CYANOBACTERIUM SPIRULINA (ARTHROSPIRA) PLATENSIS AS VALUABLE SOURCE OF ANTI-VIRAL AGENTS

Valentina BULIMAGA, Liliana ZOSIM, Alina TROFIM, Daniela ELENCIUC
CZU: 615.281:582.232
ciumac@yahoo.com

Introduction. The high virulence of some Coronavirus strains and the absence of effective therapies present an ongoing threat to the public health. Macro- and microalgae were one of the first sources of natural compounds showing in vitro anti-HIV activity. The *in vitro* or *in vivo* studies have shown the possibility of algae and cyanobacteria use against range of viruses [1-5]. This explains the intensification of investigations on algae and cyanobacteria as food and antiviral substances source in general and in some species of *Spirulina (Arthrospira)* for example in particular. *Spirulina (Arthrospira) platensis* refers to prokaryotic ¦filamentous cyanobacteria. The cyanobacterium *Spirulina platensis* are used on large scale as food biodditives due to their biochemical composition: high protein content (60-70%), including phycobiliproteins, acidic polysaccharides, polyunsaturated fatty acids, β-caroten, chlorophyll *a*, vitamins, minerals, as well as presence of secondary metabolites with beneficial health properties such as polyphenols, carotenoids, sterols [6-9]. *Spirulina* has antioxidant, hepatoprotective, nephroprotective, neuro-protective, hypoglycemic, hypolipidemic, antitumor, antimicrobial and anti-inflammatory activity [1,8]. It also induces immunomodulatory responses. All of these functions are related to maintaining homeostasis and improving the health.

Based on a literature framework about antivirals from *Spirulina (Arthrospira)* sp, this work is focused on the description of *Spirulina (Arthrospira) platensis* use as food and antiviral agents source and evaluation of the most relevant data for identification of antiviral and efficient compounds for human health.

Discussion and conclusions. Numerous studies in recent decades on the effect *in vitro* and *in vivo* of algae and cyanobacteria or their extracts on animals and humans have highlighted their antiviral and immunomodulatory properties [2, 5, 10, 11]. As a food supplement with therapeutic effect, the most used is the cyanobacterium *Spirulina platensis*, which in animal and human tests increases phagocytic activity, increases antibody production, contributes to the accumulation of NK cells in the tissue and mobilizes T and B cells in the blood [2, 4, 6, 12]. Chen et al. have identified anti-viral properties associated with cold water extract of *A. platensis*. The group demonstrated that viral plaque formation in a broad range of influenza viruses, including oseltamivir-resistant strains, was inhibited by the *A. platensis* extract. Furthermore, they observed that *Spirulina* extracts increased the lifespan of influenza-infected mice [12]. The sulfated polysaccharides, extracted from algae, present a high antiviral activity *in vitro* against HIV-1 and on other stains of viruses [2,10, 13]. These compounds interfere with the attachment of the virus to its target cells, thus inhibiting

the fusion between viral cells and the entry of the virus into its target cells. Calcium spirulan (Ca-Sp) prevents several viruses from replicating and exhibits antiviral activity against the human immunodeficiency virus type 1 (HIV-1), HSV-1, influenza virus, herpes simplex virus-1, human cytomegalovirus (HVMV and other viruses [13-18].

The Spirulina biomass has been widely used in feed and food supplement, as pharmaceutical remedy for health protection [17,19,20]. *Spirulina (Arthrospira) spp*. compounds were studied as antiviral against various viruses such as *Inluenza, Herpes simplex* virus (HSV) and Hepatitis C (HCV) *in vitro* and *in vivo*, as well as potential source to prevent and cure of SARSCoV-2 [5,11,21, 22]. In search of a natural compound that might increase the immunity and block the viral replication within the host was selected C-Phycocyanin of *Spirulina plantesis* to study its anti-viral property in-silico. In their study, the authors focused on the possibility of C-phycocyanin to inhibit the active site of nsp12, which is very much needed for viral replication. Auto Dock, Auto Grid, and Discovery Studios tools reveal that C-Phycocyanin inhibits the active site of nsp12 , thereby interfering with the replication of the virus itself [23].

