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Review Article

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Review in: Toxic effects of Cyanobacteria

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Abstract

Cyanobacteria is a phylum of photosynthetic bacteria found in aquatic and moist soil environments. As a consequence of photosynthesis, cyanobacteria have been discovered to have a role in the production of gaseous oxygen. Eutrophication contributes to major challenges to water quality. It reveals that poor-quality water and not good for drinking and causes health issues. Some species of blooms are also causing even deadness to humans as well as animals when consuming the water in the presence of algal blooms. George Francis wrote on the scientific report of the toxin nature on cyanobacteria in 1878 that the rapid death of livestock of animals at lake Alexandrina, a freshwater lake at south Australia. There is a Discussion of wild and domestic animal poisonings that can be seen in most reviews of cyanobacteria toxin and mention of field deaths and often served to introduce and contextualize reports of toxicological experimental investigations into cyanobacterial suspensions, extracts, or isolates. This review aims to collect and concisely summarize the effects of cyanobacterial toxins.

Keywords: Cyanobacteria, photosynthesis, water quality, cyanobacterial toxins, moist soil.

1.0 Introduction

Cyanobacteria belong to the phylum of Gram-negative bacteria. Its class belongs to Cyanophyceae and order belongs to Chroococcales. It is also called Cyanophyta and blue-green algae. But in recent days, blue-green algae are not a concern because algae are eukaryotes and this cyanobacterium comes under the bacterial prokaryotes. They live in colonies and each one of those colonies is made up of multiple individual cyanobacterial cells living together. The advantage of living as a colony is that when many individuals live together, tasks

can be divided among the members. When their numbers get dense enough it is called bloom. Many cyanobacterial species are bloom-forming and distinguish each species by their unique colony shapes.

It forms symbiotic associations with animals and plants. Symbiotic associations with many organisms like fungi, bryophytes, pteridophytes, gymnosperms, and angiosperms (Rai, 1990).

The endosymbiotic origin hypothesis about chloroplasts and mitochondria is the best example for endosymbiosis that is the evolutionary formation of a photosynthetic eukaryote, cyanobacteria that were engulfed by eukaryotes and co-developed by a phagotrophic host (Douglas, 1994).

Fig.1: Blooms of Cyanobacteria from Nachimuthuram village in Appakudal town.

The most prominent habitats of cyanobacteria are marine environments like a pond, lake, well, near to the street water taps, etc. They can also exist in saline, brackish, or freshwater, cold and hot springs, and other situations where no other microalgae can survive (Chorus and Welker, 2021). They also even live-in soil.

Most species in cyanobacteria are oxygenic photoautotrophs. The mode of nutrition requirement is water, carbondioxide, inorganic substance, and light. Photosynthesis is the main mode of energy metabolism. Some species in cyanobacteria are showing the ability of heterotrophic nutrition (Fay, 1965). Some species are having the ability to obtain energy from the consumption of organic substrates in the absence of light. The cyanobacterium A. microscopica was successfully grown by Meireles experiment heterotrophically with starch as an exogenous source of carbon (Meireles et al., 2017). Some of the studies show that the expanded Cyanobacteria phylum proposed three classes: Oxyphotobacteria, “Melainabacteria” and “Sericytochromatia” were living without the photosynthetic mechanism (Soo et al., 2017). The cyanobacteria species varies from the photosynthetic and non-photosynthetic-dependent modes of nutrition. Cyanobacteria are typically the first plants to colonize exposed rock and soil surfaces. UV-absorbing sheath pigments, for example, improve their fitness in the comparatively exposed terrestrial environment. Many species can live in the soil and other terrestrial habitats, where they play a significant role in ecosystem functioning processes and nutrient cycling (Whitton, 1992). Limnic and marine environments are cyanobacteria's most common habitats. Cyanobacteria are remarkable colonizers of infertile substrates including volcanic ash, desert sand, and boulders (Dor and Danin, 1996). Another notable attribute is their capacity to withstand extreme heat and cold temperatures.

They thrive in salty, brackish, or freshwater as well as cold and hot springs and other situations where no other microalgae can survive. Many freshwater and brackish water species of cyanobacteria have gotten the attention of public health experts due to their ability to create a varied range of potent toxins.

