REPUBLIQUE ALGERIENNE DEMOCRATIQUE ET POPULAIRE
MINISTERE DE L'ENSEIGENEMENT SUPERIEUR ET DE LA RECHERCHE SCIENTIFIQUE

UNIVERSITE AMAR TELIDJI-LAGHOUAT

FACULTE DES SCIENCES

DEPARTEMENT DE BIOLOGIE

Mémoire de fin d'études en vue de l'obtention du diplôme de Master

En : **Ecologie et Environnement**

Option :**Ecologie Végétale et Environnement**

THÈME

Toxic Cyanobacteria Biocontrol by Plants

Présenté par : BELHADJ Mokhtar Salah Eddine

Membres de jury :

Présidente :TAKHI Djalila MAA/Université Amar Telidji-Laghouat

Examinateur : Pr. GOUZI Hicham Professeur /Université Amar Telidji-Laghouat

Promotrice : ABDESSELAM Amira MAA/ Université Amar Telidji-Laghouat

Année Universitaire 2020-2021

Dédication

The best is yet to come; my heartfelt gratitude goes to my family, especially my mother NOUIOUA Fadhila and my grandfather NOUIOUA Abubakeur« May Allah have mercy on him », for their continuous support and encouragement since the start of my studies; I love you and dedicate my success to you which is also your achievement.

Acknowledgment

I thank Allah, great merciful, for giving me the patience, the courage, and the will to carry out this work.

I would like to express all my thanks and gratitude to my thesis supervisor, Miss ABDESSELAM Amira to her follow-up, her availability, her support, her patience and her guidance during the development of this research.

Isincerelyexpressmygratitudetothejury, Mrs TAKHI Djalila and Pr. GOUZI Hicham,whogavemehonorandpleasuretohaveagreedtoconsiderthismodestwork andgavetheirvaluabletime toread andevaluate it.

I cannot omit to express my deep gratitude to my teachers who taught me during my entire university career

Thanksto all

ملخص:

تكاثر البكتيريا الزرقاء السامة لها العديد من التاثيرات السلبية على النظام البيئي المائي كما انها تضر بالبشر. يعد استخدام التضاد البيوكيميائي للنباتات لمنع فرط نمو الطحالب الدقيقة نهجا صديقا للبيئة للتحكم في تكاثر الطحالب الضارة.يهدف هذا العمل الى ضخ كميات كبيرة من عمليات الازالة البيولوجية للبكتيريا الزرقاء السامة باستخدام النباتات الأرضية والمائية.اظهرت العديد من اعمال البحث كفاءة النباتات والمواد الكيميائية الخاصة بها في إزالة كل من الخلايا السيانوبكتيرية والايضات المنبعثة في المسطحات المائية وخاصة السموم الزرقاء.ثبت أيضا ان إزالة العناصر الغذائية من الماء عن طريق النباتات لها دور في إعادة تاهيل النظم المائية والمكافحة الحيوية لتكاثر البكتيريا الزرقاء السامة.

الكلمات المفتاحية :السمومالسيانوتينية,البكتيريا الزرقاء ,نباتات,المكافحة الحيوية للآفات,الفاعلية

ABSTRACT

Toxic cyanobacteria have several negative impacts on aquatic ecosystem, and even harm to humans.Utilization of plants allelochemicals to inhibit microalgal overgrowth is an environment-friendly approach for controllingHABs.This work aims to sumarize toxic cyanoabcteria biological removal processes using terrestrial and aquatic plants. Several reserch works showed the effiency of plants and their allelochemicals in the removal of both cyanobacterial cells and metabolits released in water bodies aspecially cyanotoxins. The removal of nutrients from water by plants is also proved to have a role in the rehabilitation of aquatic systems and harmful Algae Blooms (HABs) biocontrol.

Key words: Cyanotoxins, Cyanobacteria, plants, biocontrol, efficiency

RÉSUMÉ

Les cyanobactéries toxiques ont plusieurs effets négatifs sur l'écosystème aquatique, voire nuisent aux humains. L'utilisation d'allelochimiques végétaux pour inhiber la prolifération des microalgues est une approche respectueuse de l'environnement pour lutter contre les les cyanobactéries toxiques. Ces travaux visent à résumer les processus d'élimination biologique des cyanoabctéries toxiques à l'aide de plantes terrestres et aquatiques. Plusieurs travaux de reserch ont montré l'efficacité des plantes et de leurs produits allélochimiques dans l'élimination des cellules cyanobactériennes et des métabolits libérés dans les plans d'eau, en particulier les cyanotoxines. Il est également prouvé que l'élimination des nutriments de l'eau par les plantes a un rôle dans la remise en état des systèmes aquatiques et la lutte biologique contre les proliférations des cyanobactéries toxiques

Mots clés:cyanotoxines,Cyanobactéries,plantes,biocontrôle,Efficacité

1H-NMR Proton Nuclear Magnetic Resonance
2,4-DAB 2,4-diaminobutyric acid
ALDH2 Aldehyde Dehydrogenase 2
AOAC Association of Official Analytical Chemists
APX Aplysiatoxin
ATX-a Anatoxin-a
ATX-a(s) Anatoxin-a(s)
BGAS Blue Green Algae Supplements
BMAA β-N-methylamino-L-alanine
BMP Bacterial Magnetic Particles
cDNA Complementary Desoxyribonucleic Acid
CRL Community Reference Laboratory
CYN Cylindrospermopsin
DNA Desoxyribonucleic Acid
ELISA Enzyme-Linked Immunosorbent Assay
EPA Environmental Protection Agency
EU European Union
HABs Harmful Algal Blooms
hATX-a Homoanatoxin-a
HILIC Hydrophilic Interaction Liquid Chromatography
HPLC High Performance Liquid Chromatography
IARC International Agency for Research on Cancer
i.p. Intraperitoneal
i.v. Intravenous injection
LC-MS Liquid Chromatography Mass Spectrometry
LC-MS/MS Liquid Chromatography-Triple Quadrupole Mass Spectrometry
LC-TOF-MS Liquid Chromatography –Time–of-Flight Mass Spectrometry61
LD50 Lethal Dose 50
LOAEL Lowest Adverse Effect Level
LOQ Limit of Quantification
LPS Lypopolysaccharide
LT Lyngbyatoxin
LTA Lyngbyatoxin A
LTB Lyngbyatoxin B
LTC Lyngbyatoxin C
MCsMicrocystins
MC-LR Microcystin-LR
MC-RR Microcystin-RR
MRL Maximum Residue Limit
MS Mass Spectrometry
NER Nucleotide Excision Repair
NHEJ Non-Homologous end Joining
NOAEL No Observed Adverse Effects Level
NODsNodularins
NRPS Non-Ribosomal Peptide Synthetase
NMR Nuclear Magnetic Resonance
PHE phenylalanine
PKC Protein Kinase C
PKS Poliketide Synthase
PMAC Provisional Maximum Concentration
PMAV Provisional Maximum Value
PPIA Protein Phosphatase Inhibitor Assay
PP1 Protein Phosphatases 1
PP2A Protein Phosphatases 2A
PSP Paralytic Shellfish Poisons
qPCR Quantitative Real-Time Polymerase Chain Reaction
QqTOFQuadrupole Time-Of-Flight
rDNA Ribosomal Desoxyribonucleic Acid
62
RNA Ribonucleic Acid
ROS Reactive Oxygen Species
rRNA Ribosomal Ribonucleic Acid
STXs Saxitoxins
TPA Tumor Promoter 3H-12-*O*-Tetradecanoylphorbol-13-Acetate
UBA Umweltbundesamt
UHPLC Ultrahigh Pressure Liquid Chromatography
UK United Kingdom
USA United States of America
UV Ultraviolet
WHO World Health Organization
EO Essential Oils
CWRC Global Water Research Coalition

.

Eutrophication is one of the most serious problems affecting aquatic ecosystems, which causes Harmful Algal Blooms (HABs) especially toxic cyanobacteria. They became global concerned issues as they can induce several negative impacts on aquatic environment functioning, water quality of rivers and lakes and also affect the safety of drinking water and consequently human health(Zingone and Enevoldsen, 2000; Xiao et al., 2014; Zhang et al., 2019).

Cyanobacteria rapid proliferation is regulated by a combination of natural and anthropic factors forming a dense layer of cells on the water's surface (Sanseverino et al., 2016).Excessive growth of toxic cyanobacterial can result in financial losses in the form of decreased property prices, high-cost raw drinking water treatment, diseases, slowed recreational industries, and management and restoration costs for impaired lakes and reservoirs (Marsalek et al., 2001).

Therefore, control and elimination oftoxic cyanobacteria blooms have become a significant goal in environmental science. At present, several measures were conducted to control blue-green algal blooms, including physical, chemical and biological methods (*e.g.*, introducing fish, cultivating aquatic plants and using algicidal bacteria). Biological technology has been widely required because of its higher environmental safety and relatively low operating cost (Chang et al., 2007).

Among numerous biological approaches in HABs control, utilization of allelochemicals has attracted considerable attention. Allelochemicals are regarded as eco-friendly algicides due to the characteristic of negligible toxicity, high selectivity and excellent degradability (Wang et al., 2018c). The efficiency of both macrophytes and several terrestrial plants has been proved by scientists (Tsuda et al.,2005; Zhu et al., 2021).

In this work, we will present the scientific researches concerning the biocontrol of toxic cyanobacteria using plants. This bibliographic collection is structured in four chapters; in the first chapter, we gave some information on the biology and ecology of cyanobacteria. In the second one, it was important to briefly present cyanotoxins and their dangerousness on environment and human health. The third chapter concerns all toxic cyanobacteria removal methods. The last and the most important chapter will explain toxic cyanobacteria biocontrol approaches using plants and there compounds

Chapter I:

General information on Cyanobacteria

1.1. Biology and Ecology of Cyanobacteria

1.1.1. Biology of Cyanobacteria

Cyanobacteria are gram-negative photosynthetic prokaryotes that include over 1000 species of unicellular and multicellular microbes belonging to the orders Chroococcales, Chamaesiphonales, Pleurocapsales, and Nostocales (Oscillatoriaceae, Nostocaceae, and Rivulariaceae) (Glazer ,1977). Cyanobacteria may be unicellular (single or forming colonial aggregates) or filamentous (forming colonies) (possessing or lacking heterocysts and akinetes). The filamentous forms can be uniseriate or pluriseriate, unbranched or with true or false ramifications, without sheath or with homogeneous or stratified mucilaginous sheath(Couté & Bernard, 2001)*(Fig. 1)*.

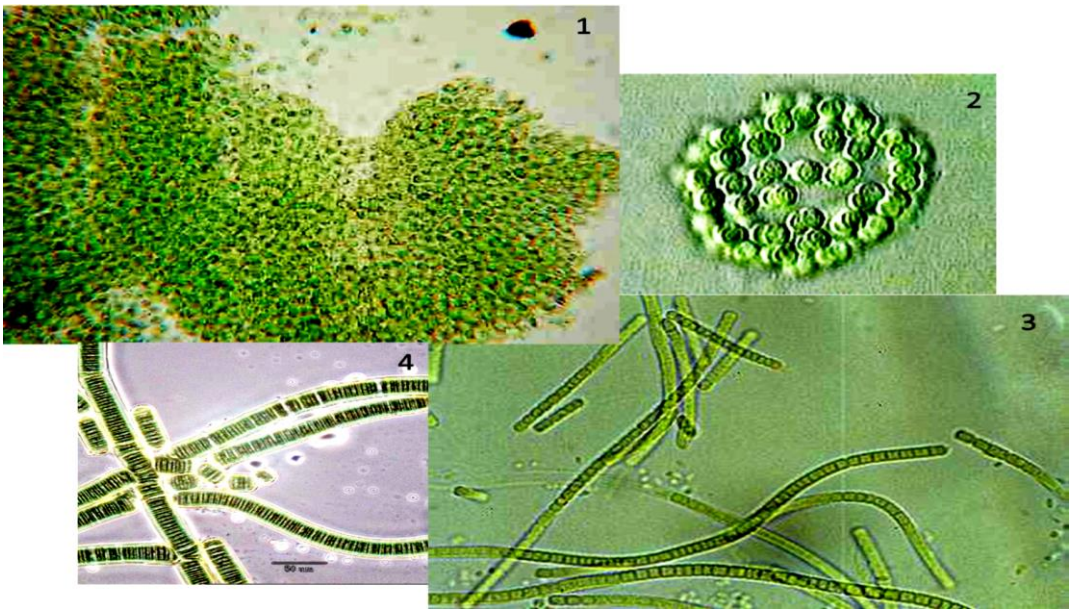

Figure 01: Morphological diversity of cyanobacteria;(1) *Microcystis spp.* (2) *Anabaena spp.* (3) *Phormidiumspp*.(4) *Lyngbya spp*. (Schneegurt, 2001)

Several cyanobacterial species, especially those with heterocyst, may fix nitrogen using the enzyme nitrogenase, compensating for any nitrogen deficiency in aquatic nitrogen, which is needed for primary production. Nitrogenase, which catalyzes the reduction of dinitrogen to ammonia, is found in filamentous cyanobacteria and is found in heterocysts, which are produced in response to nitrogen limitation, but non-heterocyst forming cyanobacteria may also fix nitrogen (Walsby,1994). In fact, certain strains of non-heterocystous cyanobacteria can fix

nitrogen aerobically. Despite this, these organisms may have a significant impact on the global nitrogen cycle. (Volgusheva et al.,2019).

The dominance of cyanobacteria in eutrophic aquatic environments has also been due to a number of cyanobacterial characteristics, such as the presence of phycobiliproteins (Pflugmacher, 2002). Phycobiliproteins are natural protein polymers found in cyanobacteria, eukaryotic red algae, and cryptophytes, where they serve as photosynthesis's accessory pigments (Pereira et al.,2020).

Cyanobacteria are an ancient and widespread group of species, many of which can photosynthesize (Blais, 2001). In fact, cyanobacteria, unlike eukaryotic algae, lack organelles and instead have intracellular membranes (thylakoids) that contain photosynthetic pigment (phycobilisomes-phycobiliproteins in a supramolecular structure) within their cells (Walsby, 1994) (*Fig. 2*).

The ability of cyanobacteria to absorb light from a broad spectrum and use it to photo synthesis is perhaps their most intriguing function. All cyanobacteria have the photosynthetic pigment chlorophyll-a, as well as the light harvesting phycobiliproteins allcophyeocyanin- B, allophycocyanin and C, or R-phycocyanin (others like phycoerythrin and C phycoerythrin may also be present in some cyanobacteria groups - red algae) that allow them to fix carbon dioxide outside of the chlorophyll (Pflugmacher, 2002).Both chlorophyll in photosystem I (PSI) and a sequence of phycobilosomes in photosystem II (PSII) capture light energy, which is then used to produce ATP and NADPH. Under low light conditions, cyanobacteria can thus outperform most algae.

Gas vesicles are hollow gas-permeable and water-impermeable protein structures that provide buoyancy in certain cyanobacteria (Whitton and Potts, 1999). The cyanobacteria's gas vesicles, which vary in width depending on the species, control buoyancy, allowing them to occupy the best location in the water column(Nierzwicki-Bauer et *al.*, 1983).

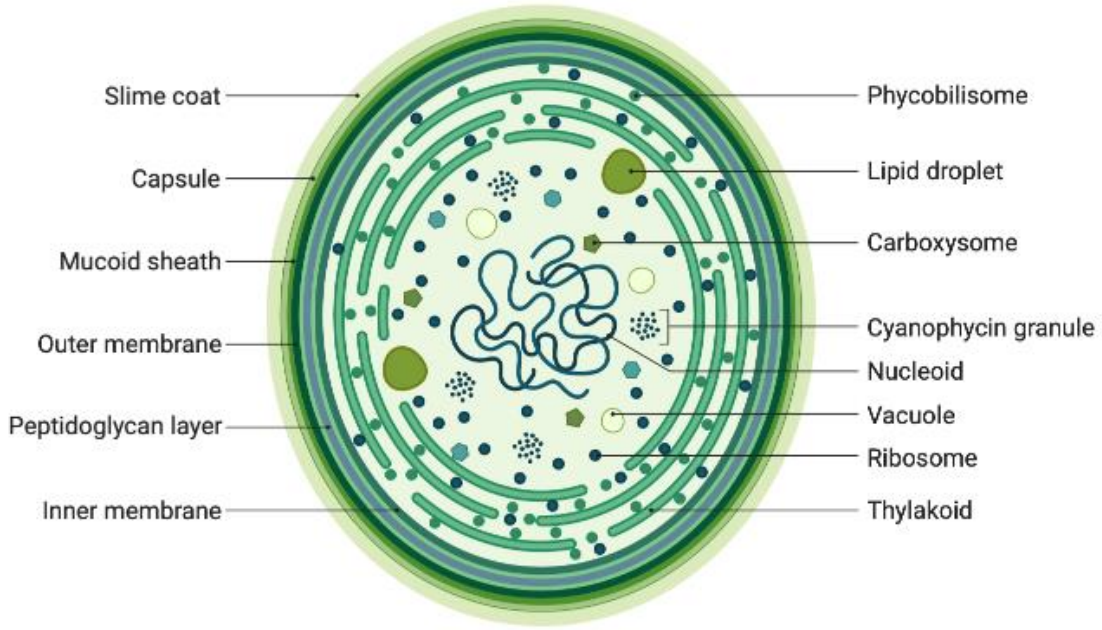

Figure 2: Cell structure of cyanobacteria (Biorender, 2021)

1.1.2. Ecology of Cyanobacteria

Cyanobacteria have a number of adaptive mechanisms that enable them to thrive in harsh environments and promote their successful growth in water. The presence of gas vesicles, the probability of partial heterotrophic metabolism, and the generation of allelopathic compounds are all important factors in the success of nuisance blue-green organisms (Mur et al., 1999).Many anti-cyanobacterial steps have different effects depending on the cyanobacterial species' susceptibility or autecology. Microcystis genus, especially *Microcystis aeruginosa*, is one of the most common bloom-forming cyanobacterial species worldwide. As a result, several studies and methods have been established to regulate these species (Kolmakov and Gladyshev, 2003).

They are common in marine, brackish, and freshwater environments, as well as freshwater surface water drinking sources (Chorus and Bartram, 1999). In aquatic environment rich in nutrients, cyanobacteria periodically reveal significantly increased reproductive rates and total population biomass known as a “bloom” (Falconer, 1999).

Shade, a rise in pH, a decrease in oxygen content in the water due to bloom respiration or degradation, and the generation of highly active cyanotoxins are all negative environmental effects of cyanobacterial blooms.

While speculation about the potential existence of cyanobacteria on Mars poses even more questions about their origin, geologists and geochemists agree that cyanobacteria have a long evolutionary history, with most - but not all - agreeing that it dates back at least 3500 Ma. The protozoic Era (2500-570 Ma) has been dubbed the " Age of Cyanobacteria" by Schopf and Walter (1982), since it is when they are most abundant in the fossil record. Many modern cyanobacteria contain derivatives of 2- methylbacteriohopanepolyols, which have been discovered in phosphate-rich sediments dating back to 2500 Ma (Summons et al., 1999). Proterozoic rocks occasionally have filamentous structures that look remarkably similar to modern filaments. Stromatolites, which were commonly deposited at the time, tend to be somewhat similar to structures developing in a few locations today, the best known of which are those at Shark Bay in western Australia. Many modern laminated structures produced by cyanobacteria, such as *Phormidiumhendersonii*, are destroyed by invertebrates and the absence of such activity in the Proterozoic. Period is likely one of the reasons why so many structures from this era survived as stromatolites (Schopf and Walter, 1982).

