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Cyanobacterial Farming for Environment Friendly Sustainable Agriculture Practices: Innovations and Perspectives

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Sustainable supply of food and energy without posing any threat to environment is the current demand of our society in view of continuous increase in global human population and depletion of natural resources of energy. Cyanobacteria have recently emerged as potential candidates who can fulfill abovementioned needs due to their ability to efficiently harvest solar energy and convert it into biomass by simple utilization of CO_2, water and nutrients. During conversion of radiant energy into chemical energy, these biological systems produce oxygen as a by-product. Cyanobacterial biomass can be used for the production of food, energy, biofertilizers, secondary metabolites of nutritional, cosmetics, and medicinal importance. Therefore, cyanobacterial farming is proposed as environment friendly sustainable agricultural practice which can produce biomass of very high value. Additionally, cyanobacterial farming helps in decreasing the level of greenhouse gas, i.e., CO_2, and it can be also used for removing various contaminants from wastewater and soil. However, utilization of cyanobacteria for resolving the abovementioned problems is subjected to economic viability. In this review, we provide details on different aspects of cyanobacterial system that can help in developing sustainable agricultural practices. We also describe different large-scale cultivation systems for cyanobacterial farming and discuss their merits and demerits in terms of economic profitability.

Keywords: biofertilizers, bioenergy, biotechnology, cyanobacterial farming, nutraceuticals, sustainable agricultural practices

INTRODUCTION

The human population of our planet is projected to reach ∼9.7 billion by 2050, and majority of this increased population would be contributed by developing countries of Asia and Africa (DESA UN, 2015). This increase in global population is associated with increased demand of food security in future. To overcome this challenge, the World Health Organization has suggested a doubling of food production by 2050, while the United Nations have suggested a 50% increase in global food production by 2030. The productivity gains resulted from the "Green Revolution" have essentially reached a plateau, and feeding the increased global population is further challenged by limited availability of agriculture land. The range of non-conventional biotechnological measures involving improvement in CO_2 fixation efficiency of crop plants can be used to enhance the food productivity per hectare of agricultural land (Parry and Hawkesford, 2010; Parry et al., 2011). Nevertheless, a production system which has a higher productivity but requires a small land area and time for cultivation would be the requirement of the future agriculture.

Several factors such as haphazard nutrient mining, water limitation, accumulation of noxious xenobiotic compounds in the soil, soil corrosion and climate change have deteriorated the quality and fertility of agricultural land (Singh, 2014). Additionally, soil salinity is a well-known stressor which affects the plant growth and crop production globally (Upadhyay et al., 2011). The social and economic activities have resulted in reduction of the cultivable area, and hence, in addition to conservation of fertile land, enhancement of the coverage of cultivable land should be one of the focused areas to feed the human population (Singh et al., 2016; Pathak et al., 2017). Modern green technologies such as biofertilizers consisting of cyanobacteria, fungi (arbuscular mycorrhizal fungi, AMF) and bacteria (plant growth promoting rhizobacteria, PGPR) could improve and restore the soil fertility and ensure the sustainable agricultural production. Moreover, these microorganisms can reduce the energy demand in the form of synthetic fertilizers, and have the capability to mitigate stressed agroecosystems and wastelands.

Microbial biotechnology plays an important role particularly in secondary metabolites, biofertilizers, bioenergy, bioprocessing, biopesticide production, waste treatment, and bioremediation (Du et al., 2007; Mohammadi and Sohrabi, 2012). The sustainable agriculture involves soil, water and pest management, crop selection, soil preservation and processing. These sustainable agricultural practices together with biotechnology have the potential to increase the productivity by developing new transgenic plants, microbes and animals (Singh, 2000). Over the last decade, biotechnology has significantly contributed to sustainable agriculture by the development of stress resistance in microbes and plants, bioremediation of polluted soils, enhanced nitrogen fixation and increased nutrient uptake efficiency (Singh, 2000). However, the cultivation of genetically modified organisms in an open area is still a matter of debate all over the world.

In recent years, microalgae, including cyanobacteria, have emerged as potential candidates for their application in development of environment friendly and sustainable agricultural practices (Singh et al., 2016, 2017). These oxygen-evolving photosynthetic organisms do not compete for arable land for their cultivation. Cyanobacteria, which can be cultivated using seawater, require residual nutrients for high areal productivity and have high protein and reasonable amount of carbohydrate as well as lipid contents per gram of their biomass (Williams and Laurens, 2010; Milledge, 2011; Hoekman et al., 2012). Globally about 25 Gt a^{-1} of carbon can be fixed into energy-dense biomass by cyanobacteria using atmospheric CO_2 and solar energy (Pisciotta et al., 2010). Therefore, generation of microbiological energy through massive solar energy transformation permits harvesting various forms of eco-friendly energy reserves (Hall et al., 1995; Paumann et al., 2005). The aforementioned characteristics make cyanobacteria potential microorganisms for their application as feedstocks for sustainable production of food and non-food commodities, including valuable chemicals and bioenergy (Wase and Wright, 2008; Sarsekeyeva et al., 2015; Rajneesh et al., 2017). Cyanobacteria produce a number of valuable compounds such as ethanol, butanol, fatty acids, and other organic acids, and therefore, are promising candidates for fulfilling our energy demands in a sustainable manner (Rajneesh et al., 2017). In addition, cyanobacteria have potential applications in agriculture as biofertilizers and in the food industry as food supplements (**Figure 1**). Recent developments in the techniques of genetic engineering, culturing and screening of cyanobacteria have enabled novel ways to utilize the potentials of available wealth of these ancient microorganisms. Genetic manipulation techniques are well developed for several cyanobacteria, and therefore, a synthetic biology approach provides an opportunity to exploit these organisms as green factories for the production of new lines of commodities. In this paper, we review various ways of cyanobacterial farming that could be utilized in the development of sustainable agriculture practice in an eco-friendly manner (**Figure 1**).

