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MEDICAL APPLICATIONS OF CYANOBACTERIA

Gulbicha Orujova
Western Caspian University

Abstract: Cyanobacteria, commonly known as blue-green algae, are vital organisms with significant industrial, medical, ecological, and biotechnological value. These prokaryotic organisms have adapted to thrive in diverse environments worldwide, making them an attractive area of study for biotechnology researchers. Currently, cyanobacteria are employed in various sectors, including agriculture, producing bioenergy and biofertilisers, enhancing soil quality, supporting aquaculture, and treating wastewater. In the food industry, they serve as additives for both food and animal feed. Additionally, cyanobacteria are a source of bioactive compounds that possess antiviral, antibacterial, anticancer, antifungal, and cytotoxic properties, contributing to their broad pharmaceutical applications. This review highlights the medical applications of cyanobacteria and explores their future potential in the field.

Keywords: cyanobacteria, Spirulina, Cladophora, antioxidants, anticancer properties.

***Corresponding Author:** gullu.ordzh@gmail.com

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Introduction:

Cyanobacteria, also referred to as blue-green algae or "Cyanophyta," constitute a group of photosynthetic prokaryotes. They are among the oldest microorganisms on Earth and the first to produce oxygen. These highly specialized microorganisms adapt to various ecological habitats and exist as individual cells, colonies, or filaments (Castenholz, 2001). As a result, cyanobacteria are found in diverse environments, including glaciers, seas, oceans, saline and freshwater bodies, terrestrial soils, and even bare rocks (Whitton, 2012). They are photoautotrophic, utilizing sunlight to produce food and energy, similar to plants. Cyanobacteria possess cellular mechanisms that enable them to adapt to environmental changes, proliferate rapidly, form dense populations, and thrive in diverse ecological niches. Their rapid growth is influenced by biotic and environmental factors, as well as fluctuations in nutrient levels (Sukenik, 2012; Paerl, 2012).

Cyanobacteria, classified under the group Cyanophyceae, lack plasmids, membrane-bound organelles, and true nuclei, characteristic of prokaryotic organisms. Due to the absence of a nuclear membrane, their DNA and pigment-related compounds are freely distributed within the cytoplasm. Their cell walls have a peptidoglycan structure; however, the presence of prokaryotic 70S ribosomes distinguishes them from eukaryotic cells, where 80S ribosomes are found. The cells are enveloped by a thin mucilaginous sheath and a double-walled capsule rich in carotenoids (Cirik, 2004).

Cyanobacteria not only exhibit filamentous structures but can also form colonies consisting of one or multiple cells. They utilize two spore forms, known as coccospore and hormogonia, in addition to vegetative division for reproduction. In certain filamentous forms, individual, robust spore cells known as akinetes can be observed between filament-forming cells. Under favourable conditions, these akinetes detach from the filamentous thallus and give rise to new thalli. Specialized cells within the thallus, known as "heterocysts," play a crucial role in nitrogen fixation by converting atmospheric nitrogen into a usable form, as they lack photosynthetic ability. These heterocysts are systematically significant due to their function and can be distinguished by their thicker walls and transparent appearance (Rinehart, 1994).

Cyanobacteria are microscopic organisms capable of accumulating commercially valuable metabolites. They contain carbohydrates, proteins, essential amino acids, vitamins, and bioactive molecules. The significant pigments produced by cyanobacteria include chlorophyll a, β-carotene, astaxanthin, phycocyanin, xanthophyll, and phycoerythrin. These pigments find extensive applications in the food, pharmaceutical, textile, cosmetic, and natural product industries.

Although cyanobacteria, often called blue-green algae due to their photosynthetic pigments, contribute beneficial compounds, they also produce toxic substances that can be harmful to other organisms. Currently, at least 46 species of cyanobacteria are known to release toxic compounds into aquatic environments, posing a threat to vertebrate life.

Materials and Methods:

The research was conducted on 23 new and In this study, various cyanobacteria species were examined to evaluate their bioactive compound production and potential pharmaceutical applications. Samples were collected from non-arable and non-productive regions, ensuring a diverse range of cyanobacteria for analysis. Specifically, Cladophora glomerata was obtained from the southern region of the Caspian Sea for further investigation.