Many freshwater and brackish species of cyanobacteria have gained the attention of public health experts due to their ability to create a variety of potent poisons. If the foregoing fatality was caused by cyanotoxin poisoning, the main public health concerns about recreational exposures revolve around the risk of being exposed to dangerous levels of cyanotoxins in untreated waters, which is presumably now a risk if the aforementioned fatality was caused by cyanotoxin poisoning. Direct contact with skin and mucous membranes, inhalation, and accidental or deliberate ingestion are all possible routes of exposure (Stewart et al., 2006). This review aims to collect and concisely summarize the problems behind the algal blooms, cyanobacterial toxins present in the environment and to understand the significance of cyanobacteria in the environment.

1.1 Origin of oxygen on earth

The earth was formed around 4.6 billion years ago (Coates, 2020). After 0.6 billion years, cellular life gets originated. The atmosphere became an anoxygenic zone and anoxygenic organisms were dominating to thrived until the Great Oxidation Event (GOE) occurred. It was one of the most prominent drivers of biological innovation throughout the Precambrian, having a significant impact on early Earth's surroundings. Earlier studies analyzing 16S rRNA have revealed that the GOE may have been involved in the emergence of multicellularity in cyanobacteria (Schirrmeister et al., 2021). They were responsible for the fast oxygenation of Earth's atmosphere at the end of the Apostolic Age during an incident known as the Great Oxidation Event (GOE). Before 3 billion years ago, cyanobacteria were originated and it uses sunlight to make sugars and then those sugars are used to energy for the cells (photosynthesis) and release oxygen as a byproduct. These photosynthesizing bacteria exhale oxygen and were almost certainly responsible for the apparent rapid increase in oxygen levels. The growth of Oxygen producing cyanobacteria that utilize water as a terminal reductant and enable the aerobic metabolism and complex life to evolve. The formation of oxygen in the atmosphere leads the way to the biological innovation of aerobic respiration, which enhances the more powerful metabolic energy source. (Dismukes et al., 2001). It is the first and only prokaryotes to have evolved oxygenic Photosynthesis and transformed the biology and chemistry of our earth (Sanchez et al., 2021). It is completely changed the earth's atmosphere, that is the earth became slowly oxygenated, and oxygenic cellular forms were formed. So, the cyanobacteria were thought to be the first organism on earth to generate oxygen.

2.0 Historical occurrence

The cyanobacteria are described in the playwright of "The Merchant of Venice" written by William Shakespeare in the 16th century that awareness of plankton scums and blooms existed in Europe for at least two millennia.

Fossils show that the prokaryotes are present before 3,450 million years ago in Warrawoona sedimentary rock of north-western Australia and these Cyanobacteria were among the colonist organisms of the early earth (Brock, 1996). These photosynthetic micro-organisms like cyanobacteria were probably the chief primary producers of organic matter, and the first organisms to release oxygen in the primitive atmosphere (Holland, 1997).

3.0 Mortalities and illnesses

George Francis wrote on the scientific report of the toxin nature on cyanobacteria in 1878 that the rapid death of livestock of animals at lake Alexandrina, a freshwater lake at south Australia. *Nodularia spumigena* is the brackish freshwater cyanobacteria that caused death to pigs, sheep, horses, and dogs within a period of 1 to 24 hours. The postmortem examination resulted in the noticeable things that the pericardial effusion in the abdominal cavity but normal looking in lungs, liver, and kidneys (Francis, 1878).

In South Africa, many thousands of cattle and sheep mortalities over above 25–30 years are due to cyanobacterial poisoning (Steyn, 1944). The

majority of animals such as horses, mules, donkeys, dogs, hares, poultry, and water birds found dead near affected water bodies were also thought to be similarly affected. Microcystis were identified in the water such as fulminant hepatic disease was observed in some animals, as were subacute cases with death ensuing after some two weeks and chronic cases with weeks or months of infection preceding either death or recovery. Necropsy results show that the findings in fulminant cases included pulmonary hemorrhage, hae61, and hepatomegaly (Steyn, 1943). There is a Discussion of wild and domestic animal poisonings that can be seen in most reviews of cyanobacteria toxin and mention of field deaths and often served to introduce and contextualize reports of toxicological experimental investigations into cyanobacterial suspensions, extracts, or isolates.

Table 1: Early reports of Animal mortalities associated with ingestion of Cyanobacteria.