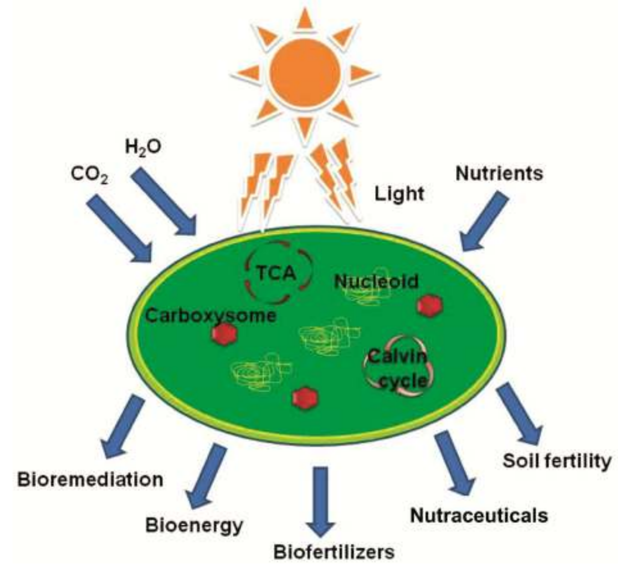

FIGURE 1 | Various outcomes of cyanobacterial growth that can be utilized for the development of sustainable agricultural practices.

SUSTAINABLE AGRICULTURE AND MICROBES

Among various streams of life sciences, agricultural biotechnology could potentially help in developing the sustainable agriculture practices. In modern agriculture, microbial intervention further strengthens the impact of transgenic organisms. Microbes play a vital role in determining the fertility and structure of soils (Vaishampayan et al., 2001;

Singh, 2014; Singh et al., 2016), in processing and preservation of crops, and in recycling the residues of crops (Saddler, 1993; Hanson, 1996). Microbial activity in soil fertility, bioremediation and biocontrol requires the introduction of genetically engineered or natural microbial inoculants; however, mere inoculation of microbes in soil is not sufficient. The monitoring of survival and establishment of inoculants in the soil, and their negative or positive interactions with other indigenous microbial population are very crucial (Molin and Molin, 1997; Van Veen et al., 1997). Maintenance of soil fertility with renewable resources is the prime requirement of sustainable agriculture in order to reduce the need for synthetic fertilizers. Among such resources, natural and transgenic N_2-fixing microbes are the most promising candidates. In the rhizosphere, the N_2-fixing microorganisms can be directly inoculated in soil or can be used as coating on seeds, however, in both cases their survival need to be assured. Several living biosensors have been developed which can be used for monitoring, management and manipulation of interacting microbial consortia (Burlage and Kuo, 1994).

The various metabolites produced by microbes have the potential to aid in the development of sustainable agriculture practice, and the best example is biocompatible microbial polymers which can be used in coating of fertilizers, pesticides, and nutrients. This will help in targeted delivery of fertilizers, pesticides, and nutrients for agriculture by preventing their application in other industry or antisocial activities. Microbial polymers can also be used in food processing units (Vandamme et al., 1996; Sutherland, 1998). One of the sustainable ways to convert wastelands to agricultural practices is bioremediation of contaminated soils and waters. For bioremediation of contaminated soils, natural, or transgenic microbes in mixed culture are used (Atlas, 1995). However, for effective bioremediation of contaminated terrestrial or aquatic ecosystem, the chemical and microbial interactions along with biogeochemical and ecological balances of concerned ecosystem should be considered (Anderson and Lovley, 1997; Tiedje, 1997). Among various beneficial microbes, cyanobacteria can be used in nutrition, energy and agriculture sector because of their ability to fix atmospheric N_2 and CO_2, and produce energy rich biomass containing myriad of metabolites of economic importance. Furthermore, recent developments in cyanobacterial screening, cultivation, and gene manipulation techniques have enabled new ways to utilize the potential of these photosynthetic microbes to deal with socio-economic problems (Sarsekeyeva et al., 2015).

CYANOBACTERIA AND SUSTAINABLE AGRICULTURE

Cyanobacteria contribute significantly to the biogeochemical cycles of carbon, nitrogen and oxygen (Karl et al., 2002; De Ruyter and Fromme, 2008). They have undergone a series of functional and structural modifications during their evolution that permit their current distribution in diverse ecological niches (Olson, 2006). Cyanobacteria can tolerate various stresses such as ultraviolet radiation (UVR; 280–400 nm), desiccation, high or low temperatures and salinity, which contribute to their advantages over different competitors/neighbors in their natural habitats (Gröniger et al., 2000; Herrero and Flores, 2008). For example, *Spirulina maxima* is known to survive under high alkaline conditions (pH 11) and high salinity which provide advantage and protection from other competitors and grazers (Habib et al., 2008). The nitrogen fixing ability of cyanobacteria aids their successful growth and survival in habitats where no or little combined nitrogen is available. This trait of cyanobacteria makes them agronomically and economically important as biofertilizers (Singh, 1961, 2014; Vaishampayan et al., 2001; Singh et al., 2016).

Several cyanobacteria are known to establish symbiotic associations, and this ability could be exploited in developing the consortia of microorganisms for their application in bioremediation of affected soils or aquatic systems (Rai et al., 2000; Subashchandrabose et al., 2011; Hamouda et al., 2016). Strains of cyanobacteria which are native and adapted to local climatic conditions have a capacity to survive in wet soils. This significantly affects the nutritional status, structural stability and crop productivity of such soils (Nisha et al., 2007). Twenty five percent of the total biomass of cyanobacteria is contributed by the exopolysaccharides (EPS) (Nisha et al., 2007). The upper crust of the soil is the site of cyanobacterial activities and the EPS act as a gluing agent on soil particles. The EPS can hold soil particles together which leads to soil aggregation, organic content accumulation and increase in water holding capacity of the top layer of soil (Malamlssa et al., 2001). This increase in soil moisture and organic content can support the survival and growth of plant-growth promoting rhizobacteria (PGPR). Thus, cyanobacterial growth positively alters the chemical and physical property of soils, and PGPRs along with EPS-producing cyanobacteria may contribute to an improvement and reclamation of infertile soils (Flaibani et al., 1989; Verrecchia et al., 1995; Zulpa et al., 2003; Paul and Nair, 2008). The consortium of PGPR and cyanobacteria increases the plant growth by improving the soil fertility and nutrient utilization. In additions, this consortium also enhances the tolerance of plants against environmental stresses such as drought and salinity (Singh et al., 2011; Prasanna et al., 2012; Singh, 2014). However, community structure and diversity of cyanobacteria should be studied in depth particularly in reference to environmental conditions and ecosystem functions before devising application of a consortium under field conditions. In following sections, different properties of cyanobacteria are presented that can be utilized for the development of sustainable agriculture practice in environment friendly manner.

