stresses

Review

Mechanisms of Stress Tolerance in Cyanobacteria under Extreme Conditions

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Abstract: Cyanobacteria are oxygen-evolving photoautotrophs with worldwide distribution in every possible habitat, and they account for half of the global primary productivity. Because of their ability to thrive in a hostile environment, cyanobacteria are categorized as "extremophiles". They have evolved a fascinating repository of distinct secondary metabolites and biomolecules to promote their development and survival in various habitats, including severe conditions. However, developing new proteins/enzymes and metabolites is mostly directed by an appropriate gene regulation system that results in stress adaptations. However, only few proteins have been characterized to date that have the potential to improve resistance against abiotic stresses. As a result, studying environmental stress responses to post-genomic analysis, such as proteome changes using latest structural proteomics and synthetic biology techniques, is critical. In this regard, scientists working on these topics will benefit greatly from the stress of proteomics research. Progress in these disciplines will aid in understanding cyanobacteria's physiology, biochemical, and metabolic systems. This review summarizes the most recent key findings of cyanobacterial proteome study under various abiotic stresses and the application of secondary metabolites formed during different abiotic conditions.

Keywords: cyanobacteria; extremophiles; proteomics; antioxidants; tolerance; secondary metabolites

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1. Introduction

Cyanobacteria are a very diverse group photosynthetic prokaryotes that originated approximately 3.5 billion years ago and performed a critical role in shifting the earth's environmental conditions from anaerobic to aerobic. The cyanobacteria are typically the first oxygen-evolving photoautotrophic colonizer of primary deglaciated environments, kicking off the first succession process. They also help to stabilize the soil by forming crusts on the top. Cyanobacteria are ubiquitous and can be found in aquatic and terrestrial ecosystems, including hot springs, deserts, and polar regions. Although these places have harsh climatic circumstances, cyanobacteria showed their ability to cope with the stresses of low temperatures and constant irradiance of high and low intensity of light, ultraviolet radiation (U.V.R.), freezing, and desiccation [1,2]

However, the stress conditions depend upon various factors, such as duration (U.V. exposure), periodicities (such as diel or annual temperature cycles), high irradiance, desiccation, and elevated and low temperatures. The cyanobacteria respond quickly after exposure to these stress factors and move under a state transition, which may be slow, with changes lasting months or years, which can lead to the emergence of a new strain [3].

The cyanobacterial strains can be used as a model to study the stress response because of a direct link with eukaryotic photosynthetic organisms or the plant [4]. The latest molecular techniques are employed at the molecular (D.N.A., R.N.A., and protein) levels to explore the physiological, biochemical, and metabolic activity of stressed organisms. However, the relationship between transcript and protein expressions still needs to be deeply studied [5] because it correlates the actual functions of genes and their transcribed products and can reflect the stress-specific cellular protein profile under defined stress circumstances.

In addition, proteomics offers advances in understanding cellular functions [6]. It can investigate the function and structure of proteins by acting as a link between the transcriptome and metabolomic profiles, allowing researchers to probe the cell's physiological and metabolic states. Furthermore, in a stressful situation, the creation of "adaptation proteins" controls long-term cellular adaptation. These adaptation proteins are being studied to determine how the cells adapt to stressful situations. Identifying unregulated proteins with the latest new-generation techniques can be beneficial for studying stress proteomics.

The production of secondary metabolites, in response to the different biotic and abiotic stresses, also protects the cyanobacteria [7,8]. Depending on the stress situation, different suites of secondary metabolites are produced. Alkaloids, UV-absorbing polyketides, and terpenoids are frequently reported metabolites. As a result, they have a wide range of protective properties for the cells, including defense against grazers and predators, antioxidant, chemosensory, and photoprotection functions. These qualities can be used in cosmeceuticals, nutraceuticals, and medicines in industrial biotechnology.

This review article briefly discussed the different abiotic stresses and their impact on cyanobacterial biology. In addition, it summarizes the proteomics associated with cyanobacteria during exposure to different stresses; lastly, we have also summarized how the cyanobacterial inoculation enhances the growth and yields of the plant.

2. Occurrence of Cyanobacteria in the Environment

Cyanobacteria are ubiquitous and present in various shapes and sizes, including unicellular, colonial, filamentous, branching, and heterocystous, in the different possible environments. Cyanobacteria can switch between autotrophic, mixotrophic, and heterotrophic feeding modes. In addition, they play an essential part in global biogeochemical cycles by transforming organic molecules into proper forms [9].

Moreover, cyanobacteria are a substantial component of marine and freshwater ecosystems with global distribution. Some cyanobacterial species, when separated from coastal settings, tolerate high concentrations of salt water (halotolerant) [10]. However, some cyanobacterial strains can survive in the terrestrial habitats and play a vital role in nutrient recycling and sustainable environmental development. The presence of UV-absorbing sheath pigments and exopolysaccharide (EPS) make the cyanobacterial strains survive in the exposed terrestrial environment. However, some cyanobacterial strains are common colonizers of euryhaline environments and survive under 3–4 molar mass salt concentrations [11]. Cyanobacteria are remarkable colonizers of infertile substrates, such as desert sand, volcanic ash, and boulders [12]. They are incredible excavators who carve out hollows in the limestone and specific sandstone. Mountain streams [13], hot springs [14], and Antarctic and Arctic lakes [15] are all the homes of cyanobacterial species [16]. Additionally, they can be found in a wide variety of water types, from katharobic waters to polysaprobic zones [17].

