Toxic cyanobacteria and antibiotics in the environment: a complex relationship

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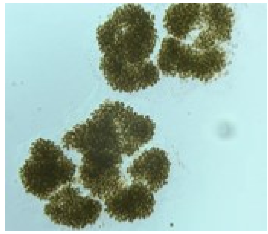
Cyanobacteria and human health

1. Cyanobacteria are important primary producers in almost every habitat, especially freshwater. Increasing blooms due to eutrophication and climate change

2. Produce an incredible array of bioactive peptides, some very well known for their toxicity, others are beginning to raise a concern

3. Being prokaryotes, they could play a role in dissemination/emergence of antibiotic resistance (AR) in the environment

Toxic cyanobacteria: major player in aquatic environment

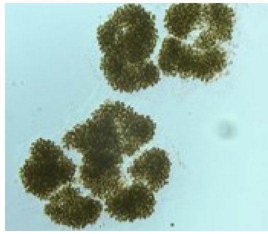


Microcystis aeruginosa in Florida, USA

Microcystis, *Anabaena*, *Aphanizomenon* in Southern Sweden

Cylindrospermopsis raciborskii, Brasilia, Brazil

Toxic cyanobacteria: major player in aquatic environment



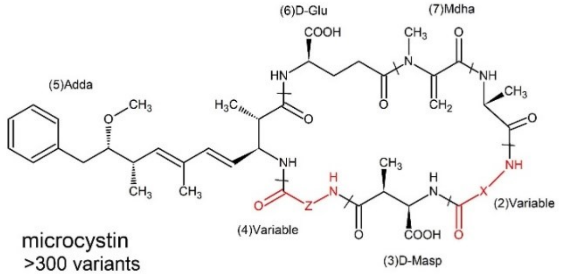
Microcystis aeruginosa in Florida, USA

Microcystis, *Anabaena*, *Aphanizomenon* in Southern Sweden

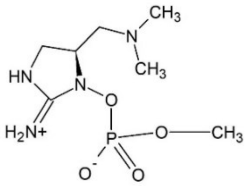
- Cyanotoxins are among the most toxic naturally occurring compounds
- Cyanotoxins occur worldwide in many lakes, reservoirs and rivers used as sources of drinking-water or for recreational activity
- Cyanotoxins are produced naturally within surface waters and are not directly introduced by human activity

(Chorus and Welker, 2021. Toxic cyanobacteria II ed. WHO)

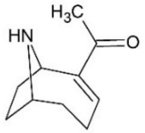
Classes of toxins produced by cyanobacteria



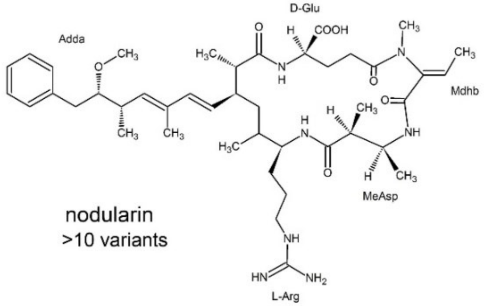
microcystin
>300 variants



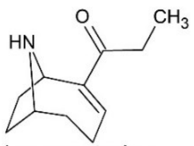
guanitoxin



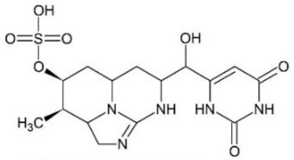
anatoxin-a



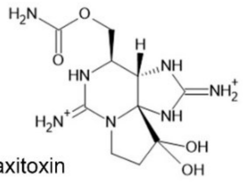
nodularin
>10 variants



homoanatoxin-a



cylindrospermopsin



saxitoxin

Cyanotoxins	Drinking Water (for Chronic Lifetime Exposure)	Drinking Water (Short- Term Exposure ≈2 Weeks)[3]	Recreational Water (Short-Term Exposure)
Microcystins[1]	1	12	24
Cylindrospermopsin[1]	0.7	3	6
Anatoxin-a[2]	Insufficient information to develop a long-term health-based GV	30	60
Guanitoxin	No toxicological data available (New Zealand has established a limit as provisional maximum acceptable value of 1 µg/L)		
Saxitoxin	Insufficient information to develop a long-term health-based GV	3[4]	30

Health-Based Guidance Values (HBGV) and other recommended values for various exposure scenarios (µg/L).