Cyanobacteria as Bioremediators

Cyanobacteria can be used for the bioremediation of several contaminants such as heavy metals, pesticides, crude oil, phenanthrene, naphthalene, phenol, catechol, and xenobiotics (Kesaano and Sims, 2014; Hamouda et al., 2016; Kumar et al., 2016; Singh et al., 2016). *Synechococcus elongatus*, *Microcystis aeruginosa* and *Anacystics nidulans* have shown potentials to remove organo-chlorine and organo-phosphorus insecticides (Vijayakumar, 2012). Cyanobacterial genera such as *Oscillatoria*, *Synechococcus*, *Nodularia*, *Nostoc*, *Anabaena,* and *Microcystis* break down lindane residues (El-Bestawy et al., 2007). *Anabaena* sp., *Lyngya* sp., *Microcystis* sp., *Nostoc* sp. and *Spirulina* sp. can utilize glyphosate as the source of phosphorus, and therefore, helps in removal of this herbicide from contaminated soil (Forlani et al., 2008; Lipok et al., 2009). Thus, an above mentioned cyanobacterial strains are potential candidates for their application in developing sustainable agricultural practice where they can be used for removing various contaminants from soil as well as water.

The consortia of cyanobacteria and chemotrophic bacteria have been effectively used to bioremediate wastewaters and oil-contaminated sediments (Abed and Köster, 2005). Cyanobacteria can oxidize oil components as well as other complex organic compounds such as herbicides and surfactants (Mansy and El-Bestway, 2002; Subashchandrabose et al., 2013). The consortium of *Oscillatoria-Gammaproteobacteria* can degrade phenanthrene, dibenzothiophene, pristine and n-octadecane (Abed and Köster, 2005). Similarly, consortia of *Microcoleus chthonoplastes* with organotrophic bacteria can fix atmospheric nitrogen and degrade aliphatic heterocyclic organo-sulfur compounds and hydrocarbons such as alkylated monocyclic and polycyclic aromatic compounds (Sánchez et al., 2005). An artificially designed biofilm consortium of hydrocarbon-degrading bacteria and cyanobacteria on gravel particles and glass plates has been developed that can be used for cleaning up crude-oil contamination of sea water samples (Al-Awadhi et al., 2003). The consortium of *Anabaena oryzae* and *Chlorella kessleri* can be used to biodegrade crude oil under mixotrophic condition (Hamouda et al., 2016). Cyanobacteria are also capable of removing heavy metals from water bodies and can reduce the excess of nitrate and phosphate from agricultural fields (Kesaano and Sims, 2014; Kumar et al., 2016). Consortia of cyanobacteria and bacteria have shown positive results in wastewater treatment. Cultures of *Aphanocapsa* sp. BDU 16, *Oscillatoria* sp. BDU 30501 and *Halobacterium* US 101 can be utilized for minimizing the amount of calcium and chloride in wastewater to a level that can support the survival of fishes (Uma and Subramanian, 1990). Similarly, *Phormidium valderianum* BDU 30501 and *Oscillatoria boryana* BDU 92181 can be utilized to remove phenol and melanoidin, respectively, from the effluents of distillery (Shashirekha et al., 1997; Kalavathi et al., 2001). Desertification is another challenge for sustainable agriculture practices which can be reversed by the application of cyanobacterial inoculums. Cyanobacteria together with bacteria, mosses, algae, lichens and fungi forms biological soil crusts (BSCs) in semiarid and arid areas of various geographical regions (Rossi et al., 2017). These BSCs play an important role in stabilization and primary colonization of desert soil surface by increasing the nutrient and moisture contents (Rossi et al., 2017). Thus, cyanobacteria can be ideally utilized for removing the various contaminants. However, for bioremediation of polluted sites, focus should be given to utilization of indigenous consortia that could potentially reduce the need of adding new microorganisms or fertilizers to the target site. Further improvement in bioremediation property can be achieved by genetic engineering of parent strains which can help in developing a maintenance-free and economical remediation technology while producing the biomass of high value for other purposes (Kuritz and Wolk, 1995; Cuellar-Bermudez et al., 2017).