Cyanobacterial Stress Tolerance

Cyanobacteria are known for their strong adaptability under different environmental conditions, such as exposure to Gamma or UV radiation, heat, salinity, desiccation, and heavy metals. However, some of the cyanobacterial strains are resistant to these stress conditions, as listed in Table 1. These environmental condition affect the morphology (cell wall alteration), biochemicals (production of screening pigments), or physiology (state transitions), or there may be some genetic changes that occur as a result of acclimatization under the environmental extremes [18].

Table 1. List of abiotic stress tolerance in cyanobacteria with their references.

S. No.	Types of Stresses		References
1	Nutrient deficiency		[19,20]
2	Light intensity		[21–23]
3	Radiation	U.V.	[24–26]
		Gamma	[27–29]
4	Temperature	High	[30,31]
		Low	[32–34]
5	Salt	Salinity	[35–37]
		Osmoticum	[38–40]
6	Chemicals	Pesticides	[41]
		Heavy metals	[42–44]
7	Desiccation		[45–47]

In addition, the imposition of stress can lead to changes in the metabolic behaviors, such as the enhanced synthesis of polyunsaturated fatty acids [48] and enhanced concentration of photosystem unit in the thylakoid membrane, which is commonly observed [49]. However, the response time of short-term reactions are usually less than a minute, and rare structural modifications have been observed [50]. However, long-term reactions can span from several hours to days and frequently entail de novo protein formation. The changes in photosystem stoichiometry and alteration in the pigment quantity are examples of long-term responses [51].

3. General Mechanisms of Cyanobacteria to Survive under Extreme Habitat

The abiotic stresses, including the presence of salt, heavy metals, light, drought, and temperature extremes, primarily affect the physiology and metabolic behavior of the cyanobacteria [52]. However, in response to stress, a variety of stimuli and other defense systems have been activated [53,54]. Changes in the osmotic pressure have been observed during various stresses, such as the enhanced concentration of salt [55], freezing stress [56], and the stress of desiccation [57].

The generation of reactive oxygen species (ROS) has been observed after high P.A.R. [58] and U.V.R. [59], and these ROS have been neutralized by different enzymatics, such as superoxide dismutases (SOD), catalases (CAT), and guaiacol peroxidase (GPX), and non-enzymatic substances, such as carotenoids and glutathione reductase (G.R.) [60]. However, the excess generation of free radicals can lead to oxidative stress, which can affect the structural integrity and nucleic acids of the cells [61]. ROS also act as secondary signal molecules, regulating photosynthetic genes and inducing antioxidant enzymes through genetic regulation. However, the cyanobacteria can recover from the oxidative damages caused due to mild UV-B exposure, thanks to their efficient defense and repair system [62]. However, the prolonged exposure to UVR stress can cause the denaturation of DNA. The principal harm is the formation of photoproducts between adjacent bases; similar types of damage were found during desiccation stress [57,63].

The fluidity and integrity of the cell membranes are critical for normal life [64]. However, stresses such as temperature [65], salinity [66], desiccation [67], and photoinhibition generally cause alternation in lipid content of the cell [68]. Different strategies employed by cyanobacteria to cope with different abiotic stresses are described in Figure 1.

