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## Bioactive Compounds from Nostoc Species

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### ABSTRACT

Recently microalgae have become commercially important because of novel compounds of potential medicinal value. *Nostoc* species are producers of structurally and functionally diverse natural biological activities such as antibacterial, antiviral, anticancer, antitumor, algicide, antifungal, enzyme inhibiting, immunostimulant, antiplatelet aggregation, cytotoxic and antiplasmodium activities. Most of the isolated substances from the alga belong to groups of hydrocarbons such as phytane; lipids such as sterol, esters, waxes and free sterols; fatty acids such as dioic acids; derivatives of amino acids such as indole-3-acetic acid and anatoxin A; terpenoids and aromatic compounds such as diterpenoid and anthraquinone; boron-containing macrocycles such as borophycin; arsenolipids such as dimethylarsenic acid; mycosporine-like amino acids such as shinorine and scytonemin; lipopeptides such as cryptophycin-1 and polyketides and several carotenoids; amides, alkaloids, peptides, monosaccharides and polysaccharides. Some extracellular metabolites secreted by cyanobacteria function as toxins or allelochemicals. Apart from these cytotoxic metabolites (e.g. nostocyclophanes, borophycin, elastase inhibitors, antitumor, antifungal agent, antiviral indolocarbazoles) they produce antimetabolic compounds. This article provides an overview of bioactive compounds produced by *Nostoc* species.

**Keywords:** Cyanobacteria, *Nostoc*, Bioactive Compounds, Biological activities, Allelochemicals.

### 1. INTRODUCTION

Chemoheterotrophic microorganisms *viz.* bacteria and fungi are the traditional sources of antibiotics and bioactive compounds. The bioactive compounds isolated from microalgae are chemically polyketides, amides, alkaloids and peptides<sup>1</sup>. The family *Nostocaceae* (order *Nostocales*) consists of nitrogen-fixing cyanobacteria, which were characterized as eubacteria that grow as autotrophs with CO<sub>2</sub> as the carbon source, utilizing an oxygen-producing photosynthetic mechanism for the generation of ATP and reductants<sup>2</sup>. *Nostoc* species are producers of structurally and functionally diverse natural biological activities such as antibacterial<sup>3, 4</sup>, antifungal<sup>5, 6</sup>, antiviral<sup>7</sup>, anticancer<sup>8, 9</sup>, antitumor, antimetabolic, algicide<sup>10</sup>, enzyme inhibiting, immunostimulant, antiplatelet aggregation<sup>11</sup> and immunosuppressive<sup>12</sup> activities, cytotoxic and antiplasmodium activities<sup>13</sup>. The secondary metabolites produced by *Nostoc* are rich sources of novel bioactive compounds applicable to the production of medicines and agriculturally important chemicals. Some of the extracellular metabolites secreted by cyanobacteria are function as toxins or allelochemicals<sup>14</sup>. Many species of cyanobacteria are known to produce intracellular and extracellular metabolites. These metabolites are known to show diverse biological activities and inhibit microbial growth<sup>15</sup>. The very high incidence of novel, biologically active compounds isolated from *Nostocaceae* indicates that cyanobacteria are a rich source of potentially useful natural products<sup>16, 17</sup>.