Cyanobacteria as Bioenergy Resource

First and second generations of biofuels have utilized feedstocks such as rapeseed, soybean, sunflower, wheat, switchgrass, peanuts, and sesame seeds. These raw materials have been used to produce different energy sources such as ethanol, propanol, butanol, and vegetable oils (Quintana et al., 2011). However, energy crops, which are used in first and second generations of biofuels production, compete with conventional food sources for water, nutrients and fertile land. Therefore, the third generation of biofuel production using microalgae has emerged as an alternative to avoid the competition between food crops and energy crops for available resources, and furthermore, cyanobacteria are one of the most promising feedstocks for the production of third generation biofuels (Quintana et al., 2011; Al-Haj et al., 2016; Rajneesh et al., 2017). Rapid growth rate and cultivation in suitable in-house bioreactors and/or on non-arable land gives cyanobacteria an advantage over plants (Singh, 2014; Sarma et al., 2016). Furthermore, cyanobacteria show higher photosynthetic efficiency (∼10%), as compared to land plants (∼3–4% maximum efficiency) (Lewis and Nocera, 2006; Melis, 2009). Cyanobacteria can be easier genetically manipulated than other algae, and hence, serve as a better candidate in comparison to eukaryotic algae for the production of targeted chemicals and fuels. The genome size of cyanobacteria is relatively small and till date genomes of several genera have been sequenced (Rajneesh et al., 2017). Therefore, cyanobacteria provide an exceptional opportunity to conduct genetic and metabolic engineering studies for improved biomass production which is comparatively difficult to do with eukaryotic algae (Rittmann, 2008). Cyanobacteria contain considerable amounts of lipids; primarily located in the thylakoid and plasma membranes, and show higher rates of growth and photosynthesis. Enhanced production of biofuel from cyanobacteria utilizing genetic engineering has been attempted mainly on *Synechocystis* sp. PCC 6803 and *S. elongatus* PCC 7942, whose genomes are fully sequenced and molecular techniques are well-established (Kaneko et al., 1996). Genetic engineering can be used for the production of various fuels such as 2,3-butanediol, acetone 1-butanol, ethylene, ethanol, fatty acids, isobutyraldehyde, isobutanol, 2-methyl-1-butanol, and isoprene in cyanobacteria. Therefore, genetically modified cyanobacteria might play a crucial role in reduction of crude oil dependency and CO_2 emissions, owing to direct photosynthetic fixation of CO_2 to biofuel and other valuable secondary metabolites (Ducat et al., 2011; Oliver et al., 2016).

However, cyanobacteria have some limitations for their application in biofuel production. The production of valuable chemicals in photoautotrophic cyanobacteria is always less than sugar-utilizing systems such as *S. cerevisiae* and *E. coli* (Savakis and Hellingwerf, 2014). Generally, photoautotrophic cyanobacterial chassis can produce only ∼100 mg of biochemicals per liter of cell culture (Gao et al., 2016), which is far too low for any commercially viable application. Theoretical yields under heterotrophic and autotrophic growth conditions for production of several chemicals have been computed for cyanobacterial chasis to find out the limiting factors in cyanobacterial metabolic network (Gudmundsson and Nogales, 2015). However, study suggests that low yield is not due to the topology of the photosynthetic metabolic networks in cyanobacteria. Therefore, it is important to optimize the inherent biological chassis for enhancing the yield of biochemicals from cyanobacteria. In recent years, several groups have emphasized on construction, designing, and expression of the biosynthetic pathways along with development of the toolboxes for metabolic engineering in cyanobacteria which could lead to economic profitability by increasing the production of existing and novel chemicals and biofuels (Wang et al., 2012; Berla et al., 2013; Desai and Atsumi, 2013; Oliver and Atsumi, 2014; Gudmundsson and Nogales, 2015; Markley et al., 2015).

TABLE 1 | List of nitrogen-fixing cyanobacteria important for their application in biofertilizer industry (adapted from Vaishampayan et al., 2001).

Filamentous		Unicellular
Heterocystous	**Non-heterocystous**	
Anabaena, Anabaenopsis, Aulosira, Calothrix, Camptylonema, Chlorogloea, Chlorogloeopsis, Cylindrospermum, Fischerella, Gloeotrichia, Haplosiphon, Mastigocladus, Nodularia, Nostoc, Nostochopsis, Rivularia, Scytonema, Scytonematopsis, Stigonema, Tolypothrix, Westiella, Westiellopsis, Wollea	*Lyngbya, Microcoleus chthonoplastes, Myxosarcina, Oscillatoria, Plectonema Boryanum, Pseudoanabaena, Schizothrix, Trichodesmium*	*Aphanothece, Chroococcidiopsis, Dermocarpa, Gloeocapsa, Myxosarcina, Pleurocapsa, Synechococcus, Xenococcus*

Cyanobacteria as Biofertilizers

It is very expensive to produce inorganic nitrogen fertilizers due to the requirement of large amount of fossil-fuel energy. This necessitated the development of alternate, sustainable and cost-effective biologically available nitrogen resources which can fulfill the nitrogen demand of agriculture in sustainable manner (Mahanty et al., 2017). For this purpose biological systems have been identified which can fix atmospheric dinitrogen (Hegde et al., 1999; Vaishampayan et al., 2001). Biological nitrogen fixation contributes $\sim 2 \times 10^2$ Mt of nitrogen annually (Guerrero et al., 1981). According to Metting (1988), the total nitrogen fixation can be ~90 kg N ha^{-1} y^{-1}. Symbiotic and free-living eubacteria, including cyanobacteria, are two groups of nitrogen-fixing organisms. The free-living cyanobacteria fix <10 kg of N $ha^{-1}y^{-1}$, however, annually ~10–30 kg of N ha^{-1} is fixed by dense mats of cyanobacteria (Aiyer et al., 1972; Watanabe et al., 1977). Therefore, cyanobacteria constitute an important component of naturally available biofertilizers (Vaishampayan et al., 2001; Prasanna et al., 2013). Rice production in tropical countries mainly depends on biological N_2 fixation by cyanobacteria which are a natural component of paddy fields (Vaishampayan et al., 2001). In these cultivated agriculture systems, annually ~32 Tg of nitrogen is fixed by biological nitrogen fixers (Singh et al., 2016), and cyanobacteria add about 20–30 kg fixed nitrogen ha^{-1} along with organic matter to the paddy fields (Subramanian and Sundaram, 1986; Issa et al., 2014). Cyanobacteria also make symbiotic associations with different photosynthetic and non-photosynthetic organisms such as algae, fungi, diatoms, bryophytes, hornworts, liverworts, mosses, pteridophytes, gymnosperms, and angiosperms (Rai et al., 2000; Sarma et al., 2016).