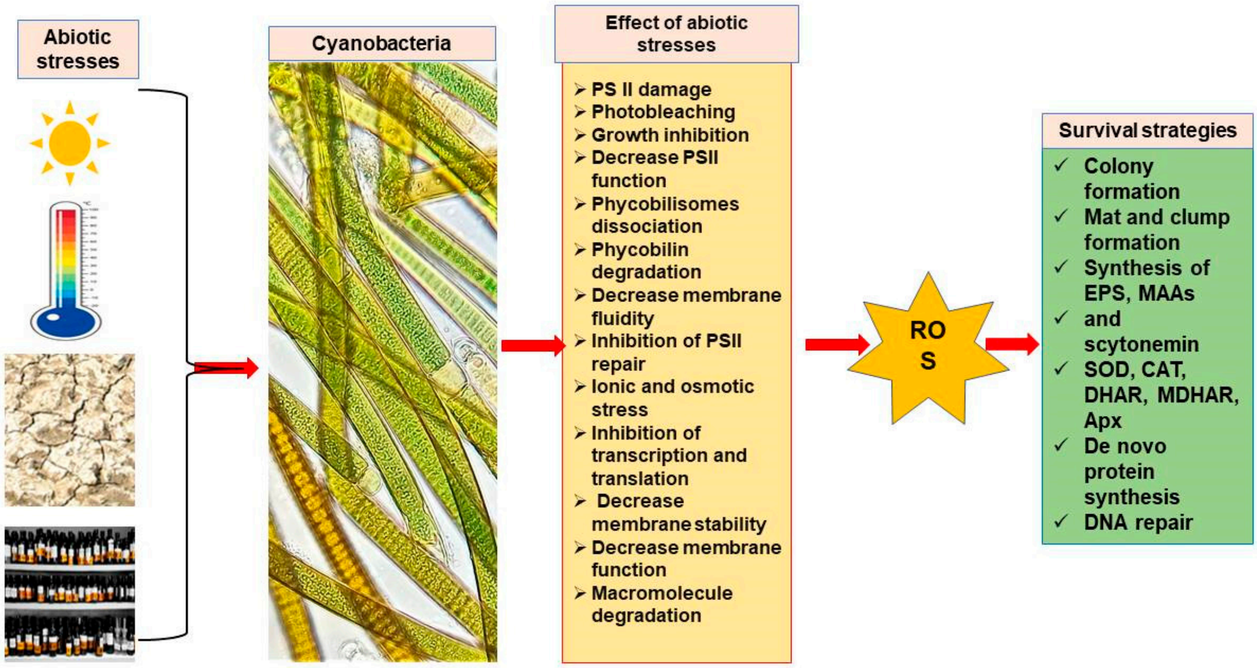

Figure 1. The overview of strategies, followed by cyanobacterial strains to cope with different abiotic stresses.

Heat-shock proteins (HSPs) were first reported in the context of high-temperature responses, but now have also been reported during different stress conditions [69,70]. However, in response to salinity stress cyanobacteria synthesizes nonreducing carbohydrates like trehalose [64]. Studies reported trehalose's involvement in maintaining the integrity of membranes, proteins, and nucleic acids, also involved in their functions in osmotic stress tolerance [71].

3.1. Photosynthetic Active Radiation (P.A.R.)

All the photoautotrophic organisms rely on light to synthesize their food and as an energy resource. However, the availability of P.A.R. and its intensity change over time [23]. The intensity can range from as low as 0.1 mol m^2 s^1 to as high as 1500 mol m^2 s^1 in full sunlight [72,73]. As a result, polar cyanobacteria adapt to an oscillation regime and a wide range of P.A.R. [23]. However, the different cyanobacterial populations compete with each other for the radiation, light-scattering, and absorbing elements in the aquatic environment. This competition leads to vertical and horizontal species distribution in aquatic and terrestrial ecosystems [74,75].

Tiny cyanobacterial filaments or unicellular cyanobacterium may reduce the self-shading, which can use poor light quality for survival. However, the cyanobacterial group, having mat-forming characteristics, showed optical properties similar to picophytoplankton [23]. Significant levels of Chl-*a* and many thylakoids are signs of acclimatization to low intensities [76]. However, high irradiances are frequent on the exposed surfaces, such as soil crusts, rock, and glaciers, which leads to decreases in the surface density of thylakoid membranes, Chl-*a* content, and the buildup of stored chemicals [76] (highly reduced ratio of PS I to PS II, it could be below one) [77].

3.2. Light Quality

The absorption of particular wavelengths of light causes cyanobacteria to modify their pigment makeup results in a complementary chromatic adaptation to maximize the use of available light [78]. However, the absorption spectrum of light varies as a result of the adaptation to light quality [79]. The alteration in the pigment is directly associated with the ability to adapt during different intensities and duration of light. However, the upper surface protects the deeper layers, where the rate of photosynthesis is higher in a layered community [80]. In a previous study, *Calothrix* sp. and *Synechococcus* sp. have been evaluated for chromatic adaptations [81]. During the study, a higher concentration of phycoerythrin (P.E.) was generated when the *Calothrix* sp. PCC 7601 cultivated under green light, while an elevated level of phycocyanin (P.C.) was observed under the red-light condition [82].

3.3. Ultraviolet Radiation (U.V.R.)

The exposure of U.V. radiation significantly affects the morphology and physiology of cyanobacteria [83,84]. Cyanobacteria travel to areas with low UV-B flux to avoid the harm of UV-B and try to make a balance for efficient photosynthesis and pigment bleaching by optimizing their position in inland mats or the water column [85]. However, to cope with the stress of UV-B radiation and photooxidative damage caused by ROS, cyanobacteria synthesize metabolites, such as mycosporine-like amino acids (M.A.A.s) and scytonemin. These metabolites scavenge the reactive oxygen species and repair the D.N.A., which was damaged due to U.V. radiation [86]. The overview of the survivability of cyanobacteria under exposure to U.V. radiation has been summarized in Figure 2.

