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Cyanobacteria: Extreme Environments and Toxic Metabolites

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Abstract: Cyanobacteria, also known as blue-green algae, are photosynthetic bacteria that can colonize different habitats, including extreme ones. They are of great interest to the scientific community, especially because of their ability to produce cyanotoxins: toxic secondary metabolites potentially harmful to organisms especially when released to surface waters.

Keywords: Bioaccumulation · Cyanobacteria · Cyanotoxins · Lichen · Water quality

Cyanobacteria belong to a photosynthetic Gram-negative bacterial phylum and are divided into two main groups: filamentous and unicellular (Fig. 1a,b).[1] They are pioneer microorganisms, and they are poikilo-tolerant: they can survive even when environmental conditions are drastically versatile. Examples include that cyanobacteria can withstand low temperatures thanks to extra-cellular polymeric substance (EPS) production; desiccation thanks to anhydrobiosis (Greek for 'life without water') by including shrinking and production of sugar metabolites; and high UV radiation thanks to their 'sunscreen' metabolites, *i.e.* pigments. Therefore, they can also colonize most parts of the world including extreme environments (*e.g.* glaciers, deserts, rock surfaces), Fig. 1c,d.[1–3]

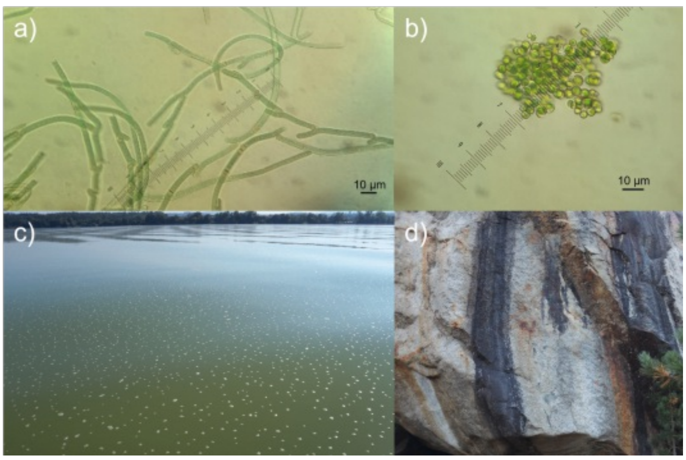

Fig. 1. a) Filamentous cyanobacteria, b) unicellular cyanobacteria, c) cyanobacterial bloom (photo credit to Francesco Pomati), d) cyanobacteria colonizing rock surface (also known as *Tintenstrich*).

Being omnipresent, cyanobacteria play a key role in many ecosystems: some of them can fix nitrogen and are predominantly responsible for nitrogen supply in both marine and terrestrial environments.[4,5] Nitrogen fixation can occur because of the enzyme nitrogenase which is inhibited by oxygen; therefore, it is generally located in the heterocysts (cells unique to cyanobacteria with a thick envelope limiting oxygen entry,[1] Fig. 2).

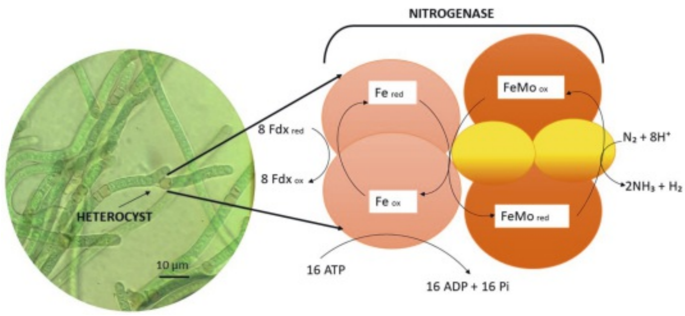

Fig. 2. Microscope image of a heterocyst-forming cyanobacterium, and a schematic illustration of the structure of nitrogenase enzyme. Subunits with Fe represent the iron-containing protein known as dinitrogenreductase; FeMo is the molybdenum–iron containing protein known as dinitrogenase; and Fdx is ferredoxin, which is the electron-donor protein of the process.

Some cyanobacteria also produce cyanotoxins: secondary metabolites that are classified according to their toxicological effects as hepatotoxins, neurotoxins, dermatotoxins, and cytotoxins according to their toxic effect.[6] Due to the toxicity of those compounds and their presence in aquatic environments, the World Health Organization (WHO) developed guideline values in drinking water for the most common cyanotoxins found worldwide. Cyanotoxins that are included in the Water Quality Guidelines of the WHO are: microcystins (MCs), nodularins (NOD), saxitoxins (STXs), anatoxins (ANTX), cylindrospermopsins (CYN) (Fig. 3).[7] While some toxicological functions are recognised, the biological functions of cyanotoxins, *i.e.* why cyanobacteria produce these complex molecules in the first place, are still not fully understood.[8] Different hypotheses of their function include defence against grazers, allelopathy, competitive advantage or cellular physiology benefits (*e.g.* retention of nutrients, attractant/repellent for heterotrophs).[9] The mechanism of toxicity of MCs, for example, involves the high affinity of these toxins for the proteins PP1 and PP2a (phospho-protein phosphatase), which are involved in various cellular processes (*e.g.* DNA damage response, glucose metabolism, transcription, cytoskeleton organization, cell cycle and meiosis); binding these proteins MCs inhibit their function.[10,11] Consequently, MCs can cause different adverse effects, for example, exposure of zebrafish embryos to MCs caused not only death but also delayed hatching, malformations, and caused lesions of the liver.[12]