Several heterocystous cyanobacterial genera such as *Nostoc, Anabaena, Nodularia, Scytonema, Cylindrospermum, Mastigocladus, Calothrix, Anabaenopsis, Aulosira, Tolypothrix, Haplosiphon, Camptylonema, Stigonema, Fischerella, Gloeotrichia, Chlorogloeopsis, Rivularia, Nostochopsis, Westiellopsis, Wollea, Westiella, Chlorogloea*, and *Schytonematopsis* have been shown to be efficient N_2 fixers (Venkataraman, 1993). **Table 1** contains a list of potential cyanobacteria which can be used as biofertilizers in agricultural fields (Vaishampayan et al., 2001). For the first time, Fritsch (1907) studied the abundance and importance of cyanobacteria with respect to maintenance of soil fertility of paddy fields through biological nitrogen fixation, which was afterwards recognized by several other workers (Singh, 1950; Fogg and Stewart, 1968; Holm-Hanson, 1968). Generally, for algalization of the rice fields, mixed cyanobacterial cultures of free-living forms are used (Venkataraman, 1972; Roger and Kulasooriya, 1980). The water fern *Azolla* harbors *Anabaena azollae* in its fronds and the cyanobacterium releases ammonium into the water when paddy fields are inoculated with foam-immobilized *A. azollae* strains (Kannaiyan et al., 1997). Significant increase in grain yield, biomass and nutritive value of rice can be achieved by inoculating *Anabaena doliolum* and *A. fertilissima* in paddy fields with or without urea (Dubey and Rai, 1995). Several cyanobacterial species such as *Anabaena iyengarii* var. *tenuis*, *A. fertilissima*, *Nostoc commune*, *N. ellipsosporum*, *N. linckia*, and *Gloeotrichia natans* are known to contribute to the productivity of rice fields in Chile (Pereira et al., 2009). Generally, application of 12.5 kg ha^{-1} of cyanobacterial biofertilizer has been recommended for quantitative and qualitative improvements in rice production (Dubey and Rai, 1995).

In addition to rice crop, cyanobacterial biofertilizers can also enhance the yield, shoot/root length, and dry weight of wheat crops (Spiller and Gunasekaran, 1990; Obreht et al., 1993; Karthikeyan et al., 2009). Inoculation of soil with various cyanobacterial strains like *Nostoc carneum*, *N. piscinale*, *Anabaena doliolum* and *A. torulosa* results in significantly higher acetylene reducing activity (Prasanna et al., 2013). Additionally, the acetylene reducing activity is highest at harvest stage when wheat fields are inoculated with an *Anabaena-Serratia* biofilm along with rock phosphate (Swarnalakshmi et al., 2013). The cyanobacteria based biofertilizers are cost-effective as they cost one third to that of chemical fertilizers (Prasanna et al., 2013). In addition to nitrogen fixation, cyanobacteria also contribute to mobilization of inorganic phosphates through excretion of organic acids and extracellular phosphatases (Bose and Nagpal, 1971; Rai and Sharma, 2006). Cyanobacteria solubilize and mobilize the insoluble organic phosphates and improve the availability of phosphorus to the crop (Dorich et al., 1985; Cameron and Julian, 1988). The humus content generated after death and decay of cyanobacteria creates strong reducing condition in soil which improve the soil structure and fertility (Abdel-Raouf et al., 2012). Different cyanobacterial strains are known to produce plant growth hormones and siderophores, and therefore, cyanobacteria can affect the development and productivity of crops (Rodriguez et al., 2006; Rastogi and Sinha, 2009). The EPS secreted by cyanobacteria induces aggregation of soil particles which improve the soil structure and fertility by enhancing the accumulation of organic content and water accumulation. These findings collectively support the importance of cyanobacteria as biofertilizers, and methods have been developed for their cultivation and utilization in fertilizer industry (Brouers et al., 1987; Shi and Hall, 1988; Vaishampayan et al., 2000).

Cyanobacteria in Nutrition and Health Sector

Cyanobacteria are a well-known non-conventional source of protein, healthy lipids, minerals, antioxidants, and vitamins (Pulz and Gross, 2004; Singh et al., 2005; Gantar and Svircev, 2008; Rosenberg et al., 2008). The cyanobacterium *Spirulina* (*Arthrospira*) has been used by the Aztec population as food supplement for a long time (Pulz and Gross, 2004). The various strains of *Nostoc, Spirulina,* and *Anabaena* are used as food supplements in Peru, Mexico, Philippines, and Chile. Cyanobacteria generally have low lipid content but 6–13% lipid on dry weight basis has been reported in *Spirulina* (Cohen, 1997). *Spirulina* is a good source of rare polyunsaturated fatty acid, i.e., gamma-linolenic acid (GLA), which has several pharmaceutical properties. GLA is 170 times more effective than linoleic acid, which is the main constituent of majority of polyunsaturated oils (Huang et al., 1982).

Arthrospira platensis is a best example of non-conventional source of food supplement which is mass cultivated in outdoor ponds or bioreactors, and commercially available in the form of flakes, powder, capsules or pills. It is very nutrient rich, containing more than 60% of proteins. *Arthrospira* is a rich source of thiamine, riboflavin, beta-carotene, and it is also considered as an excellent whole-food source of vitamin E and vitamin B_{12} (Abed et al., 2009). *Arthrospira* (∼20 g) can provide the required regular doses of vitamin B_{12} and 50% of vitamin B_2 (riboflavin), 70% of B_1 (thiamine) and 12% of B_3 (niacin) in humans (Switzer, 1981). It also contains a fair amount of tocopherol (vitamin E), which is almost three times that of pure wheat germ (Hudson and Karis, 1974). The native population of the lake Chad region of Africa uses *Spirulina (Arthrospira)* as hardened, sun dried mat (Dihé) as a food supplement rich in proteins, minerals, carotenoids, vitamin E, folate and lipids containing essential unsaturated fatty acids (Carcea et al., 2015). *Spirulina* (*Arthrospira*) is generally termed as "magic agent" because of its wide applications as feeds, food, anticancer agent and cosmetics (Vonshak, 1997). However, *Spirulina* proteins are low in methionine, lysine and cysteine contents, and therefore, inferior to milk or meat protein but it is superior to plant proteins such as legumes (Ciferri, 1983). Thus, *Spirulina* could be utilized as a source of protein and other nutrients in countries where starvation and malnutrition is the main problem for human civilization. *Spirulina* can also be used for feeding hens because it stimulates egg production with intense yolk color, while *Spirulina*-fed fish develop a pink yellow meat of high commercial value (Sharma et al., 2011). Tilapia fish shows high growth rates in outdoor and indoor cultures when fed with marine cyanobacteria (Mitsui et al., 1983). *P. valderianum* is non-toxic and possesses high nutritional value, and therefore, it can be used as a complete aquaculture feeds (Steinberg et al., 1998). Thus, cyanobacteria can be used as a quality food in aquaculture and poultry farming which increases the quality and quantity of products.

