Chapter

Potential of Cyanobacteria in Wound Healing

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Abstract

The wound care market is rapidly expanding due to the development of innumerable dressings that exhibit specific healing requirements for different wound types. The use of biomaterials as suitable wound dressing material is highly advantageous due to their biocompatibility, biodegradability, and non-toxicity. Cyanobacteria have been widely explored for their potential applications in wound healing, as they are the rich source of bioactive compounds with antibacterial, anti-tumor, antiviral, antioxidant, and antifungal activities. In recent years this group of organisms has been widely studied due to their immense potential in biomedical applications. Although their different bioactivities can support wound healing in different ways, very few forms have proven utility as a wound-healing agent. This chapter gives an insight into the potential of cyanobacteria in wound healing. Different bioactive compounds present in variable forms of cyanobacteria and their associated activities were reported to support tissue regeneration and wound healing acceleration. As the demand for cost-effective, bioactive wound care products is ever increasing, these organisms have immense potential to be utilized for the development of bioactive wound dressings. Hence, various bioactive compounds of cyanobacteria, their associated activities, and roles in wound healing have been briefly reviewed in this chapter.

Keywords: Cyanobacteria, wound healing, bioactive compounds, hemostatic, antioxidant activities

1. Introduction

Wound healing involves various interactions between cellular, molecular, biochemical, and physiological activities, making the process very complex, dynamic, and precisely programmed. Wound healing involves four phases: hemostasis, inflammation, proliferation, and remodeling to restore the structural, functional, and physiological integrities of injured tissues [1]. This process results in the regeneration and replacement of injured tissue at the wound site [2]. Several nutritional factors are required for proper cellular differentiation, immune functioning, and collagen formation [3]. Any interruption, aberrance, or prolongation in the healing process would extend the tissue damage and thus prolong the repair process, contributing to chronic wound healing [4]. In recent years there has been accelerating demand for various wound dressings, each with specific characteristics, considering the distinctive healing requirements of various wound types. Various synthetic and natural products have been widely explored for their efficiency and accelerating wound healing abilities to accomplish the need for suitable dressing for a particular wound type.

The nonabsorbent and non-biodegradable nature of synthetic products makes these products unsuitable for healing purposes [5]. Medicinal plants are widely being explored for their utility in wound healing, and the ancient knowledge of medicinally essential plants, their increased popularity and utility further raised interest in exploring new natural products useful for the healing process. Various studies confirmed the anti-inflammatory, pro-collagen synthesis, antioxidant and antibacterial activities of natural products from plants and microbes, potentially beneficial for healing purposes. Biocompatibility and the presence of various bioactive phytochemicals in natural products efficiently promote the healing process and make them economically suitable for designing and fabricating dressings [6]. To satisfy the demand for new natural therapeutic agents for wound healing and to decrease the average costs involved in their development, researchers are screening organisms from overlooked microbial sources having the potential to be used as effective wound healing agents such as proteobacteria, bacterioidetes, and cyanobacteria.

Cyanobacteria are ubiquitous, oxygenic photosynthetic bacteria having diverse nature and can be found in various forms like unicellular and filamentous, marine and freshwater, free-living symbiotic, edible, and poisonous. [7, 8]. This group of organisms has immense potential to produce many primary and secondary metabolites thus are known to perform potent biological activities. Produced secondary metabolites are low molecular weight, natural organic compounds, essential for average growth and development of these organisms. These metabolites have a wide range of applications in the field of medicines, industries, and biotechnology. These metabolites are a rich source of bioactive compounds, and cyanobacteria are the most promising organisms to produce them. In the last few decades, cyanobacteria have gained lots of attention for their medicinal values and wound healing properties. They are the choice of organisms due to their easy availability, fast regeneration, and huge diversity which have further expanded interest of researchers in their values as medicine and functional foods [9]. Thus, their potential as a good source of new therapeutic lead compounds has been realized during the last two decades. Cyanobacterial secondary metabolites show different medicinally essential activities such as antitumor, antibacterial, antifungal, antiviral, anti-inflammatory, immunomodulatory effects, and protease inhibition [10]. These biological activities are helpful to promote wound healing in different ways. Despite their potent biological activities, very few cyanobacterial forms are known to be useful in wound healing acceleration. Thus, this chapter presents an overview of bioactive compounds of cyanobacteria responsible for their various biological activities that promote the wound healing process by affecting different phases and factors of wound healing.