Year	Location	Causes	References
1878	Alexandrina lake, South Australia.	Rapid death of livestock	Francis, 1878
1944	South Africa	Death of Cattle and Sheep	Steyn, 1944
1997	Alaska	Mortality of Sea Otters	Haschek, 2013
1997	North Africa	Death of Monk Seal	Haschek, 2013
2002	Indian River lagoon	Death of Dolphins	Haschek, 2013

4.0 Toxic cyanobacterial blooms

Eutrophication contributes to major challenges in water quality. It reveals that poor-quality water and not good for drinking and causes health issues. Some species of blooms are also causing even deadness to humans as well as animals when consuming the water in the presence of algal blooms. It is mainly due to the excessive enrichment of nutrients in water bodies and it is frequently due to the excess runoff in agriculture fields such as fertilizers and manures or organic wastes that may cause the formation of this process. This process accumulated the occurrences of harmful blooms like cyanobacteria (Anderson et al., 2002), red tides algae, etc. The topics of eutrophication and global climate change effects in the response of cyanobacteria are going to be potent research in the future (Paul, 2008).

The huge distribution of cyanobacteria in some places of freshwater, brackish water, and marine ecosystem is becoming a considerable environmental problem. The effect of global climate changes such as high temperature, increased atmospheric concentration, etc. was connected with the ecology and growth of the cyanobacterial species (Beardall and Raven, 2004). The massive distribution of cyanobacteria in water bodies can cause significant problems such as making a wide range of odors, potent toxins, and low oxygen concentration in the inside of water bodies (Sivonen, 1999). The lower oxygen concentration inside water bodies causes many problems to the oxygen depending organisms.

If cyanobacterial toxins can reach a higher concentration in the water bodies, it might cause health problems and ecological risks. Cyanobacteria belong to gram-negative bacteria and have the capacity of producing a wide range of high amounts of toxins as secondary metabolites. About 200 species of 150 genera were included in the class cyanobacteria (Hitzfeld et al., 2000). All the cyanobacterial blooms are not having the capacity to produce toxins but some of the species are having the capability to produce high productivity of toxins. The cyanobacterial species which are responsible for cyanobacterial toxin poisoning (CTP) is about an estimated 40 genera. The main species are Anabaena, Aphanizomenon, Cylindrospermopsis, Lyngbya, Microcystis, Nostoc, and Oscillatoria (Carmichael, 2001). The amount of toxin production varies with the time for an individual bloom.

5.0 Cyanobacterial toxins

Cyanotoxins have a different group of compounds from chemical to toxic points of view. From the toxicological view, the Cyanophyta toxins are hepatotoxins, neurotoxins, cytotoxins, dermatoxins, and irritant toxins (Wiegand and Pflugmacher, 2005). The fresh and brackish water cyanobacterial toxins were fallen into three broad groups of chemical structures, namely the cyclic peptides (hepatotoxic microcystins and nodularin), the alkaloids (hepatotoxic cylindrospermopsins, the neurotoxins, anatoxin, and saxitoxins), and lipopolysaccharides (Carmichael, 2001), (Sivonen, 1999).