Several cyanobacteria such as *Anabaena flos-aquae*, *A. hassali*, *Nostoc punctiforme, Phormidium bijugatum,* and *Microcystis pulverana* are good source of vitamin B-complex, pentothene and nicotinic acid (Robbins et al., 1951; Koptera, 1970). Similarly, *N. commune* is a rich sources of fibers and proteins (Abed et al., 2009). Additionally, cyanobacteria are source of pigments such as phycobiliproteins, chlorophyll *a,* and carotenoids. Cyanobacteria synthesize UV screening compounds such as mycosporine-like amino acids and scytonemins which have their applications in cosmetic and pharmaceutical industry (Rajneesh et al., 2017). However, several species of cyanobacteria are known to produce various cyanotoxins such as hepatotoxins, neurotoxins, cytotoxins, and dermatotoxins, and therefore, care should be taken when toxin producing cyanobacteria are used for the production of edible chemicals (Rajneesh et al., 2017). Cyanobacteria-based diet can be also used in reducing the cholesterol levels; cyanobacterial diet has been found to reduce the lipoproteins and cholesterol levels in blood serum of rats (Nakaya et al., 1988; Hori et al., 1994). Detailed studies suggest that cyanobacterial feeding increases the lipase enzyme which helps in lowering of triglycerides (Iwata et al., 1990). The consumption of cyanobacterium *A. flos-aquae* decrease the blood cholesterol level, stimulate liver functioning and accelerate the recovery from mild traumatic brain injury (Vlad et al., 1995; Valencia and Walker, 1999).

The phycobiliproteins produced by cyanobacteria, e.g., phycocyanin, phycoerythrin, and allophycocyanin, have several applications in food, cosmetics, medicine, and diagnostics industry. Phycocyanin from *Spirulina* has been used in lipsticks, eyeliner and eye shadow (Sharma et al., 2011). In Japan, phycocyanin extracted from *A. platensis* is marketed as a colorant of cosmetics and food (Prasanna et al., 2007). Phycocyanin is highly stable in the presence of preservatives, high temperature, and light; however, reluctance in consumption of blue foods has limited the interest of industries in utilization of phycocyanin as food colorant (Jespersen et al., 2005; Mishra et al., 2008). Phycocyanin can be also used as a rich source of protein in commercially available dietary supplements. Apart from the nutritional importance, the cyanobacteria also possess anti-inflammatory, antioxidant, anti-viral, and anti-cancer properties (Jensen et al., 2001). Several biologically active compounds have been reported from cyanobacteria (**Table 2**), which may contribute to the improved health on consumption of cyanobacteria based diet, and furthermore, these compounds can be also used in the development of new drugs (Rajneesh

TABLE 2 | Cyanobacterial metabolites of pharmacological and biotechnological importance (Source: Rajneesh et al., 2017).

Antibacterial	Antifungal	Anticancerous	Antiviral	Antimalarial
Abietane diterpenes, Ambiguines, Bastadin, Bis-(v-butyrolactones), Hapalindole, Didehydromirabazole, Nostocine A, Muscoride, Noscomin, Tolyporphin	Anhydrohapaloxindole, Fischerllin, Majusculamide A–D, Tanikolide	Acutiphycin, Ankaraholide A, Aplysiatoxin, Apratoxins, Arenastatin A, Aurilide, Bisebromoamide, Biselyngbyaside, Borophycin, Calothrixins A, B, Carmabin A, B, Caylobolide, Cocosamides B, Coibamide, C-phycocyanin, Cryptophycins, Curacin A, Hoiamide, Dragonamide C, D, Dolastatins, Diacylglycerols, Homodolastatin 16, Isomalyngamide, Kalkitoxin, Jamaicamides, Lagunamide, Largazole, Lyngbyabellin B, Majusculamide, Malevamide, Malyngamide 3, Obyanamide, Palauamide, Symplocamide A Symplostatin 3, Tasiamide, Tasipeptins, Tjipanazoles, Ulongapeptin, Veraguamides, Wewakpeptins	Bauerines A–C, Calcium spirulan, Cyanovirin, Scytovirin, Sulfoglycolipid, Sulfolipids	Calothrixins A,B, Carmabin A,B, Dragonamide A, B, Dragomabin, Dolastatins, Nostocarboline, Symplocamide A, Venturamide A, B

et al., 2017). The consumption of cyanobacterial diet increases the level of IgA in serum, and therefore, cyanobacterial diet can boost our immune system to fight against different allergens (Hayashi et al., 1998). Therefore, cyanobacterial consumption may help in reducing allergies, chronic inflammatory conditions, autoimmune diseases and diseases involving a suppressed immune system.

MASS CULTIVATION OF CYANOBACTERIA

Cyanobacterial biomass can complement agricultural crops for the production of food, feeds, fuels, and chemicals. However, production of biomass at large scale is required for the application of cyanobacteria in above mentioned purposes. Cyanobacterial cultivation does not compete for resources with agricultural crops, and moreover, they have better aerial productivity than plants (Dismukes et al., 2008; Cañedo and Lizárraga, 2016; Ooms et al., 2016). Genetic modification of cyanobacteria and their usefulness have been studied mainly in the laboratory; however, for commercial production, the process needs to be standardized and applied outdoors. The idea of high-rate (non-nutrient limited) large-scale (>50 L) cultivation of cyanobacteria and microalgae was proposed in early 1950s (Cook, 1951). The recent demand of cyanobacteria and other microalgae in bioenergy, food, and valuable chemicals production sector has necessitated their large-scale cultivation. However, economic sustainability is the most critical factor which determines the success of large scale biomass production and its downstream processing for the production of different commercial products (**Figure 2**). Light, pH, temperature, carbon dioxide, and nutrient supplements are the five critical abiotic parameters which determine the success of any growth system designed for autotrophic growth of photosynthetic organisms (Pulz, 2001; Flynn et al., 2010). However, tremendous expertise and resources are required to manage all these closely linked factors. Therefore, only few cyanobacteria and microalgae such as *Arthrospira*, *Chlorella, Haematococcus*, and *Dunaliella* have been cultivated on large scale as economically and commercially viable crops (Rosenberg et al., 2008).