2. Important wound healing properties of cyanobacteria

2.1 Antibacterial activity

Antibacterial compounds are the molecules that kill or inhibit the growth of bacteria by affecting their physiological processes. Increased temperature due to inflammation caused by immune response and humidity caused by accumulation of fluid at the wound surface, make the wounds more vulnerable for bacterial infections. Once the wounded site came in contact with bacteria, they can penetrate underlying tissues, leading to life-threatening infections. To deal with such pathological conditions, effective wound management practices are essentially required. To improve the healing process and to reduce the wound bacterial colonization as well as infection at the wound site, the use of systematic antibiotics and the application of antimicrobial-loaded wound dressings are viable options to overcome the issue of infection and associated delay in healing. Considering the fact that usage of antibiotics has led to the increasing emergence of multidrug-resistant (MDR) strains of bacteria which negatively affects the healing process and worsens this issue [11]. Thus, there is a need to develop/discover an effective wound management material which can efficiently cure wound in such conditions. Several cyanobacteria are known to produce intracellular and extracellular bioactive compounds that possess antibacterial activities. [12]. These compounds are effective against various bacterial strains like *Staphylococcus epidermidis*, *Bacillus cereus*, *Escherichia coli, Staphylococcus aureus, Salmonella typhi, Staphylococcus albus, Micrococcus flavus, Bacillus subtilis, Pseudomonas aeruginosa, Serratia marcescens, Mycobacterium smegmatis, Streptococcus pyogenes*, and some other Gram-positive and Gram-negative bacteria. [13–19]. However, the production of antibacterial agents depends upon the composition of the culture medium, incubation period, pH, temperature, and light intensity during the growth of the selected cyanobacteria [20]. **Table 1** shows the bioactive compounds produced by different cyanobacterial strains, potentially useful for their antibacterial activity.

2.2 Antifungal activity

Devastating chronic wound infection is a significant reason for trauma worldwide, which causes serious public health problems. Majorly bacteria are responsible for infections in wounds, but very few recent studies analyzed both fungal and bacterial communities in the microbiome of chronic wounds, suggesting the role of fungi as underappreciated agents that leads to complications at the wound site [33].

Cyanobacterial Strain	Bioactive Compounds	Reference
Nostoc commune	Noscomin,Comnostins	[13, 21]
Nostoc sp.	Comnostin, Muscoride A, Dodecahydrophenanthrene, 4-methylchrysazin, Norharmane and 4-hydroxy-7-methylindan-1,carbamidocyclophane, Nostocarboline	[13, 16, 22]
Nostoc muscorum	Muscoride A	[23]
Lyngbya majuscula	Tanikolide	[24]
Microcoleus lacustris	Abietane	[25]
Oscillatoria redekei	Coriolic acid	[14]
Lyngbya sp.	Lyngbyazothrin, pahayokolide A	[26, 27]
Scytonema ocellatum, Tolypothrix conglutinate	Tolytoxin	[28]
Lyngbya majuscula	Pitipeptolides, malyngolid	[29, 30]
Scytonema sp.	Scytonemin	[31]
Nostocspongiaeforme	Tenuecyclamides	[31]
Micrococcus lacustris	Norbietane	[32]
Fischerella sp.	hapalindole T, ambiguine-I isonitrile	[14, 18]
Anabaena	Exopolysaccharide	[32]
Tolypothrix tenuis	Exopolysaccharide	[32]

Table 1.
Bioactive compounds of cyanobacterial strains possess antibacterial activity.