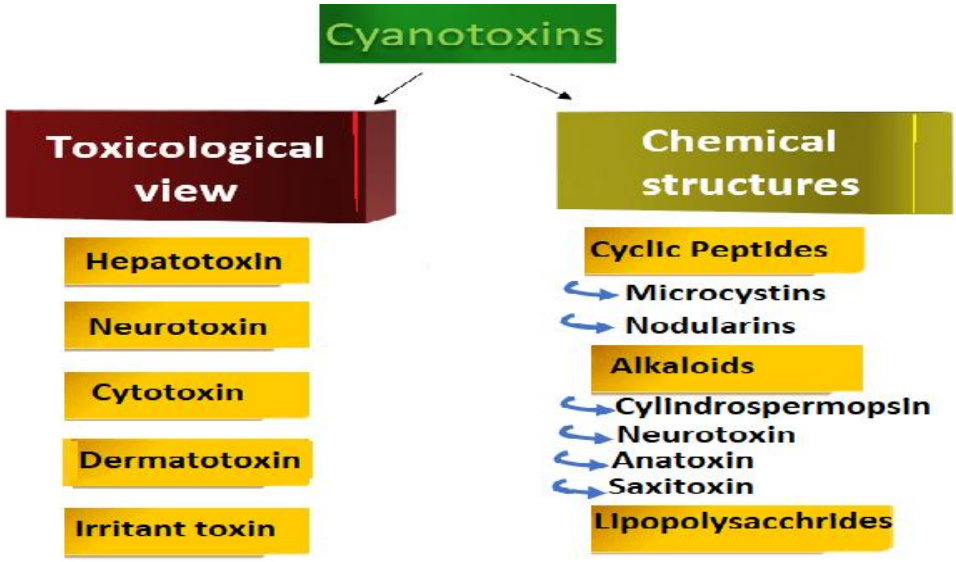

Fig.2: Groups of Cyanotoxins

Cyanotoxins produced by blooming cyanobacteria can harm and even kill animals and people in high enough concentrations. Other organisms, such as fish and shellfish, can accumulate cyanotoxins and produce poisonings, such as shellfish poisoning. It contains neurotoxins, hepatotoxins, cytotoxins, and endotoxins, among others. Despite its name, they have nothing to do with cyanides. Cyanobacteria exposure can cause gastrointestinal and hay fever symptoms, as well as pruritic skin rashes (Stewart et al., 2006). From both a chemical and toxicological point, cyanotoxins are a varied category of natural toxins. Despite their aquatic origins, the majority of cyanotoxins identified so far appear to be more dangerous to terrestrial mammals than to aquatic biota. Cyanobacteria create several unique metabolites, the natural function of which is unknown, however, some appear to influence another biota. Compounds that affect humans and livestock, either as poisons or as pharmaceutically helpful molecules, have been the focus of research. Cyanobacteria also synthesize a diverse spectrum of non-toxic substances, the biochemical and pharmacological effects of which are unknown. During the 1980s, the research used mouse bioassays to investigate the existence, distribution, and frequency of hazardous cyanobacteria in several countries (Lawton et al., 1994). Although quantitative toxin determination methods were only accessible in the late 1980s, investigations of individual cyanotoxins have been increasing since then. Cyanobacterial toxicity has a wide range of mechanisms which include hepatotoxic, neurotoxic, and dermatotoxic effects, and also general suppression of protein synthesis. Understanding the chemical and physical features of cyanobacterial toxins, their presence in human-use waters, the regulation of their production, and their fate in the environment are all important to assess the specific dangers of these toxins. Cyanotoxins are divided into three chemical groups: cyclic peptides, alkaloids, and lipopolysaccharides (LPS).

The cyclic peptide toxins of the microcystin and nodularin groups are the most commonly found cyanobacterial toxins in blooms from fresh and brackish environments around the world. They present a significant difficulty for producing safe drinking water from surface water containing cyanobacteria that produce these poisons (Aboal and Puig, 2005). cyanobacterial hepatotoxins which are liver toxins that cause mortality by liver haemorrhage within a few hours of acute dosages in mice bioassays, which have usually been used to assess the toxicity of field and laboratory materials. Microcystins have been identified in planktonic Anabaena, Microcystis, Oscillatoria (Planktothrix), Nostoc, and Anabaenopsis species, as well as terrestrial Anabaena, Microcystis, Oscillatoria (Planktothrix), Nostoc, and Anabaenopsis species. Microcystins and nodularin are hazardous to mammals because of their high binding to protein phosphatases, which are important cellular enzymes. Recent research has revealed that this area is critical for interaction with the protein phosphatase protein molecule, and the cyanotoxins toxicity (Hilborn et al., 2005). Microcystins also have the property of creating a covalent link between the DNA residue and the phosphatase molecule. Microcystins and nodularin have been identified in cyanobacterial strains that are axenic (i.e., free of contaminating bacteria), indicating that these chemicals have a cyanobacterial origin. Bloom-forming species of Microcystis, Anabaena, Oscillatoria (Planktothrix), and Nostoc, as well as a species of Anabaenopsis and a soil isolate of *Haphalosiphon hibemicus* all, generate microcystins (Srivastava, 2005). Cyanobacterial colonies can be dominated by a single species or formed up of a diverse group of species, some of which are not toxic. There may be a mix of dangerous and non-toxic strains even within a single-species bloom. Some strains are hundreds of times more hazardous than others, sometimes by three orders of magnitude. This means that one very dangerous strain cannot be distinguished from a greater number of toxic and non-toxic strains from the same cyanobacterial species by microscopic identification, even if it's present in small amounts. Microcystis sp., most often Microcystis aeruginosa, has been connected to hepatotoxic blooms all around the world. *Microcystis viridis* and *Microcystis botrys* are two species of Microcystis (Srivastava, 2005).