Cyanobacterial cultivation requires a source of light, essential nutrients such as C, N, P, S, K, Fe, etc., and water. Commercial production of photosynthetic microorganisms can be achieved in different ways (**Figure 3**):

(1) Cultivation using sunlight in open systems
(2) Cultivation using sunlight in closed systems
(3) Cultivation using artificial light in closed systems

The above mentioned systems have both positives and negatives which are discussed in the following section, however, the preference of system depends on the value of the product and the extent of control over various parameters required for the production. Supplying light to culture constitutes a common limitation to all these systems; however, light limitation can be overcome by increasing the surface area of the system to maximize the light absorption.

Cultivation Using Sunlight in Open Systems

Several designs of sunlight dependent open cultivation systems have been proposed and constructed (Oswald, 1988; Chaumont, 1993; Pushparaj et al., 1997). Generally, the raceway or circular type shallow open ponds are used for mass cultivation of cyanobacteria and microalgae (Cañedo and Lizárraga, 2016). These systems are usually large raceways or open ponds where natural light is the source of energy (**Figure 3A**). The most advantageous aspect of this system is that the source of light, i.e., solar radiation is free of cost. However, several major disadvantages compensate this advantage and limit the overall biomass production. Contamination by algae, grazers and

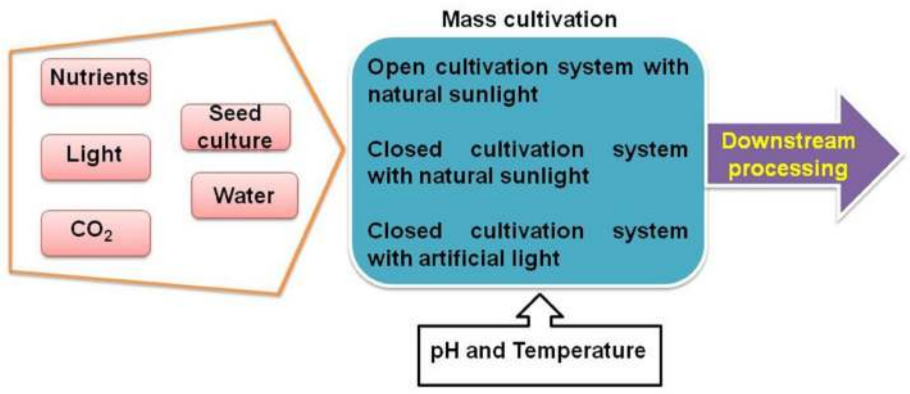

FIGURE 2 | Simplified outline for large-scale cultivation of microalgae. Photosynthetic microorganisms can be cultivated by providing nutrients, light, carbon dioxide, and water using different cultivation systems under controlled pH and temperature conditions. After mass cultivation, biomass is harvested for downstream processing.

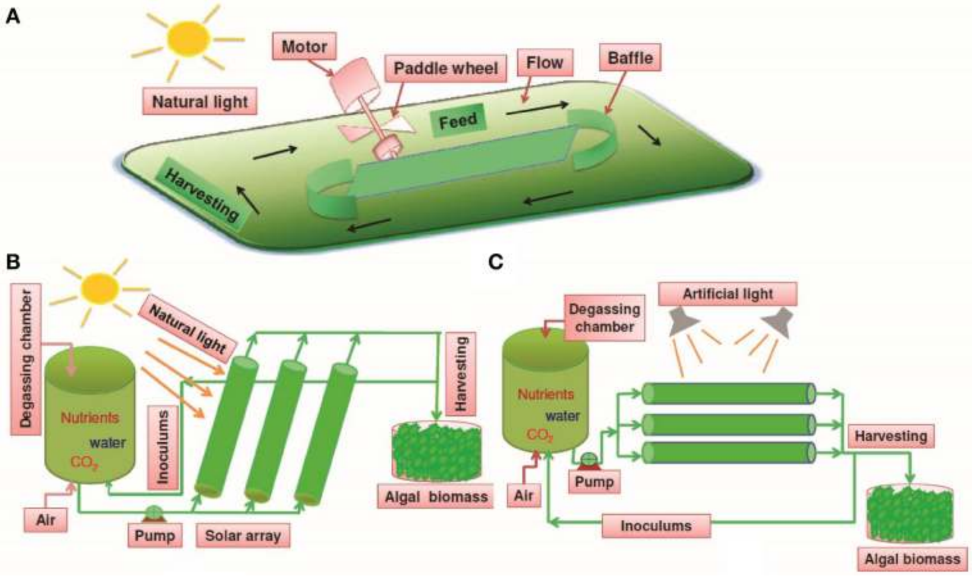

FIGURE 3 | Different cultivation systems for large-scale production of algal biomass. **(A)** Open raceway pond system using natural solar light as a source of energy; **(B)** Closed system using natural solar light as a source of energy; **(C)** Closed system using artificial light as a source of energy.

other microorganisms in open systems is unpreventable which compromise the net productivity. However, contamination problems could be avoided for organisms requiring unique growth conditions which generally prevent the growth of other organisms, however, this strategy limits the application of open systems for cultivation of only selected organisms (Costa et al., 2006; De Morais and Costa, 2007; Ugwu et al., 2008).

The outdoor open cultivation systems are also subject to diurnal fluctuation of different environmental conditions such as quality and quantity of light, temperature, evaporation, and rain, which significantly control the productivity and survival of the system. Apart from these limitations, open cultivation systems have been proven successful for the production of specific biomaterials producing tons of dried biomass (Lee, 1997). For example *Spirulina* has been extensively cultivated in Mexico, USA, China, and Thailand using open system due to its abovementioned unique growth requirement (Li and Qi, 1997; Vonshak, 1997).

