Genetics and Plant Physiology – 2016, Volume 6(1–2), pp. 85–100

Available online at http://www.ifrg-bg.com

Review

SIGNIFICANCE OF MICROALGAE – GROUNDS AND AREAS

Gigova L. **[*]** ***and G. Marinova***

Institute of Plant Physiology and Genetics, Bulgarian Academy of Sciences, Acad. G. Bonchev Str., Bldg. 21, Sofia 1113, Bulgaria

Received: *03 February 2015* Accepted: *07 March 2016*

Summary: The use of microalgae by humans dates back thousands of years. However, the cultivation of microalgae is a modern biotechnology. The recent progress in microalgal biotechnology contributes to the identification and better use of the enormous potential of these ubiquitous photosynthetic microorganisms. A growing body of literature describes their benefits for human and animal health, or their applicability in various areas of human business activity. This article, based on the accumulated literature network, summarizes the most important current topics, covering the significance of microalgae for science, ecology, agriculture and industry as well as the advantages of using microalgae.

Citation: Gigova L., G. Marinova, 2016. Significance of microalgae - grounds and areas. *Genetics and Plant Physiology*, 6(1–2): 85–100.

Keywords: Algae; applications; biotechnological advantages; useful natural products.

Contents

[*]Corresponding author: gigova01@gmail.com

INTRODUCTION

Microalgae are a large and diverse group of photoautotrophic microorganisms that includes eukaryotes such as green, red, brown and golden algae, diatoms, dinoflagellates, as well as prokaryotic cyanobacteria (blue-green algae). These organisms are ubiquitous in nature - in the water and on land. In natural habitats they are often exposed to stressors with abiogenic (low or high temperatures, drought, high/low light intensity, nutrient deficiency, etc.) and/or biogenic origin (interaction with other organisms via competition, parasitism). The basis of the survival of microalgae in harsh environments or in environments with widely varying physico-chemical parameters and/or in a highly competitive environment is their remarkable physiological and biochemical plasticity (Falkowski et al., 1997). These microorganisms have developed a variety of adaptive and defense mechanisms, ranging from a change in the ratio and composition of the main structural and functional components of the cell (proteins, carbohydrates, lipids, pigments), activation of non-enzymatic and enzymatic defense systems, to the synthesis of substances with a cytotoxic, antibacterial, alelochemical action, including various secondary metabolites (isoprenoids, toxins, etc.). Although microalgae have been known for many centuries, in recent decades they have been rediscovered as an excellent source of valuable compounds, due to the strong demand of the humans for natural, safe, eco-friendly and renewable products. This review aims to present the significance of microalgae for human community, covering their crucial role in the biosphere through photosynthesis, their impact on the research development, as well as their economic importance as a source of a vast range of substances with current and potential applications in the agriculture and wastewater treatment, in the food, feed, pharmaceutical and cosmetic industries.

1. WHAT ARE THE ADVANTAGES OF USING MICROALGAE:

- Microalgae perform a photosynthetic process similar to higher plants, but biological CO_2 fixation with microalgae is more efficient than with terrestrial plants and microalgae can grow about 10 to 50 times faster (Dismukes et al., 2008; Williams and Laurens, 2010).
- Many species could be cultivated on a large scale with the potential for growth in a bioreactor under controlled conditions.
- Microalgae cultivation in open ponds or in closed photobioreactors is characterized by less seasonality (Moheimani and Borowitzka, 2006), simple and inexpensive culture media and the use of low-productive or non-arable land.
- They have short harvesting times and the harvested biomass can be used directly or after further processing.
- Provide opportunities for their simultaneous multipurpose use.
- Some microalgae produce unique metabolites. Phycobiliproteins (phycocyanins, allophycocyanins and phycoerythrins) for example, are water-soluble fluorescent accessory light-harvesting protein pigments, characteristic of Cyanophyta,

Rhodophyta and Cryptophyta. A range of structurally novel cyclic peptides and depsipeptides are found in cyanobacteria (reviewed in Moore, 1996). Only the marine diatom *Haslea ostrearia* is shown to synthesize the pigment marennine.

