maness, J. Yu, Sustained photosynthetic conversion of CO<sub>2</sub> to ethylene in recombinant cyanobacterium *Synechocystis* 6803. *Energy Environ. Sci.* 5, (2012). 8998. doi:10.1039/c2ee22555g.CrossRef Full Text.
- [69] P. Lindberg, S. Park, A. Melis, Engineering a platform for photosynthetic isoprene production in cyanobacteria, using *Synechocystis* as the model organism. *Metab. Eng.* 12, (2010) 70–79. doi:10.1016/j.ymben.2009.10.001. Pubmed Abstract | Pubmed Full Text | CrossRef Full Text.
- [70] X. Liu, J. Sheng, R. Curtiss, III, Fatty acid production in genetically modified cyanobacteria. *Proc. Natl. Acad. Sci. U.S.A.* 108 (2011)6899–6904. doi:10.1073/pnas.1103014108. Pubmed Abstract | Pubmed Full Text | CrossRef Full Text
- [71] A.M.P. Anahas, G. Muralitharan, Characterization of heterocystous cyanobacterial strains for biodiesel production based on fatty acid content analysis and hydrocarbon production. *Energy Convers. Manag.* 157(2018) 423–437. [CrossRef]
- [72] H.W. Paerl, R.S. Fulton, P.H. Moisander, J. Dyble, Harmful freshwater algal blooms, with an emphasis on cyanobacteria, *Sci. World J.* 1 (2001) 76–113.
- [73] G.A. Donovan, C. Steenholdt, K. McGehee, K. Lundquist, Hypomagnesaemia among cows in a confinement-housed dairy herd, *J. Am. Vet. Med. Assoc.* 224 (2004) 9–96.
- [74] K.E. Havens, R.T. James, T.L. East, V.H. Smith, N:P ratios, light limitation, and cyanobacterial dominance in a subtropical lake impacted by non-point source nutrient pollution, *Environ. Pollut.* 122 (2003) 379–390.
- [75] N.N. Galalais, Nitrogen in aquatic ecosystems, *Ambio.* 31 (2002) 102–112.
- [76] V.H. Smith, Predictive models for the biomass of blue-green algae in lakes, *Water Resource Bull.* 21 (1985) 433–439.
- [77] V.H. Smith, Effects of nutrients and non-algal turbidity on blue-green algal biomass in four North Carolina reservoirs, *Lake Reserv. Manage.* 6 (1990) 125–131.
- [78] J.H. Cardellina, B.S. Moore, Editorial: Richard E Moore (1933–2007). *J. Nat. Products*, 73: (2010) 301–302.
- [79] A.M. Burja, B. Banaigs, E. Abou-Mansour, G. Burgess, P.C. Wright, Marine cyanobacteria: a prolific source of natural products. *Tetrahedron*, 57(2001) 9347–9377.
- [80] R. Bajpai, N.K. Sharma, A.K. Rai, Anticancerous/antiviral compounds from cyanobacteria. *Algas*, 43(2010) 4–6.
- [81] J.K. Nunnery, E. Mevers, W.H. Gerwick, Biologically active secondary metabolites from marine cyanobacteria. *Curr. Opin. Biotechnol.* 21 (2010) 787–793.
- [82] R.K. Singh, S.P. Tiwari, A.K. Rai, T.M. Mohapatra, Cyanobacteria: an emerging source for drug discovery. *J. Antibiotics*, 64 (2011) 401–412.
- [83] M.A. Jordan, L. Wilson, Microtubules and actin filaments: dynamic targets for cancer chemotherapy. *Curr. Opin. Cell Biol.*, 10 (1998) 123–130.
- [84] A. Catassi, A. Cesario, Arzani, D. et al., Characterization of apoptosis induced by marine natural products in non-small cell lung cancer A549 cells. *Cell. Molec. Life Sci.*, 63(2006) 2377–2386.

