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Review Article

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Cyanobacteria: an emerging source for antibacterial, antimycobacterial and antifungal properties

Abhishek Chauhan¹✉, Ritu Chauhan¹, Rupesh Kumar Basniwal² and Sachin C. Narwadiya³

¹Amity Institute of Environmental Toxicology, Safety and Management, Amity University, Sector-125, Noida, Uttar Pradesh, India

²Amity Institute for Advanced Research and Studies (M&D) Amity University, Sector-125, Noida, Uttar Pradesh, India

³Vigyan Prasar, Department of Science and Technology, Govt. of India, C-24, Qutub Institutional Area, New Delhi-110016
✉ akchauhan@amity.edu

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Abstract

Cyanobacteria are various group of gram-negative prokaryotes that originated before 3.5 billion years ago known as phototrophic blue green algae. This group is well known for their higher photosynthetic growth rate and capability to grow in adverse environmental conditions. Unique property of the algal group to grow in almost every environmental condition, makes them suitable candidate for the study of antimicrobial research. First time before 1500 BC, medicinal and nutritional properties have been investigated for *Nostoc* algal species to treat gout, fistula and cancer. In current scenario, less accessibility of life saving drugs, high cost of antibiotics and development of resistivity towards existing antibiotics, made it necessary to look forward for new research activities based on cyanobacteria and other plants for betterment of human society. The different extracts prepared from cultured cyanobacteria to isolate compounds are a common way to discover novel compounds. Most of the valuable cyanobacterial metabolites are concentrated in their biomass. For existence in nature, cyanobacteria secrete and contain various organic compounds. Compounds like proteins, fatty acids, vitamins, pigments, primary and secondary metabolites extracted from cyanobacteria are well known for different antimicrobial activities like antifungal, antiviral and antibacterial. Pharmaceutical companies have been shown commercial interest in this algal group due to presence of vast and diverse biological active compounds. In this review, we have shown panoramic view of cyanobacterial extracts and their commercial applications in different fields.

Keywords: Antibacterial, antimycobacterial and antifungal properties, cyanobacteria

Introduction

Cyanobacteria are the oxygenic, photosynthetic, gram-negative, oldest phototrophic organisms exhibited diverse biological activities. Approximately 2000 different strains of freshwater and marine cyanobacteria are found throughout world, which shows extraordinary ecological variety. Capability to grow in adverse condition and their autotrophic nature makes them eligible candidate to grow in low nutrient deficient lakes, ponds and oceans which pose serious threat for water and result into eutrophication (Chorus and Bartram, 1999; Duy et al., 2000). They are well known for different antimicrobial activity and being used for

production of various value-added products throughout the world. The first partly identified antimicrobial compound isolated from algae were obtained from unicellular green algae particularly, *Chlorella* which contained a substance termed as 'chlorellin' that exhibited inhibitory activity against Gram-positive and Gram-negative group of bacteria. In pharmaceutical companies especially in new drug discovery research division, last 40 years research is going on extraction of new compounds or drugs from cyanobacteria. Their development without supplement of organic substrate can be a practical advantage over the

Table 1: Antibacterial, antimycobacterial and antifungal properties of Cyanobacteria (from 1962 to 2019)