- Provide molecules (pigments, triacylglycerols containing polyunsaturated fatty acids) in their natural isomer proportions.
- Microalgae are the primary producers of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in the food chain.
- The variety and quantity of valuable algal products are amenable to manipulation by changing the growth conditions.
- Some algal strains are extremophyles to temperature, salt or pH.
- Last but not least, the biodiversity and extraordinary biosynthetic potential of these photoautotrophic microorganisms are still largely unexplored and unused.

2. AREAS OF MICROALGAE IMPORTANCE

2.1. Ecology and environmental research

Microalgae are responsible for over 50% of the primary photosynthetic productivity on Earth and are an essential link in the food chain. Through the biological fixation of carbon, a part of which is subsequently sequestered at ocean depth, microalgae participate in the global carbon cycle (Not et al., 2012). On the other hand, they largely contribute to the global oxygen production (between 50 to 87%). Their participation in these major global processes, as well as in the nutrient recycling, especially in aquatic environment, is important to support the majority of life on our planet. Microalgae mitigate the effects of water and soil pollution with industrial waste, such as organic and inorganic substances, heavy metals and in this way they are involved in the biodiversity conservation. Moreover, by removing excessive nitrogen and carbon from water, microalgae help reduce the eutrophication in the aquatic environment. The important role of microalgae in soil ecosystems is to improve the physical and chemical characteristics of the soil (aggregation of soil particles, increasing the water and mineral content, aeration), but is also related with the stimulation of plant growth by physiologically active substances, hormones, which they produce and secrete (Borowitzka, 1995). Furthermore, these ubiquitous microorganisms synthesize and secrete in the environment many metabolites with biocidal activity such as antibacterial, algicidal, herbicidal, insecticidal, which help maintain the ecological balance. On the other hand, microalgae make a significant contribution to environmental research. It is well known, that climatic changes and many aspects of human activity have harmful effects on ecological systems. Microalgae are excellent indicators of ecosystem change as their populations are very sensitive to changes in light quality, temperature, nutrient status (including pollution). Assessment of microalgal population dynamics is particularly informative in environmental impact assessments (Day et al., 1999). Diatoms, for example are used extensively to monitor the ecological status of lotic environments due to several reasons: methods are cost effective, data is comparable, techniques are rapid and accurate. Diatoms also have a short life cycle allowing rapid response to changes in water quality associated with urbanization and agricultural activities (acidification, eutrophication, etc.). Their fossil forms are good indicators of climate variations (Bere and Tundisi, 2010).

2.2. Importance for the development of fundamental science

Due to their small size, relatively simple morphological organization and good reproductive capacity microalgae are cultured relatively easily in the laboratory. The genome of dozens strains of several species is sequenced. These biological advantages, in combination with the developed plurality of molecular tools make some microalgae convenient models for studying of various processes in plants.

Synechocystis sp. strain PCC 6803 (Cyanoprokaryota) is widely used by scientists around the world for studying photosynthesis, directed biosynthesis of valuable metabolites (pigments, poly-β-hydroxybutyrate) and protective mechanisms in stress conditions (Lagarde et al., 2000; Wu et al., 2001; Marin et al., 2006; Vassilakaki and Pflugmacher, 2008). The filamentous cyanobacterium *Anabaena* sp. PCC 7120 is a model system to study nitrogen fixation, cell differentiation, cell pattern formation and evolution of plastids (Padhi et al., 2010). The unicellular green *Chlamydomonas reinhardtii* is the eukaryotic model alga that contributes to the understanding of chloroplast biogenesis and function (Rochaix, 2004), circadian rhythms (Mittag et al., 2005), cell cycle control (Bisova et al., 2005), plant respiration (Cardol et al., 2005), metal transporters (Hanikenne et al., 2005) and the evolution of herbicide resistance (Reboud et al., 2007).