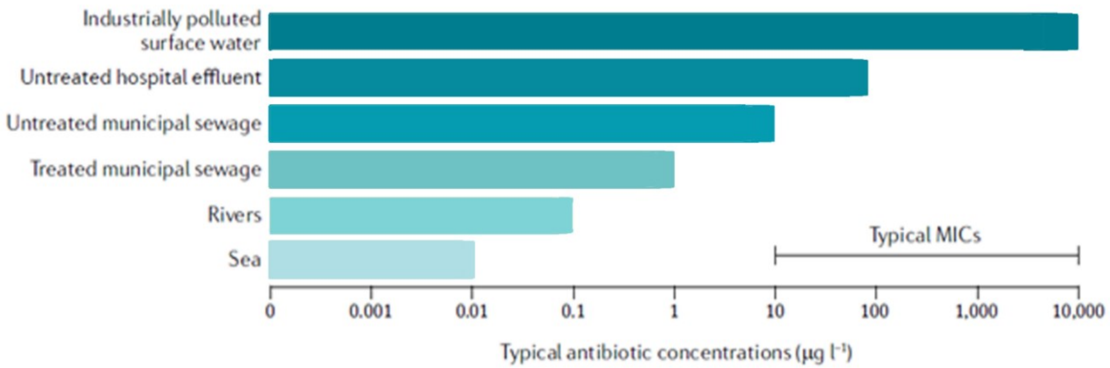
Other much less known toxins, occurring at similar concentrations

- Anabaenopeptins
- Cyanopeptolins
- Aeruginosins
- Microginins
- Aerucyclamides

Antibiotic resistance, a major threat in the future

The World Health Organization (WHO) recognized **antimicrobial resistance (AMR)** to be **one of the most serious risks to public health** in 2015, and endorsed a Global Action Plan to tackle AMR using a **One Health strategy**

Pathogenic bacteria from humans and animals, or **antibiotics and their metabolites**, are regularly discharged into the **water** environment



Larsson and Flach, 2022. Nature Reviews Microbiology

Antimicrobial resistant genes can spread from pathogenic bacteria to environmental bacteria

Antibiotics can select resistant organisms

Antibiotics can affect natural bacterial population

Antibiotics and cyanobacteria

CB can be sensitive or resistant to antibiotics, so some individuals can be selected from the selective pressure of the antibiotics

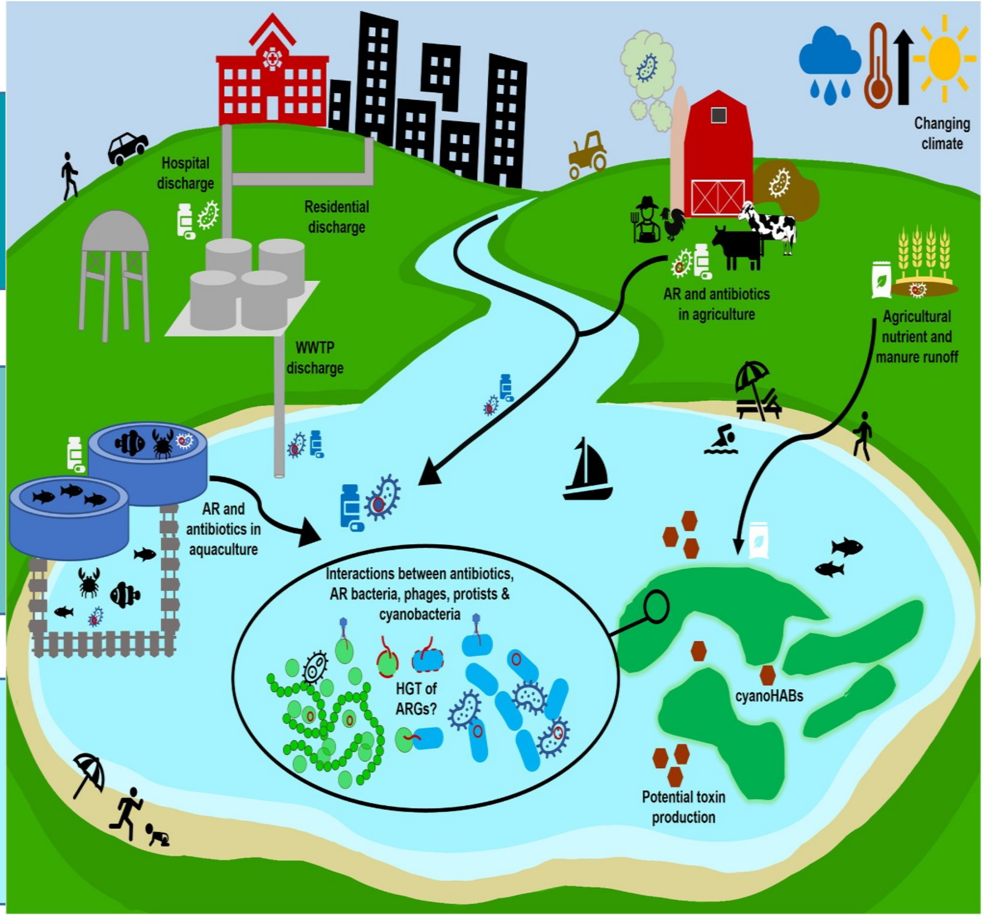
(Dias et al., 2015; LePage et al., 2019)