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The LD_{50} of cyanotoxins (lethal dose for 50% of the test population) can vary from 8 to 2100 µg/kg in mice according to the type of cyanotoxin and to the type of exposure (acute or chronic).[13] Before it was apparent that cyanobacteria produce potent toxins, several dialysis patients died from liver failure when water contaminated with cyanobacteria was used for their treatment.[14,15] Despite decades of research and evidence regarding the occurrence and toxicity of cyanobacteria in surface waters, we still encounter frequent reports about the death of animals, particularly dogs, that were exposed to contaminated water. Therefore, it is important to better understand where toxic cyanobacteria occur, which toxins they produce and which factors promote these processes in the environment.[8]

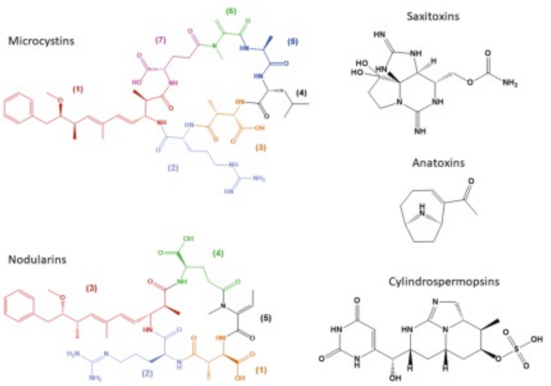

Fig. 3. Examples of compounds of the cyanotoxin classes of microcystins, nodularins, saxitoxins, anatoxins and cylindrospermopsins. The building blocks in microcystin (1–7) and nodularins (1–5) can vary, which explains the high number of different variants in these compound classes.

To evaluate the risk posed by cyanotoxins, one needs to understand not only the production from cyanobacteria but also the stability of these compounds in the environment. Studies report that microcystins can persist in surface water for several days to weeks.[16] The biodegradation of these cyclic peptides requires specific enzymes, so-called microcystinases that can cause ring cleavage resulting in less toxic linear peptides.[17] Sunlight-driven transformation can be another central fate process of organic compounds in surface waters. Although most microcystins do not absorb light in the solar spectrum, they can be transformed by other reactive species produced in sunlight, a process termed indirect photochemistry. Organic matter in surface water can act as a photosensitizer when it absorbs sunlight and forms an excited state molecule that subsequently produces other reactive species such as singlet oxygen and hydroxyl radicals.[18] Depending on the light conditions and organic matter present, the reported photochemical half-lives of microcystins range from days to months.[19] Overall, many cyanotoxins are not readily degraded in the environment. Persistent toxins are of higher concern because they can accumulate in the environment and be transported with the water.

As the multitude of studies thus far focused on aquatic environments, a critical knowledge gap for the potential risk of cyanotoxins release in terrestrial environments exists. Cyanobacteria occur just as frequently in terrestrial environments, and, despite their toxicity, they can also occur in symbiosis with other life forms including lichens[20] and plants roots.[12] An example are endolithic cyanobacteria and cyano-lichens that form so-called *Tintenstrich* ('ink stripe') communities, which mainly develop on rock surfaces in presence of variably frequent water run-off and are visible as large dark stripes (Fig. 1d). These *Tintenstrich* structures are ubiquitous, for example in the Swiss Alpine region and so far, have been largely overlooked.[3]

Alexander von Humboldt was the first to realize in 1849 that these *Tintenstrich* structures are of biological origin,[21] and almost 100 years later the Swiss biologist Otto Jaag first described and studied their cyanobacterial components.[22] Thanks to this pioneering work, these communities were further studied to identify the diversity of cyanobacteria in *Tintenstrich* and their interaction with other organisms.[3,21,23] The most abundant orders of free-living unicellular cyanobacteria widely described in these environments include: Chroococcales, Synechococcales, Chroococcidiopsidales, Pleurocapsales and Gloeobacterales; while the most abundant filamentous ones are Oscillatoriales and Nostocales.[3] *Tintenstrich* can also consist of the so-called cyano-lichens which are a symbiotic lifeform. In general, lichen interaction is an obligate and mutualistic symbiosis between at least one photobiont (cyanobacteria or algae) and a mycobiont (typically ascomycetes, less frequently basidiomycetes).[3] The main role of the photobiont is to perform photosynthesis and fix CO_2, providing organic carbon to the mycobiont while the mycobiont (*i.e.* fungus) provides a protected environment to the photobiont. When the photosynthetic component is a cyanobacterium that can fix N_2, the mycobiont can take advantage of this capability as an alternative nitrogen supply.[24] On rocks, it is possible to observe both saxicolous lichens (living on the rock surface) and endolithic ones (living inside rocks or pores). Cyano-lichen are pioneer colonizers and the most common cyanobiont is the genus Chroococcidiopsis, a non-filamentous cyanobacterium, which can produce scytonemin and mycosporine-glycine, which are UV-absorbing substances that allow the cyanobacterium to withstand high irradiation conditions on rock surfaces.[3,25]

In summary, this column has provided an insight into the occurrence and transformation of toxins from cyanobacteria, underlining especially the scarce knowledge we have so far about their occurrence in the terrestrial environment. We showcased the example of *Tintenstrich* communities of cyano-lichens on rocks in Alpine regions. *Tintenstrich* are also known to play an important role in trophic interactions, as water flowing across them collects and transports nutrients and biological material from the rock substrate to downstream water catchments. So far, we lack studies on the diversity of cyanobacteria and production of toxins from *Tintenstrich* communities and their mobility with surface water.[3] The consistent development of cyanobacteria in such environments emphasizes the need to investigate the potential release of these bacteria and their toxins.

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