Antarctic microalgae are suitable model system for the creation of survival strategies because of their ability to survive in various ecological niches and the exhibition of extreme resistance to the effects of harsh environmental factors such as high solar irradiance, increased UV radiation and low temperature. The survival of these algae is connected with the efficiency of their repair systems (error-free rejoining of double-strand DNA breaks, increased levels of HSPs, increase in carotenoids content) and the stability of cell defence mechanisms (enhanced antioxidant enzyme activities, high content of SH-groups and some pigments – carotenoids, phycobiliproteins and chlorophyll) (Pouneva and Minkova, 2010).

2.3. Economic importance

Microalgae can biosynthesize, metabolize, accumulate and secrete a great diversity of primary and secondary metabolites, many of which are valuable substances with current and potential applications in the food, pharmaceutical, cosmetic and textile industries, and in agriculture.

2.3.1. Applications of microalgae in agriculture and wastewater treatment

Algal biomass or live cultures are used as a means to enrich the soil (Nakao and Kuwazuka, 1991). Water-retention ability of polysaccharides from *Nostoc muscorum* is useful in their application as a soil stabilizer (De Caire et al., 1997). Blue-green algae are important for boosting agricultural crops as they can fix nitrogen (*Anabaena*, *Nostoc*); produce and release a wide array of compounds like amino acids, auxins, gibberellins, cytokinins with plant growth-promoting effects (*Nostoc*, *Chlorogloeopsis*, *Calothrix*, *Plectonema*, *Gloeothece*, *Anabaena*, *Cylindrospermum*, *Anabaenopsis*, *Chroococcidiopsis*); increase the fertility of soils and crop yield by adding organic matter, nitrogen, phosphorus, carbon, potassium, zinc and micronutrients; possess the ability to degrade various agrochemicals such as the insecticides methyl parathion, malathion, dichlorovos, lindane and herbicide anilofos (*Oscillatoria*, *Synechococcus*, *Nodularia*, *Nostoc*, *Cyanothece*, *Synechocystis*, *Anabaena*, *Phormidium*) (Singh et al., 2014). Algal biofertilizers promote the growth of other "useful" soil-borne microorganisms and increase the activity of soil enzymes that participate in the liberation of nutrients necessary for plants. Acting solely or in a microbial consortium, they are suitable for recovery of marginal soils (Abdel-Raouf et al., 2012). Additionally, some cyanobacteria and green algae play an effective role as antagonistic agents against plant pathogenic bacteria, fungi and insects (see Singh et al., 2014; Abdel-Raouf et al., 2012). The use of algal metabolites exhibiting biocidal activity (Wiegand and Pflugmacher, 2005) as biological control agents in agriculture is environment-friendly alternative to synthetic biocides (Gol'din, 2012).

Microalgae are able to sequester, remove or transform pollutants such as excess nutrients, xenobiotics and heavy metals from wastewater, or CO_2 from exhausts, thus having great potential in the phycoremediation. Some green algae and cyanobacteria show high efficiency in the content reduction of various nutrients (PO_4^{-2}, NO_3^{-2}, SO_4^{-2}) and chlorides as well as the electrical conductivity from/of municipal or other wastewater (Azarpira et al., 2014 and ref. therein). *Ankistrodesmus*, *Chlorella* or *Scenedesmus* species are successfully attempted to purify wastewater containing organic pollutants in the manufacture of pulp, paper and olive oil (Munoz and Guieysse, 2006). Filamentous cyanobacteria are suitable for the reduction of organic and inorganic pollutants from agro-industrial wastes and wastewaters (Markou and Georgakakis, 2011). *Scendesmus obliquus* can degrade up to 90% of the cyanide in mining wastewater (Gurbuz et al., 2009). Microalgae effectively remove heavy metals from wastewater, resulting in high quality reusable water (Perales-Vela et al., 2006). The capabilities of some algae for aerobic biodegradation of phenolic pollutants seem also to be promising **(**Lika and Papadakis, 2009**)**.