Cyanobacteria may act as a reservoir of ARGs thus contributing to AR spreading (10% of analysed genomes harbours some kind of ARGs)

(Timms et al., 2023)

Cyanotoxins (ctx) production can be stimulated by antibiotics; ctx can favour horizontal gene transfer between bacteria in the phycosphere.

(Wu et al., 2020; Xu et al., 2020)



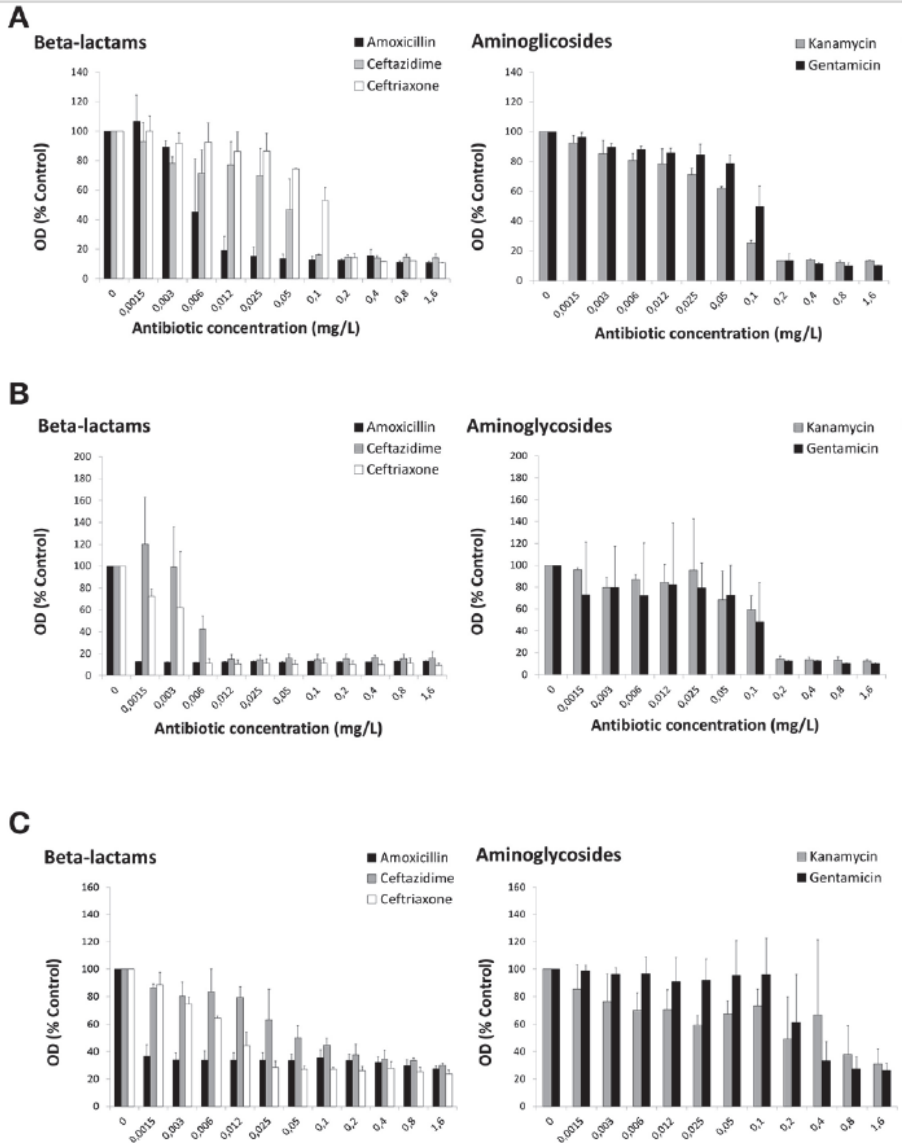
Volk and Lee, 2023. Environmental Research