The long evolutionary history of cyanobacteria can be linked to some of the reasons for their success in modern environments. investigate how the evolving metal composition of early environments during the time when O2 was first released into the atmosphere could have affected the development of new metal resistance determinants and metal-using proteins. Low oxygen tolerance is still common in cyanobacteria, and certain strains tolerate free sulphide at levels much higher than those tolerated by most eukaryotic algae (Padan and Cohen, 1982). Some eukaryotes, such as some diatoms, can use H2S as a hydrogen donor in addition to H2O (Cohen et al., 1975), a function that appears to be absent even in those eukaryotes that can withstand relatively high H2S concentrations. Another characteristic of certain strains is their high resistance to ultraviolet-B and -C radiation, which is thought to have played a key role in the early evolution ofs cyanobacteria.

Modern-day picocyanobacteria dominate both biomass and productivity in the transparent, nutrient-deficient waters that characterize vast swaths of the world's oligotrophic

oceans and some large lakes due to their adaptation to low light and efficient nutrient absorption kinetics at low ambient concentrations. However, there is still a lot to learn about these species, which were previously unknown (Johson and Sieburth,1979, Waterbury et al.,1979).

The role of circadian rhythms in aquatic cyanobacteria's behavioral responses is becoming increasingly apparent (Mann and Schmidt,1998; Kondo and Ishiura, 1999). Such rhythyms are a basic adaptation of living cells to the earth's everyday fluctuations in light and temperature (Kondo et al., 1994). The circadian rhythm is found in all species, from prokaryotes to higher eukaryotes, and it is a universal biological phenomenon. Self-sustaining molecular transcriptional/post-translational feedback loops are required for these rhythms (Guo et al.,2016). However, Periodic expression of circadian system proteins generates behavioral and physiological rhythms at the organismal level. Indeed, there is evidence that circadian rhythm-dependent transcription occurs in more than 40% of all protein-coding genes (Cedernaes et al.,2018).

In many terrestrial environments, cyanobacteria are essential, and their resistance to desiccation and water stress is a key factor (Whitton et al.,2002). Akinetes are dormant cells found in the Nostocales and Stigonematales orders of cyanobacteria that allow phototrophic bacteria to persist under severe and starving environments. In response to environmental changes, these spore-like, thick-walled, non-motile cells develop from vegetative cells. They have a perennating function because they may restore the shape and activities of vegetative cells, including cell division renewal, after a lengthy time of dormancy (Assaf Sukenik et al.,2018).

Therefore, cyanobacteria often play a key role in preserving the stability of semi-desert surface crusts and the dertility of arid-zone farming soils. Cyanobacteria, especially Chroococcidiopsis, can be found in microbial communities several millimeters below the surface in true deserts. These species are clearly approaching the limits of existence in Antarctica's dry deserts, and their doubling period has been estimated to be as long as ten thousand years (Nienow and Friedmann, 1993).

Symbiotic relationships exist between cyanobacteria and a variety of eukaryotic hosts, including fungi, plants, and animals such as sponges, ascidians, and corals. They offer the host with fixed nitrogen and carbon, and in exchange, they live in relatively safe settings free of

predators and harsh weather. Many cyanobacteria are also heterotrophic, allowing them to live in symbiotic structures that get little or no light and where photosynthetic hosts may provide them with fixed carbon, such as the roots of plants. Cyanobacterial symbionts are capable of independent development in all but a few cases, yet they typically display major morphological and physiological changes while in symbiosis. Many cyanobacterial symbionts fix nitrogen in specialized cells known as heterocysts, and the frequency of heterocysts, as well as the rate of N2 fixation, is considerably increased in many symbioses, particularly those with plant hosts. As providers of fixed nitrogen to their surroundings, cyanobacterial symbioses play an important role in the ecosystem. Some, such as diatoms, can reach vast numbers in the seas, whereas moss epiphytic associations and cyanolichens are prevalent in hostile conditions with few alternative sources of fixed nitrogen (David et al., 2012).

One of the most evident dangers to the ecosystem of lakes, rivers, and certain estuaries is the ongoing and expected global expansion in cyanobacterial dominance (Paerl and Huisman,2008). The quality and quantity of primary production for zooplankton grazers determines the structure and function of aquatic ecosystems. While high-quality phytoplankton allows for effective carbon and energy transfer to higher trophic levels, cyanobacterial characteristics (such as toxicity, size, and nutrition) may affect zooplankton fitness(Wilson et al.,2006) and the ecological interaction between primary producers and the grazers who graze on them (Elser and Goldman,1991). Indeed, when cyanobacteria dominate phytoplankton populations in extremely eutrophic conditions, this trophic uncoupling becomes more pronounced (Auer et al., 2004). However, zooplankton frequently coexists with harmful cyanobacterial blooms, and the function of plankton ecosystems is also influenced by zooplankton characteristics and abundance. Copepods, for example, may help cyanobacteria thrive (Hong et al.,2013). When liberated from planktivorous fish predation, high abundances of generalist grazers (*eg.*Daphnia) may limit blooms (Sarnelle,2007). Although bloom-forming cyanobacteria is thought to be a low-quality food with weak links to zooplankton, examples of strong top-down bloom management highlight the cyanobacteria–zooplankton interactions' complexity (Kemal et al.,2016).

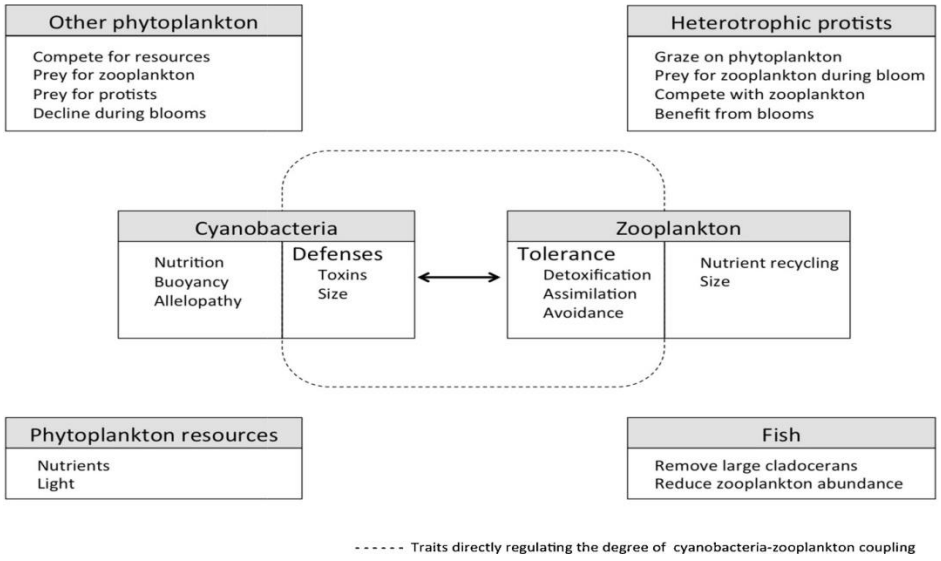

Figure 3 : The planktonic food web in relation to the drivers of cyanobacteria–zooplankton interactions during bloom conditions.

As figure 3 shows, the ecological coupling between cyanobacteria and zooplankton, which regulates the function of the plankton ecosystem, depends on the interaction of defensive and tolerance traits of cyanobacteria and zooplankton, respectively (dashed line). Increased cyanobacterial dominance of phytoplankton may shift the species composition and traits of zooplankton, resulting in smaller and selective grazing species, as well as more tolerant genotypes. Blooms also indicate an accumulation of cyanobacteria un-grazed by meso-zooplankton, and an increased role for heterotrophic protists in transmitting primary production carbon and energy to higher trophic levels. Zooplanktivorous fish also reduce the abundance of large Daphnia, which further weakens the link between cyanobacteria and zooplankton and may facilitate blooms(Kemal et al.,2016).

Chapter 2:

Cyanotoxins and their impacts

2.1.Cyanobacterial Toxins

Cyanotoxins are a group of secondary metabolites formed by various cyanobacteria genera that are highly toxic to a wide range of species, including animals, plants, algae, and humans. Bloom-forming cyanobacteria contain cyanotoxins. Cyanobacteria rapid proliferation is regulated by a combination of natural and anthropic factors. A bloom is a natural phenomenon that occurs when there is a large amount of biomass produced, and it is often characterized by the formation of a dense layer of cells on the water's surface (Sanseverino et al., 2016).

The massive growth of cyanobacteria can be triggered by a variety of physical, chemical, and biological factors, including warmer water temperatures (25°C or higher), light intensity (a species-specific requirement), and the presence of oxygen. Increased input of nutrients in aquatic environments, primarily phosphorous and nitrogen) trophic state of the water (Merel et al., 2013).

Since not all cyanobacteria strains are toxic (Blaha et al., 2009), blooms are not always linked to toxicity. Cyanobacteria develop each toxin only when the required toxin gene is present carried by a specific strain, and whether environmental conditions. During a bloom, toxic and nontoxic organisms coexist in the majority of cases, but the amount of toxins in the waterbody is not always proportional to the presence of toxin-producing cyanobacteria. Different organisms may produce different types of toxins, and a single species can produce multiple types and variants of toxins.

The majority of cyanotoxins are present inside the cells, in the cytoplasm. When an algal bloom decays, cyanobacteria normally release their intracellular toxins into the water, but toxins can also be secreted by live cells in some animals (toxins found outside the cell). Toxins released into the water can bioaccumulate in waterborne species, allowing them to pass on to aquatic fauna and humans. When toxins build up in shellfish, human populations consume them. It can result in a variety of symptoms ranging from serious illness to death. Several studies are currently underway to better understanding of the wide spectrum effects of cyanotoxines. Recently, more attention has been paid to their toxicity and potential effects on human health.

2.2.**Classification of Cyanotoxins**

Cyanotoxins are classified into four groups based on their toxicological targets(Sanseverino et al.,2017):

- Hepatotoxins: that have an effect on the liver (Microcystins and Nodularin).
- Neurotoxins: Anatoxins, Saxitoxins, and -Methylamino-LAlanine –BMAA-) are neurotoxins that cause damage to the nervous system.
- Cytotoxins: they have hepatotoxic as well as neurotoxic effects (Cylindrospermopsin).
- Dermatotoxins: that irritate people when they come into contact with them (Lypopolysaccharids, Lyngbyatoxin and Aplysiatoxin)

Table 1: **Toxins produced by cyanobacteria: their effects and primary targets** (JRC TechnicalReport, 2016)

Toxin classification	**Toxins**	**Most common Cyanobacteria Genera producing toxins**	**Main organaffected**	**Effects**	**Main targets**
Hepatotoxins	*Microcystins*	*Microcystis Anabaena, Aphanizomenon, Planktothrix, Oscillatoria, Phormidium*	Liver	Diarrhea, Vomiting, weakness liver, Inflamation, Liver, Hemorrhage, Pneumonia, dermatitis	Serine/ Threonineprotein phosphatases
	Nodularin	*Nodularia, Nostoc*	Liver	Diarrhea, Vomiting, weakness liver, Inflamation, Liver, Hemorrhage, Pneumonia, dermatitis	Serine/ Threonineprotein phosphatases
Cytotoxins	*Cylindrospermopsin*	*Cylindrospermopsis, Anabaena, Aphanizomenon, Raphidiopsis, Oscillatoria, Lyngbya, Umezakia*	Liver	Gastroenteritis, Liver, Inflammation, Hermorrhage, Pneumonia, Dermatitis	Proteinsynthesis

Neurotoxins	*Anatoxins*	*Anabaena, Aphanizomenon, Planktothrix, Cylindrospermopsis, Oscillatoria*	Nervous system	Muscle twitching, Burning, Numbness, Drownless, Salivation, Respiratory paralysis leading Burning to death	Nicotinic receptors or acetylcholinest erase
	Saxitoxins	*Anabaena, Aphanizomenon, Cylindrospermopsis, Lyngbya, Planktothrix, Rhaphidiopsis,*	Nervous system	Muscle twitching, Burning, Numbness, Drownless, Respiratory,paralysis leading Burning to death, Headache, Vertigo	Sodium channels
	*BMAA**	*Nostoc , Microcystis, Anabaena, Aphanizomenon, Nodularia*	Nervous system	No specific clinical symptoms,ALS/PDC with long –term consistent exposure	NMDA* Excitotoxicity, ROS production
Dermatotoxins	*Lypopolysaccharide*	*Synechococcus, Microcystis, Anacystis, Oscillatoria, Schizothrix, Anabaena*	Skin	Skin irritation, Eye irritation , Headache, Allergy, Asthma,fever	Toll-like receptors
	Lyngbyatoxins	*Lyngbya*	Skin	Skin and eye irritation, Respiratory problems	Proteinkinese C
	Aplysiatoxin	*Lyngbya, Schizothrix, Oscillatoria*	Skin	Skin irritation, Asthma	Proteinkinese C

***BMAA** stands for β-Methylamino-L-Alanine; NMDA stands for N-Methyl-D-Aspartate

2.2.1. *Hepatotoxins: Microcystins and Nodularins*

Microcystins (MCs) and Nodularins (NODs) are cyclic heptapeptides with similar structures and mechanisms of action. These toxins possess in their molecules the unusual molecules Adda (3-amino-9-methoxy-2, 6, 8-ethyl-10-phenyldeca-4E, 6E dienoic acid), which is found only in cyanobacterial compounds (Merel et al., 2013). To date, more than 80 variants of MCs and 9 congeners of NODs have been identified (Sanseverino et al.,2017)

Microcystins take their name from Microcystis, the first genera of cyanobacteria. The production of NODs, on the contrary, has been reported only for species

Nodulariaspumigena. Toxin's synthesis is a non-ribosomal process regulated by genes coding for Non-Ribosomal Peptide Synthetase (NRPS) and Poliketide proprietary Synthase (PKS) (Pearson et al.,2010).

MC-LR and NODs are inhibitors of serine/threonine-specific Protein Phosphatases 1 and 2A (PP1 and PP2A) (Zagura et al., 2011). It has been reported that MCs and NODs can also induce the formation of Reactive Oxygen Species (ROS), reactive products belonging to the partial reduction of oxygen. The combination of the oxidative stress and the inhibition of pathways involved in DNA repair are two cellular pathways that contribute to the genomic instability caused by the MCs-induced oxidative stress (Ohta et al., 1994).The MC- LR may induce the oxidative stress via its link with the human liver Aldehyde Dehydrogenase 2 (ALDH2) and other environmental contaminants (Chen et al., 2006).

Nodularins exert effects comparable to those induced by MC-LR; it induces the expression of TNF-alpha, proto-oncogenes, oxidative stress, DNA damages and interferes with the DNA damage repair pathway NER (Zagura et al., 2011). The UK is the only country to have set a Provisional maximum value (PMAV) for NODs in drinking water (1µg/L) (Chorus, 2012).

2.2.2. Cytotoxins: Cylindrospermopsin

Cylindrospermopsin (CYN) is a cyanobacterium enclosing a tricyclic guanidine group, which is linked through a hydroxyl bridge to a uracil moiety (Dittman et al., 2013). CYN is classified as cytotoxic and can affect both the liver (hepatotoxic) and the nervous system (neurotoxic). It is also biosynthesised by other cyanobacteria including *Anabaena bergii, Aphanizomenonovalisporum and Raphidopsiscurvata*(Funari and Testai,2008;Dettmann et al.,2013)When the LD50 was 0.18 mg/kg alkaloid equivalent after 7 days it showed a lower toxicity in the range of 4.4-6.9 mg/ kilograms. The half-life of CYN in high purity water is more than 10 days, when bacterial communities were exposed to the toxin, the biodegradation of CYN was not observed after 40 days, suggesting that this event may concur to promote the event in waterbodies. The liver is the liver, but other organs including the lungs and lungs might be affected. Cylindromic acid (CYN) has a late

and acute biased toxicity as demonstrated in a study where the bacterial Communities were not only via the urine, but also via feces 23 days after the toxicity of the toxin was 2.1mg/kg BW after 24 hours and 10 times after 120-144 hours (Furani and Tastai, 2005).

Exposure to CYN may lead to micronucleus induction, tumor initiation, fetal toxicity, Desoxyribonucleic Acid (DNA strand breaks and chromosome loss. The exact mechanism through which CYN promotes carcinogenity is not well understood and the toxin was not evaluated by the World Health Organization (WHO) The involvement of p53 in CYN toxicity needs to be investigated mainly because of the important role the protein has in growth arrest, DNA repair processes and apoptotic cell death. More studies should be a priority for future research in order to understand its genotoxic and carcinogenic potential. The WHO has inadequate information to assess carcinogenic potential of CYN (Sanseverino et al.,2017)

2.2.3. Neurotoxins

a- Anatoxin-a (ATX-a)

Homoanatoxin-a (HATX-a) is a variant that has a chemical structure different from anatoxin-a (ATX-a) but they show the same toxicity properties and both have neuromuscular and blocking agents potential. The toxicity of ATX-a has been estimated at 250–375mg/kg bw by intraperitoneal (i.p.) injection into mice. The oral Lethal Dose 50 (LD50) is >5000mg bw. No No Observed Adverse Effects Level (NOAEL) value has been proposed for these two toxins. The neurotoxin hATx-a shows a similar toxicity to ATX/a with a LD50 value around 330mg/ kg bw (Rogers et al., 2005).

b- Anatoxin-a(s) (ATX-a(s))

ATX-a(s) is a neurotoxin isolated from cyanobacteria *Anabaena flos-aquae*. It is similar in structure to synthetically produced organophosphate-based insecticides. The mechanism is the inhibition of acetylcholinesterase activity at the neuromuscular junction. It causes persistent muscle stimulation, paralysis and death due to respiratory respiratory arrest. There are no structural variants of ATX- a(s). The suffix "(s)" stands for salivation factor and refers to a rapid onset of excessive salivation in animals poisoned with ATx-a (s) The Lethal Dose 50 (LD50) of retrieve this molecule is 20-40mg/kg bw in

intraperitoneally injected mice and there are no data about oral administration (Matsunga et al.,1989).

c- Saxitoxins (STXs)

Toxins are a family of potent neurotoxins with a chemical structure which share tricyclic backbone with different chemical side-chain. More than 57 congeners have been described. All STXs share the same mechanism of action but differ in toxicity, with STX resulting the most toxic (Wiese et al., 2010). The Lethal Dose 50 (LD50) of STX is recommended in Australia, Brazil, Brazil and New Zealand and New England, but not in the UK and the U.S. It can also inhibit calcium and potassium channels in excitable cells thereby affecting the production of action potentials which can cause fatal cardiac potentials (Su et al., 2004).

d- **β-N-methylamino-L-alanine (BMAA)**

BMAA acts on motor neurons by fixation on glutamate receptor and it is involved in mechanisms inducing oxidative stress (Banack, S et al 2010). This toxin has been proposed to contribute to neurodegenerative diseases such as Parkinson's andheimer's. The BMAA toxicity is controversial and no guidelines have been suggested for the use of BMAA in drinking water. The toxin can potentiate neuronal injury induced by other insults at concentrations as low as 10 mg/ml (Lobner,D et al 2007). It has been shown to cause intraneuronal accumulation of misfolded proteins, a characteristic of neurodegnerative disorders, which is linked to Parkinson's disease and other degenerative diseases. It is a neurotoxic non-protein amino acid.

2.2.4. Dermatoxins

a- Lypopolysaccharide (LPS)

Gram-negative bacteria can act as a first line defense barrier. The LPS can cause allergy and skin disease such as eczema, sepsis, and certain strains of human papillomavirus. LPS has a toxicity value of up to 250 mg/kg bw in some animals, and in some experiments, it has reached 250mg/kg in humans. It is responsible for eliciting an immune response characterised by the release of cytokines and the activation of various

cells like monocytes (Durai et al.,2015). It can also play a role in the prevention of anti-inflammatory diseases (Sanseverino et al.,2017).

b- Lyngbyatoxin (LT)

It is an indole alkaloid that was initially discovered from the benthic cyanobacterium *Lyngbyamajuscula* during an epidemic of acute contact dermatitis in Hawaii in 1912.The cyanotoxin is slightly lipophilic and its penetration as a percentage dose in guinea pig (Cavia porcellus) and human skin was respectively 23% and 6.2% after one hour of topical exposure. There are three different isoforms of Lyngbyatoxin: A (LTA), B (LTB) and C (LTC). The intraperitoneal (i.p.) value in mice for LTA is 250mg/kg bw/kg and the lethal dose in mice is 250 mg/kg. The body's exposure to contaminated water might cause serious concerns (Jakubowska et al., 2015).

c- Aplysiatoxin (APX)

It was identified in strains of *Lyngbyamajuscula*, in the sea hare *Stylocheiluslongicauda* and in the red alga *Gracilariacoronopifolia*. Aplysiatoxin is a potent tumor promoter which exerts its effects through the activation of Protein Kinase C (PKC). The environmental concentration of APX have not been explored yet (Jaffrey and Liskamp, 1986).

