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# Biological consequences of cyanobacteria and microalgae

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*Motivation and Aim*: Microalgae and cyanobacteria are a diverse group of microorganisms that live in a variety of settings, are capable of oxygenic photosynthesis, and can create a thick microbial mat even in harsh conditions. Microalgae and cyanobacteria contain a diverse variety of physiologically active compounds that can be exploited to create promising dietary supplements and anti-inflammatory medications [1–3]. Only a few of the more than 12,000 microalgae and 5,000 cyanobacteria species are approved for human consumption. On this basis, it appeared natural to investigate the effects of numerous microalgae and cyanobacteria bioactive substances *in vitro* and *in vivo*.

*Methods and Algorithms*: Green microalgae (*Chlorella vulgaris* Beijerink, *Coelastrella sp.*, and *Tetraselmis (Platymonas) viridis* Rouchijajnen), cyanobacteria (*Arthrospira* (Spirulina) *platensis* (Nordstedt) Gomont, *Leptolyngbya cf. ectocarpi*, *Planktothrix agardhii*, and *Roholtiella mixta sp. nov.),* diatoms (*Cylindrotheca closterium* (Ehrenb.) Riemann et Lewin, and *Nanofrustulum shiloi*) and reds microalgae (*Porphyridium purpureum* (Bory) Drewet Ross) were obtained from the Kovalevsky Institute of Biology of the Southern Seas culture collection. Sample extracts were made from dry biomass by passive diffusion of physiologically active chemicals into a 1 % dimethyl sulfoxide (DMSO) solution for 24 hours or into vegetable oil for 72 hours at 37 °C. The effect of oil extracts of microalgae and cyanobacteria was assessed in an experiment on mice fed conventional pelleted food pre-soaked in oil extract; the animals were withdrawn from the experiment on the 13th day. Blood serum was taken, lymphocytes were separated from the thymus and spleen, and cell functional characteristics were assessed in vitro. An extract from kidney and liver homogenate was also obtained. The levels of IL-1β, IL-10, and TNFα were measured in serum, conditioned medium, and kidney and liver tissue extracts using commercial kits "Interleukin-1 beta-IFA-BEST", "Interleukin-10-IFA-BEST", and "TNF-IFA-BEST alpha" (Vector-Best, Russia), according to the manufacturer's instructions. The quantities of persistent nitric oxide metabolites in serum, conditioned medium, and kidney and liver tissue extracts were measured using Griess reagent. The cytotoxicity of DMSO extracts of materials was assessed against mouse splenocytes and peritoneal macrophages, as well as human and rat bone marrow mesenchymal stem cells. Furthermore, the antimicrobial potential of DMSO extracts of samples against Gram-positive and Gram-negative strains of bacteria, as well as *Mycobacterium tuberculosis* and *Mycobacterium smegmatis* was assessed using an *in vitro* micro method, and the *in vivo* effect of an alcoholic extract of Fucoxanthin in an experimental tuberculosis model in mice was evaluated. Furthermore,

the impact of intragastric administration of alcoholic and oil Fucoxanthin on blood biochemical markers and cytokines was investigated. Data is presented in the form of mean and standard deviation (M±SD) in the tables. Utilizing Statistica 10.0 for Windows, data was examined. Statistical significance of differences between samples was evaluated using one-factor analysis of variance (ANOVA) with Bonferroni post hoc test, and accepted at $p < 0.05$.

*Results*: Microalgae and cyanobacteria can impact the functional characteristics of lymphocytes and liver cells [4]. Oil extracts of microalgae and cyanobacteria have been shown to cause changes in serum levels of albumin (*Chlorella*, Spirulina, *Cylindrotheca*); low-density lipoprotein *(Chlorella*, Spirulina, *Cylindrotheca*); high-density lipoprotein (*Chlorella*, *Cylindrotheca*); total cholesterol (*Chlorella*, Spirulina, *Porphyridium*); progesterone (*Chlorella*, Spirulina, *Cylindrotheca*, *Coelastrella*) and increased albumin levels (*Coelastrella*, *Porphyridium*). In addition, there was a rise in IL-1β (*Chlorella*), TNF-α (*Coelastrella*), IL-10 (*Chlorella*, *Coelastrella*), NO (*Porphyridium*), and decrease in TNF-α levels (*Chlorella*, *Coelastrella*).