Cyanobacteria	Bacterial and Fungal species	References
<i>Lyngbya majuscula</i>	<i>Bacillus subtilis</i> , <i>Bacillus subtilis</i> , <i>Bacillus typhosus</i> , <i>Mycobacterium balnei</i> , <i>Mycobacterium phlei</i> , <i>Mycobacterium smegmatis</i> , <i>Sarcina lutea</i> , <i>Staphylococcus aureus</i> , <i>Candida albicans</i> , <i>Cryptococcus neoformans</i> , <i>Penicillium sp.</i>	Welch (1962); Gupta and Shrivastava (1965); Moikeha and Chu (1971)
<i>Oscillatoria princeps</i>	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Bacillus typhosus</i> , <i>E. coli</i>	Gupta and Srivastava, 1965
<i>Brachytrichia balani</i> , <i>Mastigocoleus testarum</i>	<i>Salmonella sp.</i> , <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Mycobacterium phlei</i> ,	Kobbia and Zaki, 1976
<i>Lyngbya majuscula</i>	<i>Mycobacterium smegmatis</i> , <i>Streptococcus pyogenes</i> , Compound identified: Malyngolide	Cardllina and Moore, 1979
<i>Oscillatoria sp.</i> 1459/8, <i>Oscillatoria redekei</i> , <i>Schizothrix sp.</i> 1470/2, <i>Synechococcus leopoliensis</i> , <i>Schizothrix sp.</i> 1470/2, <i>Synechococcus leopoliensis</i> , <i>Fischerella ambigua</i> , <i>Hapalosiphon hibernicus</i>	<i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Aspergillus oryzae</i> , <i>Candida albicans</i> , <i>Penicillium notatum</i> , <i>Saccharomyces cerevisiae</i> , <i>Trichophyton mentagrophytes</i> . Compound identified: Ambiguines	Cannell et al., 1988
<i>Nostoc muscorum</i>	<i>Staphylococcus aureus</i> , <i>Pseudomonas aeruginosa</i> , <i>Candida albicans</i> , <i>Cunninghamella blakesleeana</i> , <i>Rhizoctonia solani</i> , <i>Sclerotinia sclerotiorum</i>	De Cano et al. (1990), Bloor and England (1989)
<i>Scytonema sp.</i>	<i>S. cerevisiae</i> , <i>C. albicans</i> , <i>A. oryzae</i> , <i>P. notatum</i> , Compound identified: Tolytoxin and 6-Hydroxy-7-O-Mehtylescytophytine	Carmeli et al., 1990
<i>Tolythrix tjipanensis</i>	<i>Aspergillus oryzae</i> , <i>Candida albicans</i> , <i>Trichophyton mentagrophytes</i>	Bonjouklian et al., 1991
<i>Westiellopsis prolifica</i>	<i>C. albicans</i> , <i>A. oryzae</i> , <i>Saccharomyces cerevisiae</i> , <i>Trichophyton mentagrophytes</i> , <i>Penicillium notatum</i> Compound identified: Ambiguines	Smitka et al, 1992
<i>Fischerella ambigua 108a</i>	<i>Bacillus subtilis</i> , <i>Micrococcus luteus</i> , <i>Escherichia coli</i> . Compound identified: Ambigol A & B	Falch et al., 1993 & 1995
<i>Phormidium sp. HS-273</i>	<i>Staphylococcus aureus</i>	Ohta et al., 1993
<i>Phormidium sp.</i> , <i>Mastigocladus laminosus</i> , <i>Mastigocladus laminosus</i>	<i>Staphylococcus aureus</i> , <i>Bacillus cereus</i> , <i>B. coagulans</i> , <i>B. licheniformis</i> , <i>B. sphaericus</i> , <i>B. subtilis</i> , <i>Streptococcus faecalis</i> , <i>S. viridi</i> , <i>E. coli</i> , <i>Proteus vulgaris</i> , <i>P. morganii</i> , <i>Pseudomonas denitrificans</i> , <i>Candida albicans</i>	Fish and Codd, 1994
<i>Scytonema lyngbyoides</i> , <i>Anabaena planctonica 115b</i> , <i>Pseudoanabaena catenata U7</i> , <i>Nostoc sp. 51</i> , <i>Nostoc commune NC1</i> , <i>Oscillatoria rubescens R19</i>	<i>Bacillus subtilis</i> , <i>Micrococcus luteus</i> , <i>Escherichia coli</i> , <i>Penicillium oxalicum</i>	Falch et al., 1995