Susceptibility to antibiotics

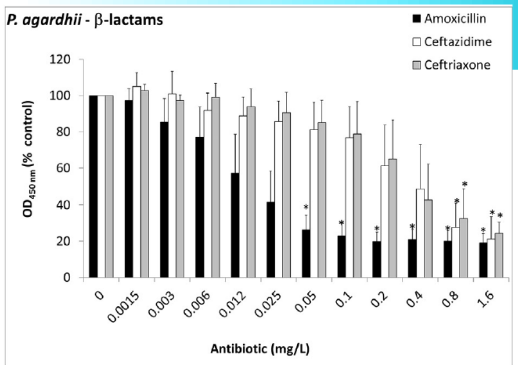
Microcystis aeruginosa

Aphanizomenon gracile

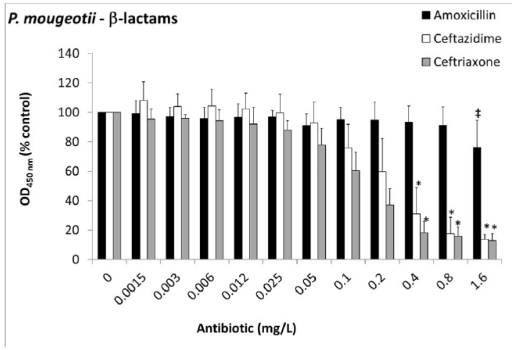
Chrisosporum bergii



Dias et al. 2015



Freshwater



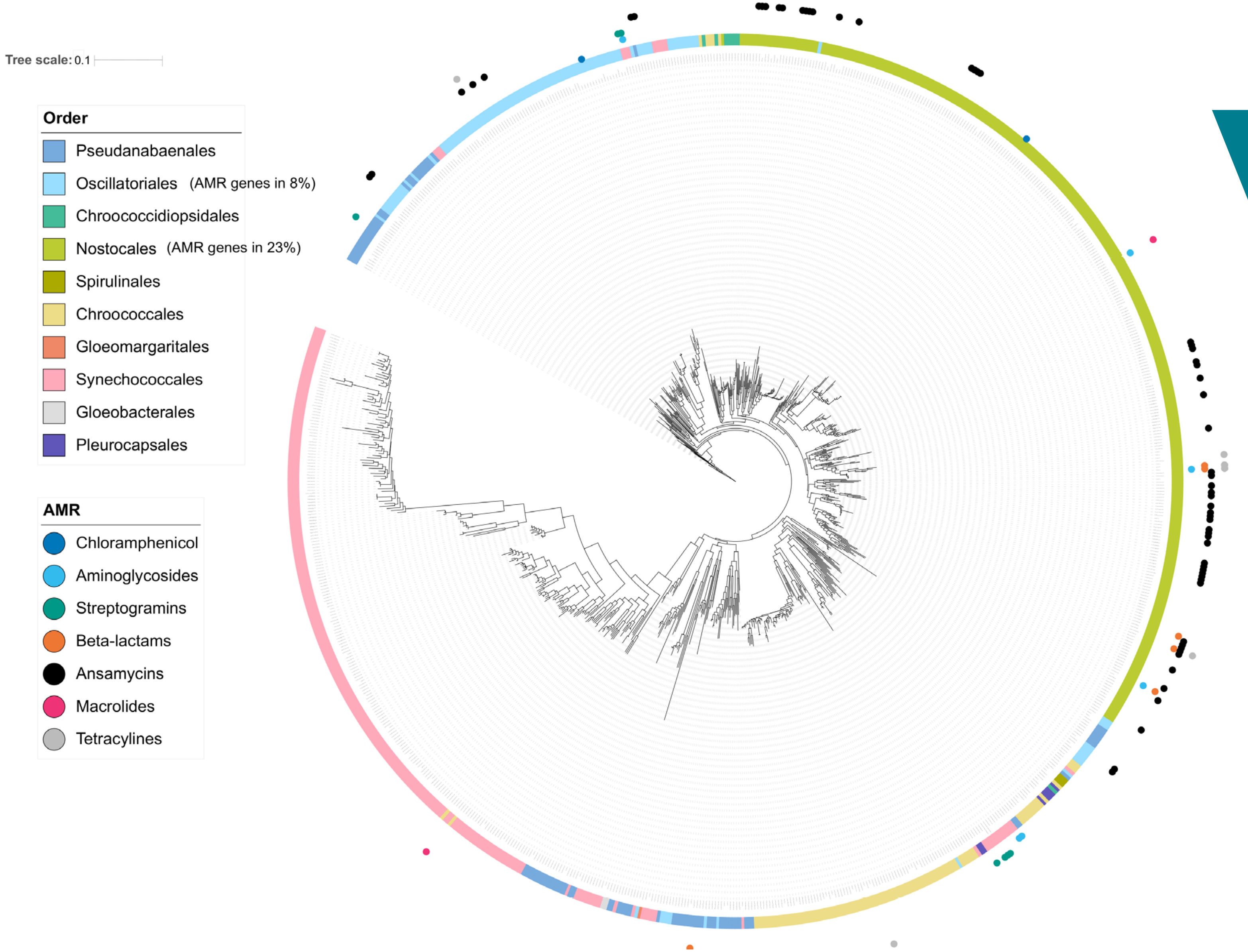
Waste Water Treatment Plant

Dias et al. 2019