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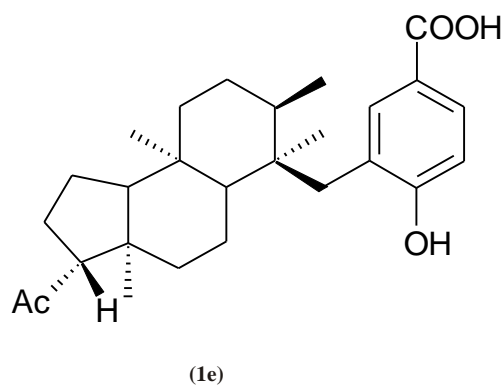
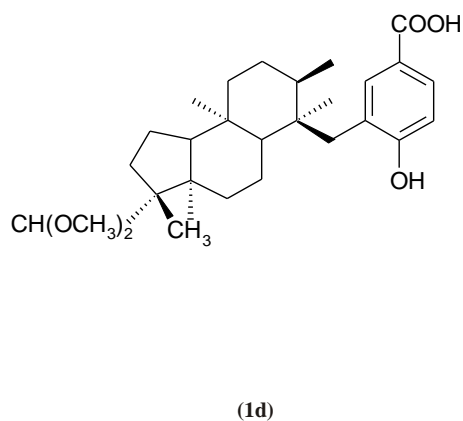
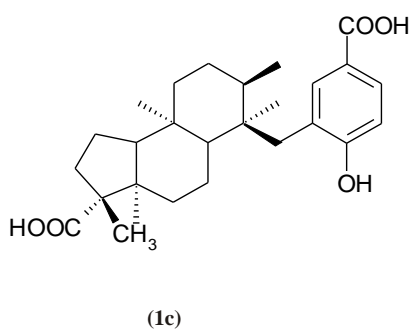
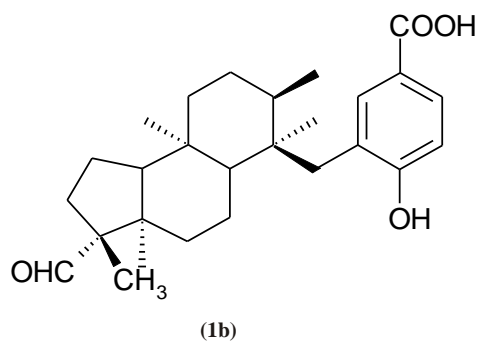
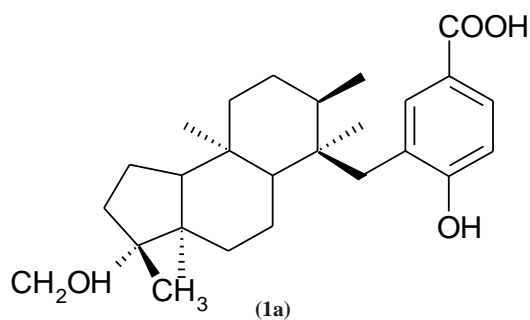
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## 2. TERPENOIDS AND AROMATIC COMPOUNDS

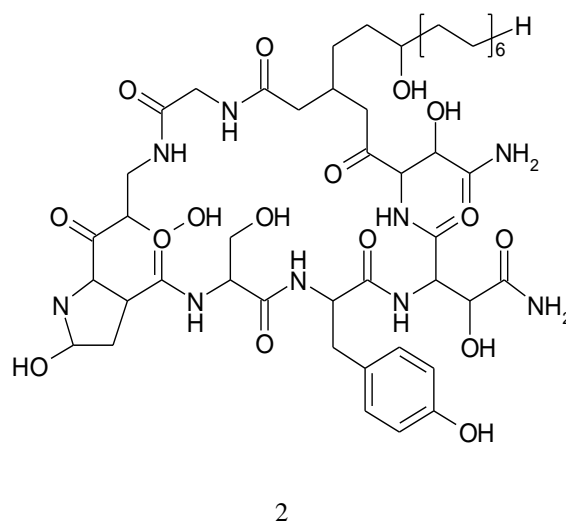
Five novel extracellular metabolites with an unprecedented diterpenoid skeleton, named as comnostin A (1a), B (1b), C (1c), D (1d), and E (1e) have been isolated from *N. commune* 18 showed antibacterial activity.