Cultivation Using Sunlight in Closed System

Several cultivation systems have been designed which are closed and utilize solar radiation as a source of energy (Qiang and Richmond, 1994; Spektorova et al., 1997; Grima et al., 1999). In these systems, transparent material made up of plastic or glass is used for making vessels which are placed outdoors in the natural light for illumination (**Figure 3B**) (Khatoon and Pal, 2015). The cost of these systems is increased significantly by application of transparent materials but the closed system helps in preventing contamination of grazers and competitors. Such systems are designed in a manner which provides a higher surface to volume ratio, and therefore, cell densities obtained are often higher than in open systems (Carvalho et al., 2006).

Outdoor systems are subjected to aforementioned abiotic factors that may affect the reproducibility of their outcome. Additionally, the removal of photosynthetically produced oxygen and maintenance of optimum temperature are other factors which need to be critically observed in closed systems. These factors, if not maintained optimally, can cause a sudden crash of cultures. Techniques have been developed to maintain these parameters; however, the associated costs usually offset the cost advantage of using natural sunlight (Khatoon and Pal, 2015).

Cultivation Using Artificial Light in Closed System

Several designs have been developed for closed (indoor) cultivation of photosynthetic microorganisms which utilize artificial light as source of energy (Ratchford and Fallowfield, 1992; Wohlgeschaffen et al., 1992; Lee and Palsson, 1994). These designs/vessels are similar to conventional fermenters in principle and are referred to as photobioreactors; however, these photobioreactors are driven by light unlike the fermenters, which are driven by an organic carbon source (**Figure 3C**). These photobioreactors empower real-time control and optimization of culture parameters using software, and therefore, could be suitable for the cultivation of various organisms (Ratchford and Fallowfield, 1992).

The cost of photobioreactor-based biomass production increases significantly in comparison to outdoor systems due to utilization of plastic or glass material in making the vessel and power consumption. However, the cost can be offset by the production of high quality and quantity biomass using these systems. Photobioreactors serve as an important tool for the production of high-value products such as stable-isotope-labeled biochemicals (Apt and Behrens, 1999). These systems are also ideal for the cultivation of genetically modified organisms because their release in the environment from closed photobioreactors is limited but not guaranteed. Therefore, analysis of the associated risks of spreading of genetically modified organism into the surrounding is suggested before starting a large-scale production.

CONCLUSIONS AND FUTURE DIRECTIONS

Cyanobacterial farming can help in developing sustainable agricultural practice by the generation of biomass that can be used for the sustainable production of bioenergy, food supplements, nutraceuticals, biofertilizers, and feeds for aquaculture and poultry. In addition, cyanobacterial farming can significantly lower the atmospheric CO_2, and therefore, helps in controlling the problems associated with global climate change. The successful utilization of cyanobacterial species or other microalga for the development of sustainable agricultural practices requires their large scale cultivation. The raceway pond and photobioreactors systems have been devised for large scale biomass production, however, cyanobacterial farming using abovementioned systems requires very high amount of investment in the form of capital and operational costs. Therefore, third farming system, i.e., hybrid system, involving both raceway and photobioreactor system, are recommended which significantly reduce the capital and operational costs of farming (Bravo-Fritz et al., 2016). The cost associated with cyanobacterial/microalgal farming is still so high that any venture will have negative net profitability considering the current scenario of capital and operational costs required for the establishment of biorefinery (Bravo-Fritz et al., 2016). Therefore, the cost associated with farming needs to be significantly reduced for net profitability and success of any venture. The economic studies conducted so far have focused only on selected species, and therefore, further economic profitability modeling with a large number of new species is needed. The production cost of photobioreactors is an important area of concern, and attention is required to cut the price to reduce the cost of commodities production.

The reduction in production cost and positive net profitability can be also achieved by production of several commodities and complete utilization of biomass without producing any waste (Bravo-Fritz et al., 2016; Rajneesh et al., 2017). For example, protein extraction before the production of bioenergy has shown the positive net profitability of biorefinery (Bravo-Fritz et al., 2016). Therefore, different aforementioned sustainable services from cyanobacteria can be combined with each other to reduce the waste which could help in reaching a positive net profitability by producing several valuable commodities. The harvesting of organisms from a large volume of water is another challenge that cost enormously to and negatively affect the profitability. The biomass composition of an alga, i.e., percentage of proteins, lipids and carbohydrates, also affects the profitability of the bioenergy business, and therefore, farming of species with high lipid and low protein contents is recommended for the profitability of bioenergy industry (Bravo-Fritz et al., 2016). The requirement of water and nutrients are other major challenges for economic profitability of large scale cyanobacterial farming, however, bioremediation property of cyanobacteria can be exploited to lower the expenditure on water and nutrients. Cyanobacterial farming needs to be optimized using wastewater at small scale before going to large scale cultivation. Outdoor open cultivation of cyanobacteria is challenged by fluctuating environmental conditions and contamination, which collectively result in lower biomass production and pose a threat to economic viability. Abiotic stresses mainly light quality and quantity, temperature, pH, salinity, availability of nutrients, and CO_2, and biotic factors such as grazers and other biological contamination controls the biomass production. Therefore, cyanobacterial species need to be identified which can sustain fluctuating environmental conditions and can give consistent and economically viable amounts of biomass throughout the year for various applications. Efforts are also needed to improve the fitness of already known species under various environmental stresses which will enhance the biomass production and profitability of cyanobacterial farming.

AUTHOR CONTRIBUTIONS

JP: Conceptualized the review, did the literature survey, and wrote the paper; Rajneesh: Helped in collecting literature and making figures; PM: Helped in making figures; SS: Critically reviewed the manuscript and helped in writing paper; D-PH: Provided the valuable suggestions and edited the MS; RS: Gave the concept and thoroughly reviewed the MS.

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