No resistant genes to amoxicillin found

Different susceptibility between species

Cyanobacteria as reservoir of ARGs



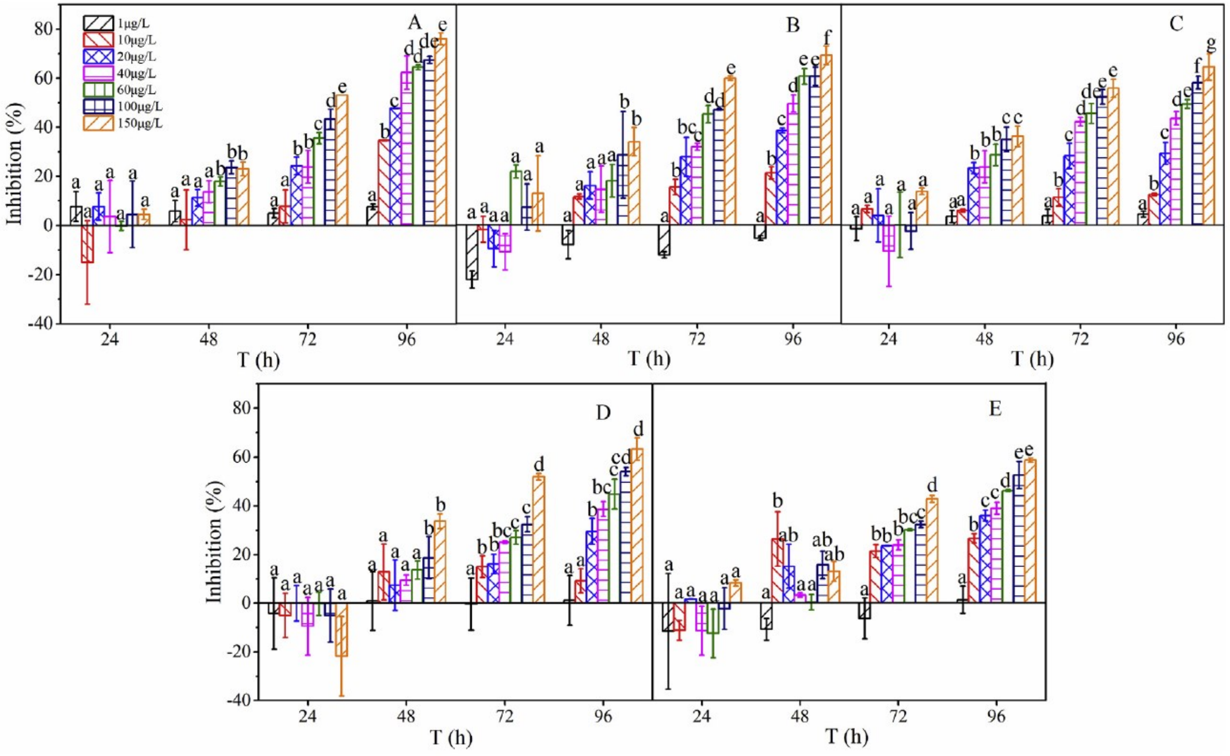
"At least one AMR gene was found in 10% of the cyanobacterial genomes and 10 (1%) had AMR genes with high homology (>99%) to equivalent genes from pathogenic bacteria"