Hard to heal wounds like diabetic foot ulcers (DFUs) are majorly infected by members of the genus *Candid*a [34, 35]. Prolong infection along with delayed healing makes these wound types chronic and challenging to manage. Over 75% *Candid*a species were isolated by DFUs. In allergic rhinitis, respiratory disease, diabetic foot ulcers, other allergic fungi such as *Cladosporium* spp., *Aspergillus* spp., *Penicillium* spp., *Alternaria* spp., *Pleospora* spp., and *Fusarium* spp. are reported as critical infection-causing agents. Pathogenic and opportunistic fungi such as *Candida* spp., *Trichosporon asahii*, and *Rhodotorula* spp. are reported to associate with stalled open wounds or wounds resulting in an amputation [33]. Antifungal drugs to cure infected wounds are limited due to their high cost and side effects. So there is an emerging need to discover a new natural fungicidal agent. Many cyanobacterial compounds have been reported to possess inhibitory effects against different pathogenic strains of fungi [36]. They are an excellent source of various bioactive compounds that belong to several different chemical classes like peptides, polyketides, and alkaloids [37]. Bioactive antifungal compounds like nostodione, nostocyclamide, carazostatin, scytophycins, tolytoxin, phytoalexin, fisherellin, hapalindole are isolated from different strains of cyanobacteria [38]. Organic extracts of several cyanobacteria like *Oscillatoria latevirens, Chrococcus minor, Phormidium corium, Lyngbya martensiana, Lyngbya aestuarii, Aphanothece bullosacrude* and *Microcystis aeruginosa* have potential antifungal activity against *Candida albicans* and *Aspergillus flavus* [19]. **Table 2** shows various bioactive compounds of cyanobacteria possessing antifungal activity.

2.3 Antioxidant activity

Antioxidants are substances that prevent oxidation. They balance oxidative stress by eliminating free radicals and allowing the regeneration of tissue by repairing the cells [50]. Respiratory burst generates oxidants during wound healing; production of these oxidants supports acceleration in healing. These produced oxidants act as a messenger and thus promote healing. However, a delicate balance between oxidants and antioxidants required to control the progress of the wound. For normal wounds, low physiology levels of reactive oxygen species and oxidative stress are required at wound sites. Whereas oxidative stress and impaired wound healing led by their overexposure. To improve the level of oxidative stress, increased level of antioxidants is expected, which further help in healing acceleration [51]. Antioxidants also preserve

Cyanobacterial Strain	Bioactive Compounds	Reference
Scytonema hofmanni	Cyanobacterin	[39]
Calothrix fusca	Calophycin	[40]
Hapalosiphon fontinalis	Fontonamide, hapalindole	[38, 41]
Tolypothrix tenuis	Toyocamycin, Tubercidin	[42, 43]
Lyngbya majuscula	Majusculamide C, Hectochlorin, Tanikolide	[24, 44, 45]
Hyella caespitosa	Carazostatin	[46]
Nostoc sp.	Nostocyclamide	[47]
Nostoc commune	Nostofungicidine, Nostodione	[48, 49]
Scytonema sp.	tolytoxin, phytoalexin, scytophycins	[38]
Fischerella muscicola	fisherellin	[38]

Table 2.
Antifungal activity of bioactive compounds isolated from different cyanobacterial strains.