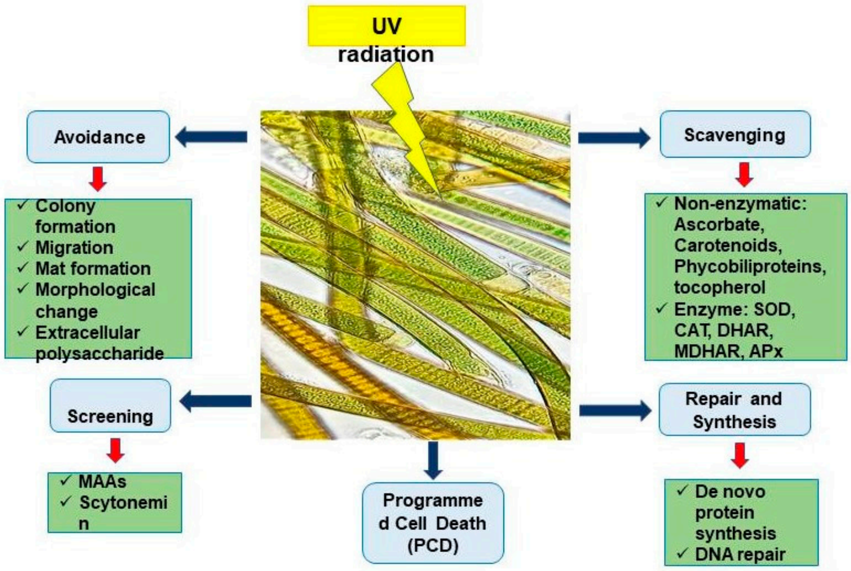

Figure 2. The overview of cyanobacterial survival strategies to cope with Ultraviolet radiation.

The U.V.R. sensitivity should be lower in the species that originated from the exposed areas. Although, resistant species have more giant cells or form coenobia, vast colonies, or mats that protect the interior cells/filaments [87,88]. In the previous study, it has been stated that the mats of resistant strains have been characterized by actively moving filaments, as well as the surface filaments, which contain modest concentration of pigments [89]. Surface cells could produce screening substances, such as sheath pigments, that have property to protect the consortium of inner cells [90]. U.V.R. at high levels slows growth and damages the photosynthetic system, including enzyme nitrogenase and membranes, but D.N.A. is the main target [91–93]. The study suggested exposure to UV-B suppresses the ATP production [94,95].

However, various changes have been observed at the protein and metabolite levels in the cyanobacteria after exposure of UV-B. Changes in the proteome during U.V. acclimation and UV-B shock, as indicated by subtractive high-resolution 2D gel electrophoresis, was investigated in the work on *Nostoc commune* [96]. However, the U.V. impact on protein synthesis has been classified into three categories, based on exposure time: (i) continuous decrease or increase of proteins after prolonged exposure, (ii) durable repression or induction of proteins after short-term exposure, and (iii) transient repression or short-term exposure [97].

3.4. Temperature

Rising global temperature is a severe threat to living organisms, and it has been estimated that temperature may rise by 0.2 °C per decade [98]. Temperature variation also influences a wide range of biological processes, including the physiology and metabolism of cyanobacteria [99]. However, the most crucial variation after temperature exposure is the variation in the membrane composition [100]. Based on temperature tolerance, cyanobacteria are divided into the psychrophilic, psychrotrophic, mesophilic, and thermophilic groups. Each of the cyanobacterial groups has a specific growth temperature. Psychotropics can withstand freezing temperatures (below 15 °C), mesophilic can withstand temperatures up to 50 °C, and thermophilic can withstand temperatures beyond 80 °C [101]. The duration and intensity of the temperature changes the components and metabolism of the cells [102]. Temperature-induced changes in membrane fluidity are one of the most immediate repercussions. The shift in membrane composition, which comprises changes in membrane fluidity, heat shock proteins (HSPs), fatty acid saturation, and protein integrity, are some common responses of temperature stress, as summarized in Figure 3.

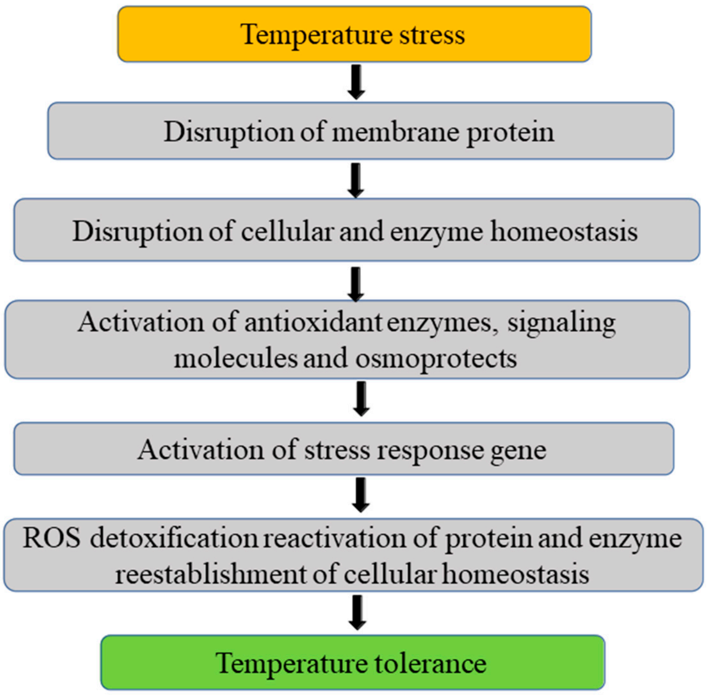

Figure 3. The overview of cyanobacterial response after varying temperature conditions.