"AMR genes were predicted most frequently in Nostocales (23%) compared to other orders"

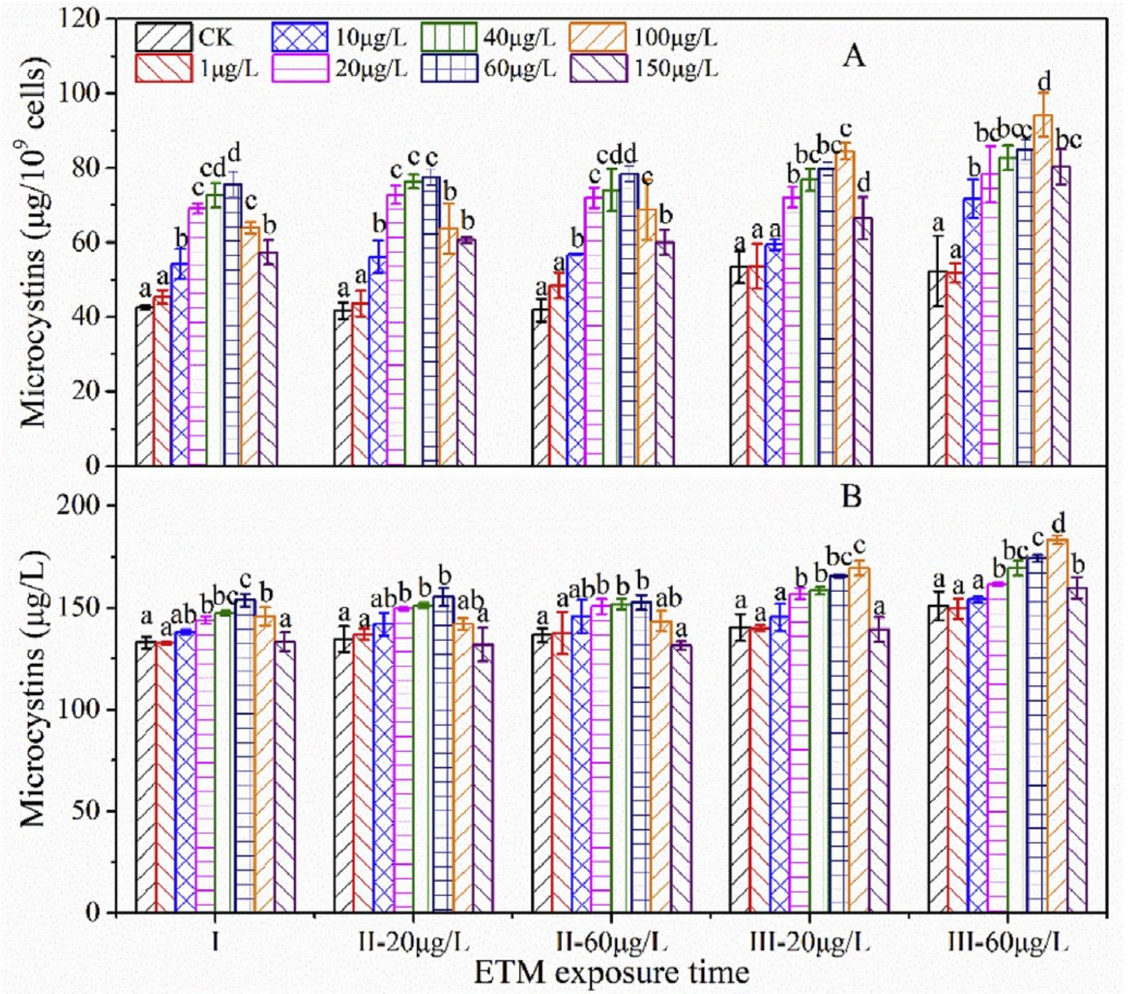
Maximum likelihood phylogeny inferred from 400 universal proteins showing distribution of predicted antimicrobial resistance (AMR) genes to antibiotic classes as indicated. Putative AMR genes were particularly abundant in Nostocalean species

