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### **Antibacterial Compounds from Non-Heterocystous Cyanobacteria: A Review**

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#### **ABSTRACT**

Heterocystous cyanobacterial genera *Nostoc*, *Fischerella*, and *Tolypothrix* were extensively explored for antibacterial compounds. Aromatic compounds (Ambigol, 2,4-dichlorobenzoic acid), Alkaloids (Ambiguine, Ambiguine isonitrile, Ambiguine kisonitrile, Ambiguine mesonitrile, Fischambiguine, Eucapsitrione, Fischerindole, Hapalindole, Tjipanazole) and Lipopeptide (Fischerellin), Cyclophane, Diterpenoid, Cyclicdepsipeptide, Linear peptide, extracellular pigments, Polyketide, Cyclic hexapeptides, Phenol, Indane, Terpenoids, Cyclic peptides, Porphinoid, Indolophenanthridine, Cyclic depsipeptides, Macrolide, Lipopeptide, Terterpene and Indole alkaloid are antibacterial compounds isolated from heterocystous cyanobacteria. Only a few genera have been searched for antibacterial compounds. Heterocystous cyanobacteria have rich diversity, and most genera and species have not been explored for antibacterial compounds. Hence, heterocystous cyanobacteria have great potential for drug discovery.

**KEYWORDS:** Cyanobacteria, Non-heterocystous, *Lyngbya*

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## INTRODUCTION

Cyanobacteria are Gram-negative, photo synthetic prokaryote. They are also known as Blue-green algae. Cyanobacteria possess properties of both prokaryote as well as eukaryote. Cyanobacteria are classified following both i.e. botanical classification system<sup>1,2</sup> and the bacteriological classification system<sup>3</sup>. Botanical classification system of cyanobacteria is based on morphological characters. All the cyanobacteria possessing specialized cells i.e., Heterocyst (Site of nitrogen fixation) are called heterocystous cyanobacteria and are clustered in two orders i.e, Nostocales and Stigonematales of Phylum Cyanophyta<sup>1</sup>. *Nostoc*, *Anabaena*, *Richelia*, *Anabaenopsis*, *Cylindrospermum*, *Aphanizomenon*, *Wollea*, *Raphidiopsis*, *Pseudanabaena*, *Homothamnion*, *Nodularia*, *Aulosira*, *Plectonema*, *Scytonema*, *Pseudoscytonema*, *Hydrocoryne*, *Scytonematopsis*, *Petalonema*, *Camptylonemopsis*, *Tolypothrix*, *Microchaete*, *Fortiea*, *Calothrix*, *Dichothrix*, *Rivularia*, *Gloeotrichia*, *Leptochaete*, *Homoeothrix*, *Stauronema*, *Mastigocoleus*, *Nostochopsis*, *Mastigocladopsis*, *Brachytrichia*, *Mastigocladus*, *Iyengariella*, *Camptylonema*, *Fischerella*, *Stigonema*, *Fischerellopsis*, *Westiella*, *Hapalosiphon* and *Westiellopsis*<sup>1</sup> are heterocystous genera. They are widely distributed from aquatic, terrestrial environment, Polar Regions to hot springs. Besides the important role in agricultural fields, cyanobacteria are of great economic importance. They produce vitamin, photosynthetic pigments, polysaccharides, sugars pharmaceutically important molecules, and other biologically active compounds. Secondary metabolites are low molecular weight organic molecules that have diverse biological activities. They are not required for normal growth and development of organisms but facilitate the survival of the organism. Antibacterial, antifungal, anticancerous, immunosuppressants, herbicidal and cholesterol-lowering properties of secondary metabolites are well established. Chemical nature of important secondary metabolites are polyketides, alkaloids, terpenoids, shikimate derived molecules and aminoglycosides. A number of cyanobacterial strains produce intracellular and extracellular metabolites with diverse biological activities including antibacterial and antifungal<sup>4,5</sup>. Cyanobacteria are the rich source of secondary metabolite with various antimicrobial activities. A large number of cyanobacteria from different habitats have shown antibacterial activity against a wide range of human pathogenic bacteria. This review article deals with the current status of the antibacterial potential of heterocystous cyanobacteria and prospects. The emergence of antibiotic-resistant bacteria is a serious problem for the whole world. Twenty-three thousand people of US died in 2013 due to infection of antibiotic resistance bacteria (CDC report 2013). Hence there is an urgent need for the discovery of new antibacterial compounds. Cyanobacteria are the rich source of secondary metabolites

and have great potential for drug discovery<sup>6,7</sup>. A score of researchers has reported a diverse group of antibacterial compounds which are listed in

## ANTIBACTERIAL COMPOUNDS FROM NON-HETEROCYSTOUS CYANOBACTERIA:

Cyanobacteria are a rich source of antibacterial compounds, but most of them have been isolated from heterocystous cyanobacteria. An updated list of antibacterial compounds isolated from Non-heterocystous cyanobacteria is presented in Table-1.

