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Review Article

LYNGBYA SP.: A SUITABLE CYANOBACTERIUM FOR HARVESTING ANTIMICROBIAL COMPOUNDS

MAHEEP KUMAR

Department of Botany, Guru Ghasidas Vishwavidyalaya, Koni, Bilaspur- 495009, India. Email: maheep.bot@gmail.com

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ABSTRACT

Lyngbya spp. is one of the most efficient groups of secondary metabolite producers and is very important from pharmaceutical point of view. Among its various species, *majuscula* is the major producers of commercially important biomolecules. Several species have been isolated and screened from the marine in the past decades. Although the chance of isolating a novel *Lyngbya* strain from a marine habitat, which would produce new biologically active metabolites, has increased, but rediscovery has also important aspect. The most relevant reason for discovering novel secondary metabolites is to circumvent the problem of resistant pathogens, which are no longer susceptible to the currently used drugs. Existence of *Lyngbya* has been reported in the hitherto untapped brackish ecosystem. Marine *Lyngbya* are efficient producers of new secondary metabolites that show a range of biological activities including antibacterial, antifungal, anticancer, insecticidal and enzyme inhibitor. Bioactive compounds from marine *Lyngbya* possess distinct chemical structures that may form the basis for synthesis of new drugs that could be used to combat resistant pathogens.

Keywords: *Lyngbya* · Bioactive compounds. Antibacterial. Antifungal. Secondary metabolites.

INTRODUCTION

Microbial natural products are an important source of both existing and new drugs. Among the producers of commercially important metabolites, cyanobacteria have proven to be a prolific source with a surprisingly small group of taxa accounting for the vast majority of compounds discovered till date [1-3]. Cyanobacteria produce a large number of compounds with varying bioactivities. A number of cyanobacteria and very few other microalgae, have been screened for antiviral activity so far, but the limited results available are promising [4]. Among these, *Lyngbya* spp. are the most economically and biotechnologically priceless prokaryotes. Representative species of *Lybngbya* include *L. aestuarii*, *L. bouillonii*, *L. confervoides*, *L. hieronymusii*, *L. kuetzingii*, *L. polychroa*, *L. semiplena*, *L. hieronymusii*, *L. hieronymusii* and several others, *L. majuscula* species has proved to be most potent. Although other species of *Lyngbya* may have potency but they are even untapped. The immense diversity of this habitat along with its underexploitation is the fundamental reason for attracting researchers towards it for discovering novel metabolite producers. *Lyngbya* spp. have also been isolated from terrestrial as well as brackish water bodies [5]. *Lyngbya* spp. as usual form bloom in marine habitat and produce noxious environment [6]. It has been found to contain a variety of chemicals that exerts a range of biological effects, including skin, eye and respiratory irritation. The toxins lyngbyatoxin A and debromoaplysiatoxins appear to give the most widely witnessed biological effects in relation to humans, and experiments involving these two toxins show the formation of acute dermal lesions. Studies into the epidemiology of the dermatitic, respiratory and eye effects of the toxins of this organism are reviewed and show that *Lyngbya* induced dermatitis has occurred in a number of locations [7]. Secondary metabolites produced by *Lyngbya* possess a wide range of biological activities [8]. The genus *Lyngbya* alone produces a large number (>100) of bioactive molecules [9-15]. It has an enormous biosynthetic potential that remains unchallenged without a potential competitor among other microbial groups. A large number of *Lyngbya* spp. have been isolated and screened from marine in the past several decades [16]. An important reason for discovering novel secondary metabolites is to circumvent the problem of resistant pathogens, which are no longer susceptible to the currently used drugs [17]. Secondary metabolites from marine *Lyngbya* strain may form the basis for the synthesis of novel therapeutic drugs, which may be efficient to combat a range of resistant microbes [18]. Many *Lyngbya* species isolates from oceans contain non-ribosomal polyketide synthetase (NRPS) and polyketide synthetase (PKS) pathways, the hallmarks of secondary metabolite production[19-21].