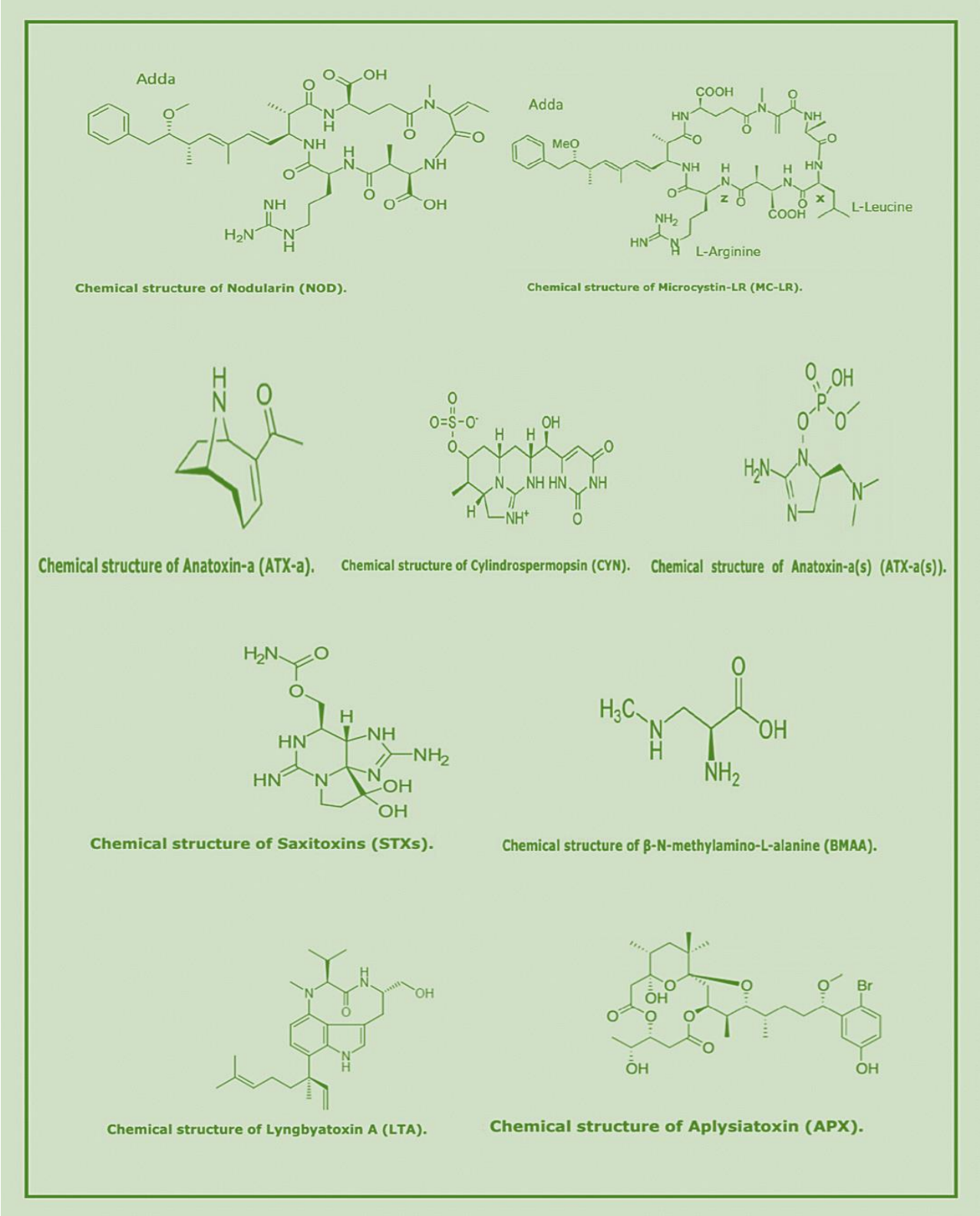

Figure 4: Representative chemical structures for cyanobacterial toxin families (Sanseverino et al., 2017)

2.3.Environnemental effects on cyanotoxicity

Blooms in the same waterbody can be Variably toxic or non-toxic from one year to the next. Different strain composition is a common explanation for this occurrence. Some species are known to exhibit high or low toxicity under different laboratory conditions. The stimuli for toxin production in such species are currently unknown (Sivonen and Jones,1999).

Because of the various intensities and strains studied, studies on light intensity and toxin development are highly variable. Low light intensities (2–20 mol photons m2 s1) have been found to have the lowest toxin concentrations, with highest levels ranging between 20 and 142 mol photons m2 s1 depending on the sample. The relationship between iron uptake and light intensity is also important. High light intensities promote cellular iron uptake, which could lead to increased toxin output (Utkilen and Gjolmen, 1995). Low iron levels, on the other hand, have been linked to slower cell growth and higher microcystin levels (Lukac and Aegerter, 1993).

Under the lowest phosphorus concentrations measured, decreased quantities of microcystin (produced by Anabaena, Microcystis, and Oscillatoria), anatoxin-a (produced by Aphanizomenon), and nodularin (produced by Nodularia) have been recorded (Sivonen and Jones, 1999). Increased microcystin in terms of dry weight was observed under phosphorus-restricted conditions as an exception (Oh H et al., 2000).

Nitrogen has a distinct effect on the formation of cyanotoxins in nitrogen-fixing cyanobacteria and non-nitrogen-fixing cyanobacteria. When grown in a nitrogen-free medium, Anabaena, Aphanizomenon, Nodularia, and Cylindrospermopsis strains, all capable of nitrogen fixation, produce the highest levels of microcystin, anatoxin-a, or nodularin (Saker et al.,1999). At high levels of nitrogen, however, Oscillatoria and Microcystis strains (non-nitrogen fixing) display the highest levels of toxin (Sivonen and Jones, 1999).

In most cyanobacteria, the influence of temperature on toxin levels is comparable. *Anabaena spp.* and Aphanizomenon produce more anatoxin-a at 20°C than at 30°C or lower temperatures (Rapala and Sivonen ,1998). Microcystin and nodularin concentrations

in Anabaena, Microcystis, and Nodularia are also highest between 18 and 25°C, with lower levels at either higher or lower temperatures tested (Sivonen and Jones,1999). Saxitoxin formation in cyanobacteria has not been studied in relation to temperature, but their concentration in the dinoflagellate *Alexandrium sp.* is increased at low temperatures and when phosphorus is limited (Anderson et al.,1990). Various temperatures have been linked to different toxin chemical types. Anabaena spp. develop microcystin-LR at temperatures below 25°C, rather than microcystin-RR, which is synthesised preferentially at higher temperatures (Rapala et al.,1997). *Microcystis sp.*, on the other hand, synthesizes more microcystin-LR than microcystin-RR in phosphorus-restricted environments (Oh et al ,2000). In comparison to [D-Asp3] microcystin-LR, which is more widespread at lower light intensities, microcystin-LR corresponds to higher levels of light (Rapala et al.,1997).

The highest toxin concentrations are also recorded under conditions that are ideal for cell development. This may be due to a direct relationship between toxin production rates and development, as Orr and Jones (Orr and Jones,1998) recently discovered. When analyzed under nitrogen and phosphorus limiting conditions, a linear association between microcystin development rates and cell division was discovered (Oh et al., 2000).

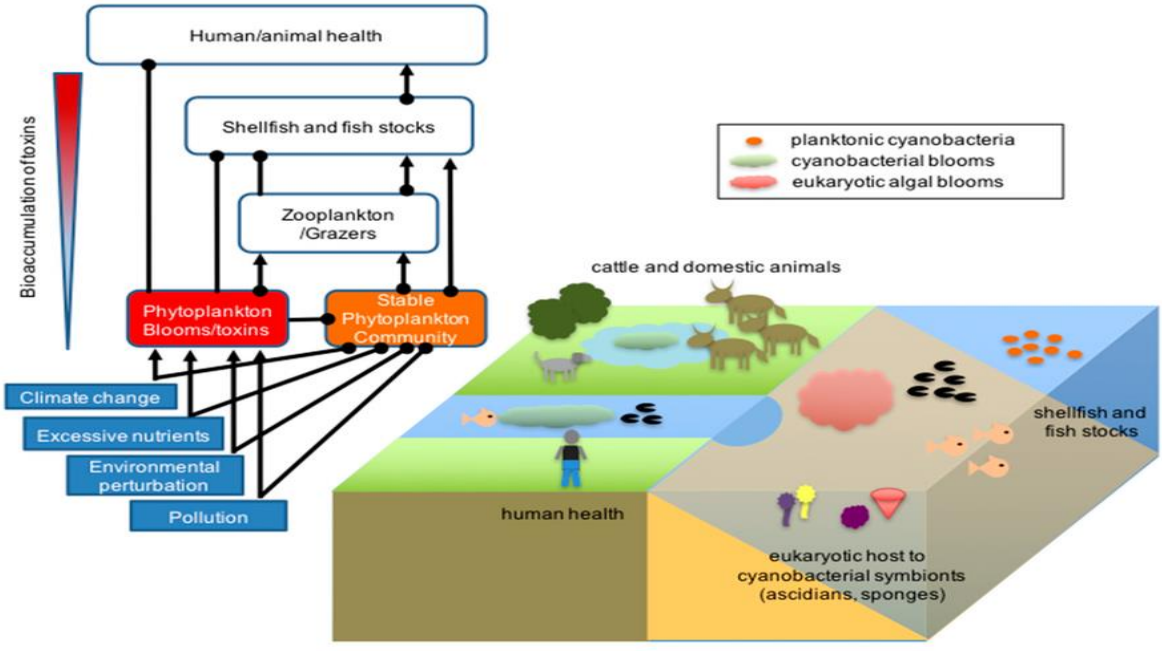

Figure 5: Environmental impact of photosynthetic microorganisms in aquatic systems (Mazard et al., 2016).

2.4. Cyanobacterial Toxins impacts

By interfering with food-web dynamics and displacing normal phytoplankton species, these effects result in aquatic organism mortality, decreased growth of submerged aquatic plants, decreased biodiversity of aquatic organisms, and decreased ecosystem stability. Furthermore, the development of odors and cyanotoxins in recreational lakes and drinking water sources has other harmful effects for humans (Falconer, 1999). The *neurotoxic, hepatotoxic, and dermatoxic* effects of cyanotoxins (blue green algal toxins) are the most common (Cooke et al., 2005). Excessive cyanobacterial growth can result in financial losses in the form of decreased property prices, high-cost raw drinking water treatment, diseases, slowed recreational industries, and management and restoration costs for impaired lakes and reservoirs (Marsalek et al., 2001).

2.4.1. Health Effects

Cyanotoxins have been linked to negative health effects in humans, who may be exposed to these compounds through oral, inhalation, or dermal routes (Sanseverino et al.,2017).

Recreational behaviors are responsible for half of the recorded episodes in humans following exposure to cyanotoxins, according to a recent analysis of data collected from 1800 to present about events in humans following exposure to cyanotoxins (Wood, 2016).

Accidental ingestion of polluted water (especially when cyanobacteria bloom or form scum), skin contact with infected waterbodies, and inhalation of aerosolized cyanotoxins are all modes of exposure to different cyanotoxins in recreational settings (Sanseverino et al.,2017).

Exposure to cyanotoxins can cause severe headache, fever, pneumonia, pneumonia and liver damage. A unique case of death was reported in the United States of America where a teenager accidentally ingested the water from a golf-course pond contaminated with the Anatoxin-a (ATX-a) Although the toxin was detected in his blood, the unusually long time between exposure and death (48h) raised doubts about this case (Stewart et al., 2006).

Humans are also at risk from inhaling cyanotoxins that have been aerosolized. Even though a study conducted in New Zealand found that aerosols collected for 4, 12, and 24 hours near two lakes did not pose a direct threat to humans, the aerosolized toxins did. When combined with other sources of exposure, such as the oral one, it may pose a danger (Wood and Dietrich, 2011).

Among all the existing cyanobacteria, the marine *Lyngbyamajuscula* has been shown to be highly toxic to human health. The toxins released by some harmful varieties of *L. majuscu a* have been reported to cause symptoms of rashes, blistering, skin and eye irritation. The toxic effects have been associated to the action of Lipopolysaccharide (LPS) (Stewart et al.,2006).

Exposure to cyanobacterial toxins through consumption of drinking water has also caused human poisonings. In 1990, in Australia, 140 children and 10 adults were hospitalised for liver and kidney damage after drinking copper sulphate-infested water. In 2000 cases of gastroenteritis and 88 deaths were reported and attributed to a bloom of Anabaena and Microcystis in the water supply in Brazil. In Kenya, 100 human deaths at Lake Embu, in Kenya, were attributable to cyanotoxins (Harding, 2006).

The World Health Organization (WHO) has defined some guidelines in order to protect human health form cyanobacterial blooms. In temperate zones, the chronic exposure to cyanotoxins is improbable while it is higher in areas often affected by cyanobacteria blooms. The value of 200.000 cells/ml has been fixed as a cyanobacteria density corresponding to a low probability of adverse effects.

Microcystins are mainly accumulated in the hepatopancreas of the shellfish and molluscs. The maximum concentration of MCs in the edible parts of fish, crustaceans and mussels has been reported to reach levels of 300, 2700 and 16,000mg/kg (Funari and Tastai,2008). The European Regulation No. 853/2004*indicates specific hygiene rules for the monitoring of toxins. The limit value for STX has been set at 800 mg/kg and the limit for Amnesic Shellfish Poison is 800mg (Sanseverino et al.,2017). Every year, more than 2000 cases of human poisoning through fish or shellfish consumption are reported worldwide. Saxitoxin is one of the most potent marine biotoxin. Symptoms include tingling

of the extremities to respiratory paralysis and death (Faber, 2012). It generally takes 24 hours to completely depurate the blood from the blood. The disease outcome depends on the timeliness of medical cares including artificial respiration (Sanseverino et al.,2017).

While evidence on the accumulation of MCs in livestock (sheep, cows, etc.) after ingestion of polluted water shows that no trace of cyanotoxins is present in milk or meat (Orr et al.,2003), eating meat may be another form of being exposed to cyanotoxins. In the case of vegetables, experiments using water infested with blooms or scums and used to water rice, rape, and lettuce revealed the presence of cyanotoxins in plant extracts. It's worth noting that cyanobacterial cells can be toxic (Sanseverino et al.,2017).

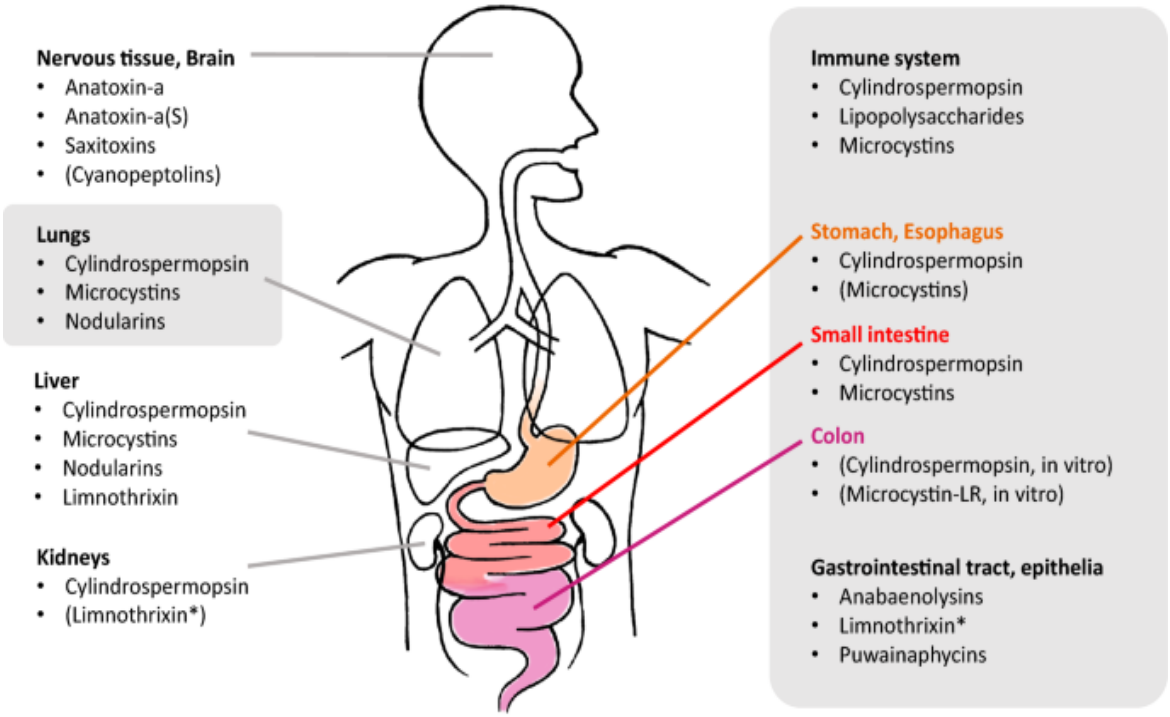

Figure 6: Organs/organ systems affected< by toxic metabolites of cyanobacteria

Organs traditionally considered targets of toxicity are on the left; organs directly subjected to oral exposure are on the right. Grey background illustrates organs with mucosal surfaces that serve as primary entry portals for environmental and dietary contaminants. The figure depicts inner organs figuratively and not anatomically correct (Kubickova et al.,2019).

2.4.2. Environmental Effects

Cyanobacterial blooms have the potential to harm aquatic ecosystems. The dense cyanobacterial blooms can form thick scums and mats, causing the bottom waters to become deoxygenated. Fish, shellfish, aquatic invertebrates, and plant populations would all suffer as a result of the lack of oxygen. Because light penetration is reduced, the blooms may have an impact on benthic fauna and flora. Toxic blooms may prevent other phytoplankton from growing by competing for sunlight and nutrients. They can also reduce the grazing of zooplankton. All of these factors cause changes in the aquatic ecosystem's community structure and composition (Quiblier et al., 2013; Zanchett& Oliveira, 2013).

Cyanobacteria blooms are linked to taste and odor problems in drinking water, in addition to the generation of toxins. Algal scums can form in shallow bays and stay together for a long period. Cells may dissolve and die during this time. The contents of the dead cells are released into the water, including poisons as well as a range of odor and taste chemicals (Danni cong,2015)

Geosmin and 2–methylisoborneol (MIB), which are not harmful but are a nuisance to the public, are two of the substances generated by blooms. Drinking water and fish have a foul odor and flavor due to odor and taste chemicals. Additionally, it will result in a loss of recreational and aquacultural revenue as well as an increase in the cost of bloom treatment (EPA,2013).