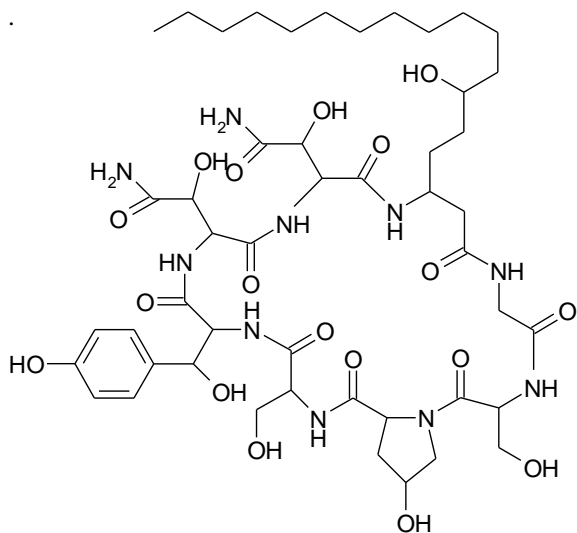
## 3. PEPTIDES AND LIPOPEPTIDES

A novel lipopeptide, nostofungicide (2), was isolated from the methanolic extract of a field-grown terrestrial *N. commune* <sup>5</sup>, showed potent antifungal activity against *Aspergillus candidus*.

A novel antifungal lipopeptide (3), 3-amino-6-hydroxy stearic acid containing cyclic peptide was isolated from a terrestrial blue-green alga *Nostoc commune*.



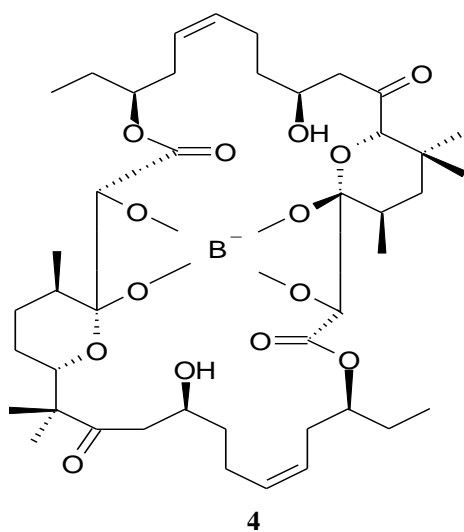
Some species of *N. flagelliforme* has been used as a food source <sup>19</sup>, as medicine to treat cancer and gout, as antimicrobial compounds <sup>20, 21</sup> and antitumor activity <sup>22, 23</sup>, but no characterization has been done.



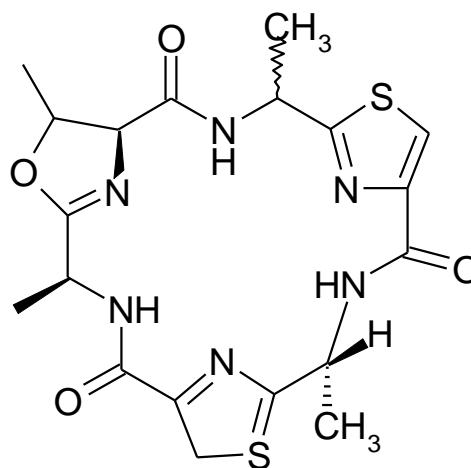
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#### 4. BORON-CONTAINING MACROCYCLES

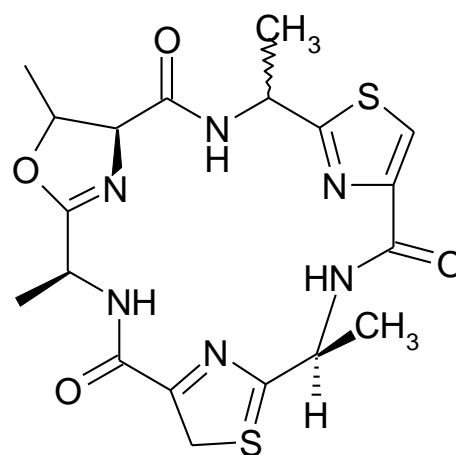
Borophycin (**4**, as sodium salt) is the potent cytotoxin in the lipophilic extract of a marine strain of the cyanobacterium *N. linckia*<sup>24, 25, 26</sup>, and from *Nostoc spongiaeforme* var. Tenue. Four new cyclic hexapeptides containing no boron, tenuecyclamides (**5**) A–D, were also isolated from the methanol extract of *Nostoc spongiaeforme* var. Tenue<sup>27</sup>.