Timms et al. 2023

Antibiotics and cyanotoxins



Microcystis aeruginosa
exposed to erythromycin

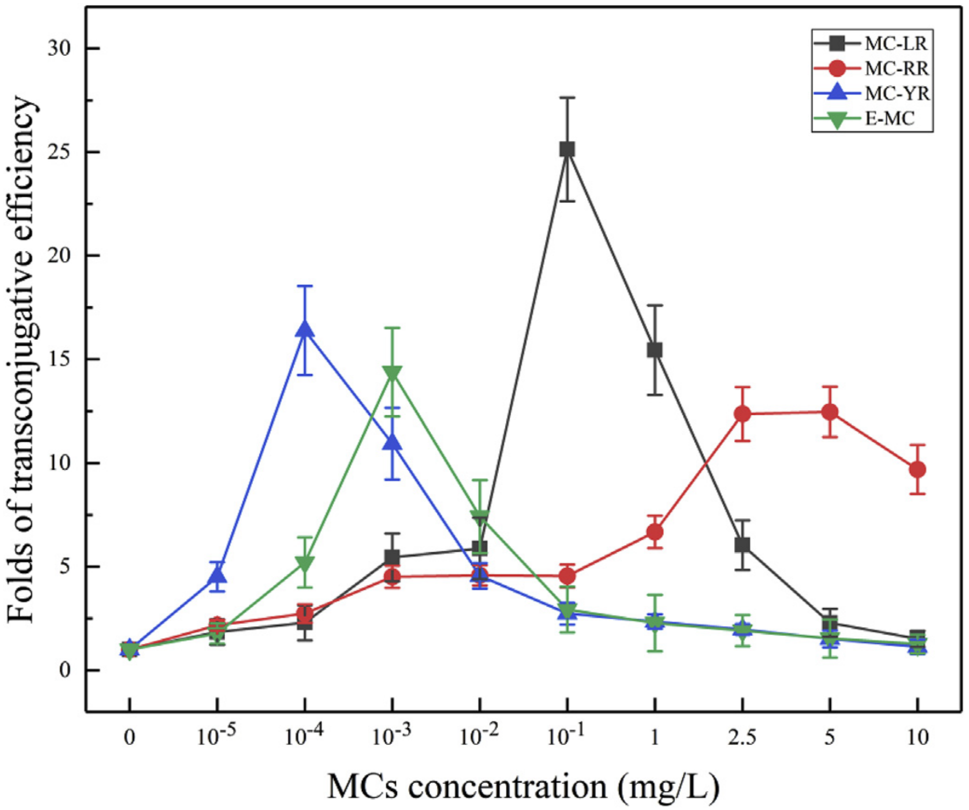


- ✓ Decrease of % of inhibition after repeated exposure to 20 and 60 μg/L erythromycin;
- ✓ Increase in MCs production