2.3.2. Applications in food and nutraceuticals industries

Chlorella, *Nostoc*, *Spirulina* and *Aphanizomenon* have been used as food since ancient times. Due to the original chemical composition of microalgae (high protein content, with balanced amino acids ratio, essential minerals, carotenoids, polyunsaturated fatty acids, vitamins, polysaccharides, carotenoids, phycobilins and other biologically active compounds), their biomass has extremely high nutritional value and health benefits (Batista et al., 2013). The application of microalgal biomass and/or metabolites is a contemporary approach for obtaining healthy food and food supplements (nutraceuticals) (Gouveia et al., 2008). The commercial applications in human nutrition are dominated by *Arthrospira, Chlorella, Haematococcus*, *Dunaliella salina* and *Aphanizomenon flos-aquae*. Therapeutic supplements from micro-algae comprise an important market in which compounds such as β-carotene, astaxanthin, lutein, polyunsaturated fatty acid (PUFA) such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) and polysaccharides such as β-glucan dominate. The great potential of microalgae and microalgae products for functional foods has been recently reviewed by Gouveia et al. (2008), Plaza et al. (2009), Chacón-Lee and González-Mariño (2010) and Buono et al. (2014). In addition, as a rich source of antibacterial and fungicidal activities, microalgae including cyanobacteria are able to propose innovative compounds as preservatives in food (Guedes et al., 2011; Najdenski et al., 2013).

Algae are the typical natural food for many animals used in aquaculture and it is not surprising that they are considered the best food source for production of bivalve molluscs (oysters, scallops and mussels), for juvenile stages of abalone, crustaceans and some fish species and for zooplankton, used in aquaculture food chain. The most frequently used species in aquaculture are *Isochrysis galbana*, *Pavlova lutheri*, *Chaetoceros calcitrans*, *Skeletonema costatum*, *Tetraselmis suecica* and *Pseudoisochrysis paradoxa*. Other genera include *Spirulina*, *Chlorell*a, *Dunaliella*, *Isochrysis*, *Thalassiosira* and *Nannochloropsis* (Guedes and Malcata, 2012 and ref. therein). Some algae (e.g. *Spirulina, Chlorella*, *Haematococcus*, *Scenedesmus*, *Tetraselmis*) are suitable healthy food for both aquatic and terrestrial animals (Harel and Clayton, 2004). Using even small amounts of microalgal biomass can positively affect the physiology of animals by improved immune response resulting in growth promotion, disease resistance, improved gut function, probiotic colonization stimulation, as well as by improved reproductive performance (Harel and Clayton, 2004). According to Becker (2004), 30% of the "current" world algal production is sold for animal feed applications.

2.3.3. Pharmaceutical applications of microalgae

Microalgae produce many compounds, which exhibit various biological activities and pharmacological properties, such as antibacterial, antifungal, antiviral and anticancer activities, immunostimulating, anti-inflammatory, fibrinolytic, antidiabetic, anti-oxidant and free radical scavenging properties. Some of these compounds are currently exploited or have potential applications as pharmaceuticals. Microalgal antibiotics show great chemical diversity (fatty acids, bromophenols, tannins, polyketides, terpenoids, polysaccharides, peptides). Among the others, the polysaccharides, fatty acids and pigments synthesized by microalgae from different phyla exhibit the widest spectrum of activity, and thus are of greater pharmacological importance.