Annual cyanobacterial blooms (Fig. 07) have certain properties that have an impact on water quality, vegetation, and **(Havens, 2008).**The formation of cyanobacterial blooms therefore has consequencesharmful to water quality. The flora and fauna are found to be completely modified since, for example, the growth of plants is no longer allowed (due to the turbidity of the water) and that certain blooms produce toxins with the effectsallelopathic (refers tocompounds produced by a plant which has positive or negative consequences on other plants). In addition, the fish in the lake eventually die due to the lack of dissolved oxygen in the lake. Water (hypoxia then anoxia) when the density of cyanobacterial flowering becomes very high (which we find at the level of the “Bloom collapse” (Fig. 07).In addition, the blooms disrupt human activities since they cause

problems in the extraction and treatment of lake water. They also have impacts on agriculture and fishing, and they prevent recreational activities (swimming, boating, sailing, etc.) **(Sigee, 2005).**

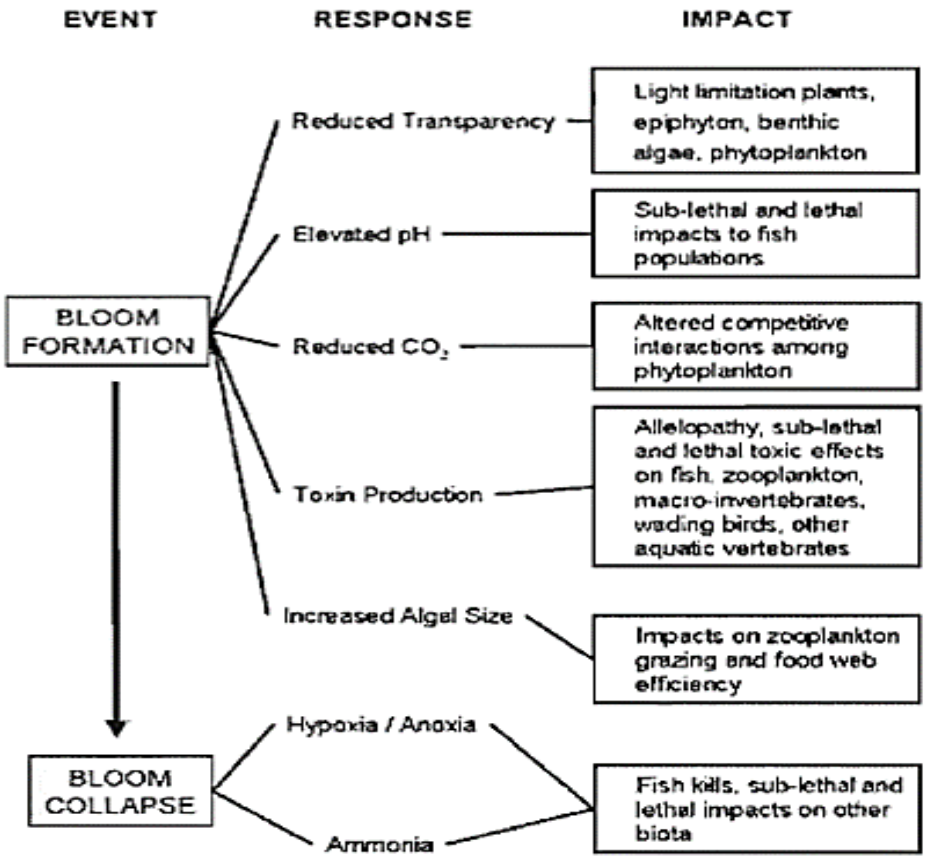

Figure 07**:** Consequences associated with the formation of cyanobacterial blooms **(Havens, 2008)**

The potential changes caused by microcystins on zooplankton populations could cause a dietary imbalance for the upper trophic compartments and increase their stress, cyanobacteria influence the structure and distribution of zooplankton communities, potentially through a negative effect on the abundance of zooplankton and their filtration rate **(Vincent 1989).**

The ecological nuisances linked to the production of Cyanobacteria toxins could affect all links in the ecosystem, namely zooplankton, green algae, plants and fish as well

as humans who consume products capable of accumulating these toxins**(Saqrane et *al.*, 2007).**

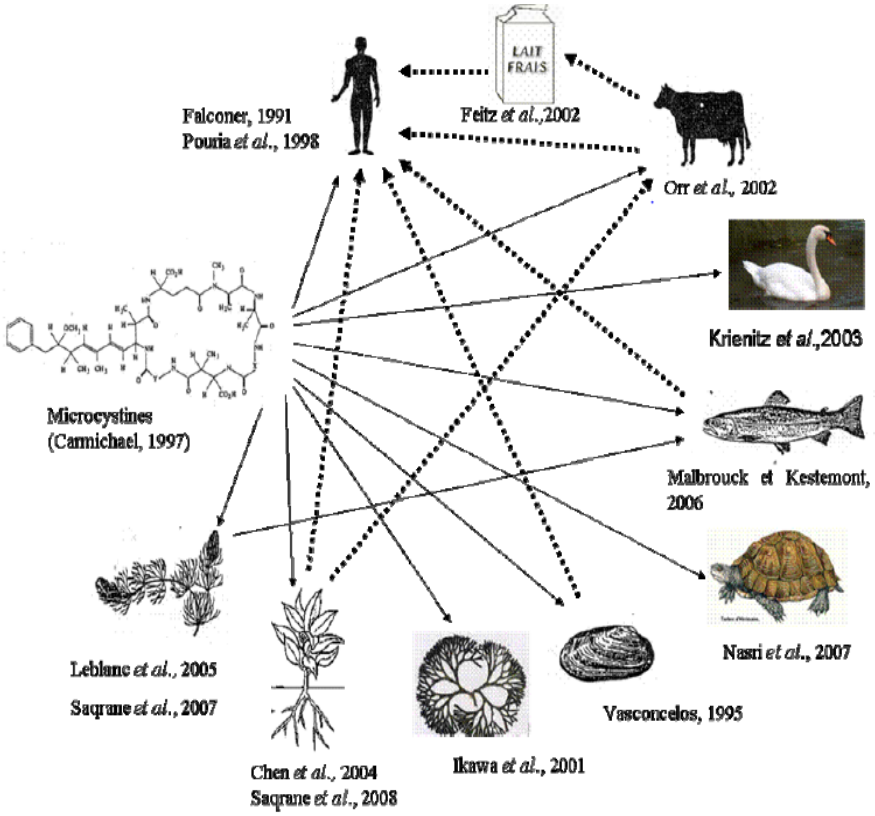

Figure 08**:**Diagram of the effect of cyanotoxins on different organisms in the environment **(Saqrane et *al.*, 2007).**

Routes of exposure reported in the literature

Routes of exposure that are not yet scientifically confirmed

Chapter 3:

Removal of toxic Cyanobacteria processes

3.1. Cyanobacterial Cells RemovalProcesses

A healthy cyanobacterial cell can have high levels of toxin – or taste and odor compounds – confined within its walls. Dissolved toxin is not removed by conventional treatment technologies. The most effective way to deal with high total toxin concentrations is to remove the cells intact and without damage. Any damage may lead to toxin leakage, and an increase in dissolved toxin entering the treatment plant (GWRC,2009).

Removal of intact cells and associated intracellular toxin should be the primary aim in the treatment of cyanobacteria. Most water treatment processes are designed to remove particulate material (GWRC,2009).

3.1.1. Pre-Oxidation

Pre-oxidation is not recommended in the presence of potentially-toxic cyanobacteria. The risk of damaging the cells and releasing toxin into the dissolved state is high. The effect will depend on the oxidant and its reactivity with the particular cyanobacteria (Petruševski et al.,1996).

Lab tests should be carried out to determine the effect, if any, on cyanobacterial cells in the inlet to the plant. The levels of oxidant needed to meet the demand of the water including cells should be sufficient for destruction of dissolved toxins (GWRC,2009).

If insufficient oxidant is applied there is a risk of high levels of dissolved toxin and organic carbon entering the treatment plant and adversely influencing subsequent removal processes. However, this effect willdepend on the reactivity of the particular oxidant (GWRC,2009).

3.1.2. Microstaining

Microstraining is a technique that can be used to remove fine particles including algae and cyanobacteria. A microstrainer consists of a horizontally mounted, slowly rotating drum with sides of fabric. Water is fed into the center and flows out through the sides. The screenings are collected in a trough suspended towards the top of the drum

interior. They are sieved, the solids disposed of and the water returned to the inlet (GWRC,2009).

Microstraining is used to remove mineral and biological solids from surface water. It is normally used as pre-treatment before slow sand filtration or coagulation processes. It can be used as a sole treatment prior to disinfection (GWRC,2009).

3.1.3. Riverbank, Slow Sand and Biological Filtration

Riverbank filtration is a simple and effective treatment process, which is widely used in some parts of the world. Water is abstracted from rivers by using bores (wells) close by, effectively filtering the raw water through the riverbank. This process removes particulates including algae and cyanobacteria. Many soluble contaminants are also removed by adsorption or by biological processes (Grutzmacher et al., 2002).

Slow sand filtration is capable of providing a high degree of removal of algal cells and associated cyanotoxins. Biological activity within slow sand filters may also provide some removal of extracellular toxin (GWRC,2009).

3.1.4. Conventional Treatment

In a natural bloom there will probably be cells in all stages of growth. However, an optimised process will provide a very effective first barrier to toxic algae in the treatment plant. The health of the cells and the stage in the growth of the bloom will affect the success of the process. The amount of damage caused by the process depends on the number of cells and their growth stage. The effect of damage to the cells during the process depends on the type of cells involved (Chow et al., 1998).

Coagulation and Flocculation:

The coagulation mechanism must be optimized under all circumstances, but it is especially necessary during a toxic cyanobacteria bloom. The following factors play a role in achieving successful chemical coagulation and flocculation (GWRC,2009):

- ✓ The best coagulant to use and the pH factors to use.

- ✓ Good control of coagulant dose and pH is needed to maintain optimum conditions. Underdosing can produce poor floc. overdosing increases the quantity of solids for removal.
- ✓ Good mixing at the point of chemical dosing to ensure rapid.
- ✓ Optimum paddle speeds need to be determined based on performance of the subsequent treatment process.
- ✓ Avoidance of excessive floc shear after flocculation, which could result from turbulence at weirs, pipe bends or constrict.
- ✓ Laboratory jar tests used to select the best combination of coagulation chemicals and pH.

3.1.5. Sludge and Backwash Disposal

Once confined in sludge of any type, cyanobacteria may lose viability, die, and release dissolved toxin. This can occur within one day of treatment and can result in very high dissolved toxin levels. All sludge and sludge supernatant should be isolated from the plant until toxins have degraded sufficiently.*Microcystins*are readily biodegradable so this process should take 1-4 weeks (Senogles et al., 2002). *Cylindrospermopsin* appears to be slower to degrade and the biological degradation of saxitoxins and anatoxins has not yet been widely studied (GWRC,2009)

3.1.6. Membrane filtration

Membrane technologies are becoming a more feasible alternative for treating microbiologically contaminated small supplies as well as larger sources (*e.g.*, *Cryptosporidium*). Membranes used in water treatment can be divided into the following categories (GWRC,2009):

- ✓ Microfiltration (MF) membranes are used to remove small particulate content larger than 1 micron in dimension, such as Cryptosporidium and bacteria.
- ✓ Ultrafiltration (UF) membranes are used to remove colloidal particles smaller than 0.1m and organic molecules with a high molecular weight.
- ✓ Nanofiltration (NF) membranes are used to remove low-molecular-weight organics, color, and divalent ions including calcium and sulfate.

- ✓ Desalination of seawater or brackish water using reverse osmosis (RO) membranes

Generally cyanobacterial cells and/or filaments or colonies can be expected to be 1 micron in size or larger. Membranes with a pore size smaller than this will remove cyanobacterial cells. The efficiency of these membranes will also depend on the integrity of the membranes. The extent of damage to the cells will depend on the flux through the membranes, pressure and the time period between backwashes and removal of the waste streams. (Chow et al.,1997). optimisation of the processes is recommended, with frequent backwashing and isolation of the backwash water from the plant due to the risk of the cells releasing dissolved toxin (GWRC,2009).

Submerged membrane systems may offer advantages over pressurised systems for waters with high cyanobacterial concentrations. The potential for cell lysis is reduced, but this benefit may be offset by greater accumulation of cells in the membrane tanks (GWRC,2009).

3.1.7. Bio-manipulation

The term bio manipulation was coined by (Hrbáček et al,1961) and later used by Shapiro,1995. The principle is based on manipulations of a trophic ascade. The effectiveness of the top-down bio manipulation method is limited, according to some critics. The desired composition of fish populations can be achieved by harvesting non-predatory fish and by introducing predatory fish. The method can only be successful if a specific condition needs to be fulfilled for it to be effective.Most effective examples of bio manipulation apply. to relatively small water bodies because of a great difficulty to. manipulate fish populations in large ones. Bio manipulation can be performed only with the participation of a skilled limnologist. Often, the continuous maintenance is required to maintain a lake. (Lazzaro,1997).

In the case of Microcystis dominance the zooplankton grazing wrathfulis limited, mainly because of bigger colonies. The toxic effects of cyanobacteria are reported, which may also play a role in bio manipulation. Daphnids in lakes might be resistant to cyanotoxins, which could make it difficult to control cyanobacterial blooms (Nandini and Rao ,1998).

The removal of substantial amount of benthivorous fishes is strongly recommended if control of cyanobacterial blooms is the aim of lake-restoration project. The bio manipulation may reduce cyanobacterial growth via the bottom-up effect in the case of fish removal. The removal of benthvorous fishes can help to reduce the water levels in lakes and ponds (Gehrke and Harris, 1994).

3.1.8. Use of aquatic organisms

Many aquatic organisms have been considered and studied to limit potentially the cyanobacterial growth (Fig. 9). Their use is based on principles of predation, parasitism or release of metabolites suppressing cyanobacterial growth. Studies with viruses, bacteria, algae, fungi, and protozoa have been reported. However, the large-scale cultivation of many of these organisms is problematic. No successful direct applications in the whole lake scale have been reports (Erhard and Gross, 2006).

a- Herbivorous fishes: Potential method how to reduce cyanobacterial blooms is direct grazing by herbivorous fishes. Phytoplankton is the main food especially for the silver carp. Nile tilapia is known to have a low pH value in its stomach, therefore enhanced damage of ingested cyanobacteria is probable. However, studies show metabolic activity of phytoplankton after gut passage remains unaffected or even increases (Getachew,1989).

b- Virus:Cyanobacteria viruses (cyanophages) are widespread in both marine and freshwater aquatic environments. (Bergh et al.,1989; Suttle et al.,1990). They serve a crucial function in determining the presence of cyanobacteria throughout the season. Safferman and Morris reported the first evidence of viruses being used to reduce cyanobacterial blooms. (Safferman and Morris ,1964). A dramatic drop in cyanobacterial biomass has been observed, accompanied by the appearance of cyanophages. (Gons et al.,2002). A few recent researches have looked into the possibility of viruses controlling cyanobacterial growth. (Yoshida et al.,2006). However, there are a slew of issues that make using viruses in practice extremely hard. Isolation and culture of cyanophage are difficult or impossible to achieve. Because cyanobacteria have developed resistance to cyanophage, the effect will only be transitory. (Cannon et al., 1976). Furthermore, the virus is strain-specific, and it seldom affects cyanobacteria from other locations, even if the species is the same. (Waterbury and Valois ,1993). Even when viruses have wiped off a specific

cyanobacteria, other cyanobacterial species might quickly take its place. (Van Hannen et al., 1999).

c- Bacteria:Bacteria can lyse cyanobacteria via producing extracellular lytic enzymes or by direct contact. In the instance of the bacterium Alcaligenes denitrificans, lytic effects specific to bloom-forming cyanobacteria have been documented. (Manage et al.,2000). *Bacillus sp.* (Reim et al.,1974).Bdellovibrio-like bacteria (Sallal,1994), *Myxococcus sp.* (Daft et al.,1985), Flexibacterium (Gromov et al.,1972), and Pseudomonas sp. or *Spingomonas sp*. producing lytic agent Argimicin A (Imamura et al.,2000). Anabaena and *Microcystis Oscillatoria* were both killed by the actinomycete Streptomyces exfoliatus (Sigee et al.,1999). Cyanobacterial growth, photosynthesis, and metabolism are all inhibited by several extracellular compounds. The cyanobacterium *Oscillatoria williamsi* was reduced in photosynthesis and enzymatic activity by a Flexibacterium metabolite that was comparable to lysozymes. In recent years (Ahn et al.,2003). Surfactin generated by *Bacillus subtilis C1* inhibits the development of the cyanobacterium *Microcystis aeruginosa* and *Anabaenaaffinis* selectively. Similarly, a cyanobacteriolytic compound from *Bacillus cereus* has been identified, as well as its lytic activity against *Aphanizomenonflos-aquae*. *Streptomyces neyagawaensis*has been shown to lyse *Microcystis aeruginosa* (Choi et al.,2005).

d- Algae:Some planktonic algae, in addition to macrophytes, may generate allelopathic chemicals that limit cyanobacterial development (Pajdak et al.,2001).In the cyanobacterium *Microcystis aeruginosa*, extract from the dinophyte *Peridiniumbipes* produces alterations in membrane permeability.

e- Fungi:The *chytridiaceous fungusRhizophidiumplanktonicum* parasitizes a cyanobacterium (Canter et al., 1990). However, due to challenges in large-scale production, *chytridiaceous fungi* were eventually regarded to be of little benefit. Redhead and colleagues found that 62 non-chytrid fungus have particular antagonistic effects on *Anabaenaflos-aquae* and other filamentous or unicellular cyanobacteria (Kotak et al.,1990).

f- Protozoa: Protozoa play an essential role in the lowering of phytoplankton populations in aquatic ecosystems by grazing and phagocytosis (Canter et al.,1990). Predation on cyanobacteria has been shown in the case of ciliates Furgasonia (Canter et al.,1990). *Nassula* and *PseudomicrothoraxStos* (Fialkowska and Pajdak-Stos, 2002).

Amoeba (Ho and Alexander, 1974) and flagellate *Monas guttula* (Sugiura et al.,1990). Most bloom-forming cyanobacterial species, on the other hand, form colonies, which protect them against protozoan nibbling. As a result, the use of protozoa as biocontrol agents is extremely restricted and controversial.

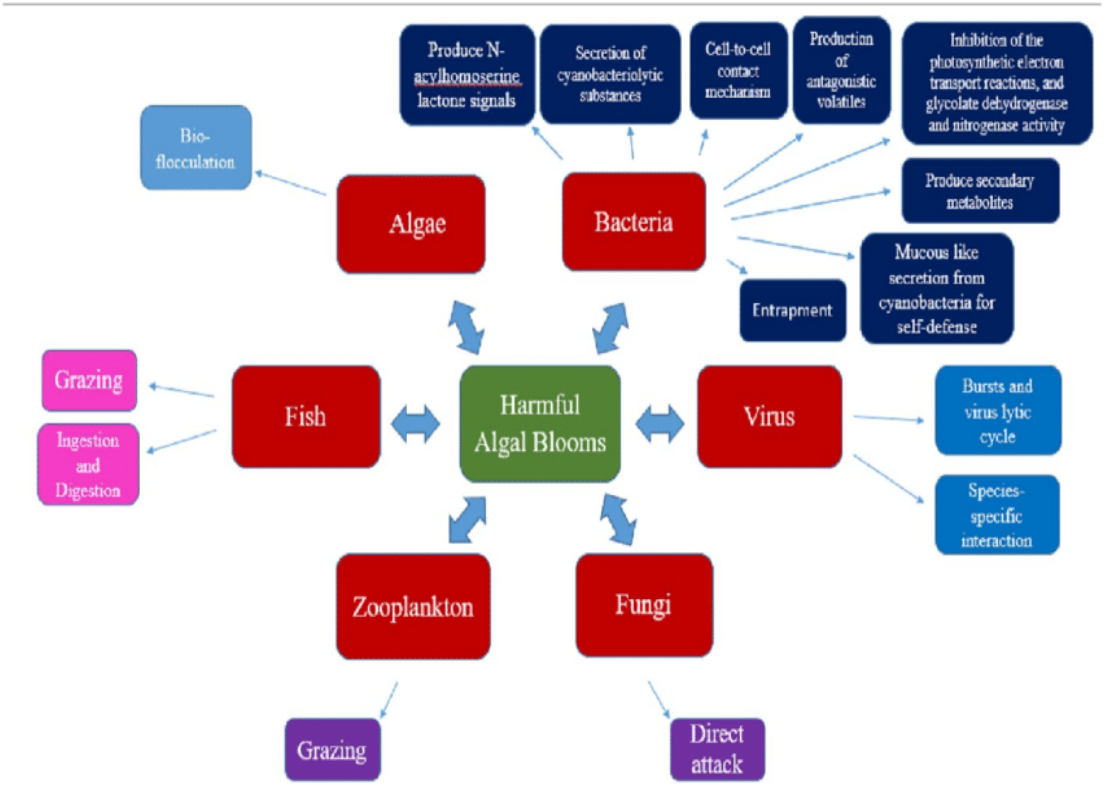

Figure 9:Interaction events of microorganism with Harmful Algal Blooms (Pal et al., 2020)

3.2. Cyanotoxins Removal processes

As previously mentioned, traditional treatments such as coagulation and others are ineffective in removing dissolved cyanotoxins. The below are the three types of water treatment systems that can be used to effectively remove dissolved toxins:

- ✓ Physical processes such as activated carbon removal and membranes.
- ✓ Chemical processessuch as chlorine, ozone, and potassium permanganate oxidation.
- ✓ Biological processes that maintain a stable biofilm include sand filtration and granular activated carbon (GAC).