In other publication Petit et al. were performed the docking and in silico toxicity assessment of some *Arthrospira* compounds as potential antiviral agents against SARS-CoV-2. Using largely widespread docking software, three *Arthrospira* molecules (folic acid, phycocyanobilin and phycoerythrobilin) among 51 were identified as candidates for antiviral development drugs [22].

In our investigations some procedure of obtaining of spirulina biomass with high phycobiliproteins (phycocyanin) and acidic polysaccharides content, as well as polysaccharides, phycocyanin and *Se-phycocyanin* technologies obtaining have been proposed [24-28]. The purified preparations of phycocyanin and Se-phycocyanin with high nutritive value have many health benefits and an essential antioxidant activity [29]. Acidic polysaccharides are well known for its antiviral activity. The spirulina polysaccharides could be used as anti-viral agents in nasal spray. Phycocyanin with antioxidation, anti-inflammation and anticancer properties is a promising candidate as alternative drug for virus suppression.

Thanks to the very valuable spirulina biochemical composition (high content of proteins, peptides, amino acids, vitamins, antioxidants, acidic polysaccharides, phycobiliproteins, 3 and 6 omega fatty acids with proven immunomodulatory, antioxidant and other properties, administration of biomass and various extracts can increase human body resistance. Both the ability to improve immunity and the property of suppressing the activity of various viruses in humans and animals make cyanobacteria *Spirulina (Arthrospira*) platensis to be successfully recommended as a preventive remedy and an alternative source of anti-viral agents against infection with Covid-19.

References:

1. EL-BAY, F., EL-SENOUSY, W., EL-SAYED, A., KAMEL, M. In vitro antiviral and antimicrobial activities of *Spirulina platensis* extract. In: *Journal of Applied Pharmaceutical Science*, 2013, 3(12):52-56.

2. LUESCHER-MATTLI, M. Algae, a Possible source for new drugs in the treatment of HIV and other Viral Diseases. In: *Curr. Med. Chem.- Anti-Infective Agents*. 2003, 2, (3): 219-225.
3. SCHNITZLER, P. et al. Antiherpetic eficacy of aqueous extracts of the cyanobacterium *Arthrospira fusiformis* from Chad. In: *Pharmazie*. 2013, 68:376-380.
4. NAGULENDRAN, Kr., KAVITHA, N. Antiviral and Immuno Modulating Role of Super Food *Spirulina* and Covid-19 IJTSRD. 2020, 4:621-626.
5. RATHA, S., RENUKA, N., RAWAT. I., BUX, F. Prospective options of algae-derived nutraceuticals as supplements to combat COVID-19 and human coronavirus diseases. In: *Nutrition*. 2021; 83:1-6.
6. ANDRADE, L. et al. *Chlorella* and *Spirulina* microalgae as sources of functional foods, nutraceuticals, and food supplements; an overview. In: *MOJ Food Process. Technol*. 2018, 6, 00144.
7. MATHUR, Meeta. Bioactive Molecules of *Spirulina*: A Food Supplement. In: *Bioactive Molecules in Food. Springer, Cham*. 2018: 1621-1642
8. HETTA, M. et al. Antiviral and antimicrobial activities of *Spirulina platensis*. In: *World J Pharm Sci*. 2014, 3:31-39.
9. RUDIC, V. et al. *Phycobiotechnology, fundamental research and practical achievements*. Chişinău: S.n., Tipogr. „Elena V.I.” SRL, 2007. 365 p.
10. AHMADI, A. et al. Antiviral Potential of Algae Polysaccharides Isolated from Marine Sources. In: *A Review BioMed Research International*. 2015, Article ID 825203. 10 p.
11. PERUMAL, E., SUNDARARAJ, R. Algae: A Potential Source to Prevent and Cure the Novel Coronavirus. In: *A review. Int J Emerg Technol*. 2020, 11:479-483.
12. CHEN, Y. Et al. Well-tolerated Spirulina extract inhibits influenza virus replication and reduces virus-induced mortality. In: *Scientific Reports*, 2016, 6: 24253.
13. JANG, I., PARK, S. A *Spirulina maxima*-derived peptide inhibits HIV-1 infection in a human T cell line MT4. In: *Fish Aquat Sci*. 2016, 19:37.
14. BARRÓN, B. et al. Chapter 11. Spirulina as an antiviral agent. In: *Spirulina in Human Nutrition and Health*. 2007, 227-242.
15. DIRAMAN, H., KORU, E., DIBEKLIOGLU, H. FattyAcid Profile of *Spirulina platensis* used as a food supplement. In: *The Israeli Journal of Aquaculture – Bamidgeh*. 61(2), 2009: 134-142.
16. HAYASHI, T. Studies on evaluation of natural products for antiviral effects and their applications. In: *Yakugaku Zasshi.* 2008, 128: 61-79.
17. JIN, S., LEE, J., KIM, Y., PARK, C. Spirulina powder as a feed supplement to enhance abalone growth. In: *Aquaculture Reports.* v.17, 2020. 100318:1-8.
18. RAMAKRISHNAN, R. Antiviral properties of Cyanobacterium, *Spirulina platensis* a review. IJPSM. 2013, 3: 1-10.
19. SONI, R., SUDHAKAR, K., RANA, R. Spirulina – From growth to nutritional product. In: *A review. Trends Food Sci Technol.* 69. 2017, 171:157-161.
20. PARODI, A. et al. The potential of future foods for sustainable and healthy diets. In: *Nature Sustainability*. 2018, 1 (12): 782-789.
21. YAKOOT, M., SALEM, A. *Spirulina platensis* versus Silymarin in the treatment of chronic hepatitis C virus infection. A pilot randomized, comparative clinical trial. In: *BMC Gastroenterol*. 2012, 12:32.