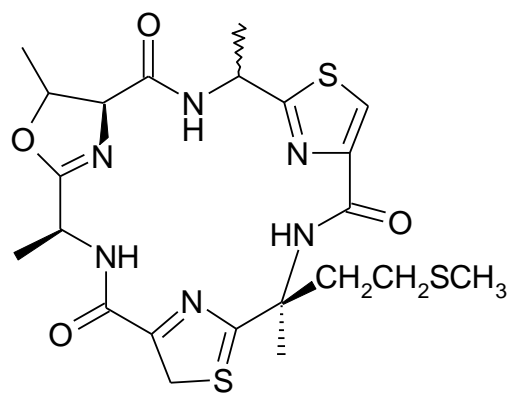
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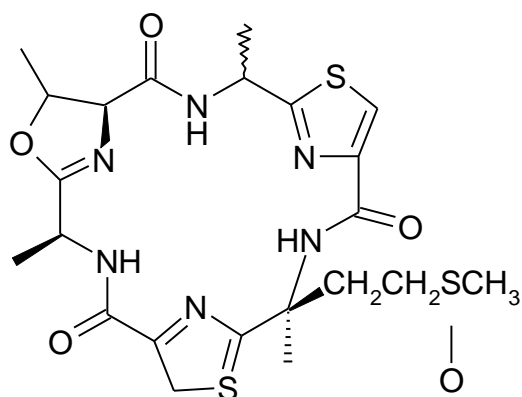
5A



5B



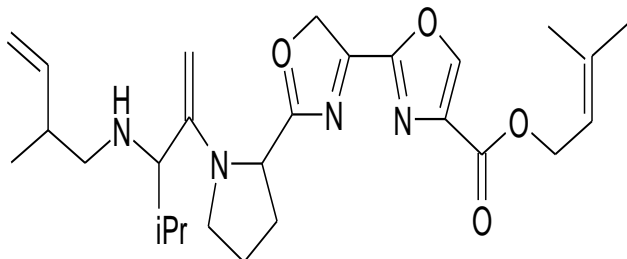
5C



5D

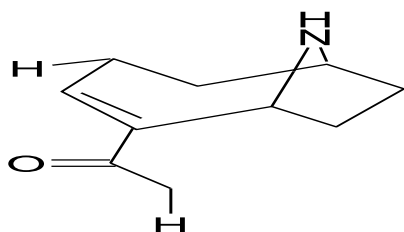
### 5. DERIVATIVES OF AMINO ACIDS

A novel oligopeptide alkaloid, muscoride A (**6**), was isolated from terrestrial freshwater *N. muscorum*<sup>28</sup>. Muscoride A showed weak antibacterial activity against *Bacillus subtilis* and *Escherichia coli*<sup>29</sup>.



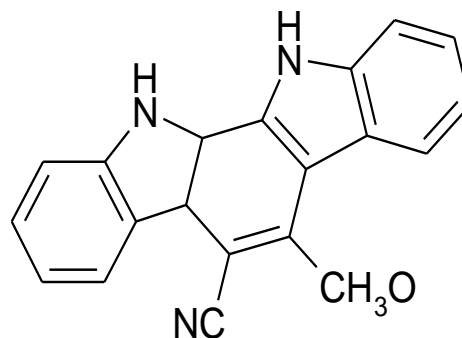
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Anatoxin A (**7**), the neuromuscular blocking agent was first isolated from the freshwater cyanobacterium *Anabaena flos-aquae*<sup>30</sup>; later it has been isolated from other cyanobacterial species including *N. muscorum*<sup>31</sup>.