3.2.1. Physical processes

a- Activated Carbon: Activated carbon is a porous material with a very high surface area. The internal surface provides the sites for the targeting contaminants such as algal toxins to adsorb. It is used extensively in water treatment for organic contaminants.Activated carbon is available in two forms, granular activated carbon (GAC) and powdered activated carbon (PAC) GAC can be added before coagulation, during chemical addition or during the settling stage. PAC is in particulate form, with particle size typically between 10 and 100mm in diameter. It is dosed as a slurry into the water, and is removed by subsequent treatment processes. It can be applied for short periods when problems arise, then stopped when it is no longer required. It cannot be reused and is disposed of with waste.

b- ***Membrane Filtration:*** Membranes are physical filtration barriers. The main factor influencing removal of microcontaminants is the size, hydrodynamic diameter, of the compound compared with the pore size distribution of the membrane. Microcystins should be rejected by reverse osmosis (RO) membranes and nanofiltration (NF) membranes. However, even RO membranes may allow the smaller toxin molecules to permeate the membrane. The crucial issues are the pores in the membrane, which should be available from the manufacturer, as well as the integrity of the membranes.

3.2.2. Chemical processes

The ability of most oxidants used in water treatment to react with cyanobacterial toxins varies depending on the type of oxidant, dosage, and composition of the toxin.

a- Chlorine:Chlorine is an oxidant that reacts with a variety of organic compounds, such as algal toxins and NOM. Hypochlorous acid (HOCl), the most reactive type of chlorine, is in contact with the hypochlorite ion (OCl^-) in water.The concentration of hypochlorous acid is dependent on the pH of the water. A small change in pH can result in a large change in the concentration of the most reactive form. The reaction of chlorine with any compound will be dependent on pH.Chlorine reacts rapidly with a range of molecules, depending on their molecular structure and susceptibility

to oxidation. Some molecules are more reactive than others and the rates of reaction between chlorine and organic compounds will depend on their structure.

b- **Chloramines:**Chloramine is a far weaker oxidant than chlorine or ozone, and only extremely strong concentrations and long contact periods have been seen to affect microcystin levels (Nicholson et al.,1994). Based on the scant evidence available for the other toxins, chloramination cannot be deemed an appropriate toxin shield.

c- **Ozone and Ozone/peroxide:**Chlorine, like ozone, is an oxidant. The formation of hydroxyl radicals is dependent on pH. High alkalinity water may maintain an ozone residual for longer, but this is at the expense of the formation of the most reactive species. When ozone is used in combination with hydrogen peroxide, the formation of Hydrogen peroxide radicals is increased, therefore the oxidising potential of the treatment is increased. The reaction can be described as a chain reaction where NOM plays a part as both an initiator and inhibitor in the chain reaction, and plays a strong role (Ho et al.,2002).

d- **Potassium Permanganate:** Potassium permanganate has been shown to reduce the concentration of Microcystins and anatoxin-a considerably (Carlile, 1994). Unfortunately, the data currently available are not sufficient to allow recommendations for dose requirements or to allow potassium to be considered as an effective barrier (Rodriguez et al.,2007).

e- **UV and UV/Hydrogen Peroxide:**Ultraviolet irradiation is capable of degrading Microcystin-LR and Cylindrospermopsin, but only at impractically high levels. As with ozone, the presence of hydrogen peroxide promotes the formation of hydroxyl radicals (Senogles et al., 2001).

f- **Hydrogen peroxide:**On its own, it is ineffective. It creates hydroxyl radicals, which are very potent oxidizing agents, when combined with ozone or UV. There is no data to make dosage recommendations.

3.2.3 Biological processes

In the past,scientists has focused on the engineering aspects of biological filtration with such assumptions as expecting that the presence of a biofilm should result in efficient

biodegradation of the cyanobacterial metabolites. Moreover, genetic technology has allowed for significant improvements in the understanding of many biodegradation processes. Consequently, further work is required to ensure that biological treatment, such as biological filtration, can be confidently applied for the removal of these metabolites. To date, only the genes responsible for microcystin degradation have been identified (Ho et al., 2012).

The advancements in molecular microbiology and genetic technology should also promote future researches in other cyanobacterial metabolites, in terms of gene discovery; however, the lack of key findings in this area to date (apart from the microcystin-degrading genes) indicates that this is not a trivial exercise. While it is evident that climate change is predicted to increase the intensity of cyanobacterial blooms and subsequently, the production of these unwanted metabolites, it is clear that climate change could also significantly influence the biological processes, which can be implemented to remove them. This conundrum should foster research into further understanding such biological processes, particularly with the recent shift away from chemical- and energy-intensive processes towards carbon and climate neutrality (Table 2) (Ho et al., 2012).

Table 2: organisms implicated in the degradation of microcystins (Ho et al., 2012)

Organisms	**Reference (s)**	***Mlr A* gene detected**
Arthrobacter sp.	Manage et al., 2009; Lawton et al., 2011	No
Brevibacterium sp.	Manage et al., 2009; Lawton et al., 2011	No
Burkholderia sp.	Lemes et al., 2008	Unknown
Methylobacillussp.	Hu et al., 2009	Unknown
Morganellamorganii	Eleuterio and Batista, 2010	Unknown
Paucibactertoxinivor	Rapala et al., 2005	Unknown
Poterioochromonassp.	Ou et al., 2005 ; Zhang et al., 2008	Unknown
Pseudomonas aeroginosa	Takenaka and Watanabe , 1997	Unknown
Ralstoniasolanacearum	Yan et al., 2004	Unknown
Rhodococcussp.	Manage et al., 2009 ; Lawton et al., 2011	No
Sphingomonassp. 7CY	Tshii et al., 2004	Unknown
Sphingomonassp. ACM-3962	Jones et al., 1994 ; Bourne et al., 1996, 2001	yes
Sphingomonassp. B9 (Sphingosinicellasp.)	Harada et al., 2004 ; Imanishi et al., 2005 ;Tsuji et al., 2006 ; Kato et al., 2007	Unknown
Sphingomonassp. CBA4	Valeria et al., 2006	Unknown
Sphingomonassp. MD-1	Saitou et al., 2003 ; Saito et al., 2003	yes
Sphingomonassp. MDB2 (Sphingosinicellasp.)	Maruyama et al., 2006	Unknown
Sphingomonassp. MBD3	Maruyama et al., 2006	Unknown

(Sphingosinicellasp.)		
Sphingomonassp. Y2 (Sphingosinicellamicrocystinivorans)	Park et al., 2001 ; Maruyama et al., 2003, 2006	Yes
Sphingopyxissp. LH21	Ho et al., 2007a, 2007d ; Hoefel et al., 2009a	Yes
Sphingopyxissp. USTB-05	Wang et al., 2010 ; Zhang et al., 2010	Unknown
Stenotrophomonassp. EMS	Chen et al., 2010a	Yes

Nodularins has been documented to be biodegraded by bacteria with the Adda amino acid shown to be a by-product (Imanishi et al., 2005; Edwards et al., 2008; Torunska et al., 2008; Mazur-Marzec et al., 2009). Many of the reported NOD-degrading organisms also have the ability to degrade microcystins (Table 3). It is believed that this may be due to the enzymes (*eg.*mlrA) acting similarly for both cyanotoxins by cleaving their cyclic structures at the Adda-Arg peptide bond (Kato et al., 2007; Edwards et al., 2008). Kato et al. (2007) and Edwards et al. (2008), provided evidence to support this contention through detection of NOD biodegradation by-products, including linear NOD (NH2-Adda-GluMdhb-MeAsp-Arg-OH).

Table 3: Organisms implicated in the degradation of nodularin (Ho et al., 2012)

Organisms	**Reference(s)**
Arthrobacter sp.	Manage et al., 2009; Lawton et al., 2011
Brevibacterium sp.	Manage et al., 2009; Lawton et al., 2011
Paucibactertoxinivorans	Rapala et al., 2005
Rhodococcussp.	Manage et al., 2009; Lawton et al., 2011
Spingomonassp. B9 (Sphingosinicellasp.)	Harada et al., 2004 ; Imanishi et al., 2005 ; Tsuji et al., 2006 ; Kato et al., 2007

Chapter 4:

Biocontrol of toxic cyanobacteria by plants

4.1. Biocontrol of Toxic Cyanobacteria by aquatic plants

In aquatic environments, seaweeds are one of the most basic and dominating creatures. Because of their capacity to create a wide range of bioactive chemicals, they may provide an eco- friendly method to Harmful cyanobacteria blooms management (Zerrif et al., 2018; Zerrifi et al.,2019).Phytoplankton blooms can be dominated by submerged macrophytes in temperate regions due to their allelopathy effect or nutrient rivalry. Indeed, underwater macrophytes can use a lot of nitrogen and phosphorous, which can be used to eradicate unwanted and dominant phytoplankton indirectly. According to the report of Vanderstukken et al. (2011), Submerged macrophytes species have a drastic negative impact on phytoplankton productivity, which has been used to regulate phytoplankton biomass for long periods of time. The negative associations between macrophytes and phytoplankton biomass have also been identified in tropical or warm regions. Any of the most effective predators, such as copepods and ciliates, are suggested biological algal bloom management methods. Submerged aquatic macrophytes and floating plants such as water lilies and lotus are used to limit direct sunlight in the pond and regulate algal growth.

Macrophyte, as a rooted plant, can minimize sediment resuspension caused by wind or boat, provide a safe haven for daphnia that graze algae, and provide shade to keep the water cool in the littoral areas. Macrophytes can also deplete nutrients and produce allelopathic chemicals that inhibit cyanobacteria development (Drabkova and Marsalek, 2007). However, there are a few factors that go against this. For example, lakes are resistant to nutrient load reduction, but even though nutrient loads are significantly decreased, water quality may not improve (Cooke et al.,2005). Second, wave motion, light restriction, animals consuming the plants, and dormant seeds can all obstruct macrophyte development. (Drabkova and Marsalek, 2007). Finally, the macrophyte can only dominate shallow lakes, where the colonized macrophyte can theoretically engulf the entire region. The macrophyte impact is confined in deep lakes with narrow littoral areas (Cooke et al.,2005).

Aquatic plants have mostly a positive effect on the removal of nutrients such as total nitrogen (TN), ammonia (NH^{4+}), total phosphorus (TP) (Table 4) and orthophosphate (PO_4^{3-}) (Table 5) in water by restraining the release of nutrients from sediment and adsorbing nutrients from water and sediment (Wang et al., 2014).

Table 4: Nitrogen removal efficiency (%) by aquatic plants in water bodies (Wang et al., 2014).

Location	**Plants**	**Removal efficiency (%)**			**References**
		TN	**NO^{3-}**	**NH^{4+}**	
Australia	*Phragmites australis*	16.00	-	62.00	SUN and AUSTIN, 2007
China	*Acorus calamus* *Cyperus flabelliformis* *Canna indica* *Iris tectorum* *Scirpusvalidus*	46.00-68.00 53.00-76.00 49.00-67.00 36.00-53.00 46.00-61.00	-	-	MEI et al.,2014
Germany	*Phragmites australis*	48.00-93.80		74.00-93.70	LUEDERITZ et al., 2001
Mauritius	*Eichhorniacrassipes* *Hydrocotyle umbellataPistiastratiotes*			99.60 99.00 99.20	SOOKNAH and WILKIE, 2004
Korea	*Trapajaponica*	80.00-99.00			IAMCHATURAPATR et al., 2007
Taiwan Island	*Ipomoeaaquatica*	74.49-94.93			KO et al., 2011
USA	*Scirpuscalifornicus*	19.00-31.00	60.00-88.00	40.00-62.00	CHANG et al., c2012
USA	*Ipomoeaaquatica*		84.00	38.00	NAHLIK and MITSCH, 2006

Table 5: Phosphorus removal efficiency (%) by aquatic plants in water bodies (Wang et al., 2014)

Location	**Plants**	**Removal efficiency (%)**				**References**
		TP	**TDP**	**PP**	**PO43--P**	
Australia	*Phragmites australis*				17.00	SUN and AUSTIN, 2007
China	*Ceratophyllumdemersum* *Elodea canadensis* *Myriophyllum spicatum* *Vallisneria spiralis*	91.75 84.71 68.29 84.63	90.93 86.09 71.36 89.51	97.92 87.20 49.47 54.69		GAO et al., 2009
	Acorus calamus *Cyperus flabelliformis* *Canna indica* *Iris tectorum* *Scirpusvalidus*	27.30-47.60 40.50-62.50 37.80-59.50 21.80-34.50 27.10-46.00				MEI et al., 2014
Germany	*Phragmites australis*	60.50-95.80	74-93.70	74-93.70		LUEDERITZ et al., 2001
Mauritius	*Eichhorniacrassipes* *Hydrocotyle umbellata* *Pistiastratiotes*	98.50 71.30 64.20			96.50 60.90 48.50	SOOKNAH and WILKIE, 2004
Korea	*Trapajaponica*	81.00-97.00				IAMCHATURAPATR et al., 2007
USA	*Scirpuscalifornicus*	39.00-62.00			40-67	CHANG et al., 2012
	Ipomoeaaquatica				83.00	NAHLIK and MITSCH, 2006

Macrophytes are crucial for stabilizing the clear water state in shallow, mesotrophic and eutrophic lakes, as they can reduce the microalgalgrowth (Hilt et al., 2006b). The involved mechanisms includelight shading, sediment resuspension, nutrients competition and allelopathy(Mulderij et al., 2007b). In the allelopathic way, macrophytessustainably excrete algae-inhibiting allelochemicals to ambient environment,resulting in reductions of phytoplankton biomass (Parket al., 2006). The typical macrophytes with their derived

allelochemicalsthat have been proven to be effective on microalgae inhibition areelucidated in Table 6.

Utilization of allelopathy to inhibit microalgal growth can beachieved by cultivating aquatic plants directly (Declerck et al., 2007). But aiming to overcome the above disadvantages in cultivating plants,direct addition of allelochemicals for HABs control has been proposed,and large amount of allelochemicals have been purified, identified,manufactured, and even artificial synthesized, such as gramine, pyrogallol,gallic acid, ellagic acid and (+)-catechin (Hong and Hu, 2007,2008b, 2009; Zhu et al., 2010). Despite the lack of practical cases andrelevant experience, direct addition of purified allelochemicals is muchsimpler than cultivating aquatic plants.

Table 6: Typical aquatic allelopathic plants with algistatic or algicidal effects (Zhu et al., 2021)

Categories	**Species**	**Allelochemicals**	**Re**
Emergent macrophyte	*Arundo donax*	Gramine	(Hong
	Elodea nuttallii	Apignin,caffeic acid, luteolin,nonanoic acid, N-phenyl-1-naphtylamine,	(Gao et 2015 ;H al.,201
	Oryza sativa	b-Sitosterol-b-D-glucoside,diclohexanylorizane, fumaric acid,p-coumaric acid, salicylic acid, vanillic acid	(Park e al.,200
	Nelumbo nucifera	Apignin,isoquercitrin,linoleic acid, palmitic acid p-coumaric acid,hydroxybenzoic acid(PHBA),protocatevhuic acid, quercetin ,stearic acid	(Dong Huang Park et al.2006 ,2019 ; et al.,2
Floating macrophyte	*Phragmites australis*	Ethyl 2-methylacetoacetate(EMA)	(Men e
	Stratiotesaloides	Choline,luteolin	(Conra al.,200
	Zantedeschiaspp	α-lineleic acid, lineleic acid	al.,200
	AlternantheraPhiloxeroides	Coumarin,p-aminobenzene-sulfonic acid, p-hydroxybenzoic acid Protocatechuic acid ,stearic acid	(Della e (Zuo et
		1-Linoleoyl-glycerol,lineleicacid,nonanoic acid, N-phenyl-2-	

	crassipe	naphthylamine,propionamide.	(Liu et
	Nymphaea tetragona	Apignin,ellagicacid,gallic acid, kaempherol,p-coumaric acid,quercetin,vanillic acid	(Huang al.,201 al.,201
Submerged macrophyte	*Pistiastratiotes*	Luteolin ,palmitic acid	(Liu et
	CeratophyllumDemersum	α-Linolenic acid, azelaic acid, butenoic,hexanoicacid,octanedioicacid,palmiticacid,pentanedioicacid,phthalic acid	(Dong
	Chara	Hexadecanoic acid 9,12-octadecadienoic acid ,tetradecanoic acid Caffeic acid, ferulic acid,protocatechuic acid,	(Zhang
	Hydrillaverticillata	nonanoic acid,pyrogallol,tellimagrandin 2	(Gao et
	Myriophyllum spicatum	α-Asarone,phenylpropanoidglucosides,hydrolysable tannins	(Leu et
	MyriophyllumVerticillatum	Caffeic acid, ferulic acid,protocatechuic acid. 2-Ethyl-3-methylmaleimide,3-hyfroxy-5,6-epopxy-β-innone,4-oxo –β-ionone,loliolide,dihydroactinidiolide,6-hydroxy-3-oxo-a-ionone	al.,200 Hosom et al.,2
	Vallisneria natans		(Aliotta al.,199
	Vallisneria spiralis		(Gao et
			(Xian e

The brown edible seaweed *Undaria pinnatifida* EO obtained from the Korean shore has this unsaturated fatty acid as one of the primary components (22.39 %). Palmitic acid is abundant in this product (9.2 % and 16.57%) (Petra et al.,2017; Petra et al.,2015). EOs of *Porphyratenera*and *Laminaria japonica* were used. The EO composition of *Cystoseira*genus seaweed species other than *C. tamariscifolia* has already been reported(Ozdemir et al.,2006).

The brown seaweed *C.barbata* EO (Cystoseira genus) contains many chemicals distinct from those found in *C.tamariscifolia*EO, including docosane (7.61%), tetratriacontane (7.47%), eicosane (5.05%), tricosane (4.43%), hexadecane (4.16%), and heptadecan Furthermore, 1-chloro-2,2-diethoxyethane (21.5%), 2,3-butanediol (6.5%), chloroacetic acid (3.7%), and 1,1-dichloro-2,2-diethoxyethane (2%), were found in the volatile compounds composition of C. crinite (Cystoseira genus) collected from the eastern Mediterranean(Kamenarska et al.,2002).Nonetheless, it's worth noting that research into the chemical makeup of seaweed EOs

is still in its infancy. The polyunsaturated fatty acid eicosapentaenoic acid (8%) was the most prominent element in the chemical makeup of the green macroalgae *U. lactuca* EO.