5.1 Microcystin

Microcystins are also known as Cyanoginosin and it is the common widespread cytotoxins in the environment. These are large amounts in cyanobacterial biomass. It belongs to the family of monocyclic heptapeptides and it is identified more than 70 variants and which all are characterized by some characteristic features of unusual β amino acids (Blaha et al., 2009). The world health organization (WHO) derived that the microcystin- LR, the value of tolerably daily intake (TDI) for the assessment purpose for human health risks. It is taken by some exposure routes such as consumption of contaminated food or cyanobacterial food supplements, reaction exposure, etc. (WHO, 2003). Drinking water consumption is the most common way for humans to be exposed to cyanobacterial toxins. Recreational usage of lakes and rivers is a minor source of exposure; however, because microcystin-LR cannot readily penetrate cell membranes, absorption by skin contact is rare (Eriksson et al., 1990). Some humans are also exposed to cyanobacterial toxins as a result of consuming algal food tablets. Inhalation of microcystin-LR during showering is another small route of exposure; however, because microcystin-LR is very water-soluble and non-volatile, inhalation and absorption through the lungs are improbable unless the toxin is inhaled as an aqueous aerosol in the air (Lambert., *et al*, 1994b). Microcystin-LR was found to have a half-life of less than a week in studies conducted in reservoir water in the United Kingdom. Microcystin had also been found to be quickly biodegraded in ambient waters, with a half-life of around 1 week (Cousins et al., 1996). Microcystin was found up to 21 days after an algicide treatment of bloom in one study. This could have been caused by the copper sulphate shock dosage. Microcystin-LR is extremely stable in water and can withstand pH variations as well as temperatures of up to 300°C (Wannemacher, 1989). It may be useful to distinguish screening

methods, such as the Mouse bioassay, Enzyme-linked immunosorbent assay (ELISA), and phosphatase bioassay, which are carried out before clean-up and indicate the presence of toxins in samples, from methods that are carried out for the identification and quantification of the various individual microcystins, including their detection limits. In many cases, a sample contains more than one toxin. A single method will not be enough for the identification and accurate quantification of several microcystins, according to researchers who use analytical methods. But using a combination of screening and more complex quantification methods is the best approach for monitoring (Harada, 1994). The mouse bioassay is significant as a screening method because it can determine the entire toxic potential of a substance in a short time and distinguish hepatotoxins from neurotoxins. The assay calculates the least quantity of toxin required to kill a mouse and compares that value to known toxin lethal doses. The drawback is that it cannot detect poisons at low concentrations, particularly in finished drinking water, and it cannot identify the individual harmful agent (Lambert et al., 1994a).

The important biochemical mechanism of microcystin toxicity is oxidative stress. It produces reactive oxygen species (ROS) and it may cause severe cellular damage such as peroxidation of lipid membranes, genotoxicity, or modulation of cell death (Ding and Ong, 2003). The formation of this reactive oxygen species is also likely to be the process responsible for the oxidative damage of DNA, clastogenic effects of microcystins (Humpage et al., 2000).

Several experimental pieces of evidence with mammals showed that the significant chronic and subchronic toxicity of microcystins were big effects such as increased mortality rate, histopathological changes, inflammation in chronic, increased liver enzyme level, etc. (Falconer, 2006).

5.2 Saxitoxin

Saxitoxin (STX) is a kind of neurotoxin and it belongs to the family of Heterocyclic guanidines. The name saxitoxin was originated from the butter clam, *Saxidomus giganticus*, from which the toxin was first segregated (Haschek et al, 2013). It is mostly found in a small number of cyanobacterial groups from large genera such as Anabaena, Cylindrospermopsis, Lyngbya, Aphanizomenon, Planktothrix, and Raphidiopsis. It is found in the two groups of organisms from various domains of life such as cyanobacteria and dinoflagellates (Wiese et al., 2010) which is one of the most dangerous marine poisons. Saxitoxins are produced in both freshwater and marine water ecosystem. In marine environments, they are often called PSPs (Paralytic shellfish poisoning). Saxitoxins are produced in both freshwater and marine water ecosystem. In marine environments, they are often called PSPs. It produces a variety of secondary metabolites toxic material that plays a significant impact in the water ecosystem and fisheries (Hackett et al., 2013). Saxitoxin binds to voltage-gated sodium channels, interrupting nerve signals. The positively charged guanidinium groups interact with negatively charged carboxyl groups at a site on the sodium channel of neurons and muscle cells, causing action potentials to be inhibited and transmissions to be disrupted (Wexler, 2014).