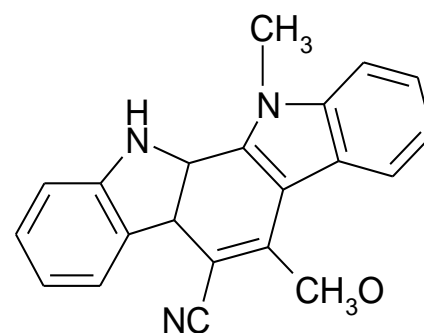


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Indolo [2,3-*a*]-3-methoxy-4-cyanocarbazole (**8a**) and *N*-methylindolo [2,3-*a*]-3-methoxy-4-cyanocarbazole (**8b**) are responsible for most of the cytotoxicity and antiviral activity associated with the blue green alga *N. sphaericum*<sup>32</sup>.

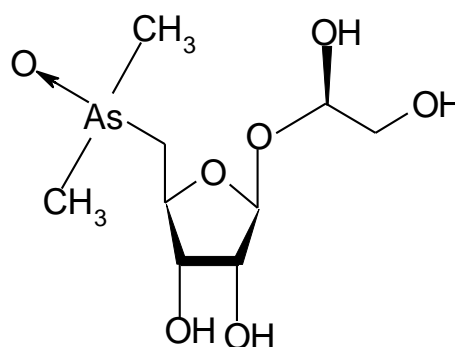


8a



8b

Recently, a freshwater *Nostoc* sp. was found to contain a 3 ppm concentration of arsenic and only 1/3 was extractable. The extract representing 1 ppm of arsenic contained one arsenosugar (**9**), the rest being dimethylarsenic acid<sup>33</sup>.

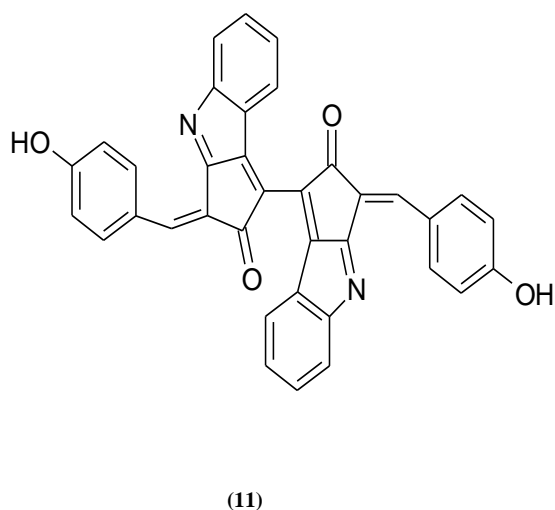
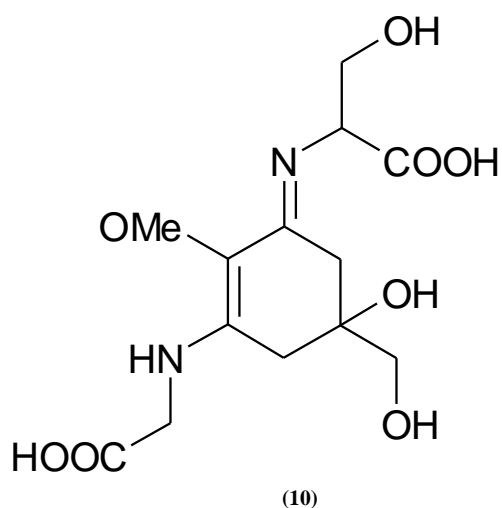


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Řezanka *et al.*<sup>34</sup> has found some dioic acid in *N. Linkia*. Aliphatic dicarboxylic acids surprisingly afforded potent cytotoxicity and antineoplastic activity<sup>35</sup>, and could serve as