Other polyunsaturated fatty acids found in the Dictyopterispolypodioides EO obtained from the Algerian coast were cis- and trans-5,8,11,14-eicosatetraenoic acids (Riad et al.,2020). Some terpenes, such as -caryophyllene (0.02 %) and -pinene (0.015%), were only discovered in trace levels, whilst others, such as dihydroactinidiolide (6.6–7.8%), -Ionone (not detected to 7.6%), and phytol (0.23–4.1 %), were discovered in larger concentrations. Safranal and other terpenes have recently been discovered in the essential oil produced from the brown algae D. polypodioides (Riad et al.,2020). Similarly, the terpenic chemicals dihydroactinidiolide, -Ionone, and phytol have been found in marine algae earlier (Gressler et al.,2009). Aside from terpenes, a variety of other chemicals were found in low levels, including alcohols, aldehydes, and ketones. Gressler et al. (2009), indicated that marine algae may create a wide range of metabolites, including hydrocarbons, terpenes, fatty acids, esters, alcohols, aldehydes, and ketones (Gressler et al.,2009).

The green m**ac**roalgae *U. lactuca* showed no inhibitory action against the Gram-negative bacteria M. aeruginosa in a qualitative screening utilizing the paperdisk diffusion technique insolid medium (Zerrifi et al.,2019). Researchers looked into the anti-cyanobacterial properties of a methanolic extract of *U. lactuca*.

Ulva seaweeds of the genus *Ulva* did not show antibacterial activity against any assayed Gram-negative bacteria. *U. lactuca* extract also did not have an effect against *M. aeruginosa* (Salvador et al.,2007).

Marine macroalgae EOs are potential producers of anti-cyanobacteria compounds. They should be subject to a comprehensive study as natural sources of bioactive substances, say researchers. Further research will need to be conducted using other seaweeds and/or phytoplankton species in macrocosms and natural field conditions (Zerrifi et al.,2020).

Figure 10: *Ulvalactuca(*Ingrediënten | Collagen Lift Paris)

Figure 11: *Sargassum nuticum(*Sargassum muticum - Nobanis)

Figure12:*Cystoseriatemariscifolia*(www.marlin.ac.uk)

4.2.Biocontrol of toxic Cyanobacteria by terrestrial plants

Direct addition of extracted allelochemicals can break through therestraint on macrophytes, as several terrestrial plants were also provenwith abundant antialgal alleleochemicals, as shown in Table 2. The ideaof utilizing terrestrial plants in HABs control was come out from thephenomenon that mi-croalgal biomass in the limnic ecosystem was significantly lower than that in the natural aquatic ecosystem, attributedto existence of defoliation in the limnic ecosystem (Tsuda et al.,2005). The proposal for inhibiting microalgal growth by terrestrialplants broadened the margin of allelopathy application in HABs control.

density of 100 g/L in terms of fresh weight, while the 50 % of effectiveconcentration (EC50) of those polyphenolic-allelochemicals were0.65–5.5 mg/L on M. aeruginosa (Nakai et al., 2000). Even so, such aconcentration level at mg/L was not yet marked with toxicities on otheraquatic organisms, like the brine shrimp (Artemia franciscana) and giantriver prawn (Macrobrachiumrosenbergii) (Defoirdt et al., 2013).

Benefitfrom the high biodegradability of allelochemicals (Steinmetz et al.,2019), the effects of residual allelochemicals on the drinking watertreatment were negligible. Allelochemicals with concentration lowerthan 10 mg/L could be dissipated without disposal in 30 days, such as Llysineand gramine, by either photo-assimilation or biodegradation(Canton et al., 2019; Kaya et al., 2005).

4.2.1. Barley straw use and efficiency

Through manufacturing allelochemicals from plants, many uselessplants or organs turned to be useful, such as barley straw (Fig. 14) (Xiao et al.,2014), an algae-inhibitor proven with 90 % of reduction on algalgrowth over 3 years under an in-situ condition in Chesterfield Canalbetween Shireoaks and Thorpe Salvin (Welch et al., 1990).Though the effective dosages of direct addition of allelochemicalswere much higher than the environmentally relevant concentrations(Hilt et al., 2006a; Zhu et al., 2010), rare obvious deleterious ecologicaleffects were observed (Welch et al., 1990). For example, the polyphenolicsreleased by *M. spicatum* were 5.2–76.6 μg/L with a plant

Figure 13: Barley straw application (http://www.clearwaterplm.co.uk)

Since the early 1990s, the use of decomposing barley straw for the management of algae and cyanobacteria has sparked a lot of attention and research (Welch et al., 1990; Newman and Barrett 1993, Jelbart, 1993; Barrett et al., 1996). Both green algae and cyanobacteria have been found to exhibit algistatic effects in lab investigations. The release of phenolic chemicals such as ferulic acid and p - coumaric acid from the degradation of straw cell walls have been

postulated aspossible explanations for the observed effects, including the generation of antibiotics by the fungal flora responsible for the decomposition (Newman and Barrett 1993).

While reservoir testing with barley straw seemed to back up these lab findings (Barrett et al. 1996, Everall and Lees 1996) Other experiments yielded no discernible impact (Jelbart 1993, Cheng et al. 1995). More recent studies have validated the efficacy of barley straw treatment for in situ therapy, with one case study observing a shift in algal populations from cyanobacteria to diatoms (Islami&Filizadeh 2011). In another, it was suggested that this may be a viable strategy in larger lakes in the US (Haggard et al. 2013).

Barley straw is utilized in numerous reservoirs and dams in the United Kingdom with good results due to its low cost and ease of application. The use and mechanism of the impact of barley straw for the management of algae in a variety of water bodies is detailed in a fact sheet issued by the Centre for Hydrology and Ecology's Centre for Aquatic Plant Management (2004) in the United Kingdom. Algae growth suppression is thought to be caused by DOC from barley straw generating hydrogen peroxide in the water (Rajabi et al.,2010).

To utilize straw efficiently, you must first have a basic understanding of how the process works. When barley straw is placed in water, it begins to decompose, and a chemical is generated during this process that prevents algae development. Rotting is a microbiological process that is temperature sensitive, with summer being quicker than winter. When the water temperature is below 10°C, it may take 6-8 weeks for straw to become active, but just 1-2 weeks when the water temperature is over 20°C. Algal growth will continue unabated throughout this time. Once the chemical is released, the straw will continue to emit it until it has nearly fully dissolved. The length of this interval varies depending on the temperature and the way the straw is applied; we'll go over this in more depth later. Straw, on the other hand, is likely to remain active for around six months, after which it will progressively diminish in activity (Rajabi et al.,2010).

Although the specific method by which straw inhibits algae has yet to be determined, we believe the following is how it works. Chemicals in the cell walls of straw degrade at varying rates when it rots. Lignins are quite persistent, and when the other components decompose, they will likely stay and be discharged into the water. Lignins can be oxidized to humic acids and

other humic compounds if there is enough oxygen in the water. These humic substances are found in many waterways naturally, and it has been demonstrated that when sunlight falls on water with dissolved oxygen and humic compounds, hydrogen peroxide is generated. Low amounts of peroxide are known to limit algae development, and tests have shown that low concentrations of hydrogen peroxide can have an impact on algae that is very similar to that of straw. Peroxides are highly reactive chemicals that only persist a short period in water.However, When humic substances are present, peroxides are continually produced anytime enough sunshine is available. Because the straw decomposes slowly, humic chemicals are constantly available to catalyse this process (Rajabi et al.,2010).

This idea is supported by a number of elements that influence the performance of straw. To guarantee that algal issues are successfully treated using straw, several aspects must be considered.

The volume of the water does not appear to affect the performance of the straw as might be expected. The majority of algal growth takes place in the surface layers of water and so it is not necessary to measure the depth of the lake when calculating the quantity of straw.

In still waters such as lakes, ponds and reservoirs, the minimum quantity of straw is about 10g straw m-2 of water surface. However, when a water body with a history of severe algal problems is first treated, a higher dose is preferable. quantities up to 100 g m- 2 have been used(Rajabi et al.,2010).

the quantity of straw needed can vary considerably and it is better to apply too much initially and then to reduce the quantity gradually each time straw is added until the dose has been reduced to 10g m-2 or until algal growth starts to increase again when the dose should be increased to a previously effective level.

There is a theoretical level at which straw could cause problems by deoxygenating the water. This is caused by the microorganisms which colonise the straw and absorb oxygen. Deoxygenation is often caused by algal blooms and so the presence of straw can reduce the risk of this. However, straw should not be applied during prolonged periods of hot weather as the combined oxygen demand from the algal bloom and the straw could temporarily increase the risk

The risk of causing deoxygenation in flowing waters is very small. The distance between straw masses has usually been between 30-50m. The size of each straw mass was chosen, for convenience, as about one bale (20kg).

The best way of applying straw varies with the size and type of water body. Straw should be applied in a loose form, either in gabions or as straw sausages. In slow flowing water, bales should not normally be used as they are too tightly packed and do not allow adequate water movement through the straw. It is preferable to apply the straw in a loose form retained in some form of netting or cage.

In all instances, it is essential to ensure that the straw container is well anchored to the bank or to stakes in the bottom which will hold it in place during periods of high flow. The best way to prevent the straw from becoming anaerobic is to use small bales (around 20kg) and to keep oxygen levels high in the straw high. The most appropriate methods for different types of water bodies are given below.

Applying multiple modest amounts of straw to a water body rather than one huge one is always preferred. This enhances the active factor distribution throughout the water body. Straw works best when held close to the surface, where the most water flow occurs. This helps to oxygenate the straw and disseminate the anti-algal chemical. This also guarantees that the chemical is created near where the majority of the algae are growing and away from the bottom dirt, which would render the chemical inactive. When determining where to lay the straw in a water body, keep the following factors in mind:

- ✓ When only a single net of straw is necessary in small ponds, it should be positioned in the center of the pond. The straw net should be set where there is a continuous flow of water over and through the straw if there is an incoming flow of water, such as a stream or fountain. This will assist to oxygenate the straw and disperse the chemical throughout the pond.
- ✓ In any still body of water, the anti-algal chemical will diffuse outwards in all directions from each net of straw, slowly being absorbed by algae and inactivated by mud until the concentration is too low to be effective. Algal development will continue unabated beyond this distance, and these algae will eventually drift back into the treated regions,

creating the impression that the straw is ineffective. It is crucial to determine how much straw is required, how many nets should be used, and how far apart each net should be in order to ensure that no sections inside the water body are untouched by the straw. The straw nets or sausages should then be put in such a way that each net is about equidistant from its neighbors and the bank.

- ✓ -There hasn't been much study done with straw in seawater, therefore any treatments done in these settings should be considered experimental. Straw appears to function in both salt and fresh water, according to results from a small number of testing in salt water lagoons and artificial pools. However, due of the limitations of short persistence time and exposure, it is highly doubtful that it would have any effect on the huge marine algae commonly seen on rocky coasts or kelp beds in the oceans. It's also improbable that enough straw could be deposited and retained in the open sea for lengthy periods of time.

Although straw may be put at any time of year, it is most beneficial when applied before to the onset of algal bloom. This is due to the fact that the anti-algal chemicals produced by the straw are more effective at preventing algal development than they are at killing existing algae. As a result, when the water temperature is low, straw is best sprayed in the autumn, winter, or very early spring. Within one month, the straw will become active and will continue to suppress algal development for roughly six months. However, after the straw has rotted away, fast algal growth can occur, thus more treatments should be done every 6 months.

It is important to note that the rate at which straw rots varies greatly, so keep an eye on it and make regular inspections so that new straw may be put before the conclusion of the six-month period if required. Because it is not always feasible to forecast when an algal issue will arise, it is occasionally required to address one that has already arisen. By adding straw to existing blooms, some algae, primarily tiny unicellular species and cyanobacteria (blue-green algae), can be reduced.

The length of time it takes to manage the algae is determined by a variety of elements, the most important of which is the water temperature. Straw has been shown to be efficient in suppressing algal blooms in water temperatures over 20°C within 4-5 weeks, and occasionally even quicker. Applying straw during lengthy periods of hot weather may raise the danger of

deoxygenation due to the combined effect of dying algae and decomposing straw. The process is slower at lower temperatures, and it may take 8 to 10 weeks to control the algae, although the risk of deoxygenation is negligible(Rajabi et al.,2010).

When filamentous algae are the major issue, straw applied to dense floating mats will have little effect unless it is supplemented with additional treatments that will be discussed later. Additional applications will be necessary after the initial straw treatment to keep the algae from returning. Although a 6-month gap is advised as the most likely time between straw treatments, more frequent treatments may be required. Waiting until all of the straw has decayed before applying a second dose is not recommended since there will be a period when no chemical is generated and rapid algae growth can occur. For the same reason, the old straw should be left in place for at least one month after the new straw is added. This gives the new straw time to become active.

Once filamentous algae have created floating mats, straw is ineffective in controlling them. Other measures, on the other hand, can be used to control them. Filamentous algae can be brushed out in some cases. Many shards, however, will remain in the water, and fast regeneration is expected. Straw should be placed approximately a month before the alga is scraped out to prevent this(Rajabi et al.,2010).

4.2.2. Use of Eucalyptus

In a very interesting work realized by Xu et al. (2020), an iron oxide nanoparticle-zeolite hybrid (EL-MNP@zeolite) was green synthesizedusing eucalyptus leaf extract (Fig. 15) and the factors affecting theremoval efficiency of ammonium and phosphate ions determined..EL-MNP@zeolite was synthesized using green syntheticmethods, where iron nanoparticles were successfully decoratedonto zeolite. Zeolite not only plays the role of an inorganiccarrier to improve the dispersion of iron nanoparticles and preventagglomeration and oxidation, but it also provides adsorption sitesfor NH4 + ions and promotes the simultaneous removal of NH4 + -PO4 3_. The removal efficiency was positively correlated with theamount of adsorbent, but when the pH of the reaction solutionwas between 4.00 and 10.00, the adsorption effectwas reduced.The removal efficiencies of NH4 + and PO4 3_ were 43.3% and 99.8%,respectively. Adsorption of NH4 + and PO4 3_ was exothermic andlow temperature was favorable for the

simultaneous removal ofboth NH4 + and PO4 3_ by EL-MNP@zeolite. The adsorption of NH_4^+-PO_4^{3-}ontoEL-MNP@zeolite was via chemical adsorption, whichwas consistent with the good fit to the pseudo-second-orderkinetics.

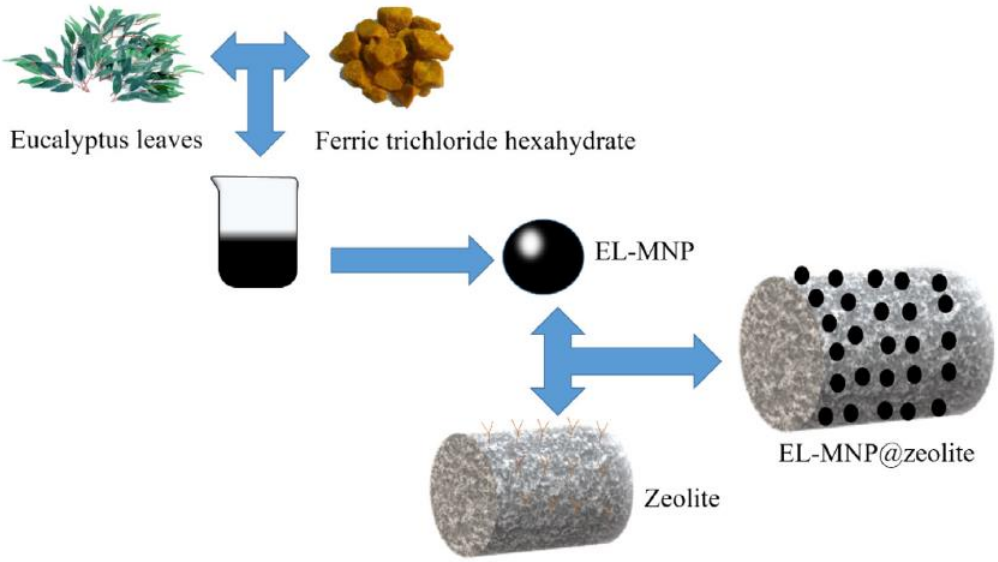

Figure 14: Synthesized mechanism of El-MNP@zeolite (Xu et al., 2020)

4.2.3. Other terrestrial plants

The table 7 gathers other terrestrial plants that were proved to have allelochemicals with efficiency in the biocontrol of harmful algae.

Table 7: Typical terrestrial allelopathic plants with algistatic or algicidal effects (Zhu et al., 2021)

Categories	Species	Allelochemicals	References
Herbaceous plants	*Allium sativum*	Diallyl trisulfide.	(Zhou et al.,2008)
	Artemisia vulagaris	1,2-Benzenedicaboxylic acid,hexanedioic acid Butanedioic acid, 2,4-bis-hydroxy butanoic acid, 9-cis-octadecenoic	(Choe and Jung,2002)
	Canna generalis	acid,dodecanoicacid,hexadecanoic acid,2-hydroxyheptanoic acid, 4-hydroxybenzoic acid, 3-methoxy-4- hydroxybenzoic acid ,3-methoxy-4-hydroxycinamic acid,octadenoicacid,protocatechuic acid	((Zhou et al.,2019)
	Chelidonium majus	Berberine,cheleryhtrince,chelirubine,coptisine,magnoflorine,protopine,sanguinarine	(Jancula et al.,2007)
	Coptis chinensis	Berberine,coptisine,jatrorrhizine,palmatine	(Zhang,2011)
	Cyperus alternifolius	1,2-Bezenedicarboxylic acid2,6-bis(dimethylethyl)-4-methyl phenol ,butanedioicacid, 9-cis- octa-decenoicacid ,2,3-dihyfroxy propanoicacid,dodecanoicacid,hexadecanoicacid ,2-hydroxyheptanoic acid, 4-hydroxybenzoic acid,tetra/octa-decanoicacid	(Zhou et al.,2019)
	Dicranostigma	Cheleryhtrine,chelirubine, magnoflorine,protopine,sanguinarine	(Jancula et al.,2007)
	Hordeum vulgare	Acetophenone,benzaldehyde,benzoicacid, benzyl cyanide, 2,6-dimethoxy phenol,heptanoicacid,hexanoicacid,hydrocinnamicacid ,2-methylbutanoic acid, 3-methylbutanoic acid,2-pjenyl-phenol-p-cresol,salcolins,trans-cinnamic acid	(Murray et al.,2010 ;Xiao et al.,2014)
Ligneous plants	*Lanceatibetica*	5,4-Dihydroxyflavone	(Huang et al.,2015)
	Macleaya microcarpa	Allocryptopine,cheleryhtrine,chelirubine,macarpine,protopine,sanguinarine	(Jancula et al.,2007)
	Polygonatum odoratum	L-Azetidinecarboxylicacid	(Kim et al.,2006)
	Salvia miltiorrhiza	Przewaquinone A	(Zhang et al.,2013
	Sanguinaria Canadensis	Cheleryhtrine,chelirubine,chelilutine,sanguinarine,sanguirubine,sanguilutine	(Jancula et al.,2007)
	Spartina alterrniflora	Cyclohexane , 2-cyclohexen-1-one,hexadecanoic, heptane,hydrocinnamic acid	(Yuan et al.,2010)
	Camellia	Epicatechin-3-gallate,epigallocatechin-3-gallate	(Lu et al.,2013)

	sinensis Cinnamomum camphora	Camphor,linalool,a-terpineol	(Chen et al.,2018)
	Dracontomelon Duperreanum	1,3-bis-1,1-dimethylethyl-benzene,cis-vaccenic acid, 5-dodecene , n-hexadecanoicacid,octadecanoic acid,9-octadecenamide,oleic acid	(Wang et al.,2018b)
	Ficus microcarpa	2-Propyl phenol	(Jiang et al.,2014)
	Latanacanara	LantadeneA ,Lantadene B	(Kong et al.,2006
	Litchi chinensis	n-Hexadecanoic acid	(Wang et al2018a)
	Magnolia Grandiflora	Cglestan-3-ol, 1-heptatriacotanol,2-H-cyclohepta(b)furan-2-one,mono-2-ethyl-phthalate , 9,10-secocholesta-5,7,10(19)-3,25,26-triol	(Li ,2009)
	Salix babylonica	Ethyl 4-hydroxy cinnamate,ethyl 4-hydoxy -3-methoxycinnamate,methyl 3-oxo-(2-pentenyl)-cyclopentaneacetate,methyl 4-hydroxycinnamate,palmitic acid	(Jiang et al.,2013)

In this work, we tried to gather scientific researches concerning toxic cyanobacteria especially removal biological processes using both aquatic and terrestrial plants and explain mechanisms of removal.The key points are as follows:

- Both aquatic and terrestrial are used in toxic cyanobacteria biocontrol;
- Removal of nutrients from aquatic bodies using macrophytes is one of HABs removal mechanisms;
- Allelopathic application is a promising strategy to control HABs. Asa method inspired by nature phenomena, the effectiveness of allelochemicalson inhibiting microalgae cells has been discovered andconfirmed for many years;
- Both planting macrophytes and adding extracted allelochemicalswere effective for introducing inhibition effects on microalgae cells.
- The sensitivities of microalgal species upon allelochemicals weresignificant different and *M. aeruginosa* was widely confirmed as themost sensitive microalgal species to allelochemicals.