Temperature variations have an impact on membrane lipid saturation and protein integrity. Therefore, 2-DE and MALDI-TOF analysis has been carried out to assess the influence of high temperature on the proteome of different cyanobacterial strains. For example, *Anabaena doliolum*, *Synechocystis* PCC 6803, and *Spirulina platensis* showed high denaturation and protein aggregation during analysis [103–105].

3.4.1. Low Temperature

It is well-known that cyanobacteria can survive at very low temperatures, even up to −20 °C [106]. However, exposure to low temperatures causes desaturation of fatty acids in the membrane and activates certain enzymes that boost transcription and translation efficiency [9,12,15,107]. In the previous study, it has been reported that exposure of cold stress can trigger more than 100 genes. In addition, the Desa, DesB, DesC, and DesD are cyanobacterial acyl-lipid desaturases that cause the unsaturation of fatty acids by forming a double bond in the 12, 15, 9, and 6 positions under the cold stress [108,109]. Respiration and photosynthesis, membrane and cell wall maintenance, transcription and translation, signal detection and transduction, and other cellular processes (nucleotide metabolism, cofactor biosynthesis) and unknown functions are all grouped into six groups. Other cold-temperature adaptation strategies include the formation of antifreeze and cold shock proteins, modifying critical protein kinetics, and building polyunsaturated fatty acids (PUFA) in membranes [107].

3.4.2. High Temperature

High temperatures cause excessive fluidity in the membrane and also change the nature of bonding (electrostatic and hydrogen) between different polar groups of proteins, resulting in structural changes and ion leakage [110]. However, the aggregation and denaturation of proteins are common phenomenon occurring during high-temperature stress, disturbing protein functions and trafficking. The HSPs then act as proteases and chaperonins and assist in protein refolding and causing high-temperature tolerance [105,111,112].

3.5. pH Stress

pH has an impact on cyanobacteria's physiological and metabolic activities, as well as their growth. Changes in pH severally affect cellular physiology and metabolic functions, such as nutritional bioavailability and substance transfer across the cytoplasmic membranes. However, the ability of cyanobacteria for everyday functioning is precise under a fixed pH range. Cyanobacteria maintain a pH of 7.1–7.5 on the inside and nearly 5–10 on the outside of the cell. Extracellular pH reduction lowers the intracellular pH and affects several processes, such as cell wall biosynthesis and solute transfer, and it may limit the growth [113]. The enzymes carbonic anhydrase and oxalate decarboxylase are known to play a crucial role in pH regulation and activation. The upregulation of ATP-substrate binding proteins implies that the phosphate absorption mechanism is highly vulnerable to higher medium pH.

3.6. Salinity and Osmotic Stress

Salinity affects 20% of agriculture and 7% of the world's land area and significantly limits crop productivity [114]. However, osmotic stress is a type of physical stress that occurs due to differences in the ion concentration of inside or outside of the cell. In general, both the salinity and osmotic stresses have comparable effects on cyanobacterial cells [115]. Salinity changes water potential and induces water loss and raises ionic concentration of the cell [116,117]. However, higher concentrations of inorganic ions can harm the cellular growth and metabolism of cyanobacteria [118], but in comparison to higher plants, cyanobacteria are much more resistant to salt stress [117]. The plasma membrane of the cell, which controls intracellular trafficking, is one of the critical aspects for the cyanobacteria to acclimatize under salty concentrations [119–121]

In general, cyanobacteria follow limited sodium absorption and active sodium efflux via Na^+/H^+ antiport as a control mechanism during accumulation of increased Na^+ ions in the cytoplasm of cyanobacterial cells [122]. In addition, the cyanobacterial cell follows some other mechanisms during encounter Na^+ toxicity: (1) collecting organic molecules to keep the osmoticum constant [123], (2) antioxidant defense system activation to detoxify R.O.S. [119], and (3) induction of salt-inducible proteins [124]. Nowadays, blue native SDS-PAGE, followed by MALDI-TOF/MS, analysis has been carried out to deem alteration in membrane dynamics at high salt concentrations in cyanobacteria The proteins involved in cell wall production have been discovered in *Synechocystis* [125]. These changes likely create a strong diffusion barrier, resulting in decreased inorganic ion flow into the periplasm [126].

Ionic stress has a significant impact on the cyanobacterial nitrogen fixation. The exposure of NaCl results in the inhibition of nitrogenase activity [127,128]. However, in the *Microcoleus vaginitis*, sucrose phosphate synthase (S.P.S.) activity increases with the elevated concentration of NaCl [129]. Differential stimulation of antioxidative systems in response to higher saline concentration has been observed in *Synechocystis* and *Anabaena*. In a study, the author reported a decrease in the S.O.D. enzyme in *Anabaena doliolum* after 24 hrs of exposure to 150 mM salt [119]. However, a higher concentration of saline conditions is also related to the production of glucosyl glycerol via glycolate metabolism and photorespiration; this is also a critical metabolic alteration observed during salinity stress conditions [130,131].