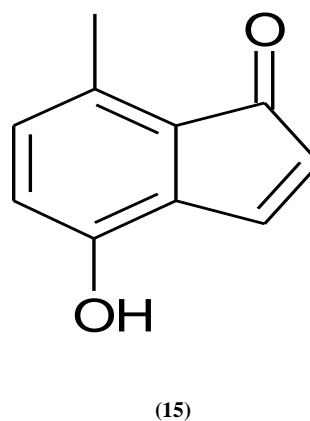
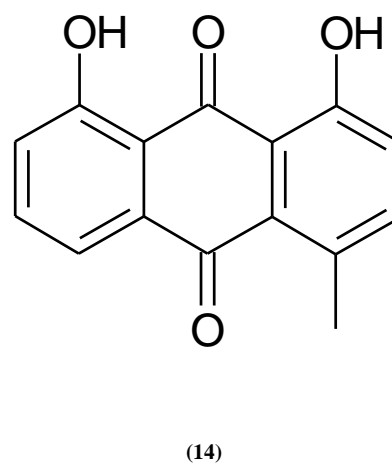
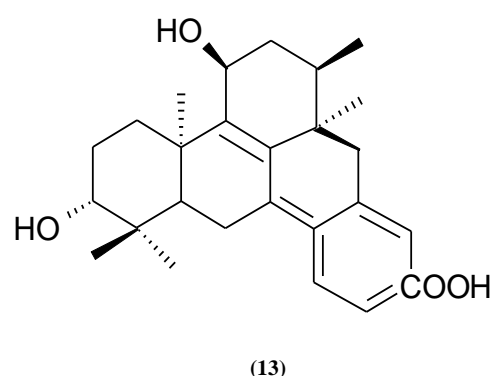
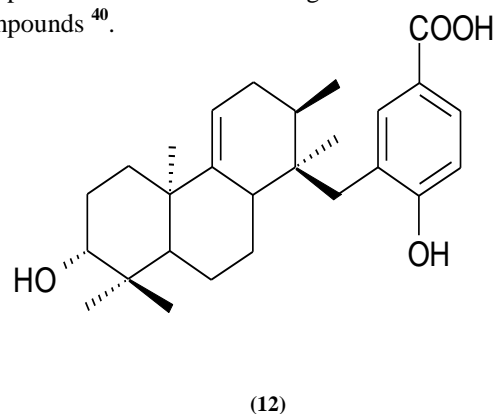
lipidic markers for identification of some human and animal diseases<sup>36, 37</sup>. These acids are of major interest for medical specialists and biochemists.

Two mycosporine like amino acids such as shinorine (10) and scytonemin (11) have been isolated from some *Nostoc* species<sup>38</sup>.



Two new compounds, diterpenoid compound, noscomin (12)<sup>39</sup> and an anthraquinone, as well as an indane derivative, which was reported as a natural product for the first time, have been isolated from *N. commune*<sup>18</sup>. Noscomin showed antibacterial activity against *Bacillus cereus*, *Staphylococcus epidermidis*, and *Escherichia coli*. In a continuation of this investigation the isolation, structure elucidation, and biological activity of further three compounds, i.e. a derivative of dodecahydrophenanthrene (13), 4-methylchryszazin (14), and 4-hydroxy-7-methylindan-1-one (15), from the cells were reported. Compound 13 displays a selective potent antibacterial activity against *Staphylococcus epidermidis* equal to chloramphenicol. Moderate antibacterial activity against *S. epidermidis* could be also detected for

compounds 14 and 15 are against *Bacillus cereus* for all 3 compounds<sup>40</sup>.



## 6. CONCLUSION

This paper provides a comprehensive overview of metabolites produced by cyanobacteria of the genus *Nostoc*. The article provides us an overview of different elements and acids containing compounds such as Borophycin contain Boron and noscomin contain diterpenoid compounds which was reported as natural product and showed antibacterial activity against *Bacillus cereus*, *Staphylococcus epidermidis* and *Escherichia coli*. All these compounds are used for the treatment of various human and animal disorders.

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