Wu et al. 2020

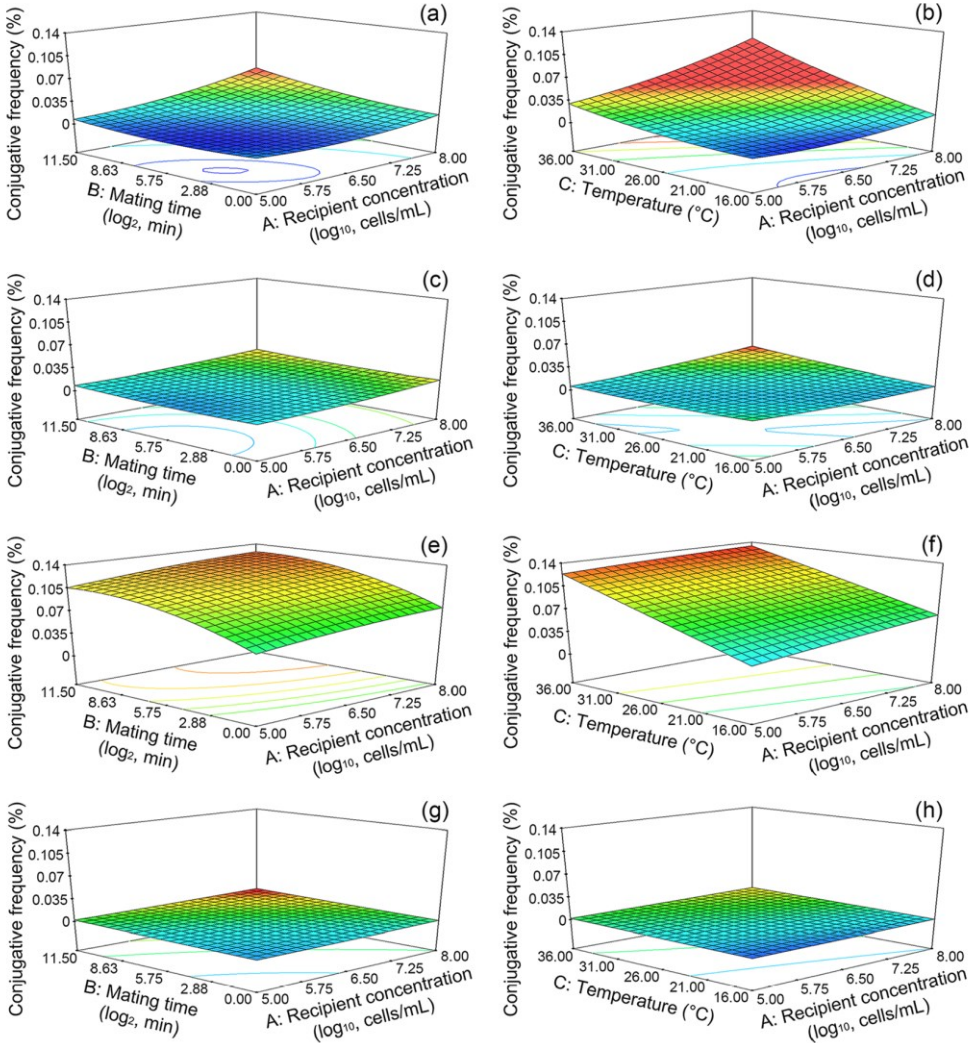
Cyanobacteria and Horizontal Gene Transfer

E. coli HB101 with RP4 plasmid as donor and *E. coli* NK5449



Xu et al. 2020

E. coli K12 with RP4 plasmid as donor and 4 cyanobacteria



Wang et al. 2020

- ✓ Toxic blooms can increase the HGT of ARG carrying plasmid between associated bacteria
- ✓ CB seem able to receive ARG carrying plasmid, as a function of T and density

Conclusions and research gaps

Cianobacteria have an intricate role in influencing the evolution and dissemination of AMR

⇩

One link between environmental AMR and humans and animals via environmental aquatic exposure, water consumption and the food chains

Need to:

- Include the environment and cyanobacteria in assessing the risk of AMR for human and animals
- Investigate whether and how much CTX, an increasing health concern in drinking water, may exacerbate horizontal gene transfer or be stimulated by environmental Abs or acquired AMR, thereby heightening the risk of CTX exposure via waterborne routes

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