2.3.3.1. Microalgal polysaccharides

Highly sulphated polysaccharides, originating from Cyanophyta, Rhodophyta and Chlorophyta have impressive efficiency in triggering either the cellular or the humoral stimulation of the human immune system. They are also hypolipidaemic, hypocholesterolaemic and hypoglycaemic agents. Some sulphated polysaccharides exhibit antitumor and antiviral activities and activity against the attachment of pathogens. Polysaccharides of red algae *Porphyridium cruentum* and *Rhodella reticulata* are powerful antioxidants with anti-inflammatory effect. Calcium-"spirulan" of *Arhrospira* (*Spirulina*) has antiviral activity and the ability to prevent pulmonary metastasis. It is also promising in treating spinal cord injuries and as matrices for stem cell cultures. The bioactivities and applications of sulphated polysaccharides from microalgae have been recently reviewed by De Jesus Raposo et al. (2013).

2.3.3.2. Polyunsaturated fatty acids

The health benefits of long-chain polyunsaturated fatty acids are well known. Both ω-3 and ω-6 PUFAs play a central role in the normal development and functioning of the brain and central nervous system (Schuchardt et al., 2010). Omega-3 fatty acids such as EPA and DHA increase the high-density lipoprotein/low-density lipoprotein (HDL/LDL) ratio and decrease the total cholesterol/HDL ratio, the impacts of which are crucial for the cardiovascular health. Due to their immuno-modulatory effects, ω-3 fatty acids are effective in treating inflammatory diseases such as rheumatoid arthritis, Crohn's disease, lupus, psoriasis, ulcerative colitis, asthma and cystic fibrosis (Adarme-Vega et al., 2012 and ref. therein). Many studies show that the microalgal fatty acids have antibacterial, antiviral and antitumor potential. "Chlorellin", isolated from *Chlorella*, is a first example for the broad antibacterial activity of the microalgal fatty acids (Pratt et al., 1944). Later on, El Semary et al. (2009) report on the antibacterial activity of palmitic acid from *Chlorococcum* sp. Eicosapentaenoic acid isolated from the marine diatom *Phaeodactylum tricornutum* is active against both Gram-positive and Gram-negative bacteria, including multi-resistant *Staphylococcus aureus* (Desbois et al., 2009). Antimicrobial activity detected in different pressurized liquid extracts from *Dunaliella salina* is related to several fatty acids (mainly palmitic, alpha-linolenic, and oleic acids) and some volatile compounds (such as phytol, neophytadiene, β-Cyclocitral, α- and β-ionone (Herrero et al., 2006). Almost the same constituents are responsible for the antiviral (HSV-1) activity of the ethanol extracts from both *Dunaliella salina* and *Haematococcus pluvialis* (Santoyo et al., 2012). The free fatty acids from the Bulgarian isolates *Gloeocapsa* sp., *Synechocystis* sp., *Chlorella* sp. and *Coelastrella* sp. significantly decrease the viability of a human cervical carcinoma cells (HeLa), with IC_{50} values lower than 15 μg/ml (Gigova et al., 2011). Normally, PUFAs are extracted from fatty fish, putting additional pressures on global fish stocks. Moreover, fish tend to accumulate poisonous substances via the food chain, and new sources of PUFAs are therefore required. As primary producers, many microalgae are rich in PUFAs and present a promising source of them because of the simple microalgal fatty acid composition, as well as opportunities for selection of the best strains-producers and controlled PUFAs production (Adarme-Vega et al., 2012).