<i>Aphanizomenon flos-aquae</i> , <i>Anabaena lemmermannii</i> , <i>Microcystis aeruginosa</i>	<i>Bacillus subtilis</i> , <i>Bacillus cereus</i> , <i>Escherichia coli</i>	Stensvik et al., 1998
<i>Nostoc commune</i>	<i>Aspergillus candidus</i> Compound identified: Nostofungicide	Kajiyama et al., 1998
<i>Nostoc muscorum</i> 1453/12a	<i>Bacillus subtilis</i>	Cannell et al., 1988
<i>Tychonema bourrellyi</i>	<i>Bacillus subtilis</i> , <i>Bacillus cereus</i> , <i>Escherichia coli</i>	Stensvik et al., 1998
<i>Oscillatoria rubescens</i>	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Micrococcus flavus</i>	Kreitlow et al., 1999
<i>Nostoc commune</i> 259	<i>Staphylococcus epidermidis</i>	Jaki et al., 1999
<i>Limnothrix</i> sp.	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Micrococcus flavus</i> .	Kreitlow et al., 1999
<i>Fischerella ambigua</i> 108b	<i>Bacillus cereus</i> , <i>Staphylococcus epidermidis</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Micrococcus luteus</i> .	Jaki et al., 1999
<i>Anabaena</i> sp., <i>A. solitaria</i>	<i>Micrococcus flavus</i> and <i>Bacillus subtilis</i>	Kreitlow et al., 1999
<i>Lyngbya majuscula</i>	<i>Candida albicans</i> . Compound identified: Tanikolide	Singh et al., 1999
<i>Lyngbya majuscula</i>	<i>Candida albicans</i> compound identified: Tanikolide	Singh et al., 1999
<i>Langbya</i> sp. 91/50, <i>Langbya</i> sp. 163, <i>Langbya</i> sp. 164,	<i>Bacillus cereus</i> , <i>Escherichia coli</i> , <i>Staphylococcus epidermidis</i>	Jaki et al., 1999
<i>Limnothrix</i> sp.	<i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Micrococcus flavus</i> .	Kreitlow et al., 1999
<i>Langbya</i> sp. 91/50, <i>Langbya</i> sp. 163, <i>Langbya</i> sp. 164, <i>Nostoc commune</i> 122b, <i>Nostoc commune</i> 123b, <i>Nostoc commune</i> 124b, <i>Tolypothrix distorta</i> 153a, <i>Tolypothrix distorta</i> 96c, <i>Scytonema myochrous</i> 200b, <i>Symploca muscorum</i> 176, <i>Tolypothrix byssoidea</i> 195, <i>Phormidium</i> sp. 178, <i>Phormidium</i> sp. 211	<i>Bacillus cereus</i> , <i>Staphylococcus epidermidis</i> , <i>Candida albicans</i>	Jaki et al., 1999
<i>Anabaena variabilis</i> 1	<i>Bacillus subtilis</i> , <i>Chaetomium globosum</i> ,	Mundt et al., 2001; Kellam et al., 1988
<i>Gloeocapsa caldariorum</i> 127, <i>Calothrix gracilis</i> 96, <i>Limnothrix redekei</i> HUB 052, <i>Limnothrix redekei</i> HUB 052, <i>Nostoc species</i> 104, <i>Oscillatoria species</i> 234, <i>Pseudoanabaena catenata</i>	<i>Bacillus subtilis</i>	Mundt et al., 2001
<i>Tolypothrix byssoidea</i> (EAWAG195)	<i>Candida albicans</i> . Compound identified: Tolybyssidin A (1) Tolybyssidin B (2)	Jaki et al., 2001