Saxitoxin poisoning has been associated with the mortality of sea otters in Alaska, and 67 percent of an endangered Mediterranean monk seal population off the coast of Cap Blanc in western North Africa died in 1997 after suffering neurologic symptoms. Saxitoxins are frequently linked to massive fish fatalities caused by poisonous blooms. Humpback whales may have died as a result of exposure to saxitoxins from contaminated mackerel. It was also related to the deaths of dolphins in Florida's Indian River Lagoon in 2002 after they ate pufferfish. Intoxication in humans in Florida, New Jersey, New York, and Virginia was related to consuming pufferfish from the Indian River Lagoon around

the same period. (Haschek et al., 2013). It can be found in filter-feeding molluscs that intake planktonic algae, including *Alexandrium tamarense, Gymnodinium catenatum*, and *Pyrodinium bahamense*.

When humans consume these molluscs, they get paralytic shellfish poisoning, which can kill them in a matter of hours if enough toxin is ingested. STX poisoning has almost not had the documented antidote. It's only utilized as a research tool to explore voltage-dependent sodium channels (Simmons et al., 2007). Mussels, clams, and oysters consume the dinoflagellates or red algae with which they may be related, and as a result, they become toxic. Carnivorous fish that consume these bacteria will become toxic as well. As a result, human consumption of seafood obtained from regions where these dinoflagellates grow in abundance, such as algal blooms, can result in paralytic poisoning outbreaks. Saxitoxin effectively blocks sodium channels. A guanidino group is identified in all paralytic shellfish toxins. On the extracellular side of the plasma membrane of nerve and muscle cells, the positively charged guanidino group interacts with a negatively charged carboxyl group near the mouth of the sodium channel. Paralysis develops when sodium ion transport through nerve and muscle cell membranes is blocked. Aphanizomenon, a cyanobacteria genus, also produces saxitoxin (Robinson, 2014). It binds to receptors that aren't related to the sodium channel. The first is saxiphilin, a protein found in many animals' circulatory fluid and exploited in a receptor binding assay similar to the sodium channel. Antibodies to saxitoxin are used instead of natural receptors. Saxitoxin does not stimulate an immunological response in animals, and the animal used to generate the antibodies should not respond to the toxin. To create an antigenic epitope and reduce toxicity, the toxin is subsequently attached to a carrier protein. The enzyme horseradish peroxidase is an example carrier that may also be employed to provide an assay signal by transforming a colorless substrate to a visible result. Saxitoxin will diminish any assay signal by interfering with the binding of the saxitoxin–horseradish peroxidase conjugate to the antibody produced to the toxin protein complex. Antibodies produced against one member of the saxitoxin family may not detect other chemical cousins, therefore such assays are limited (Worsfold, 2005).

Paralytic shellfish poisoning (PSP) is one of the most important harmful algal blooms poisoning syndrome causes severe illness that results when consuming that shellfish and chances to accumulate the toxins. It mainly binds to the sodium channel which is responsible for the flux of sodium in nerve cells and muscle cells (Cembella, 1998). The sodium channel bindings are interfering with axonal conduction. So, death is very rapid within minutes when purified saxitoxin is administered parenterally (Stewart, 2008).

5.3 Cylindrospermopsin

Cylindrospermopsin is one of the most dangerous cyanotoxins found in freshwater, with significant cytotoxicity, developmental toxicity, and carcinogenic potential. Cylindrospermopsin is generated by cyanobacteria belonging to the genera of Aphanizomenon, Umezakia, Raphidiopsis, etc. (Metcalf and Codd, 2012). Cylindrospermopsin producing toxins are abundant in tropical waters, where gastrointestinal disorders of unknown origin are common (Snider and Xie, 2004). It is an alkaloid made up of hydroxymethyluracil and a tricyclic guanidine moiety. At 100°C for 15 minutes, it remains zwitterionic, extremely water-soluble, and stable at acidic pH. The most common symptoms are liver damage and lesions in the kidney, heart, and thymus have been observed in mice and rats. (Robillot and Llewellyn, 2005). The existence of Cylindrospermopsin was identified when 149 people were poisoned on Palm Island, off the coast of northeast Australia, when their freshwater dam was contaminated by *C. raciborskii*.