and stimulate the function of immune cells against homeostatic disorders. Therefore, their increased levels can improve the immune response and accelerate wound healing [52]. Accumulation of low molecular weight iron at the wound site also increases inflammation and microbial invasion of the wound [53], suggesting the requirement of a chelating agent to achieve proper healing. Production of various, chemically diverse groups of secondary metabolites from cyanobacteria established their industrial significance and made them an excellent source of antioxidants that facilitate the formation of the body's defense mechanism against free radical induced damages to cells. Their antioxidant and metal chelating ability are reportedly due to phytonutrients and pigments present in them [54]. Their cell-free extracts possess free radical scavenging property, metal chelating activity, and deoxyribose protection [55]. The antioxidant properties of the cyanobacterial cell extracts are imparted by the total phenol and total flavonoid content present in the extracts. The free radical scavenging, metal chelating, and antioxidative damage protecting properties of cyanobacterial cell extracts are presumably linked with varied quantities of polyphenolics, gallic, chlorogenic, caffeic, vanillic, and ferulic acids, flavonoids, quercetin, and kaempferol present in them. Exopolysaccharides of cyanobacteria also exhibit good antioxidant and anticoagulant activities. They can also induce oxidants and antioxidant enzymes and are known as immunostimulators [56]. Exopolymers of three strains of *Anabaena* and *Tolypothrix tenuis* exhibited antioxidant activities against $O_2\cdot$, H_2O_2, $OH\cdot$, and $NO\cdot$. These polymers also possess $Fe2^+$ chelating activity, helps in preventing the invasion of pathogenic organisms at the wound site. A strong correlation of sulfate content against superoxide and nitric oxide radicals scavenging activity of exopolymers was found, whereas H_2O_2 scavenging ability and reducing power were contributed by phenols present in them. The overall reducing power and superoxide control strongly related to their iron chelation ability [57]. The highest phenolic, flavanoid, and phycobiliprotein content in *Lyngbya* sp. possessed the highest 2,2-diphenyl-1-picrylhydrazyl (DPPH) activity. The antioxidant potential of *Spirulina* sp. was presumable related to the presence of alcoholic and phenolic OH groups in the cellular structure of the organism [54]. Phenolic content in methanolic extracts of *Anabaena* sp., *Nostoc* sp., *Nostoc commune, Nodularia spumigena, Leptolyngbya protospira, Phormidiochaete* sp. and *Arthrospira* platensis reported higher antioxidant activity than their aqueous extracts [58, 59]. Similarly, ethanolic extracts of *Phormidium fragile, Lyngbya limnetica, Scytonema bohnerii* and *Calothrix fusca* possess antioxidant ability [60]. Cyanobacterial pigments also possess antioxidant activities. In *Lyngbya* and *Phormidium* sp. peroxyl and hydroxyl radicals, scavenging ability was reported to be linked with the presence of covalently linked tetrapyrrole chromophore with phycocyanobilin [61]. Phycocyanin, a type of phycobiliprotein isolated from *Spirulina platensis* and *Geitlerinema* sp., reported to have antioxidant and anti-inflammatory properties and ability to scavenge peroxyl, hydroxyl, and superoxide radicals [62]. Phytonutrients, pigments, and polysaccharides of cyanobacteria exhibit good antioxidant, anticoagulant, and metal chelating ability [54, 56]. Polysaccharidic exopolymers of three strains of *Anabaena* and *Tolypothrix tenuis* possessed antiradical and Fe^{2+} chelating activity. All these exopolymers exhibited antioxidant activities against $O_2^{\bullet}$, H_2O_2, $OH^{\bullet}$, and $NO^{\bullet}$, thus helps in the rapid healing of the wound [57].