We propose as perspectives to explore more aquatic and terrestrial plants because it is one of the most eco-friendly benign methods. In fact, biocontrol of toxic cyanobacteria by plants, as well as the removal of cyanotoxins released by toxic cyanobacteria in water, is today recognized as one of the most significant concerns that the world confronts.

1. Ahn CY, Joung SH, Jeon JW, Kim HS, Yoon BD, Oh HM. Selective control of cyanobacteria by surfactincontaining culture broth of Bacillus subtilis C1. Biotechnology Letters 2003b; 25:1137-1142.
2. Anderson D.M. Kulis D.M. Sullivan J.J. Hall S. Lee C. (1990) Dynamics and physiology of saxitoxin production by the dinoflagellates Alexandrium spp. Mar. Biol.104, 511–524.
3. AndersonD,M,(2009).Approaches to monitoring, control, and management of harmful algal blooms (HABs). Ocean Coast Manag, 52(7): 342
4. Banack, S. A., Caller, T. A. &Stommel, E. W. The cyanobacteria derived toxin Beta-Nmethylamino-L-alanine and amyotrophic lateral sclerosis. Toxins (Basel) 2, 2837-2850, doi:10.3390/toxins2122837 (2010).
5. Bergh O, Borsheim KY, Bratbak G, Heldal M. High abundance of viruses found in aquatic environments. Nature 1989; 340:467-468.
6. Bibak, M., and Hosseini, S. A. (2013). Review ways to control harmful algal bloom (HAB). World J Fish Mar Sci, 5, 42-44.
7. Blaha, L., Babica, P. &Marsalek, B. Toxins produced in cyanobacterial water blooms - toxicity and risks. InterdiscipToxicol 2, 36-41, doi:10.2478/v10102-009-0006-2 (2009).
8. Blais S., 2001. Cyanobacterias issue in Missisquoibay 2001, profile.Agrosol. 13 (2): 103-110.
9. Boopathi, T. & Ki, J. S. Impact of environmental factors on the regulation of cyanotoxin production. Toxins (Basel) 6, 1951-1978, doi:10.3390/toxins6071951 (2014).
10. Bourne, D.G., Jones, G.J., Blakeley, R.L., Jones, A., Negri, A.P., Riddles, P., 1996. Enzymatic pathway for the bacterial degradation of the cyanobacterial cyclic peptide toxin microcystin LR. Applied & Environmental Microbiology 62, 4086-4094.
11. Bourne, D.G., Riddles, P., Jones, G.J., Smith, W., Blakely, R.L., 2001. Characterisation of a gene cluster involved in bacterial degradation of the cyanobacterial toxin microcystin LR. Environmental Toxicology 16, 523-534.
12. Cannon RE, Shane MS, Whitaker JM. Interaction of Plectonemaboryanum (Cyanophyceae) and the LPPcyanophages in continuous culture, J Phycol.1976. 12:418-421.
13. Canter HM, Heaney SI, Lund JWG. The Ecological Significance of Grazing on Planctonic Populations of Cyanobacteria by the Ciliate Nassula. New Phytol 1990; 114:247-263.
14. Carlile P.R. (1994) Further studies to investigate microcystin-LR and anatoxin-a removal from water. Foundation for Water Research Report, FR 0458, Swindon, UK.
15. Chang X X, Wu C, Zhao J. Advance of allelopathic inhibitory effects of aquatic macrophytes on algae and its application. In: Duan C Q ed. Advance in Ecological Science. Beijing: Higher Education Press, 2007, 3: 147–174.

16. Chen, J., Hu, L.B., Zhou, W., Yan, S.H., Yang, J.D., Xue, Y.F., Shi, Z.Q., 2010a. Degradation of microcystin-LR and RR by a Stenotrophomonas sp. strain EMS isolated from Lake Taihu, China. International Journal of Molecular Sciences 11, 896-911
17. Chen, T. et al. Identification of human liver mitochondrial aldehyde dehydrogenase as a potential target for microcystin-LR. Toxicology 220, 71-80, doi:10.1016/j.tox.2005.12.001 (2006).
18. Choi HJ, Kim BH, Kim JD, Han MS. Streptomyces neyagawaensis as a control for the hazardous biomass of Microcystis aeruginosa (Cyanobacteria) in eutrophic freshwaters. Biological Control 2005; 33(3):335-343
19. Chorus I, Bartram J. (Eds.) Toxic Cyanobacteria in Water: A Guide to their Public Health Consequences, Monitoring and Management. WHO & E & FN Spon, London, 1999.
20. Chorus, I. Current Approaches to Cyanotoxin Risk Assessment, Risk Management and Regulations in Different Countries. (2012).
21. Chow C.W.K., House J., Velzeboer R.M.A., Drikas M., Burch M.D. and Steffensen D.A. (1998). The effect of ferric chloride flocculation on cyanobacterial cells. Water Research, 32(3): 808-814.
22. Chow C.W.K., Panglisch S., House J., Drikas M., Burch M.D. and Gimbel R. (1997) A study of membrane filtration for the removal of cyanobacterial cells. Journal of Water Supply: Research and Technology – Aqua, 46(6): 324-334.
23. Cooke GD, Welch EB, Peterson SA, Nichols SA. Restoration and Management of Lakes and Reservoirs. 3rd edition. Editor - Cooke, G.D., Taylor an Francis, Boca Raton, Florida, 2005, 591
24. Cooke, G. D., Welch, E. B., Peterson, S. A., Nichols, S. A . (2005). Restoration and Management of Lakes and Reservoirs (G. D. Cooke, Taylor a Francis, Boca Raton Ed. 3rd ed.). Florida.
25. Cooke, G. D., Welch, E. B., Peterson, S. A., Nichols, S. A. (2005). Restoration and Management of Lakes and Reservoirs (G. D. Cooke, Taylor a Francis, Boca Raton Ed. 3rd ed.). Florida.
26. Couté A., Bernard C., 2001. Les cyanobactéries toxiques, in: Frémy J.M., Lassus P. (Coord.), Toxines d'algues dans l'alimentation, Ed. Ifremer, Paris, 2001, pp. 89–108.
27. Daft MJ, Burnham JC, Yamamoto Y. Lyses of Phormidiumluridum by Myxococcus fulvus in continuous flow cultures, J Appl. Bacter. 1985; 59:73-80.
28. Dietrich, D. R., Ernst, B. & Day, B. W. 132 (In: 7th International Conference on Toxic Cyanobacteria (ICTC), Brazil, 2007).
29. Dittmann, E., Fewer, D. P. &Neilan, B. A. Cyanobacterial toxins: biosynthetic routes and evolutionary roots. FEMS MicrobiolRev 37, 23-43, doi:10.1111/j.1574-6976.2012.12000.x (2013).
30. Drabkova, M., &Marsalek, B. (2007). A review of in-lake methods of cyanobacterial blooms control and management. The Glogal Database of Methods for Cyanobacterial

Blooms Management. Retrieved September, 1st, 2014, from http://www.cyanodata.net/review.php.

31. Drabkova, M., &Marsalek, B. (2007). A review of in-lake methods of cyanobacterial blooms control and management. The Glogal Database of Methods for Cyanobacterial Blooms Management. Retrieved September, 1st, 2014, from http://www.cyanodata.net/review.php
32. Durai, P., Batool, M. & Choi, S. Structure and Effects of Cyanobacterial Lipopolysaccharides. Mar Drugs 13, 4217-4230, doi:10.3390/md13074217 (2015).
33. Edwards, C., Graham, D., Fowler, N., Lawton, L.A., 2008. Biodegradation of microcystins and nodularin in freshwaters. Chemosphere 73, 1315-1321.
34. Eleuterio, L., Batista, J.R., 2010. Biodegradation studies and sequencing of microcystin-LR degrading bacteria isolated from a drinking water biofilter and a fresh water lake. Toxicon 55, 1434-1442.
35. EPA. California Environmental Protection Agency. Microcystins. A brief overview of their toxicity and effects, with special reference to fish, wildlife, and livestock. (2009).
36. EPA. United States Environmental Protection Agency. Cyanobacteria and Cyanotoxins: Information for Drinking Water Systems. EPA-810F11001. (2014).
37. Erhard D, Gross EM. Allelopathic activity of Elodea canadensis and Elodea nuttallii against epiphytes and phytoplankton. Aguatic Botany 2006; 85:203-211.
38. Faber, S. Saxitoxin and the induction of paralytic shellfish poisoning. Journal of Young Investigators (2012).
39. Falconer IR. An overview of problems caused by toxic blue green algae (cyanobacteria) in drinking and recreational water. Environ. Toxicol 1999; 14:5-12.
40. Falconer IR. An overview of problems caused by toxic blue green algae (cyanobacteria) in drinking and recreational water. *Environ.Toxicol* .1999; 14:5-12.
41. Fawell, J. K., James, C. P. & James, H. A. Toxins from blue-green algae: toxicological assessment of microcystin-LR and a method for its determination in water. Marlow, UK: Foundation of Water Research (Report No. FR 0359/2/DoE 3358/2) (1994).
42. Fawell, J. K., Mitchell, R. E., Everett, D. J. & Hill, R. E. The toxicity of cyanobacterial toxins in the mouse: I Microcystin-LR. Human Exp Toxicol 18, 162-167 (1999).
43. FEMS Microbiology Ecology, Volume 35, Issue 1, March 2001, Page vii,
44. Fialkowska E, Pajdak-Stos A. Dependence of cyanobacteria defense mode on grazer pressure. Aquatic Microbial Ecology 2002; 27:149-157.
45. Fischer, W. J. et al. Organic anion transporting polypeptides expressed in liver and brain mediate uptake of microcystin. Toxicol Appl Pharmacol 203, 257-263, doi: 10.1016/j.taap .2004.08.012 (2005).
46. Funari, E. &Testai, E. Human health risk assessment related to cyanotoxins exposure. Crit Rev Toxicol 38, 97-125, doi:10.1080/10408440701749454 (2008).
47. Gantar M, JP Berry, S Thomas, ML Wang, R Perez, KS Rein. Allelopathic activity among Cyanobacteria and microalgae isolated from Florida freshwater habitats. FEMS Microbiology Ecology 2008; 64:55-64.

48. Gaysinski, M.; Ortalo-Magné, A.P.; Thomas, O.; Culioli, G. Extraction, purification, and NMR analysis of terpenes from brown algae. In Natural Products from Marine Algae: Methods and Protocols; Humana Press: New York City, NY, USA, 2015; pp. 207–223. ISBN 9781493926848
49. Gehrke PC, Harris JH. The role of fish in cyanobacterial blooms in Australia. Aust. J Mar. Freshwater Res. 1994; 45:905-915.
50. Getachew T. Stomach pH, feeding rhythm and ingestion rate in Oreochromis-Niloticus L. (Pisces, Cichlidae) in Lake Awasa, Ethiopia. Hydrobiologia 1989b; 174:43-48.
51. Glazer AN. Structure and molecular-organization of photosynthetic accessory pigments of cyanobacteria and red algae. Molecular and Cellular Biochemistry 1977; 18:125-140.
52. Gons HJ, Ebert J, Hoogveld HL, van den Hove, L Pel, Woldringh CJ. et al. Observations on cyanobacterial population collapse in eutrophic lake water. Antonie Van Leeuwenhoek International Journal of General and Molecular Microbiology. 2002; 81:319-326
53. Gressler, V.; Colepicolo, P.; Pinto, E. Useful strategies for algal volatile analysis. Curr. Anal. Chem. 2009, 5, 271–292.
54. Gromov BV, Ivanov OG, Mamkaeva KA, Avilov IA. The Flexibacteriumlyzing Blue-Green Algae. Microbiological 1972; 41:1074-1079.
55. Grutzmacher G., Bottcher G., Chorus I., et al (2002) Removal of microcystins by slow sand filtration. Environmental Toxicology, 17(4): 386-394.
56. Harada, K.-I., Imanishi, S., Kato, H., Masayoshi, M., Ito, E., Tsuji, K., 2004. Isolation of Adda from microcystin-LR by microbial degradation. Toxicon 44, 107-109.
57. Harding, W. R. A research strategy for the detection and management of algal toxins in water sources. (Water Research Commission of South Africa (TT 277/06), 2006).
58. Ho L., Gaudieux A.-L., Fanok S., Newcombe G. and Humpage A.R. (2007) Bacterial degradation of microcystin toxins in drinking water eliminates their toxicity. Toxicon, 50(3): 438-441.
59. Ho L., Newcombe G., Croue J.P. (2002) Influence of the character of NOM on the ozonation of MIB and geosmin. Water Research, 36(3): 511-518.
60. Ho L., Sawade E., Newcombe G. Biological treatment options for cyanobacteria metabolite removal e A review. Water Research. 46 (2012) 1536-1548
61. Ho TS-S, Alexander M. The feeding of amebae on algae in culture, J Phycol. 1974; 10:95-100.
62. Ho, L., Gaudieux, A.-L., Fanok, S., Newcombe, G., Humpage, A.R., 2007a. Bacterial degradation of microcystin toxins in drinking water eliminates their toxicity. Toxicon 50, 438-441.
63. Ho, L., Hoefel, D., Saint, C.P., Newcombe, G., 2007c. Degradation of microcystin-LR through biological sand filters. Practice Periodical of Hazardous, Toxic, and Radioactive Waste Management 11, 191-196.

64. Hoefel, D., Adriansen, C., Bouyssou, M., Saint, C.P., Newcombe, G., Ho, L., 2009a. Development of an mlrA gene-directed TaqMan PCR assay for quantitative assessment of microcystindegrading bacteria within water treatment plant sand filter biofilms. Applied & Environmental Microbiology 75, 5167-5169
65. Hrbáček J, Dvořáková M, Kořínek V, Procházková L. Demonstration of the effect of the fish stock on the species composition of zooplankton and the intensity of metabolism of the whole plankton association. Verh. Intern. Ver. Limnol 1961; 14:192-195.
66. Hu L, Yang Z, Pan X, Zhao N, Peng J, Wan, C. (2017). Use of fish species from different trophic levels to control algae and water quality: An enclosure experiment in eutrophic area of Xiaojiang River. PLoS ONE 12(3): e0171953. doi:10.1371/ journal. pone.0171953.
67. Hu, L.B., Yang, J.D., Zhou, W., Yin, Y.F., Chen, J., Shi, Z.Q., 2009. Isolation of a Methylobacillussp that degrades microcystin toxins associated with cyanobacteria. New Biotechnology 26, 205-211.
68. IARC. Cyanobacterial peptide toxins (2006).
69. Imamura N, Motoike I, Noda M, Adachi K, Konno A, Fukami H. Argimicin A, a novel anti-cyanobacterial compound produced by an algae-lysing bacterium. Journal of Antibiotics. 2000; 53:1317-1319.
70. Imanishi, S., Kato, H., Mizuno, M., Tsuji, K., Harada, K.-I., 2005. Bacterial degradation of microcystins and nodularin. Chemical Research in Toxicology 18, 591-598.
71. Jakubowska, N. &Szelag-Wasielewska, E. Toxic picoplanktonic cyanobacteria--review. Mar Drugs 13, 1497-1518, doi:10.3390/md13031497 (2015).
72. Jarvenpaa, S. et al. Effects of microcystins on broccoli and mustard, and analysis of accumulated toxin by liquid chromatography-mass spectrometry. Toxicon 49, 865-874, doi: 10.1016/j.toxicon.2006.12.008 (2007).
73. Jeffrey, A. M. &Liskamp, R. M. Computer-assisted molecular modeling of tumor promoters: rationale for the activity of phorbol esters, teleocidin B, and aplysiatoxin. Proc Natl Acad Sci U S A 83, 241-245 (1986).
74. Jia, Y., Han, G., Wang, C., Guo, P., Jiang, W., Li, X., &Tian, X. (2010). The efficacy and mechanisms of fungal suppression of freshwater harmful algal bloom species. Journal of hazardous materials, 183(1-3), 176-181.
75. Jones, G.J., Bourne, D.G., Blakeley, R.L., Doelle, H., 1994. Degradation of the cyanobacterial hepatotoxin microcystin by aquatic bacteria. Natural Toxins 2, 228-235.
76. Kamenarska, Z.; Yalçin, F.N.; Ersöz, T.; Çali¸s, I.; Stefanov, K.; Popov, S. Chemical composition of CystoseiracrinitaBory from the Eastern Mediterranean. Z. Nat. 2002, 57, 584–590.
77. Kato, H., Imanishi, S.Y., Tsuji, K., Harada, K.-I., 2007. Microbial degradation of cyanobacterial cyclic peptides. Water Research 41, 1754-1762.
78. Kolmakov VI, Gladyshev MI. Growth and potential photosynthesis of cyanobacteria are stimulated by viable gut passage in crucian carp. Aquatic Ecology 2003; 37:237-242.

79. Kotak BG, S Semalulu, DL Fritz, EE Prepas, SE Hrudey, RW Coppock. Hepatic and renal pathology of intraperitoneally administered microcystin-LR in rainbow trout (Oncorhynchus mykiss). Toxicon 1996; 34:517-525.
80. Kull T.P.J., Backlund P.H., Karlsson K.M. (2004) Oxidation of the cyanobacterial hepatotoxin microcystin-LR by chlorine dioxide: Reaction kinetics, characterization, and toxicity of reaction products. Environmental Science & Technology, 38(22): 6025-6031.
81. Lawton, L.A., Welgamage, A., Manage, P.M., Edwards, C., 2011. Novel bacterial strains for the removal of microcystins from drinking water. Water Science & Technology 63, 1137-1142.
82. Lazzaro X. Do the trophic cascade hypothesis and classical bio manipulation approaches apply to tropical lakes and reservoirs.Verh. Int. Verein, Limnol 1997; 26:719-730.
83. Lemes, G.A.F., Kersanach, R., Pinto, L.S., Dellagostin, O.A., Yunes, J.S., Matthiensen, A., 2008. Biodegradation of microcystins by aquatic Burkholderia sp. from a South Brazilian coastal lagoon. Ecotoxicology and Environmental Safety 69, 358-365
84. Lobner, D., Piana, P. M., Salous, A. K. & Peoples, R. W. Beta-N-methylamino-L-alanine enhances neurotoxicity through multiple mechanisms. Neurobiol Dis 25, 360-366, doi: 10.1016/j.nbd.2006.10.002 (2007).
85. Lukac M. Aegerter R. (1993) Influence of trace metals on growth and toxin production of Microcystis aeruginosa. Toxicon31, 293–305.
86. Manage PM, Kawabata Z, Nakano S. Algicidal effect of the bacterium Alcaligenes denitrificans on Microcystis spp. Aquatic Microbial Ecology 2000; 22:111-117
87. Manage, P.M., Pathmalal, M., Edwards, C., Singh, B.K., Lawton, L.A., 2009. Isolation and identification of novel microcystin-degrading bacteria. Applied & Environmental Microbiology 75, 6924-6928.
88. Maršálek B, Bláha L, Turánek J, Neča J. Microcystin-LR and total microcystins in cyanobacterial blooms in the Czech Republic In Cyanotoxins Occurrence, Causes, Consequences (ISBN 3-540-64999-9), I. Chorus, ed., pp. Springer-Verlag, Berlin, Germany 2001; 56-62:1993- 2000.
89. Maršálek B, Bláha L, Turánek J, Neča J. Microcystin-LR and total microcystins in cyanobacterial blooms in the Czech Republic In Cyanotoxins Occurrence, Causes, Consequences (ISBN 3-540-64999-9), I. Chorus, ed., pp. Springer-Verlag, Berlin, Germany 2001; 56-62:1993- 2000.
90. Maruyama, T., Kato, K., Yokoyama, A., Tanaka, T., Hiraishi, A., Park, H.-D., 2003. Dynamics of microcystin-degrading bacteria in mucilage of Microcystis. Microbial Ecology 46, 279-288.
91. Maruyama, T., Park, H.-D., Ozawa, K., Tanaka, Y., Sumino, T., Hamana, K., Hiraishi, A., Kato, K., 2006. Sphingosinicellamicrocystinivorans gen. nov., sp. nov., a microcystin-degrading bacterium. International Journal of Systematic and Evolutionary Microbiology 56, 85-89.