- [85] G.P. Kalemkerian, X.L. Ou, Adil M.R. et al., Activity of dolastatin 10 against small-cell lung cancer in vitro and in vivo: induction of apoptosis and bcl-2 modification. *Cancer Chemother. Pharmacol.* 43(1999) 507–515.
- [86] D.G. Nagle, R.S. Geraldts, H. Yoo, W.H. Gerwick, Absolute configuration of curacin A, a novel antimitotic agent from the tropical marine cyanobacterium *Lyngbya majuscula*. *Tetrahedron Lett.* 36 (1995) 1189–1192.
- [87] J.C. Muir, G. Pattenden, T. Ye, Total synthesis of (+)-curacin A, a novel antimitotic metabolite from a cyanobacterium. *J. Chem. Soc. Perkin Transactions*, 1 (2002) 2243–2250.
- [88] N. Biondi, M.R. Tredici, Taton A. et al., Cyanobacteria from benthic mats of Antarctic lakes as a new source of bioactivities. *J. Appl. Microbiol.*, 105 (2008) 105–115.
- [89] S. Kreitlow, S. Mundt, U. Lindequist, Cyanobacteria – a potential source of new biologically active substance. *J. Biotechnol.*, 70 (1999) 61–73.
- [90] O.M. Skulberg, Microalgae as a source of bioactive molecules: experience from cyanophyte research. *J. Appl. Phycol.*, 1 (2000) 341–348.
- [91] B. Jaki, J. Orjala, J. Heilmann, A. Linden, B. Vogler, O. Sticher, Novel extracellular diterpenoids with biological activity from the cyanobacterium *Nostoc commune*. *J. Nat. Products*, 63(2000) 339–343.
- [92] J.F. Blom, T. Brutsch, Barbaras D. et al., Potent algicides based on the cyanobacterial alkaloid nostocarboline. *Organic Lett.* 8 (2006) 737–740.
- [93] K. Hirata, S. Yoshitomi, Dwi S. et al., Bioactivities of nostocine A produced by a freshwater cyanobacterium *Nostoc spongiaeforme* TISTR 8169. *J. Biosci. Bioeng.* 95 (2003) 512–517.
- [94] R.K. Asthana, M.K. Tripathi, Deepali A. et al., Isolation and identification of a new antibacterial entity from the Antarctic cyanobacterium *Nostoc* CCC 537. *J. Appl. Phycol.*, 21 (2009) 81–88.
- [95] M. Luescher-Mattli, Algae as a possible source of new antiviral agents. *Curr. Med. Chem. Anti-Infect. Agents*, 2(2003) 219–225.
- [96] K.R. Gustafson, J.H. Cardellina, R.W. Fuller et al., AIDS antiviral sulfolipids from cyanobacteria (blue-green algae). *J. Natl Cancer Inst.*, 81 (1989) 254–258.
- [97] H. Yang, E. Lee, H. Kim, *Spirulina platensis* inhibits anaphylactic reaction. *Life Sci.*, 61(1997) 1237–1244.
- [98] L.T. Simmons, N. Engene, L.D. Ureña, et al. Viridamides A and B, lipodepsipeptides with antiprotozoal activity from marine cyanobacterium *Oscillatoria nigroviridis*. *J. Nat. Products*, 71(2008) 1544–1550.
- [99] M.R. Lanzer, P. Rohrbach, Subcellular pH and Ca<sup>2+</sup> in *Plasmodium falciparum*: implications for understanding drug resistance mechanisms. *Curr. Sci.*, 92 (2007) 1561–1570.
- [100] G. Kasparian, S. Ngouama, D. et al., Nifurtimox-eflornithine combination therapy for second-stage *Trypanosoma brucei* gambiense sleeping sickness: a randomized clinical trial in Congo. *Clin. Infect. Dis.*, 45(2007) 1435–1442.
- [101] K. Sheifert, A. Lunke, S.L. Croft, O. Kayser, Antileishmanial structure activity relationships of synthetic phospholipids: in-vitro and in-vivo activities of selected derivatives. *Antimicrob. Agents Chemother.* 51 (2007) 4525–4528.
- [102] D. Barbaraus, M. Kaiser, R. Brun, K. Gademann, Potent and selective antiplasmodial activity of the cyanobacterial alkaloid nostocarboline and its dimers. *Bioorganic Medicinal Chem. Lett.*, 18 (2008) 4413–4415.

[103] C. Portmann, J.F. Blom, M. Kaiser, R. Brun, F. Jüttner, K. Gademann, Isolation of aerucyclamides C and D and structure revision of microcyclamide 7806A, heterocyclic ribosomal peptides from *Microcystis aeruginosa* PCC 7806 and their antiparasite evaluation. *J. Nat. Products*, 71(2008) 1891–1896.

[104] B.R. Clark, N. Engene, M.E. Teasdale et al., Natural products chemistry and taxonomy of the marine cyanobacterium, *Blennothrix cantharidosmum*. *J. Nat. Products*.71 (2008) 1530–1537.

[105] V. V.Chaugule, Microbial synthesis of copper oxide nanoparticles from endophytic Actinomycetes and its postharvest application on *Solanum lycopersicum*. *Journal of Postharvest Technology*. 9(3) ( 2021) 68-83.

[106] D. Chittora, M. Mukesh , B.Tansukh , S.Prashant , K. Sharma, Cyanobacteria as a source of biofertilizers for sustainable agriculture *Biochemistry and Biophysics Reports* 22 (2020) 100737.