3.7. Desiccation

Desiccation/draught is one of the common stress factors of terrestrial and polar hydro-terrestrial ecosystems [132]. Cyanobacteria have been considered poikilohydric creatures, which means they can endure dehydration [133]. In the previous study, various authors have reported the desiccation potential of cyanobacteria. For example, the survival of dried *Nostoc commune* samples have been reported after 55 years [134] and 87 years [135], and also for more than a century [136]. Cyanobacteria follow numerous methods to decrease mechanical and osmotic stresses, similar to salt and freezing stress [137]. The desiccation adversely affected several physiological processes in consecutive order: firstly, stop the nitrogen fixation then slow rate of photosynthesis, and ultimately slow down the respiration although these physiological processes can be restored after rehydration. The ability of cyanobacteria to endure low water potential exemplifies their excellent desiccation tolerance (Figure 4). In a study, *Chroococcus cryptoendolithic* and *Chroococcidiopsis* have been reported to fix carbon dioxide at lower water potentials [138].

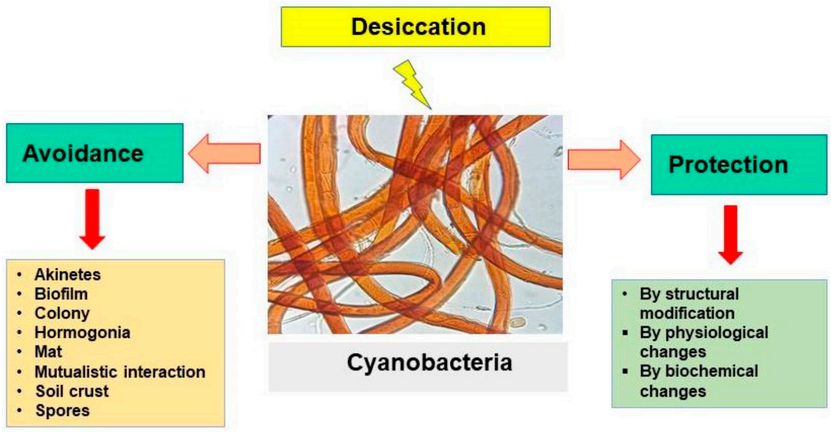

Figure 4. Schematic representation of the general mechanism of desiccation tolerance by cyanobacteria.

3.8. Freeze and Melting Cycles

In polar areas, cyanobacterial populations are frequently vulnerable to freeze/melt cycles [139,140]. Various cyanobacterial groups under low temperatures, especially in the Antarctica region, showed modifications in the structural characteristics [141]. The ice crystals can penetrate the intracellular structures, and the changing osmotic gradient can harm the cell [56,142]. However, the presence of anti-freezing proteins and other cryoprotectants, such as Dimethylsulfoxide (DMSO), inhibit the ice crystals' formation [143].

3.9. Metals and Metalloid Stress

In general, cyanobacteria require significantly higher concentration of metals than non-photosynthetic organisms, since they perform oxygenic photosynthesis. Metal ions, such as Mg and Mn, play various roles in the photosynthetic complex. However, copper (Cu) is present in the cytochrome oxidase and plastocyanin of cyanobacteria. [144]. Cyanobacteria safeguard metallic homeostasis by various methods, including membrane alterations, transfer pump activation or inactivation, biotransformation, and sequestration [145]. However, the higher concentrations of Zn and Cu can lead to the generation of reactive oxygen species (R.O.S.), which affect normal physiology [146]. In addition, the excess Cu can disturb the photosynthesis and redox equilibrium of the cells, disrupting the cells' ultrastructure and, finally, leading to death [147–149]. Metallothioneins (M.T.) are small cysteine-rich proteins associated with metals (such as Cd, As, Cu, Zn, and Hg) that were discovered for the first time in cyanobacteria that helps in surviving even under high Cd or Zn concentrations [150]. Similarly, rather than using proteomic research, most work on metal stress has relied on genomic methods, such as D.N.A. microarrays and targeted mutagenesis [151]. Only a few proteome-based studies have been documented [152,153].

4. Proteomics and Cyanobacteria

Proteomics reflects the cell's functionality, bringing the '*virtual life of genes to the actual life of proteins*' [5,154]. This represents an organism's complete protein composition at a specific moment, under specific conditions. With recent discoveries in biotechnology, high proteomic techniques provide crucial improvements in detecting the integration, regulation, and function of the proteome [155]. In cyanobacteria, stress tolerance is regulated by significant gene expression, which changes the centre dogma's downstream process. As a result, analyzing alterations in the metabolome and proteome is critical, since they are direct mediators of stress responses [4,156–158]. The elucidation of subcellular compartments, such as plasma periplasm [124], PSII complex [159], and thylakoid proteins, showed recent success in proteomic investigations [160]. Proteomics allows for a more precise knowledge of how environmental perturbations affect a system. Several proteomics investigations with different cyanobacterial species have been completed under various abiotic stresses (Table 2).

Table 2. Proteome analyses in response to different abiotic stresses in cyanobacteria.