In liver tissues, protein (*Coelastrella*, *Porphiridium*), transaminases (*Porphiridium*), IL-1β, and NO (*Porphiridium*) increased while protein (C*ylindrotheca*), IL-1β, TNF-α, and IL-10 decreased (*Chlorella*, Spirulina). The study found increased levels of protein (Spirulina, *Cylindrotheca*, *Porphiridium*), creatinine (C*ylindrotheca*, *Porphiridium*), urea (*Chlorella*, *Cylindrotheca*) in kidney tissues.

A decrease in spontaneous IL-10 synthesis by splenocytes was seen in the *Chlorella*, *Coelastrella*, Spirulina, and *Cylindrotheca* groups, whereas mitogen increased IL-10 production in all experimental groups of animals. *Cylindrotheca* increased IL-1β production by splenocytes, but *Chlorella*, Spirulina, and *Porphiridium* decreased it. Additionally, Spirulina lowered splenocytes' production of TNF-α. Thymocytes in the Spirulina and *Cylindrotheca* group produced more IL-1β, IL-10, and TNFα compared to other experimental groups. Mitogen boosted IL-1β synthesis (*Chlorella*, Spirulina, *Porphiridium*) while decreasing IL-10 production (*Coelastrella*, *Cylindrotheca*) in thymocytes.

Microalgae and cyanobacteria, with their ability to resist and protect against pathogens, are a valuable source of such molecules [5]. A significant cytotoxic activity tested microalgae and cyanobacteria extracts on splenocytes were obtained. DMSO extracts of microalgae and cyanobacteria enhanced the proliferation and NO secretion of human and rat bone marrow mesenchymal stem cells, except *Nanofrustulum*.

Fucoxanthin from Spirulina and *Nanofrustulum* decreased the growth of Gram-positive (*S. aureus, E. faecalis, S. pyogenes*) and Gram-negative (*Kl. pneumoniae, A. baumannii, Ps. aeruginosa*) bacteria compared to control and Ceftazidime on days 14 and 21, especially on day 14. DMSO extracts of microalgae and cyanobacteria, as well as Spirulina Fucoxanthin, suppress the growth of *Kl. pneumoniae*, *S. aureus* MRSA, *A. baumannii*, *E. faecalis* (excluding Fucoxanthin), and *Ps. aeruginosa*, with the exception of *Planktothrix* and *Leptolyngbya*. In comparison to Chlorophyllipt and Rifampicin, DMSO extracts of microalgae and cyanobacteria, particularly *Nanofrustulum*, *Leptolynbya*, and Fucoxanthin, shown antimycotic activity. Furthermore, administering Fucoxanthin alcoholic solution intragastrically to mice with tuberculosis caused by *Mycobacterium tuberculosis* strain H37Rv reduces colony counts in the lungs and spleens.

Fucoxanthin is a carotenoid with fat-burning, anti-inflammatory, antioxidant, anti-infectious, and anti-tumor properties [6]. Intragastric administration of Fucoxanthin

alcohol solution reduces albumin, uric acid, creatinine, cholesterol, high-density lipoprotein, hepatic transaminases, and IL-6, IL-10, and INFγ levels in serum while increasing triglycerides, low-density lipoprotein, and TNFα. In turn, Fucoxanthin oil solution increases serum creatinine, low-density lipoproteins, urea, and TNFα while decreasing albumin, uric acid, triglycerides, cholesterol, high-density lipoproteins, hepatic transaminases, lactate, IL-1β, IL-6, IL-10, and INFγ.

*Conclusion*: Thus, microalgae and cyanobacteria from various systematic groups influence the levels of proteins, fats, aminotransaminase activity, sex hormones, and filtration function in rodents, as well as the balance of pro-inflammatory and anti-inflammatory cytokines in blood serum, immunocyte conditioned media (mature and naive), kidney, and liver tissues, which should be considered when selecting microalgae and cyanobacteria as an additive in animal and human diets. Data present here showed that extracts from different microalgae and cyanobacteria taxa, especially Fucoxanthin were effective against bacteria (Gram-positive and Gram-negative) and mycobacteria (*Mycobacterium tuberculosis* strain $H_{37}$Rv and *Mycobacterium smegmatis*). However, it must be emphasized that some microalgae potentiated bacteria growth.

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