<i>Fischerella ambigua</i>	<i>Staphylococcus epidermidis</i> , <i>Candida krusei</i> . Compound identified: Parsiguine	Ghasemi et al., 2004
<i>Spirulina platensis</i>	<i>B. subtilis</i> , <i>S. faecalis</i> , <i>S. aureus</i> , <i>E. aerogenes</i> , <i>S. epidermidis</i> , <i>E. cloacae</i> , <i>P. aeruginosa</i> , <i>E. coli</i> <i>S. typhimurium</i> , <i>P. vulgaris</i> , <i>C. albicans</i> Compound Identified: Heptadecane	Ozdemir et al. 2004
<i>Fischerella ambigua</i> FS2, <i>Fischerella ambigua</i> FS18, <i>Hapalosiphon aureus</i> FS3, <i>Hapalosiphon brasiliensis</i> FS6, <i>Hapalosiphon fontinalis</i> FS7, <i>Fischerella ambigua</i> FS2, <i>Hapalosiphon hibernicus</i> FS33, <i>Nostoc linckia</i> FS8, <i>Nostoc muscorum</i> FS13, <i>Nostoc punctiforme</i> FS5, <i>Stigonema ocellatum</i> FS23, FS 30 & FS 14	<i>Staphylococcus epidermidis</i> , <i>Escherichia coli</i> , <i>Bacillus subtilis</i> , <i>Candida kefyr</i> , <i>Candida kefyr</i> , <i>Salmonella typhi</i> , <i>Candida kefyr</i> , <i>Candida albicans</i> , <i>salmonella typhi</i>	Soltani et al., 2005
<i>Anabaena</i> sp., <i>Chroococcus</i> sp., <i>Oscillatoria</i> sp.	<i>Bacillus megaterium</i> , <i>Bacillus thuringiensis</i>	Katircioglu et al., 2006
<i>Fischerella</i> sp.	<i>E. aerogenes</i> <i>M. tuberculosis</i> , <i>S. typhi</i> , <i>S. aureus</i> , <i>P. aeruginosa</i> , <i>E. coli</i> . Compound identified: Hapalindole	Asthana et al., 2006
<i>Spirulina platensis</i>	<i>E. coli</i> , <i>S. aureus</i> , <i>P. aeruginosa</i> , <i>S. typhi</i> and <i>K. pneumonia</i>	Kaushik and Chauhan, 2008
<i>Nostoc commune</i>	<i>B. subtilis</i> , <i>B. cereus</i> , <i>B. pumilus</i> , <i>E. coli</i> , <i>S. aureus</i> , <i>P. aeruginosa</i> , <i>S. typhi</i> and <i>K. pneumonia</i>	Chauhan et al., 2008
<i>Lyngbya majuscula</i>	<i>S. epidermidis</i> , <i>B. subtilis</i> , <i>B. cereus</i> , <i>S. faecalis</i> , <i>E. coli</i> , <i>C. albicans</i>	Kaushik et al., 2009
<i>Anabaena variabilis</i>	<i>S. aureus</i> , <i>E. coli</i> , <i>P. aeruginosa</i> , <i>S. typhi</i> and <i>K. pneumonia</i>	Kaushik et al., 2009
<i>Phormidium</i> sp.	<i>B. cereus</i> , <i>B. subtilis</i> , <i>S. epidermidis</i> , <i>S. faecalis</i> , <i>E. coli</i> , <i>C. albicans</i>	Garima et al., 2013
<i>Tolypothrix tenuis</i> , <i>Anabaena variabilis</i> and <i>Cylindrospermum</i> sp	<i>Bacillus subtilis</i> , <i>Pseudomonas aeruginosa</i>	Malathi, et al., 2014
<i>Lyngbya</i> sp.	<i>Escherichia coli</i> and <i>Pseudomonas aeruginosa</i> ,	Sundaramanickam et al., 2015
<i>Microcystis aeruginosa</i>	<i>A. parasiticus</i> , <i>A. flavus</i> , <i>A. westerdijikia</i> , <i>A. ochraceus</i> ITAL 14, <i>A. carbonarius</i> ITAL 204, <i>A. steynii</i> IBT LKN 23096, <i>Penicillium verrucosum</i> BFE 500, <i>Fusarium verticillioides</i> ITEM 10027, <i>F. proliferatum</i> MPVP 328.	Marrez et al., 2016
<i>Synechococcus</i> spp. PCC7942	<i>S. aureus</i> (NCIM 2099), <i>Pseudomonas aeruginosa</i> (NCIM 5029), <i>Klebsiella pneumonia</i> (NCIM 2957), <i>Enterobacter aerogenes</i> (NCIM 5139) and <i>Escherichia coli</i> (NCIM 2065)	Fatima et al., 2017
<i>Oscillatoria</i> sp.	<i>S. aureus</i> (MRSA) ATCC 25923 Gram-positive Methicillin-resistant, <i>B. anthracis</i> and <i>P. aeruginosa</i>	Wijsekara et al., 2017

	(ATCC 25853) <i>E. coli</i> and <i>S. typhi</i> (ATCC 25922 and <i>C. tropicalis</i>)	
<i>Nostoc linckia</i>	<i>Pseudomonas aeruginosa</i> <i>Bacillus subtilis</i> , and <i>Staphylococcus aureus</i> susp. <i>aureus</i> , and two tested fungal strains <i>Aspergillus niger</i> and <i>Candida albicans</i>	Vanlalveni et al., 2018
<i>Anabaena circinalis</i> , <i>Nostoc entophyllum</i>	<i>Staphylococcus aureus</i> ATCC 25923, <i>E. coli</i> O 157:H7, <i>L. monocytogenes</i> , <i>Bacillus subtilis</i> ATCC 6633, <i>Pseudomonas aeruginosa</i> ATCC 27853, <i>Salmonella typhimurium</i> CCM 5445	Yücer et al., 2018
35 cyanobacterial extracts	<i>Bacillus subtilis</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus sanguinis</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> , <i>Candida friedricki</i> , <i>Fusarium oxysporum</i> , <i>Aspergillus fumigatus</i> , <i>Monographella cucumerina</i> , <i>Alternaria alternata</i>	Saurav et al., 2019

microorganisms. The benefit of microbes, which can be cultured, such as cyanobacteria, is that a sustainable amount of anticipated bioactive compounds can be attained, which is not always possible for a product derived from a microbe other than cyanobacteria. Blue Green algae promise greater opportunities with all relatively inexpensive and easier approaches against some expensive and technically complex methods presently in use for new drug discovery.