2.4 Immunomodulatory and anti-inflammatory effects

Inflammation is a local, protective and physiological response to microbial invasion or injury. The magnitude of the inflammatory response is crucial: insufficient responses result in immunodeficiency, whereas excessive responses cause morbidity and mortality. Therefore, homeostasis and health are restored when inflammation is limited by anti-inflammatory responses [63]. Natural compounds have gained lots of attention in treating various types of inflammations to reduce the reaction of the immune system against pathogens, toxic compounds, and damaged cells. The immune system actively participates in homeostasis, re-establishment, following tissue injury via multiple mechanisms, and plays a critical role throughout the wound healing process. Immune system control to promote tissue repair and regeneration is an attractive approach when designing regenerative strategies. Now a day, the multifunctional immunomodulatory properties of cyanobacteria are gaining much attention in the field of medicine. Cyanobacteria produce various metabolites with different chemical structures, including small molecules of peptides and proteins, polysaccharides, fatty acids, and their derivatives, possessing anti-inflammatory activities [64]. Different cyanobacterial components control the release of certain cytokines from human monocytes and macrophages. Depending on the wound microenvironment, they also can reduce or activate the production of reactive oxygen species from neutrophils [65]. Immunomodulatory effects of cyanobacteria highly induce activation of both types of immune cells which could promote wound debridement, accelerate re-epithelization, and wound closure [66]. Edible cyanobacterial forms are known for their immune-boosting abilities, and many studies have proven their immunomodulatory and anti-inflammatory effects. *Spirulina* is a widely consumed cyanobacterial strain because of its extraordinary neutraceutical and pharmaceutical values. Dietary effects of *Spirulina platensis* showed increased phagocytic and increased antigen production and increased natural killer cell-mediated antitumor activity in the test animals under study [67]. Daily consumption of *Spirulina* stimulates and promotes the immune system by increasing the phagocytic activity of macrophages, induces antibodies and cytokines production, increases accumulation of natural killer cells into tissues, and activates T and B cells [68]. Daily consumption of *Spirulina* for 16 consecutive weeks reported a significant rise in plasma IL- 2 concentration and a significant reduction in IL-6 concentration in humans [69]. Nonadecane and 9-Eicosyne in *Spirulina* were supposed to be responsible for the anti-inflammatory effects [70]. A high-molecular-weight polysaccharide extracted from the cyanobacterium *Spirulina* is known as Immulina®, a potent activator of innate immune cells and exerts inhibitory effects in the induced allergic inflammatory response [71, 72]. It also exhibits anti-inflammatory properties and can inhibit the release of histamine from mast cells [47]. Gama and alpha-linolenic acid are the fatty substances extracted from *Spirulina* and *Aphanizomenon flos-aquae*, respectively, which inhibit the formation of inflammatory mediators [48]. Similarly, *Nostoc* is an edible, largely consumed cyanobacterial form after *Spirulina.* Polysaccharide-rich extracts of *Nostoc commune* could be potentially used for macrophage activation and consequently inhibit the leukemic cell growth and induce monocytes/macrophages when used to treat human monoblastoid leukemia U937 cells [73]. Different immunomodulating activities of *Microcystis aeruginosa, Synechocystis aquatilis, Oscillatoria redekei, Anabaena flos-aque, Aphanizomenon flos-aquae, Oscillatoria rubescens, Oscillatoria tenuis* have also been reported [74] their different cell extracts variably promote the proliferation of lymphocytes. On the other hand, some species of cyanobacteria that contain cytotoxic metabolites (cyanotoxins) can cause immunotoxicity and immunosuppression. The property of immunotoxicity is well reported in cyanobacterial bloom extracts containing microcystin [75]. Treatment with microcystin showed inhibition of lipopolysaccharide-induced lymphoproliferation and decreased numbers of antibody-forming cells; this results in immunosuppression in mice that were immunized using T-dependent antigen sheep red blood cells. A form of cyanobacterial toxin, cylindrospermopsin, is an important water pollutant having broad biological activity. Cylindrospermopsin promotes significant production of pro-inflammatory mediator tumor necrosis factor α and reactive oxygen species when introduced in macrophages cells [76]. Effmert in 1991 reported aqueous extracts of different cyanobacterial species *Microcystis aeruginosa, Synechocystis aquatilis, Oscillatoria redekei, Anabaena flos-aque, Aphanizomenon flos-aquae, Oscillatoria rubescens, Oscillatoria tenuis* possess strong immunomodulating activities [74]. Aqueous extract of the marine cyanobacterium, *Trichodesmium erythraeum*, ethyl acetate extract of non-edible blue-green algae *Geitlerinema splendidum* exhibit anti-inflammatory activity [77, 78]. In chronic wounds where a coordinated wound healing cascade fails to progress beyond the inflammatory phase, the anti-inflammatory activity of cyanobacteria helps in the wound healing by proliferation, matrix deposition, and ultimately, wound resolution [79]. During the last decade, several bioactive compounds have been isolated from cyanobacteria having anti-inflammatory properties that suggest their importance and potential in developing a huge market of wound healing aids [10]. Different classes of cyanobacterial bioactive compounds like phycobilins, phenols, polysaccharides, steroids, and terpenoids possess potential anti-inflammatory effects. Selected anti-inflammatory compounds of different cyanobacterial strains are listed in **Table 3**.

2.5 Hemostatic activity

For people throughout the world, traumatic injuries have been a challenge. Considering technological advancements made through age's trauma remains a leading cause of human morbidity and mortality [90]. Excess bleeding can cause delayed wound healing, hematoma formation, infection, dehiscence, and necrosis. Patients suffering from trauma and its consequent hemorrhage essentially require the establishment of hemostasis by topical wound dressings. Constriction of blood vessels, the activation of the coagulation cascade, and the formation of blood clots are essential

Chemical group of bioactive compound	Bioactive Compound	Cyanobacterial Strain	References
Amino acids and peptides	Aeruginosin	*Nostoc* sp.	[80]
	Porphyra	*Aphanizomenon flos-aquae*	[81]
	Shinorine	*Anabaena variabilis*	[82]
	Phycocyanin	*Spirulina* sp	[72]
	Ethyl tumonoate A	*Oscillatoria margaritifera*	[83]
	Cyanopeptolin	*Microcystis* spp	[84]
Polysaccharide	Sacran	*Aphanothece sacrum*	[85]
Lipids	Monogalactosyl diacylglycerol, Digalactosyl diacylglycerol, Sulphoquinovosyl diacylglycerol, Phosphatidyl glycerol	*Phormidium* sp.	[86]
Pigment	Scytonemin	*Scytonema*	[87]
Others	Coibacin A	*Oscillatoria* sp.	[88]
	Honaucins A–C	*Leptolyngbya crossbyana*	[89]