Antibacterial compounds

The filamentous Cyanobacterial genus *Lyngbya* is being found to be a rich source of toxic and otherwise bioactive metabolites. Only bioassay of active fraction were done to prove that it has some antimicrobial activity Many of the compounds isolated from marine cyanobacteria have been shown to have specific targets in higher eukaryotic organisms (e.g., tubulin, actin) and have minimal or no antibacterial activity. Many novel structures have been elucidated as a result of systematic screenings for anticancer, antibacterial, antifungal, and protease inhibitory effects [22, 23]. Few are as follows. Four novel cyclic undecapeptides, lyngbyazothrins A, B, C , and D , were isolated from the cultured *Lyngbya* sp. The mixture of lyngbyazothrins A and B shows only low antimicrobial activity against *Micrococcus flavus*, whereas the mixture of lyngbyazothrins C and D was active against *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Serratia marcescens* [24]. Malyngolide is natural δ-lactones obtained from different strains of the marine cyanobacterium *Lyngbya* and characterized by a hydroxymethyl group and a long aliphatic chain attached to the δ-position of a six-membered lactone ring. Malyngolide was isolated from *L. majuscula* collected in Hawaii [25]. Malyngolide displayed antibacterial activity against *Mycobacterium smegmatis* and *Streptococcus pyogenes*. Pahayokolide A showed specific inhibition of the two representatives of Gram-positive *Bacillus* sp. [26].

Antifungal compounds

Methanol extracts obtained by mechanical agitation of solvent with lyophilized coral sand sediment and *L. confervoides* filaments showed significant in vitro antifungal activity against *Candida albicans*. It was Lobocyclamides A-C which exhibited modest antifungal activity [27]. Lyngbyabellin B was isolated from a marine cyanobacterium, *L. majuscula*,. This new cyclic depsipeptide displayed potent toxicity toward brine shrimp and the fungus *Candida albicans* [28].

Other valuable compounds

Cytotoxic/Anticancer

A new stereoisomer of malyngamide C, 8-*epi*-malyngamide C, and the known compound lyngbic acid [(4*E*,7*S*)-7-methoxytetradec-4-

enoic acid] were isolated from a sample of *L. majuscula*. Lyngbic acid and malyngamide C were found cytotoxic against HT29 colon cancer and to inhibit bacterial quorum sensing [29]. Apratoxin A, a potent cytotoxin with a novel skeleton, has been isolated from the marine cyanobacterium *L. majuscula*. Apratoxin A has cytotoxicity against human tumor cell lines [30]. Cancer cell toxicity-guided fractionation of extracts of the marine cyanobacteria *L. majuscula* and *L. sordida* led to the isolation of apratoxin D [31]. Marine cyanobacterium *L. bouillonii* produces apratoxin E, a new peptide-polyketide hybrid of the apratoxin class of cytotoxins[30]. A new 36-membered macrolactone, (25*S*,27*S*,29*S*,33*S*)-caylobolide A, was isolated from *L. majuscula*. Caylobolide A exhibited in vitro cytotoxicity against human colon tumor cells [32]. Marine cyanobacterium *L. bouillonii* afforded three hitherto undescribed analogues of the glycosidic macrolide lyngbyaloside, namely, 2-*epi*-lyngbyaloside and the regioisomeric 18*E*- and 18*Z* lyngbyalosides C . Concurrently we discovered two new analogues of the cytoskeletal actin-disrupting lyngbyabellins, 27-deoxylyngbyabellin A and lyngbyabellin J , a novel macrolide of the laingolide family, laingolide B, and a linear modified peptide, lyngbyapeptin D, along with known lyngbyabellins A and B, lyngbyapeptin A, and lyngbyaloside. The structures contains either brominated or chlorinated consistent with halogenation being a hallmark of many marine natural products. All extracts derived from these *L. bouillonii* collections were highly cytotoxic due to the presence of apratoxin A or apratoxin C [33]. In continuing investigations of this organism for minor metabolites of related structure, we have isolated and characterized two new natural products, curacins B and C**.** Both of these are toxic to brine shrimp, demonstrate strong cytotoxicity against murine L-1210 leukemia and human CA46 Burkitt lymphoma cell lines [34].Two new linear lipopeptides, 1 and 2, and a known compound, curacin D, have been isolated from a marine cyanobacterium, brown *L. polychroa*. The new compounds were assigned the trivial names dragonamide C and dragonamide D, as their peptide moiety is related to previously reported dragonamides A and B [36]. Bioassay-guided fractionation of the organic extract of a Curaqao collection of *L. majuscula* led to the isolation of a new lipid, curacin A, with exceptional brine shrimp toxic and antiproliferative activities [37]. A lipophilic extract of an eastern Caribbean collection of *L. majuscula* yielded two new halogenated fatty acid amides, grenadamides B and C, and two new depsipeptides, itralamides A and B, along with the known compounds hectochlorin and deacetylhectochlorin. The recently reported depsipeptide carriebowmide was also present in the extract and isolated as its sulfone artifact, grenadamides B and **C** displayed marginal activity against the beet armyworm (*Spodoptera exigua*), rest others were assessed for general cell toxicity in human embryonic kidney (HEK293) cells, only itralamide B displayed significant cytotoxicity[36]. Investigation of the marine cyanobacterium *L. majuscula* has led to the isolation of a cyclodepsipeptide, hantupeptin A. Hantupeptin A showed cytotoxicity to MOLT-4 leukemia cells and MCF-7 breast cancer cells [39]. Hantupeptins B and C were isolated, along with the previously reported hantupeptin A, from the marine cyanobacterium, *L. majuscula*. Hantupeptins B and C showed moderate in vitro cytotoxicity when tested against MOLT-4 (leukemic) and MCF-7 (breast cancer) cell lines [40]. An organic extract of the cyanobacterium *L. majuscula*, led to the isolation of the known cyclic depsipeptide antanapeptin A. a new bioactive cyclic depsipeptide, homodolastatin 16. Homodolastatin 16, a higher homologue of the potential anticancer agent dolastatin 16, exhibited moderate activity against oesophageal and cervical cancer cell lines [41]. Lyngbyabellin A, a significantly cytotoxic compound with unusual structural features, was isolated from a Guamanian strain of the marine cyanobacterium *L. majuscula*. This novel peptolide is structurally related to dolabellin. Lyngbyabellin A was found to be a potent disrupter of the cellular microfilament network [42]. Kalkipyrone, a novel R-methoxy-*â*,*â*¢-dimethyl-*ç*-pyrone possessing an alkyl side chain, was isolated from an assemblage of the marine cyanobacteria *L. majuscula* and *Tolypothrix* Kalkipyrone, a novel R-methoxy-*â*,*â*¢-dimethyl-*ç*-pyrone possessing an alkyl side chain, was isolated from an assemblage of the marine cyanobacteria *L. majuscula* and *Tolypothrix sp.* Kalkipyrone is toxic to brine shrimp and gold fish and is structurally related to the actinopyrones that were previously isolated from *Streptomyces* spp. Kalkipyrone is toxic to brine shrimp and gold fish and is structurally related to the actinopyrones that were previously isolated from *Streptomyces* spp[43].