5.4 Anatoxin

Anatoxins are poisonous compounds produced by Anabaena flos-aquae and other freshwater cyanobacteria species. The poisons are water-

soluble alkaloids that have been linked to several human poisoning cases, some of which have resulted in death (Harris, 2017). It's a cholinergic agonist that binds to nicotinic acetylcholine receptors (nAChRs), which are present in neurons and at neuromuscular junctions (NMJs) (Humbert, 2009). There have been numerous reports of animal poisoning. The consumption of benthic anatoxin-a-producing cyanobacteria has been associated with the death of many dogs in France (Gugger et al., 2005). Anatoxin-a is a powerful agonist of acetylcholine receptors being many times better than acetylcholine itself in stimulating the receptor to open. Anatoxin-a therefore outcompetes and displaces acetylcholine overstimulating the receptor, impairing its function, and incapacitating nerve and muscle. Anatoxin-a is a potent agonist of acetylcholine receptors, many times more effective than acetylcholine in getting them to open. As a result, anatoxin-a outcompetes and displaces acetylcholine, overstimulating the receptor, compromising its function, and rendering nerve and muscle paralyzed (Robillot, and Llewellyn, 2005).

6.0 Bioaccumulation in the environment

The process by which toxin substances enter to accumulating individual organism is called Bioaccumulation. In this process, where toxin substances were passed from one to the next trophic level to increase their concentration in the food web. The bioaccumulation caused by microcystin in the food chain is becoming one of the main concerns for public health. It is all over the food in phytoplankton, zooplankton, and gastropods (Duy et al., 2000). The microcystins were bioaccumulated in fish and also freshwater mussels and clams. The higher amount of microcystin concentration is found in the mussel in the hepatopancreases and fish, the higher concentration is found in the liver (Duy et al., 2000).

If humans consume that bioaccumulated fish, it may cause severe health issues. So, the common advice given in Duy et al., is that not to eat the viscera of fish, because, the contaminations were mostly struck into the viscera so if it is eaten, it causes severe health issues. In an aquatic ecosystem, the species called Phyto planktivorous fish which consumes the food as phytoplankton and mostly algal blooms Microcystis aeruginosa bloom are mostly grazed out by silver carp and bighead carp fish. So, this is suggested that those fishes were counteracted with the cyanotoxin contamination when they consume the toxic cyanobacteria (Xie et al., 2004).

Aquatic field workers who are eager and/or required to take samples may be concerned in waters that are discolored or affected by cyanobacteria scums. The two incidents involving British soldiers and sea cadets conducting canoe capsizing activities in waters were reportedly affected by a "heavy bloom of Microcystis species" and a "scum of Oscillatoria". Many recreational users may avoid waters that are visibly suffering from a loss of visual amenity, yet avoidance behavior in such situations cannot be assumed. Microcystis aeruginosa (Chorus et al., 2000), (Codd et al, 1999). Fever, headache, lassitude, arthralgia, myalgia, sore throat, cough, diarrhea, and vomiting are mentioned in several sources as symptoms and symptoms of a flu-like disease. A coordinated, cytokine-mediated innate immune response has been offered as a possible explanation for this group of symptoms. Endogenous mediators regulate the occurrences of fever and malaise (Stewart, 2005).

7.0 Toxic effects in laboratory animals

Microcystin- LR is an extra ordinally acute toxin (WHO, 2003). The experiment is that 31.3 µg microcystin LR/kg BW is repeatedly given daily for 7 days to mice and caused a 75% increase in liver weight (Chorus and Welker, 2021). Another microcystin LR effect is that 150 µg microcystin-LR/kg was received to the groups of ten adult male rats for 28 days via their drinking water. It also results in increased liver weight (Heinze, 1999). The other experiment is that three vervet monkeys received microcystin LK by 3 times per week by gavage throughout the study. The doses

were gradually increased from 20 to 80 µg/kg. But the result is that there are no significant changes seen in clinical or hematological parameters (Van Apeldoorn et al., 2007). The extract from *M. aeruginosa* was given to the 5 pigs for 44 days as drinking water and doses are 280-1312 µg of total Microcystins. The result depicted is that the liver changes were reported in the 280 µg microcystin- LR eq/kg (lowest dose level) (Duy et al., 2000).