**Table-1 List of antibacterial compounds isolated from Non-heterocystous cyanobacteria**

S.N.	Name of active compounds	Cyanobacteria/ Activity	References
1	Abietane (Diterpenoid), C <sub>20</sub> H <sub>36</sub>	<i>Microcoleus lacustris</i> / Antibacterial	<sup>4</sup> Thajuddin & Subramanian, 2005
2	Brunsvicamides A (Cyclic peptide) C <sub>45</sub> H <sub>64</sub> N <sub>8</sub> O <sub>8</sub> Brunsvicamides B (Cyclic peptide), C <sub>46</sub> H <sub>66</sub> N <sub>8</sub> O <sub>8</sub> Brunsvicamides C (Cyclic peptide), C <sub>45</sub> H <sub>64</sub> N <sub>8</sub> O <sub>10</sub>	<i>Tychonema sp.</i> / Antimycobacterial	<sup>5</sup> Muller et al., 2006
3	Coriolic acid (Fatty acid) C <sub>18</sub> H <sub>32</sub> O <sub>3</sub> & α-dimorphecolic acid (Fatty acid) C <sub>18</sub> H <sub>32</sub> O <sub>3</sub>	<i>Oscillatoria redekei</i> / Antibacterial	<sup>6</sup> Mundit et al., 2003
4	Crossbyanol A (Polyphenyl ether ) C <sub>30</sub> H <sub>15</sub> Br <sub>7</sub> O <sub>6</sub> , Crossbyanol B (Polyphenyl ether) C <sub>30</sub> H <sub>15</sub> Br <sub>7</sub> O <sub>12</sub> S <sub>2</sub> , Crossbyanol C (Polyphenyl ether ) C <sub>30</sub> H <sub>15</sub> Br <sub>7</sub> O <sub>9</sub> S, Crossbyanol D ( Polyphenyl ether ) C <sub>30</sub> H <sub>15</sub> Br <sub>7</sub> O <sub>9</sub> S	<i>Leptolyngbya crosbyana</i> / Antibacterial	<sup>7</sup> Choi et al., 2010
5	Diterpenoid and majusculoic acid	<i>Microcystisaeruginosa</i> / Antibacterial	<sup>8</sup> Kumar et al., 2014
6	Kawaguchipectin A (Cyclic undecapeptide) C <sub>68</sub> H <sub>92</sub> N <sub>16</sub> O <sub>18</sub> , Kawaguchipectin B (Cyclic undecapeptide), C <sub>58</sub> H <sub>76</sub> N <sub>16</sub> O <sub>18</sub>	<i>Microcystisaeruginosa</i> / Antibacterial	<sup>9</sup> Ishida et al., 1997.
7	Lyngbyazothrin A (Cyclic undecapeptide) C <sub>62</sub> H <sub>96</sub> N <sub>12</sub> O <sub>19</sub> , Lyngbyazothrin B (Cyclic undecapeptide) C <sub>61</sub> H <sub>94</sub> N <sub>12</sub> O <sub>18</sub> , Lyngbyazothrin C (Cyclic undecapeptide) C <sub>74</sub> H <sub>109</sub> N <sub>13</sub> O <sub>21</sub> , Lyngbyazothrin D (Cyclic undecapeptide) C <sub>73</sub> H <sub>107</sub> N <sub>13</sub> O <sub>20</sub>	<i>Lyngbya sp.</i> / Antibacterial	<sup>10</sup> Zainuddin et al., 2009
8	Malyngolide (Polyketide hybrid), C <sub>16</sub> H <sub>30</sub> O <sub>3</sub>	<i>Lyngbya majuscula</i> / Antifungal & Antibacterial	<sup>11</sup> Bruja et al., 2001
9	Malyngamides, amides of the fatty acid (&)-7(S)-methoxytetradec-4(E)-enoate,	<i>Lyngbya majuscula</i> / Antibacterial	<sup>12</sup> Gerwick et al., 1987
10	20-nor-3a-acetoxy-12-hydroxy-abieta-5,7,9,11,13 - pentaene (Terpenoid), Norbietaene (Diterpenoid), C <sub>19</sub> H <sub>34</sub>	<i>Microcoleus lacustris</i> / Antibacterial	<sup>13</sup> Pérez-Gutiérrez et al., 2008
11	Pahayokolide A (Cyclic peptide) C <sub>72</sub> H <sub>105</sub> N <sub>13</sub> O <sub>20</sub>	<i>Lyngbyasp.</i> / Antibacterial	<sup>14</sup> Berry et al., 2004.
12	Pahayokolide B (Cyclic peptide)	<i>Lyngbyasp.</i> / Antibacterial	<sup>15</sup> Luesch et al., 2001