The cyanobacteria samples were cultured under controlled laboratory conditions using standard growth media to optimize biomass production. Environmental parameters, including temperature, light intensity, and nutrient composition, were carefully maintained to simulate natural growth conditions. The harvested biomass was processed for biochemical analysis, focusing on the identification of bioactive compounds such as microcystins, anatoxins, and cyanotoxins.

To assess the pharmaceutical potential of cyanobacteria-derived compounds, various bioassays were conducted. The antimicrobial and anti-cancer activities were evaluated using in vitro assays against selected bacterial strains and cancer cell lines. High-performance liquid chromatography (HPLC) and mass spectrometry (MS) techniques were employed to characterize the chemical structure of the bioactive compounds.

Additionally, Spirulina samples were analyzed for their nutritional composition, including protein, vitamin, and mineral content. The presence of essential fatty acids such as gamma-linolenic acid (GLA) was quantified to determine their potential health benefits. Statistical analyses were performed to assess the significance of the findings, ensuring the reliability and reproducibility of the results.

Results and discussions:

The diversity of cyanobacteria depends on their numerous unique characteristics. The most important feature of cyanobacteria is their ability to produce molecular oxygen as a byproduct of photosynthesis. Additionally, due to their rapid growth capabilities, they possess a higher productive potential compared to traditional food crops. This is because they can grow in non-productive and non-arable areas (Alberto, 2018). Cyanobacteria also produce bioactive compounds known as microcystins, anatoxins, cyanotoxins, etc. Due to this characteristic, cyanobacteria can form populations that significantly impact human health (Buratti, 2017). On the other hand, some cyanotoxins have the potential to be used in the development of anti-cancer drugs.

Cyanobacteria are widely utilized in the medical field through biotechnological applications. Recently, these microorganisms have attracted the attention of scientists for their production of bioactive compounds that can be used in drug formulations. Although they produce some potent toxins, they also generate numerous compounds with antifungal, antibiotic, antiviral, antimalarial, antifungal, anti-tuberculosis, anti-HIV, and anti-cancer properties (Dittmann, 2001; Volk, 2008). Researchers worldwide have discovered various drugs containing bioactive substances derived from cyanobacteria for the treatment of such diseases. For instance, aflatoxins and their derivatives, obtained from various cyanobacteria, exhibit potential against different cancerous tumour cells. Curacin A, derived from L. majuscula, is highly effective against breast cancer (Gerwick, 1994). Cryptophycins were first discovered in 1990 in cyanobacteria of the genus Nostoc. Cryptophycin is a natural analogue and is considered a powerful anti-cancer drug due to its ability to target various solid tumours, including breast, lung, pancreatic, prostate, ovarian, colon, and brain cancers. Additionally, several synthetic analogues of cryptophycin have been developed, which are used to explore potent anti-cancer agents (Magarvey, 2006).

Fig. 1. Cladophora glomerata obtained from the southern region of the Caspian Sea.

To date, approximately 80% of antibacterial and anti-cancer drugs have been derived from natural product sources. Cyanobacteria are rich in valuable substances that can be used as supplements for improving health. For example, Spirulina contains sustainable dietary supplements—proteins, iron, copper, vitamins B3, B2, and B1—along with powerful antioxidants, anti-inflammatory, anti-cancer bioactive compounds, and low-density lipopolysaccharides. Studies have shown that bioactive compound-rich cyanobacteria reduce blood pressure, regulate cholesterol levels, boost immunity, and strengthen muscles. They also positively affect health by producing gamma-linolenic acid (GLA), which is beneficial for cardiovascular diseases. These properties arise from the presence of carotenoids, chlorophylls, phycocyanins, various amino acids, and minerals (Furmaniak, 2017).

Table 1. Phenolic and flavonoid content, as well as antioxidant activity, of C. glomerata extracts.