8.0 Effects on humans

Humans can mostly be exposed orally by consuming water or algal food and it also happens when the recreational use of lakes and rivers. Sometimes, it may cause by the use of a shower and occur inhalation exposure. The effects in humans may be of short-term or long-term effect.

8.1 Short term effects

Cyanobacterial toxins caused a greater number of human birth defect rates in a community where they consume water in the reservoir which is contaminated by cyanobacterial blooms (Duy et al., 2000). Murray river of Australia had been used as the water reservoir for six towns. Among the population from six towns were gastroenteritis and allergic conditions (Falconer, 2001). The two most lethal poisonings accredited to cyanobacteria in drinking water take place in Brazil. A massive Anabaena and Microcystis bloom in Itaparica Dam were responsible for 2000 cases of gastroenteritis causing 88 deaths, mostly children (Rao et al., 2002).

In 1996, Acute liver failure at a hemodialysis center in Caruaru occurred in the clinic of 116 out of 131 patients who experienced visual disturbances, nausea, and vomiting after routine hemodialysis treatment on 13–20 February 1996. Eventually, 100 patients cause acute liver failure, and of these 76 died. Comparison of victim's symptoms and pathology using animal studies of the two suspected cyanotoxins such as microcystins and cylindrospermopsin led to the result of a major contributing factor to the death of the dialysis patients were intravenous exposure to microcystins, specifically, microcystin-YR, -LR and -AR. From liver concentrations and exposure volumes, it was estimated that 19.5 LG microcystin/L was present in the water used for dialysis treatment (Carmichael et al., 2001).

8.2 Long term effects

The studies were performed in China that whether the cyanobacterial toxins are part of risk factors in the development of human hepatocellular carcinoma (HCC). The distribution of this human hepatocellular carcinoma varies geographically. Maize and the hepatitis B virus are the food items that are responsible for the intake of aflatoxin B1 were the two proven risk factors. The third element of association was the source of consuming water. On a village base, lower cancer mortality rates were seen when the water was taken from deep wells compared with much higher rates when the water came from ponds and ditches. Cyanobacteria are large in surface waters in southeast China, where the incidence of human hepatocellular carcinoma is the highest (Chorus and Welker, 2021).

Table 2: Reports of Human health issues related to the exposure of Cyanobacterial blooms and toxins.

Year	Location	Source	Cyanobacteria	Health issues
1931	Ohio River, USA.	Drinking water	Microcystis	Gastroenteritis, Abdominal pain, Vomiting.
1959	Saskatchewan, Canada.	Recreational/ Occupational water contact	Microcystis, Anabaena.	Headache, Nausea, Vomiting, Muscular pain, Diarrhea.
1972-1996	China	Drinking water	Microcystis	Colorectal cancer, Primary liver cancer.
1974	Washington, USA	Haemodialysis	Lipopolysaccharides	Fever, Vomiting.
1979	Palm Island, Australia.	Drinking water	Cylindrospermopsis	Gastroenteritis, Abdominal pain, Vomiting.
1981	Armidale, Australia.	Drinking water	Microcystis	Liver damage
1995	Australia	Recreational/ Occupational water contact	Microcystis, Anabaena, Nodularia.	Gastroenteritis, Fever, eye and ear irritation.
2001	Rio de Janeiro, Brazil	Recreational/ Occupational water contact	Microcystis, Anabaena.	Visual disturbance, Tinitus, nausea, liver damage, vomiting.

(Blaha et al., 2009, Chorus and Batram, 1999, Codd et al, 2005, Duy et al, 2000, Falconer, 2006, Rapala et al., 2005, WHO, 1998)

9.0 Conclusion

- There are a greater number of toxic species in cyanobacteria that are harmful to human and animal health as well as cyanobacteria contributes a major role in the biogeochemical cycle.
- To avoid the harmful effects, should be properly maintained the drinking water bodies and other ecosystems.
- Eutrophication is the main effect and it is caused due to excess nutrition and waste materials entering into the water bodies. So, the excess runoff and wastewaters should be properly monitored before leaving to the ecosystem.

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