Cyanobacterial Strain	Stress	Methodologies	Proteins Identified	References
Anabaena sp. PCC 7120	Arsenic	2-DE, MALDI-TOF/MS, RT-PCR	45	[153]
Arthrospira plantensis-YZ	Salt	2DE, MALDI-TOF/TOF, qRT-PCR	141	[161]
Anabaena Doliolum, *Anabaena* PCC7120, and *Anabaena* L-31	Methyl viologen	2DE, MALDI-TOF MS/MS	103, 92, and 41, respectively	[162,163]
Anabaena sp. strain 90	Inorganic phosphorus (Pi)	2D-DIGE and LC-MS/MS	43	[164]
Anabaena L31, *Anabaena doliolum*, and *Anabaena* sp. PCC 7120	UV-B stress	2DE, MALDI-TOF MS/MS	90, 91, and 98, respectively	[165]
Anabaena sp. strain L31	UV-B	2DE, MALDI TOF MS/MS, Bioinformatics	21	[166]
Synechocystis sp. PCC 6803	3-hydroxypro pionic acid (3-HP)	iTRAQ-LC -MS/MS L.C.–MS-based targeted metabolomics	2264	[167]
Synechocystis sp. PCC 6803	Cobalt, cadmium, and nickel	2-DE MALDI TOF/MS RT-PCR	20 (Nickel) 26 (Cobalt) 13 (Cadmium)	[168]
Synechocystis sp. PCC 6803	Butanol	iTRAQ and LC-MS/MS	303	[169,170]

5. Application of Cyanobacterial Secondary Metabolites in Imparting Abiotic Stress Tolerance

The interaction of cyanobacteria with plant species have a long history, and they interact with each other in both positive and negative ways. The symbiotic relationships of rice with nitrogen fixing cyanobacteria in rice fields have been broadly studied. However, cyanobacteria synthesize a range of bioactive compounds that show plant growth promoting potential, and nowadays, cyanobacterial inoculants have been frequently utilized as a biofertilizers in the agricultural fields [171]. In previous studies, several authors reported constructive cyanobacterial functions, such as fixing atmospheric carbon and nitrogen, improving nutrient recycling, and producing various bioactive compounds [172]. They have much potential to store nitrogen and phosphorus in their protoplasm and can help in restoring soil fertility. In the previous study, several authors reported the enhancement in growth and yields after cyanobacteria filtrate. For example, Hashtroudi et al. [172] reported the growth of some horticultural crops by using water extracts of different cyanobacterial strains. The extract contained significant amount of auxin, which showed a stimulatory effect on root growth, dry weight, and plant height. Similar types of observation were reported by Haroun et al. [173] after applying *Cylindrospermum muscicola* and *Anabaena oryzae* filterate, which, after application, enhanced the chlorophyll, carbon, and nitrogen contents.

In cyanobacterial extracts, varying amounts of caffeic, polyphenolics gallic, vanillic, ferulic acids, kaempferol, flavonoids, rutin, and quercetin have been reported. The existence of these polyphenolics showed their ability to scavenge free radicals, chelate metals, and protect themselves from oxidative damage [174]. In addition, the predominance of polyphenols in cyanobacterial strains can lead to their better ecological adaptation under various stress conditions [174]. By generating and releasing a wide variety of bioactive chemicals, cyanobacteria can enhance plant growth and development [175]. In addition, they can also be used to impart abiotic stress tolerance in plants, as listed in Table 3.

Many abiotic variables (drought, salinity, and severe temperatures) manifest as osmotic stresses in plants, resulting in the formation of R.O.S. that damage carbohydrates, proteins, lipids, and D.N.A. and produce abnormal cell signaling [176]. However, soil inoculation with cyanobacterial-based biostimulants increased the antioxidant potential [177]. Similarly, Singh et al. [178] reported that soil inoculation with *Plectonema boryanum* and *Oscillatoria acuta* increased the enzymatic activity of phenylalanine ammonia-lyase and peroxidase in rice leaves, resulting in systemic tolerance against the stress.

Table 3. Role of cyanobacteria and its mechanism in imparting abiotic stress tolerance in plants.

Stress	Cyanobacteria	Plant	Mechanism	References
Cold	*Anabaena* sp.	*Agrostissto lonifera* L.	Growth modulation in plants via transformation in flavodoxin gene	[179]
	Aphanothece halophytic	*Populus alba*	With the transformation in HSP70 gene	[180]
	Synechocystis sp. *Synechococcus vulcanus*	*Nicotiana tabacum*	Plant transformation with a Δ9 and Δ12 acyl–lipid desaturase genes	[181]
Salinity	*Nostoc flagelliforme*	*Arabidopsis thaliana*	Transformation in plants using P-loop NTPase domain gene	[182]
	Anabaena vaginicola ISB42, *Nostoc calcicola* ISB43, *Trichormus ellipsosporus* ISB44, and *Cylindrospermum michailovskoense* ISB45	*Mentha piperita*	Growth promotion plant	[183]
	Nostoc carneum TUBT04 and *N. carneum* TUBT05	*Oryza sativa*	Growth and yield enhancement in plants	[184]
	Lyngbya mucicola; Oscillatoria Princeps L.; *Lyngbya phormidium Gloeocapsa* sp.; *Cryophilic* sp.	*Oryza sativa*	Enhancement in soil organic matter and enhanced concentration of plant nutrients	[185]