92. Matsunaga, S., Moore, R. E., Niemczura, W. P. & Carmichael, W. W. Anatoxin-a(s), a potent anticholinesterase from Anabaena flos-aquae. J Am Chem Soc 111, 8021-8023 (1989).
93. Mazur-Marzec, H., Torunska, A., B1o nska, M.J., Moskot, M., Plinski, M., Jako ´bkiewicz-Banecka, J., We˛grzyn, G., 2009. Biodegradation of nodularin and effects of the toxin on bacterial isolates from the Gulf of Gdansk. Water Research 43, 2801-2810.
94. McComas, S. (2004). Lake and pond management guidebook. Lewis publishers.
95. Merel, S. et al. State of knowledge and concerns on cyanobacterial blooms and cyanotoxins. Environment International 59, 303-327, doi:http://dx.doi.org/10.1016/j.envint.2013.06.013 (2013).
96. Mur LR, Skulberg OM, Utkilen H. (edit.) Cyanobacteria in the environment. in: Chorus, I., Bartram, J. (edit.): Toxic cyanobacteria in water. WHO & E & FN SPON. London and New York, 1999, 15-40.
97. Nandini S, Rao TR. Somatic and population growth in selected cladoceran and rotifer species offered the cyanobacterium Microcystis aeruginosa as a food. Aquatic Ecology 1998; 31:283-298.
98. NHMRC Australian Drinking Water Guidelines (2004). Information sheet 1. Disinfection http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/adwg_11_06_info_sheets.pdf
99. Nicholson B.C., Rositano J. and Burch M.D. (1994) Destruction of cyanobacterial peptide hepatotoxins by chlorine and chloramine. Water Research, 28(6): 1297-1303.
100. Nierzwicki-Bauer S., Balkwill L., Stevens Jr., 1983. Three-dimensional ultrastructure of a unicellular cyanobacterium. *The Journal of cell biology*, *97*(3), 713-722.
101. Oh H.-M. Lee S.J. Jang M.-H. Yoon B.-D. (2000) Microcystin production by Microcystis aeruginosa in a phosphorous-limited chemostat. Appl. Environ. Microbiol.66, 176–179.
102. Ohta, T. et al. Nodularin, a potent inhibitor of protein phosphatases 1 and 2A, is a new environmental carcinogen in male F344 rat liver. Cancer Res 54, 6402-6406 (1994).
103. Orr P.T. Jones G.J. (1998) Relationship between microcystin production and cell division rates in nitrogen limited Microcystis aeruginosa cultures. Limnol. Oceanogr.43, 1604–1614.
104. Orr, P. T., Jones, G. J., Hunter, R. A. & Berger, K. Exposure of beef cattle to sub-clinical doses of Microcystis aeruginosa: toxin bioaccumulation, physiological effects and human health risk assessment. Toxicon 41, 613-620 (2003).
105. Ou, D.Y., Song, L.R., Gan, N.Q., Chen, W., 2005. Effects of microcystins on and toxin degradation by Poterioochromonas sp. EnvironmentalToxicology 20, 373-380.

106. Ozdemir, G.; Horzum, Z.; Sukatar, A.; Karabay-yavasoglu, N.U. Antimicrobial activities of volatile components and various extracts of Dictyopterismembranaceae and Cystoseirabarbata from the coast of Izmir, Turkey. Pharm. Biol. 2006, 44, 183–188.
107. Pajdak-Stos A, Fialkowska E, Fyda J. Phormidiumautumnale (Cyanobacteria) defenses against three ciliate grazer species. Aquatic Microbial Ecology 2001; 23:237-244.
108. Park, H.-D., Sasaki, Y., Maruyama, T., Yanagisawa, E., Hiraishi, A., Kato, K., 2001. Degradation of cyanobacterial hepatotoxin microcystin by a new bacterium isolated from a hypertrophic lake. Environmental Toxicology 16, 337-343.
109. Patra, J.K.; Das, G.; Baek, K. Chemical composition and antioxidant and antibacterial activities of an essential oil extracted from an edible seaweed, Laminaria japonica L. Molecules 2015, 20, 12093–12113.
110. Patra, J.K.; Lee, S.; Park, J.G.; Baek, K. Antioxidant and antibacterial properties of essential oil extracted from an edible seaweed Undaria pinnatifida. J. Food Biochem. 2017, 41, e12278.
111. Patra, J.K.; Lee, S.-W.; Kwon, Y.-S.; Park, J.G.; Baek, K.-H. Chemical characterization and antioxidant potential of volatile oil from an edible seaweed Porphyratenera (Kjellman, 1897). Chem. Cent. J. 2017, 11, 34.
112. Pearson, L., Mihali, T., Moffitt, M., Kellmann, R. &Neilan, B. On the chemistry, toxicology and genetics of the cyanobacterial toxins, microcystin, nodularin, saxitoxin and cylindrospermopsin. Mar Drugs 8, 1650-1680, doi:10.3390/md8051650 (2010)
113. Petruševski B., van Breemen A.N. and Alaerts G. (1996) Effect of permanganate pre-treatment and coagulation with dual coagulants on algae removal in direct filtration. Journal of Water Supply: Research and Technology – Aqua, 45(5): 316-326.
114. Pflugmacher S. Possible allelopathic effects of cyanotoxins, with reference to microcystin-LR, in aquatic ecosystems. Environmental Toxicology 2002; 17:407-413.
115. Rapala J. Sivonen K. (1998) Assessment of environmental conditions that favour hepatotoxic and neurotoxic Anabaena spp. strains in culture under light-limitation and different temperatures. Microb. Ecol.36, 181–192.
116. Rapala J. Sivonen K. Lyra C. Niemelae S.I. (1997) Variation of microcystins, cyanobacterial hepatotoxins, in Anabaena spp. as a function of growth stimuli. Appl. Environ. Microbiol.63, 2206–2212.
117. Rapala, J., Berg, K.A., Lyra, C., Niemi, R.M., Manz, W., Suomalainen, S., Paulin, L., Lahti, K., 2005. Paucibactertoxinivorans gen. nov., sp. nov., a bacterium that degrades cyclic cyanobacterial hepatotoxins microcystins and nodularin. International Journal of Systematic and Evolutionary Microbiology 55, 1563-1568.
118. Regulation (EC) No 853/2004 of the European Parliament and of the Council of 29 April 2004 laying down specific hygiene rules for on the hygiene of foodstuffs.
119. Reim RL, Shane MS, Cannon RE. The characterization of a Bacillus capable of blue-green bactericidal activity. Can. J Microbial. 1974; 20:981-986.

120. Riad, N.; Zahi, M.R.; Trovato, E.; Bouzidi, N.; Daghbouche, Y.; Utczás, M.; Mondello, L.; El Hattab, M. Chemical screening and antibacterial activity of essential oil and volatile fraction of Dictyopterispolypodioides. Microchem. J. 2020, 152, 104415.
121. Rodriguez E., Onstad G.D., Kull T.P.J. (2007) Oxidative elimination of cyanotoxins: Comparison of ozone, chlorine, chlorine dioxide and permanganate. Water Research, 41(15): 3381-3393.
122. Rogers, E. H. et al. Potential developmental toxicity of anatoxin-a, a cyanobacterial toxin. J Appl Toxicol 25, 527-534, doi:10.1002/jat.1091 (2005).
123. Safferman RS, Morris ME. Control of algae with viruses. J Am. Water Works Assoc. 1964; 56:1217-1224.
124. Saito, T., Okana, K., Park, H.-D., Itayama, T., Inamori, Y., Neilan, B.A., Burns, B.P., Sugiura, N., 2003. Detection and sequencing of the microcystin LR-degrading gene, mlrA, from new bacteria isolated from Japanese lakes. FEMS MicrobiologyLetters 229, 271-276.
125. Saitou, T., Sugiura, N., Itayama, T., Inamori, Y., Matsumura, M., 2003. Degradation characteristics of microcystins isolated bacteria from Lake Kasumigaura. Journal of Water Supply: Research and Technology - AQUA 52, 13-18.
126. Saker M.L. Neilan B.A. Griffiths D.J. (1999) Two morpholgical forms of Cylindrospermopsisraciborskii (cyanobacteria) isolated from Solomon dam, Palm Island, Queensland. J. Phycol.35, 599–606.
127. Sallal AKJ. Lyses of cyanobacteria with Flexibacter spp. Isolated from domestic sewage. Microbios 1994; 77:57- 67.
128. Salvador, N.; Garreta, A.G.; Lavelli, L.; Ribera, M.A. Antimicrobial activity of Iberian macroalgae. Sci. Mar. 2007, 71, 101–113
129. Sanseverino, I., Conduto, D., Pozzoli, L., Dobricic, S. &Lettieri, T. Algal bloom and its economic impact. Report No. EUR 27905 EN, (2016).
130. Senogles P., Smith M. and Shaw G. (2002) Physical, chemical and biological methods for the degradation of the cyanobacterial toxin, cylindrospermopsin. In Proceedings of the Water Quality Technology Conference, November 10-14, 2002, Seattle, Washington, USA.
131. Senogles P.-J., Scott J.A., Shaw G. and Stratton H. (2001) Photocatalytic degradation of the cyanotoxin cylindrospermopsin, using titanium dioxide and UV irradiation. Water Research, 35: 1245-1255.
132. Shapiro J. Lake restoration by bio manipulation-a personal view. Environ. Rev 1995; 3:83-93.
133. Sigee DC, Glenn R, Andrews MJ, Bellinger EG, Butler RD, Epton HAS et al. biological control of cyanobacteria: principles and possibilities. Hydrobiologia 1999; 396:161- 172.

134. Sivonen K. Jones G. (1999) Cyanobacterial toxins. In: Toxic Cyanobacteria in Water. A Guide to their Public Health Consequences, Monitoring and Management (Chorus I. Bartram J., Eds.), pp. 41–111. E and FN Spoon, London.
135. Sivonen, K. & Jones, G. Cyanobacterial toxins. In: Chorus I, Bartram J, editors. Toxic cyanobacteria in water: a guide to their public health consequences, monitoring and management. London, UK: E & FN Spon. 41-111 (1999).
136. Stewart, I. et al. Epidemiology of recreational exposure to freshwater cyanobacteria--an international prospective cohort study. BMC Public Health 6, 93, doi:10.1186/1471-2458-6- 93 (2006).
137. Stewart, I., Schluter, P. J. & Shaw, G. R. Cyanobacterial lipopolysaccharides and human health - a review. Environ Health 5, 7, doi:10.1186/1476-069X-5-7 (2006).
138. Stewart, I., Webb, P. M., Schluter, P. J. & Shaw, G. R. Recreational and occupational field exposure to freshwater cyanobacteria--a review of anecdotal and case reports, epidemiological studies and the challenges for epidemiologic assessment. Environ Health 5, 6, doi:10.1186/1476-069X-5-6 (2006).
139. Su, Z., Sheets, M., Ishida, H., Li, F. & Barry, W. H. Saxitoxin blocks L-type ICa. J Pharmacol Exp Ther 308, 324-329, doi:10.1124/jpet.103.056564 (2004).
140. Sugiura N, Inamori Y, Sudo R, Ouchiyama T, Miyoshi Y. Degradation of blue green alga, Microcystis aeruginosa by Flagellata, Monas guttula. Environmental Technology 1990; 11:739-746
141. Sun, R., Sun, P., Zhang, J., Esquivel-Elizondo, S., and Wu, Y. (2018). Microorganisms-based methods for harmful algal blooms control: a review. Bioresource technology, 248: 12-20.
142. Suttle CA, Chan AM, Cottrell MT. Infection of phytoplankton by viruses and reduction of primary productivity. Nature 1990; 347:467-469.
143. Takenaka, S., Watanabe, M.F., 1997. Microcystin LR degradation by Pseudomonas aeruginosa alkaline protease. Chemosphere 34, 749-757
144. Torunska, A., Bolałek, J., Plinksi, M., Mazur-Marzec, H., 2008. Biodegradation and sorption of nodularin (NOD) in finegrained sediments. Chemosphere 70, 2039-2046
145. Tsuda, K., Takamura, N., Matsuyama, M., Fujii, Y., 2005. Assessment method for leaf litters allelopathic effect on cyanobacteria. J. Aquat. Plant Manage. 43, 43–46.
146. Tsuji, K., Asakawa, M., Anzai, Y., Sumino, T., Harada, K.-I., 2006. Degradation of microcystins using immobilized microorganism isolated in an eutrophic lake. Chemosphere 65, 117-124.
147. Utkilen H. Gjolme N. (1995) Iron-stimulated toxin production in Microcystis aeruginosa. Appl. Environ. Microbiol.61, 797–800.
148. Valeria, A.M., Ricardo, E.J., Stephan, P., Alberto, W.D., 2006. Degradation of microcystin-RR by Sphingomonas sp. CBA4 isolated from San Roque reservoir (Co´ rdoba - Argentina). Biodegradation 17, 447-455.

149. Van Hannen EJ, Zwart G, van Agterveld MP, Gons HJ, Ebert J, Laanbroek HJ. Changes in bacterial and eukaryotic community structure after mass lyses of filamentous cyanobacteria associated with viruses. Applied and Environmental Microbiology 1999; 65:795- 801

150. Vanderstukken, M., Mazzeo, N., Van Colen, W., Declerck, S.A.,andMuylaert,K.(2011). Biological control of phytoplankton by the subtropical submerged macrophytes Egeria densa and Potamogetonillinoensis: a mesocosm study. Freshwater Biology, 56(9), 1837-1849.

151. Walsby AE. Gas vesicles. Microbiological Reviews 1994; 58:94-144.

152. WANG C., ZHENG S., WANG P., QIAN J. Effects of vegetations on the removal of contaminants in aquatic environments:A review. Journal of Hydrodinamics. 2014, 26(4):497-511

153. Wang, J., Wu, P., Chen, J., Yan, H., 2010. Biodegradation of microcystin-RR by a new isolated Sphingopyxis sp. USTB-05. Chinese Journal of Chemical Engineering 18, 108-112.

154. Wang, Y., Liu, Q., Wei, Z., Liu, N., Li, Y., Li, D., Jin, Z., Xu, X., 2018c. Thiazole amides, a novel class of algaecides against freshwater harmful algae. Sci. Rep. 8 (1), 8555.

155. Waterbury JB, Valois FW Resistance to co-occurring phages enables marine Synechococcus communities to coexist with cyanophages abundant in seawater. Appl. Environm. Microbial 1993; 59:3393-3399.

156. Whitton B.A., Potts M., 2012. Introduction to the Cyanobacteria. In: Witton B. (eds) Ecology of Cyanobacteria II. Springer, Dordrecht. https://doi.org/10.1007/978-94-007-3855-3 1

157. Whitton BA, Potts M. The Ecology of Cyanobacteria - Their Diversity in Time and Space. Kluwer Academic, 1999.

158. Wiese, M., D'Agostino, P. M., Mihali, T. K., Moffitt, M. C. &Neilan, B. A. Neurotoxic alkaloids: saxitoxin and its analogs. Mar Drugs 8, 2185-2211, doi:10.3390/md8072185 (2010)

159. Wood, R. Acute animal and human poisonings from cyanotoxin exposure - A review of the literature. Environ Int 91, 276-282, doi: 10.1016/j.envint.2016.02.026 (2016).

160. Wood, S. A. & Dietrich, D. R. Quantitative assessment of aerosolized cyanobacterial toxins at two New Zealand lakes. Journal of Environmental Monitoring 13, 1617-1624, doi:10.1039/C1EM10102A (2011).

161. Xiao, X., Huang, H., Ge, Z., Rounge, T.B., Shi, J., Xu, X., Li, R., Chen, Y., 2014. A pair of chiral flavonolignans as novel anti-cyanobacterial allelochemicals derived from barley straw (Hordeum vulgare): characterization and comparison of their anti-cyanobacterial activities. Environ. Microbiol. 16 (5), 1238–1251.

162. Yan, H., Pan, G., Zou, H., Li, X.L., Chen, H., 2004. Effective removal of microcystins using carbon nanotubes embedded with bacteria. Chinese Science Bulletin 49, 1694-1698.

163. Yavasoglu, A. et al. Toxic effects of anatoxin-a on testes and sperm counts of male mice. Exp ToxicolPathol 60, 391-396, doi:10.1016/j.etp.2008.04.001 (2008).

164. Yoshida T, Takashima Y, Tomaru Y, Shirai Y, Takao Y, Hiroishi S, Nagasaki K. Isolation and characterization of a cyanophage infecting the toxic cyanobacterium Microcystis aeruginosa. Applied and Environmental Microbiology 2006; 72(2):1239-1247.

165. Zegura, B., Straser, A. &Filipic, M. Genotoxicity and potential carcinogenicity of cyanobacterial toxins - a review. Mutat Res 727, 16-41, doi: 10.1016/j.mrrev.2011.01.002 (2011).

166. Zerrif, S.E.A.; El Ghazi, N.; Douma, M.; El Khalloufi, F.; Oudra, B. Potential uses of seaweed bioactive compounds forharmful microalgae blooms control: Algicidal effects and algal growth inhibition of Phormidiumsp (freshwater toxic cyanobacteria). Smetox J. 2018, 1, 59–62

167. Zerrifi, S.E.A.; Tazart, Z.; El Khalloufi, F.; Oudra, B.; Campos, A.; Vasconcelos, V. Potential control of toxic cyanobacteria blooms with Moroccan seaweed extracts. Environ. Sci. Pollut. Res. 2019, 1–11.

168. Zhang, M., Pan, G., Yan, H., 2010. Microbial biodegradation of microcystin-RR by bacterium Sphingopyxis sp. USTB-05. Journal of Environmental Sciences 22, 168-175.

169. Zhang, R., Qi, F., Liu, C., Zhang, Y., Wang, Y., Song, Z., 2019. Cyanobacteria derived taste and odor characteristics in various lakes in China: Songhua Lake, Chaohu Lake and Taihu Lake. Ecotoxicol. Environ. Saf. 181, 499–507.

170. Zhang, X., Hu, H.-Y., Hong, Y., Yang, J., 2008. Isolation of a Poterioochromonas capable of feeding on Microcystis aeruginosa and degrading microcystin-LR. FEMS Microbiology Letters 288, 241-246.

171. Zhu X., Dao G., Tao Y., Zhan X., Hu H. A review on control of harmful algal blooms by plant-derived allelochemicals. Journal of Hazardous Materials. 401 (2021) 123403

172. Zingone, A., Enevoldsen, H.O., 2000. The diversity of harmful algal blooms: a challenge for science and management. Ocean Coast. Manag. 43, 25–748.