Lagunamides A and B are new cyclic depsipeptides isolated from the marine cyanobacterium *L. majuscula*. Lagunamides A and B displayed significant antimalarial properties, against *Plasmodium falciparum*. Lagunamides A and B also possessed potent cytotoxic activity against P388 murine leukemia cell lines, respectively [44].

A new cyclic depsipeptide Lyngbyabellin B was also isolated from *L. majuscula* which show toxicity against brine shrimp and fungus *Candida albicans* [45]. This cyanobacterium also produce series of Lynbyabellin E-I, analogues of Lyngbyabellin B which has same toxicity activity towards human lung tunor and neurobalstoma cell line [46]. *L. majuscula* also produces Lyngbyastatin 1, a new cytotoxic analogue of dolastatins 12 and 11. These compounds proved toxic with only marginal or no antitumor activity when tested against colon adenocarcinoma or mammary adenocarcinoma [47]. There are lot of cytotoxic compounds isolated from *L. majuscula,* Lyngbyastatin and norlyngbyastatin,are new cytotoxic analogues of dolastatin G and nordolastatin G, respectively[48]. Another but least cytotoxic compound Malyngamide, cocosamide A and B were isolated from lipophilic extract of *L. majuscula*. These compound show weak cytotoxicity against MCF 7 breast cancer and HT-29 colon cancer cells [49]. There are other compound which show resemblance with malyngamide, malyngamide C, 8-O-acetyl-8-epi-malyngamide C and 8-epi-malyngamide C. these Compounds show moderate cytotoxicity to NCI-H460 human lung tumor and neuro-2a cancer cell lines [50].

CONCLUSION

Thus there are various species of *Lyngbya* found in various environment. Specially the marine strains of *Lyngbya* are more potent to produce multiple of structurally diverse compound/ secondary metabolites which act as diverse. This cyanobacterium not only produce bioactive antibacterial, antifungal but also a good source of anticancerous compounds.

As with the discovery of novel antimicrobial drugs from microorganism, the resistant against this also originated and not the situation become more difficult, those resistant microbes become multidrug resistant. In such situation screening of antimicrobial compounds from the cyanobacteria is become necessary. We have seen that various metabolites isolated from that single genus *Lyngbya* which are very effective. This give the information and excitation to search for novel drugs from that microorganism of similar to that microorganism.

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