Table 3.
Bioactive compounds of cyanobacterial strains possessing anti-inflammatory properties.

and significant steps of hemostasis. Therefore, any effort made to accelerate any or all phases above can help achieve hemostasis [91]. The role of cyanobacteria and algae in hemostasis is significantly less known and identified. In the majority, their antithrombic activities useful to cure thrombosis-related diseases are reported. The antithrombic activity of Spirulan, a sulfated polysaccharide of *Arthrospira platensis* has been widely known. Spirulan is helpful to directly decrease the activity of thrombin and factor X activated, procoagulant proteins that can be used to prevent thrombus formation and partial lysis of thrombus [92]. Similarly, *Microcystis aeruginosa* and different cyanobacteria blooms produce probable fVIIa-soluble Tissue Factor (fVIIa-sTF) inhibitors [93]. Vitamin-K-dependent clotting factors like thrombin and fVIIa are associated with bleeding, related complications, and disorders. These factors can induce excessive bleeding when treated with vitamin-K antagonists. *M. aeruginosa* produces bioactive compound Aeruginosin, which shows positive fVIIa-sTF inhibitory activity. Daily consumption of aqueous extract of *Spirulina platensis*, containing a high dose of phycocyanin was found safe for when tried on the human to test its anticoagulant activity and platelet activation ability. The studied extract is also suitable for providing rapid and robust relief in chronic pain. The extract also improved the liver function and metabolism by reducing the activity of aspartate transaminase and alanine transaminase enzymes [94]. C-phycocyanins extracted from *Spirulina platensis* possess significant anticoagulation, antioxidant, and prevention of DNA damage activities [95]. Exopolysaccharides of *A. platensis* possess antiatherogenic and anti-thrombogenic activities [96]. Although the significant roles of cyanobacterial and algal polysaccharides as antioxidants, antiviral, antitumoral, and anticoagulant have been well-documented and reviewed [10] the single report was found to date mentioning the role of cyanobacterial exopolymers (EPs) isolated from four desert cyanobacteria (*Tolypothrix tenuis* and three species of *Anabaena*) in hemostasis. These exopolymers were potentially beneficial to reduce activated partial thromboplastin time (APTT, a measure of how long blood takes to clot) and prothrombin time (PT, a measure of how long blood plasma takes to clot) by 16–41% and 12–65% respectively. The gravimetric method of thrombogenicity assessment showed that the blood clot formed by the cyanobacterial EPs was heavier vis a vis glass (positive control) and thus was thrombogenic. Similar studies can open the treasure of hidden potential of bioactive compounds of cyanobacteria in hemostasis which needs to be explored more.