Table 3. *Cont.*

Stress	Cyanobacteria	Plant	Mechanism	References
Salinity	*Anabaena oryzae*, *Anabaena doliolum*, *Phormidium fragile*, *Calothrix geitonos*, *Hapalosiphon intricatus*, *Aulosira fertilissima*, *Tolypothrix tenuis*, *Oscillatoria Acuta*, and *Plectonema boryanum*	*Oryza sativa*	Growth promotion and modulation of phytohormone concentration	[186]
	Scytonema hofmanni	*Oryza sativa*	Production of gibberellin-like hormone	[187]
	Nostoc kihlmani and *Anabaena cylindrica*	*Triticum aestivum*	Enhanced growth and improved soil structure	[188]
	Anabaena sphaerica		Production of extracellular polysaccharides and proteins	[189]
	Nostoc flagelliforme	*Arabidopsis thaliana*	Transformation in plants with P-loop NTPase domain gene	[182]
	Nostoc muscorum; Anabaena fertilissima, A. anomala	*Oryza sativa*	Increase in the rhizosphere biology or phytohormone	[190]
	Nostoc calcicola, *Nostoc spongiaeformae*, *Nostoc linckia*, and *Nostoc muscorum*	Wheat, maize, and rice	Increased seed vigor index and germination, vigor index	[191]
	Anabaena variabilis	*Medicago truncatula*	Transformation in plants with flavodoxin gene	[192]
	Anabaena sphaerica	*Oryza sativa*	Production of extracellular polysaccharides and proteins	[193]
Drought	*Nostoc flagelliforme*	*Arabidopsis thaliana*	Enhance seed germination under salinity stress	[182]
	Nostoc sp. and *Microcoleus* sp.	*Senna notabilis* and *Acacia hilliana*	Seeds priming and enhanced germination	[194]
	Anabaena sp.	*Agrostis stolonifera* L.	Transformation in plants with a flavodoxin gene	[179]
	Leptolyngbya sp., *Microcoleus* sp., *Nostoc* sp., and *Scytonema* sp.	*Eucalyptus gamophylla* and *Grevillea wickhamii*	Enhanced radicle initiation and improved shoot and root growth	[195]
	Anabaena sp.	*Nicotiana tabacum*	Plant transformation with a flavodoxin gene	[196,197]
Osmotic stress	*Anabaena* sp.	*Nicotiana tabacum*	Transformation in plants with flavodoxin and a ferredoxin–NADP+ reductase gene	[198]
Heat	*Anabaena* sp.	*Agrostis stolonifera* L.	Plant transformation with a flavodoxin gene	[179]
	Nostoc sp., *Anabaena doliolum*, *Calothrix* sp., *Westiellopsis* sp., and *Phormidium papyraceum*	*Oryza sativa*	Heavy metal stress tolerance and improved plant growth	[199]
Heavy metal	*Nostoc muscorum*	*Trigonella foenumgracum*	Enhancement in the sugar, protein, and lipid content	[200]
	Synechococcus sp.	*A. thaliana*	Transformation in plants with a metallothionein gene	[201]
	Nostoc sp., *Anabaena doliolum*, *Calothrix* sp., *Westiellopsis* sp., and *Phormidium papyraceum*	*Oryza sativa*	Tolerance of heavy metal stress and enhancement in plant growth	[202]
	Spirulina platensis	*Zea mays* L.	Activation of plant mechanisms	[203]

6. Future Perspective

In the last few years, various authors have studied the impact of abiotic stresses on cyanobacterial biology and reported their observations. However, the proteins are the most essential ingredients of the cell, largely affected under stress conditions. Proteins are essential parts of the cell that are severally affected and the main effectors of metabolic disorders caused by abiotic stress. Stresses such as cold, salt, thirst, metals, and metalloids cause similar harm. Almost all stimuli have been linked to increased production of proteins linked to oxidative damage. Photorespiration is primarily induced by salt and, in some situations, UV-B induces D.N.A. damage directly. Temperature and pesticides primarily target membrane dynamics, while metals impact the system's redox status.

However, certain stress conditions are used during the production of specific metabolites because cyanobacteria have been reported to acclimate to changing environmental conditions by modulating the concentration of metabolites. Detailed biochemical research could lead to the discovery of new biotechnologically essential substances. These molecules could be employed in food supplements, cosmetics, cryopreservation, medicine, and other applications. In addition, cyanobacteria could be used as part of regenerative waste disposal system in future aquatic and terrestrial environments.

Many of the proteins examined during cyanobacterial stress biology are linked with the higher plants, confirming their close evolutionary link. However, the proteomics in cyanobacteria is still in its early stages and needs an extensive study to understand stress responses. More research into the intricate web of metabolites and proteins under different combined stress situations is needed to address the types and ranges of proteins and their involvement in cyanobacterial survival and nourishment.

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