Algal Extract	Total Phenolic Content (mg g^{-1})	Total Flavonoid Content (mg g^{-1})
C. glomerata	3077±105	595±23

Cladophora, widely found in the southern Caspian Sea (Figure 1), is one of the largest filamentous green algae genera. The antimicrobial and antioxidant activity of Cladophora glomerata, along with its total phenolic and flavonoid content, has been investigated (Table 1). Using disk diffusion methods, their potential antimicrobial effects at various concentrations were analyzed, resulting in varying degrees of antibacterial activity against different bacteria (Table 2) (Soltani, 2011).

Table 2. Antibacterial activity of Cladophora glomerata extract.

Bacteria	Inhibition Zone (mm)				
	100 mg ml^{-1}	50 mg ml^{-1}	25 mg ml^{-1}	12.5 mg ml^{-1}	7.5 mg ml^{-1}
Salmonella typhimurium	7.7	6.3	-	-	-
Staphylococcus aureus	22.5	21.5	18	13.8	8.7
Pseudomonas aeruginosa	-	-	-	-	-
Bacillus subtilis	11.5	9.2	8.2	-	-
Proteus mirabilis	15	13.8	12	-	-

Among natural resources, cyanobacteria serve as a promising reservoir offering a broad spectrum of compounds for the discovery of new drugs. Several researchers have determined that purified phycocyanin from different cyanobacteria exhibits antioxidant and radical-scavenging activity. It has been reported that purified C-PC from these cyanobacteria has the potential for use in nutrition and pharmaceuticals (Soni, 2006; Spolaore, 2006).

Studies have revealed that C-PC applications can treat various physiological disorders, and its antioxidant and radical-scavenging properties significantly contribute to health benefits. Furthermore, C-PC has been observed to affect mammalian cells and experimental mice by regulating gene expression, inhibiting certain enzymes, such as NADH oxidase, halting cell growth, and inducing programmed cell death in cancerous cells. Due to these findings, interest in using C-PC as a drug or nutritional supplement has increased (Eriksen, 2008).

According to Bousibba and Richmond, phycocyanin is a reserve nutrient used by Spirulina for storage. The commercial production of phycocyanin occurs, with an estimated monthly production of 600 kilograms. In Japan, it is used as a natural colorant in animal feed and cosmetics. Phycocyanin is most commonly used as a food pigment and has been reported to play a role as a biological isotope in immunological research. Additionally, due to its fluorescent properties, this pigment is utilized in flow cytometry and microscopy studies. It is one of the most widely used pigments for colouring confectionery, ice cream, daily commodities, and beverages. Phycocyanin has been generally recognized for supporting the immune system and providing protection against various diseases.

Phycocyanin is commercially produced by various companies worldwide. Its primary applications include food colouring for gum, cheese, jam, and candies. In countries like China, Thailand, and Japan, it is widely used in cosmetic products. According to Benedetti and colleagues, this blue pigment is used in cosmetics such as lipsticks, eye shadows, and eyeliners (Benedetti, 2006).

Phycobilins find applications in the food and cosmetic industries, as well as in biotechnological diagnostics and pharmaceutical preparations. Beyond its nutritional significance, phycocyanin derived from cyanobacteria possesses immunomodulatory, cholesterol-lowering, antioxidant, anti-inflammatory, antiviral, and anti-cancer properties (Boussiba, 1980) (Figure 2).

Fig. 2. Spirulina in tablet, cream, and capsule forms.

Among natural resources, cyanobacteria

In the modern world, the demand for natural minerals, colourants, antioxidants, and dietary supplements with high nutritional value, minimal processing, and no adverse health effects is increasing. Apart from its nutritional benefits, phycocyanin obtained from cyanobacteria enhances the immune system and exhibits significant pharmacological potential in various therapeutic applications (Cornejo, 1997).

Conclusıon:

Molecular analysis of various pigments, antibacterial and antifungal compounds, and vitamins found in cyanobacteria indicates that these organisms could have extensive applications in biotechnology, particularly in the medical field. To optimize their use, it is important to identify new strains that produce these beneficial compounds, develop effective purification methods, and conduct genetic and protein engineering studies to enhance their production potential and stability. By doing so, we can achieve higher purity and yield of these substances, making them more suitable for use in various applications.

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