2.6 Wound healing effect of cyanobacteria

Specific healing requirements of a wound widen the scope of identifying more natural, economic, and effective wound healing agents, which gave extraordinary rise to the development of many synthetic and natural products useful as suitable wound healing dressing materials. Various natural products obtained by plants are widely known for their medicinal properties, facilitating wound healing. Bioactive secondary metabolites like alkaloids, essential oils, flavonoids, tannins, terpenoids, saponins, and phenolics are present in plant-based natural products. These compounds possess various activities like anti-inflammatory, antioxidant, antibacterial, procollagen synthesis, etc., and efficacy to modulate one or more phases of the wound healing process which further help in accelerated tissue regeneration during healing [97]. Similarly, cyanobacterial bioactive compounds possess important medicinal properties like immunostimulating, antiviral, antioxidant, antibacterial, antifungal, antialgal, and anticancerous activities [38, 98] but very few are known for their wound healing potential. The blue-green microalgae *Spirulina* has been widely studied for its wound healing potential and possess antioxidant, antimutagenic, antiviral, anticancer, anti-allergic, immune-enhancing, hepatoprotective, blood vessel relaxing, and blood lipid-lowering activities [99, 100]. The C-phycocyanin pigment of *Spirulina* promoted proliferation, regeneration, and migration of cells tested on cultured human keratinocytes. A similar set of experiments on Sprague–Dawley male rats showed re-epithelization, neovascularization, presence of inflammatory cells, granulation of tissue amount, and maturation during wound healing [101]. Aqueous extract of *Spirulina platensis* showed proliferation, migration, and enhanced closure rate of wound area within 24 hours when tested on human dermal fibroblast cells (HDF) [102]. Compounds like cinnamic acid, narigenin, kaempferol, temsirolimus, phosphatidylserine, and isomeric derivatives were presumably involved in the accelerated wound healing activity of the studied aqueous extract of *Spirulina platensis*. Antibacterial and antioxidant activities of *Spirulina* are useful to improve the immunity of skin cells, and thus burn cream of ethanolic extract of *Spirulina* along with gold nanoparticles has been formulated. To reduce the pain by numbing the injured area, Lidocaine has been added to the cream as an anesthetic, sodium dodecyl sulfate, and glycerine used for skin moisturization [103]. Polylactic acid (PLA), polyethylene oxide, and PHB (polyhydroxybutyrate) extracted from *Arthrospira* LEB 18 strain used to prepare biodegradable, biocompatible nanofibrous scaffolds. Properties of prepared scaffolds like increased conductivity, higher mechanical durability with enhanced elasticity, tensile strength, and breaking elongation supported nutrient, growth factors, and metabolism byproducts distribution at the wound site [104]. Scaffolds of poly-D, L-lactic acid (PDLLA) associated with LEB 18 biomass showed better adherence to the wound, increased cell viability, and more moldable when compared with classic PDDLA [105]. Natural wound healing processes can be promoted by such biomatrices produced from *Arthrospira*, and also they can minimize the risk of infection [104]. PCL nanofiber loaded with *Spirulina* extract was fabricated as a cutaneous wound dressing material. The designed dressing showed enhanced wound regeneration ability by modulating intra- and extracellular ROS with enhancing antioxidant mechanism and increased fibroblast viability under oxidative stress [106]. *Synechococcus elongatusa*, a naturally occurring photoautotrophic cyanobacterium promoted angiogenesis and burn wound repair in mice. The promotion of interleukin-6 expression and secretion of extracellular vesicles probably induced pro-angiogenic and wound healing effects in the studied animals [107]. In diverse marine, freshwater, and terrestrial organisms, ultraviolet-absorbing mycosporine-like amino acids (MAAs) are found as secondary metabolites. *Nostoc flagelliforme* and *Nostoc commune*, are widely known for their edible values and reported as natural resources of MAAs. These secondary metabolites possess several beneficial effects and are useful as sun-screening cosmetics, antioxidants, and pharmaceuticals [108]. In wound healing, MAAs modulate skin fibroblast proliferation and activate adhesion kinases, extracellular signal-regulated kinases that promote acceleration in wound healing. Extensive researches are conducting on MAAs to identify their potential as a new wound healing agent to be explored as a novel biomaterial for wound healing therapies [109]. Cyanobacterial glycans are known as hydrogels that imbibe large amounts of biofluids [110]. This property of glycans extremely useful for targeted drug delivery in chronic wound cases [111], where they have been exploited for delivery of low molecular weight drugs and macro-molecular payloads (hormones, peptide, and protein drugs) [112]. Cyanobacteria have been widely explored and studied for their immense potential in various biomedical applications, but very few are reported for their accelerated wound healing abilities. Most of the studies have been conducted on *Spirulina* which is known for its extraordinary neutraceutical and pharmaceutical values. As these organisms are phototrophic and have minimal growth requirements, they can be easily regenerated, and also their huge diversity makes them suitable candidates for research, having hidden potential for wound healing. Further, they can be explored to develop bioactive and cost-effective wound dressing materials, suitable for all sections of society.

3. Conclusions

The ever-increasing demand for effective bioactive dressings suitable for different types of wounds is rapidly expanding the wound care market at diverse levels. Cyanobacteria are known for their numerous biomedical applications; thus, recently, they are a widely explored group of organisms. The cyanobacterial bioactive compounds possess antiviral, antifungal, antibacterial, antitumor, anti-inflammatory, and antioxidant activities suitable to accelerate wound healing even in chronic conditions by controlling different phases and factors of the wound. Cyanobacteria are known for the abundant availability of versatile bioactive compounds and their associated properties, but unfortunately, very few forms of cyanobacteria are known for their role in wound healing. Their easy cultivation, colossal diversity, and different biological activities can make them suitable candidates for research. Further, they can be explored more in the field of biomaterials for designing and fabrication of low-cost, biocompatible, and biodegradable wound dressings.

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Conflict of interest

The authors declare no conflict of interest.

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