	C <sub>63</sub> H <sub>90</sub> N <sub>12</sub> O <sub>18</sub>	Antibacterial	
13	Pitipeptolide A (Cyclic depsipeptide) C <sub>44</sub> H <sub>65</sub> N <sub>5</sub> O <sub>9</sub> , Pitipeptolides B (Cyclicdepsipeptide) C <sub>44</sub> H <sub>67</sub> N <sub>5</sub> O <sub>9</sub>	<i>Lyngbyamajuscula</i> / Antimycobacterial	<sup>15</sup> Luesch et al., 2001
	Pitipeptolides C (Cyclicdepsipeptide) C <sub>44</sub> H <sub>69</sub> N <sub>5</sub> O <sub>9</sub> , Pitipeptolides D (Cyclic depsipeptide), C <sub>43</sub> H <sub>63</sub> N <sub>5</sub> O <sub>9</sub> , Pitipeptolides E (Cyclic depsipeptide) C <sub>43</sub> H <sub>63</sub> N <sub>5</sub> O <sub>9</sub> , Pitipeptolides F (Cyclic depsipeptide) C <sub>43</sub> H <sub>63</sub> N <sub>5</sub> O <sub>9</sub>		
14	Schizotrin A (Lipoptide)	<i>Schizothrix</i> sp/ Antibacterial &Antifungal	<sup>16</sup> Pergament et al., 1994

## DISCUSSION:

Cyanobacteria are a well-known source of biologically active metabolites. A number of antibacterial compounds have been isolated and characterized from cyanobacteria. Only eight non-heterocystous cyanobacterial genera, i.e., *Microcoleus*, *Microcystis*, *Tychonema*, *Oscillatoria*, *Leptolyngbya*, *Microcystis*, *Lyngbya*, and *Schizothrix* were explored for antibacterial compounds (Tab.1). Diterpenoids (Abietane), Cyclic peptide (Brunsvicamides A, Brunsvicamides B, Brunsvicamides C), Fatty acid (Coriolic acid and  $\alpha$ -dimorphelic acid), Polyphenyl ether (Crossbyanol A, Crossbyanol B, Crossbyanol C, Crossbyanol D), Cyclic undecapeptide (Kawaguchipectin A and Kawaguchipectin B, Lyngbyazothrin A, Lyngbyazothrin B, Lyngbyazothrin C, Lyngbyazothrin D), Polyketide hybrid (Malyngolide), Diterpenoid (Norbieta-5,7,9,11,13-pentaene) are diverse group of antibacterial compounds isolated and characterized from non-heterocystous cyanobacteria (Tab.1). Genus *Lyngbya* is extensively explored among non-heterocystous cyanobacteria (Tab.1). Most of non-heterocystous genera i.e. *Synechocystis*, *Gloeocapsa*, *Chroococcus*, *Gloeotheca*, *Dactylococcopsis*, *Synechococcus*, *Rhabdoderma*, *Aphanocapsa*, *Aphanothece*, *Chroococcus*, *Merismopedia*, *Eucapsis*, *Coelosphaerium*, *Gomphosphaeria*, *Johannesbaptistia*, *Chlorogloea*, *Entophysalis*, *Placoma*, *Chroococcidiopsis*, *Chamaesiphon*, *Dermocarpa*, *Stichosiphon*, *Myxosarcina*, *Hyella*, *Scopulonema*, *Hydrococcus*, *Xenococcus*, *Crinalium*, *Sirocoleus*, *Polychlamydom*, *Dasygloea*, *Hydrocoleum*, *Porphyrosiphon*, *Lyngbya*, *Symploca*, *Trichodesmium*, *Spirulina*, *Arthrospira*, *Katagnymene* and *Phormidium* are not explored for antibacterial compounds (Tab.1). Each

cyanobacterial genera have a score of species and strains with worldwide distribution. Hence, there is a wide scope for mining of antibacterial compounds from Non-heterocystous cyanobacteria.

## CONCLUSION:

Diterpenoids (Abietane), Cyclic peptide (Brunsvicamides A, Brunsvicamides B, Brunsvicamides C), Fatty acid (Coriolic acid and  $\alpha$ -dimorphecolic acid), Polyphenyl ether (Crossbyanol A, Crossbyanol B, Crossbyanol C, Crossbyanol D), Cyclic undecapeptide (Kawaguchipectin A and Kawaguchipectin B, Lyngbyazothrin A, Lyngbyazothrin B, Lyngbyazothrin C, Lyngbyazothrin D), Polyketide hybrid (Malyngolide), Diterpenoid (Norbietaene), Cyclic peptide (Pahayokolide A and Pahayokolide B), Cyclic depsipeptide (Pitipeptolide A, Pitipeptolide B), Lipopeptide (Schizotrin A) and Terpenoid (20-nor-3 $\alpha$ -acetoxy-12-hydroxy-abieta-5,7,9,11,13-pentaene) are diverse group of antibacterial compounds isolated and characterized from non-heterocystous cyanobacteria (Tab.1). Genus *Lyngbya* is extensively explored among non-heterocystous cyanobacteria (Tab.1). Most of the non-heterocystous genera are not investigated for antibacterial compounds.

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