22. PETIT, L., VERNES, L., CADORET, J. *Docking and in silico toxicity assessment of Arthrospira compounds as potential antiviral agents against SARS-CoV-2*. https://doi.org/10.21203/rs.3.rs-40890/v1.
23. KIRAN RAJ, T., RANJITHKUMAR, R., KANTHESH, B. M., GOPENATH, T.S. C-phycocyanin of *Spirulina plantesis* inhibits nsp12 required for replication of SARS-Cov-2: a novel finding in-silico. In: *IJPSR*, 2020; 11(9): 4271-4278.
24. BULIMAGA, V., PISOVA, M., ZOSIM, L. Acidic polysaccharides directed synthesis at cyanobacterium *Spirulina platensis* CNM CB-02. În: *Studia Universitatis, Real and Natural Sciences*. 2017, 1(101): 46-50.
25. BULIMAGA. V., ZOSIM. L., TROFIM. A., REVA. V., BULIMAGA. M.-B. Study of polysacharides produced by cyanobacteria *Spirulina platensis* in mixtrophic cultivation. În: *Studia Universitatis Moldaviae. Ştiinţe reale şi ale naturii.* 2019, nr. 1(121):34-41.
26. BULIMAGA, V., ZOSIM, L., PISOVA, M., REVA, V. Process for obtaining of Se-exopolisaharides produced by cyanobacterium *Spirulina platensis*. In: *Studia universitatis, Real and Natural Sciences*. 2017, 6(106): 24-29.
27. BULIMAGA, V., ZOSIM, L., TROFIM, A., PISOVA, M. Procedures of obtaning of exopolysaccharides produced by cyanobacteria *Spirulina (Arthrospira) platensis* and *Nostoc linckia*. In: *Annals of the University of Oradea, Fascicula biology*. 2018, 25(1), pp.7-13.
28. ZOSIM, L., BULIMAGA, V., RUDIC, V., GULEA, A., ŢAPCOV, V. Innovative process for increasing the content of acidic polysaccharides in the cyanobacterium *Spirulina platensis*. In: *Intelectus*, 2019, 1-2:139-142.
29. BULIMAGA, V. et al. Antioxidant capacity of peptide fractions obtained from phycocyanin in enzymatic hydrolysis: *Theses at the Scientific Conference "Integration through research and innovation*, 28-29 septembrie 2016, Chişinău, pp. 46-49.