Antimicrobial potential of cyanobacteria

Culturable microorganisms for screening of novel pharmaceuticals are of paramount importance. Historically, actinomycetes have been the most prolific producers of metabolites with significant antimicrobial activities. According to Bradner, actinomycetes are most closely examined group of organisms and presently known for production of more than 95% antimicrobial compounds in primary screening (Bradner, 1980). They can be cultured in the laboratory with relative ease to provide a consistent source of biologically active secondary metabolites (Patterson et al., 1993). Screening of cyanobacteria for antimicrobial compounds with pharmaceutical value received more attention. The molecules isolated from several cyanobacteria have broad spectrum of potential including fungicides and algicides toxins, antibiotics (Browitzka, 1995) (Table 1). Random screening of cyanobacteria will continue play an important role in the drug discovery process for unforeseeable future.

Cyanobacteria as a source of antifungal compounds

Flavanoid type compounds, Fischerellin A, Phytoalexin, Tolytoxin, Laxaphycins, Ambiguines, Calophycin, Sctophytin and Laxaphycins have been isolated from *Oscillatoria*, *Scytonema pseudohofmanii*, and *Anabaena laxa* and from other cyanobacterial species also which supposed to have anticandidal and antibacterial activity (Frankmolle et al., 1992). (Table 1)

Cyanobacteria as a source of antibacterial compounds



Fig.1. Inhibition zone showed by different extracts of Cyanobacteria against *Staphylococcus aureus*

Kaushik and Chauhan (2008) have been reported the antibacterial activity of several species of cyanobacteria such as *Anabaena*, *Lyngbya*, *Calothrix*, *Spirulina*, *Nostoc*, *Hapalosiphone*, *Phormidium* and *Oscillatoria* etc. against both Gram-positive (*S. aureus*, *B. subtilis*, *B. cereus* etc.) as well as Gram-negative bacteria (*E. coli*, *P. aeruginosa*, *S. typhi* etc.). These organisms can be genetically modified by using different biotechnological techniques to produce biological active compounds like Bacteriocin, Ambigol A, Parsiguine, Hapalindole, Hormothamnin A etc. Garima et al. (2013) have evaluated *Phormidium* for its significant antibacterial and anticandidal activity. Various species of *Anabaena* were evaluated for their antimicrobial activity and for active extracts which further screened for presence of chemical constituents through HPTLC and UV-HPLC techniques (Kaushik et al., 2009a; Chauhan et al., 2010). They have been also examined *Nostoc commune* and *Lyngbya majuscula* for potent antimicrobial activity against clinically significant microorganisms and further analyzed

their methanolic extract through UV-HPLC and HPTLC analysis. (Table 1)

Cyanobacteria as a source of antimycobacterial compounds

This has been reported by Rao et al. in 2007 for different spp. of cyanobacteria viz. *Hapalosiphon* sp., *Anabaena* sp., *Lyngbya* sp., *Westiellopsis prolifica*, *Spirulina* sp., *Anabaena variabilis*, *Anabaena cylindrica*, *Oscillatoria* sp. and *Scytonema* sp. against various species of Mycobacteria (*Mycobacterium tuberculosis* ATCC 27294, *M. tuberculosis* MDR, *M. avium*, *M. intracellulare* and *M. aurum*). (Table 1)

Conclusion and future prospects

Cyanobacteria produce plenty potential antimicrobial agents which are useful for human as well as for animals' welfare. Worldwide attention is drawn towards micro-algae for their possible use in several therapeutic and other products. Keeping in view the applied applications, it has been concluded that now this area is exploring rapidly. The major challenge in front of the current world is to fight effectively against the new emerging diseases especially multiple drug resistant microbial infections and to discover new compounds for the welfare of mankind and society. Now mostly antibiotics are becoming useless due to development of multiple drug resistivities in pathogens. This is an alarming situation for human species. To overcome from this situation, continuous research in basic as well as applied filed necessary for discovery of new active drug compounds from cyanobacteria.

Conflict of Interest

Authors hereby declare no conflict of interest.

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