2.3.3.3. Pigments

The pharmacological properties of microalgal pigments (chlorophylls, carotenoids and phycobiliproteins) are also widely demonstrated and evidenced. Astaxanthin, zeaxanthin, lutein, β-carotene and fucoxanthin have strong *in vitro* and *in vivo* antioxidant and anti-inflammation activities in animal models (Zhang et al., 2014). The effect of fucoxanthin in cancer and various mechanisms by which the fucoxanthin exerts its antiproliferative and cancer preventing activities are summarized by Kumar et al. (2013). Carotenoids have also the ability to stimulate the immune system, and thus are potential participants in combating various life-threatening diseases. Particularly, astaxanthin has a great potential in the prevention and treatment of chronic inflammatory diseases, cancers, cardiovascular diseases, metabolic syndrome, diabetes, diabetic nephropathy, gastrointestinal and liver dysfunctions, neurodegenerative, eye and skin diseases (reviewed in Ambati et al., 2014). Violaxanthin is cytotoxic at very low concentrations in cancer cells. Isolated from *Dunaliella tetriolecta*, it has a dose-dependent suppressing effect on human breast cancer cells (MCF-7), being active even at concentration of 0.1 μg/ml (Pasquet et al., 2011). Also, carotenoids from *Chlorella ellipsoidea* (mainly violaxanthin with two minor xanthophylls, antheraxanthin and zeaxanthin) inhibit the proliferation of human colon cancer cells (HCT-116) with the concentration required for 50% inhibition (IC_{50}) of 40.73±3.71 μg/ml and strong apoptosis-inducing effect (Cha et al., 2008). Extracts from *Chlorella* sp. containing β-carotene and lutein exert significant prevention of cognitive impairment in mice (Nakashima et al., 2009). The main pigments (β-carotene and chlorophyll) of *Chlorococcum himicola* cells show a dose-dependent negative effect on the microbial growth (Bhagavathy et al., 2011).

Isomer composition of astaxanthin (in *H. pluvialis*) and β-carotene (in *D. salina*) is very different from that of synthetic ones. It is believed that the natural forms of these pigments are the major contributor to human health benefits. Indeed, epidemiologic studies demonstrate that β-carotene from *Dunalliela* sp., which contains readily bioavailable 9-*cis* and all-*trans* stereoisomers (*ca*. 40% and 50%, respectively), lowers the incidence of several types of cancer and degenerative diseases (Ben-Amotz, 1999).

C-phycocyanin (C-PC), synthesized in high amount by *Spirulina* (*Arthrospira*) *platensis*, shows antibacterial, antifungal, antiviral and anticancer activities, as well as anti-inflammatory, fibrinolytic, antidiabetic, anti-oxidant and free radical scavenging properties (ref. in Gardeva et al., 2014). In our experiments, a highly purified C-PC from *Arthronema africanum*, another rich source of this valuable pigment, was used to reveal its *in vivo* and *in vitro* antitumor effects on myeloid Graffi tumor in hamsters (Gardeva et al., 2014). The results demonstrated the abilities of this C-PC to decrease significantly tumor transplantability and to delay the development of the Graffi tumors as well as to improve substantially the survival of tumor-bearing hamsters. The proliferation of Graffi tumor cells treated with *A. africanum* C-PC was significantly inhibited, which was related to the concentration- and time-dependent ladder-like DNA fragmentation pattern, typical for apoptosis. Moreover, an increase in the activities of manganese and copper/zinc superoxide dismutases and glutathione reductase, coupled with a low catalase activity was observed in tumor cells, thus providing new data on the mechanism of the C-PC-induced apoptosis in which the imbalance of antioxidant enzymes that favoured hydrogen peroxide accumulation might play a leading role. Focusing on the antioxidant activity of phycocyanin, Fernández-Rojas et al. (2014) summarize the ability of this colored protein to prevent the imbalance „antioxidant/oxidant" in various *in vitro* and *in vivo* models, and its potential benefits in the treatment and prevention of numerous disorders associated with oxidative stress.

Although comparatively less studied, phycoerythrin (PE), the major photosynthetic accessory pigment in red algae also shows promising biological activities. Recombinant PE of *Gracilaria lemaneiformis*, expressed in *Escherichia coli*, can scavenge free radicals and has antitumor activity (Wen et al., 2007). We isolated pure B-phycoerythrin from *Porphyridium cruentum* and investigated his actions against various pathogenic bacteria, fungus *Candida albicans* and Graffi tumor cells. This PE was microbicidal both for *C. albicans* and the bacterial species *Staphylococcus aureus*, *Streptococcus pyogenes* and *Salmonella typhimurium* (Najdenski et al., 2013). Concerning tumor cells, about 50 and 63% growth suppression was recorded using 50 and 100 µg/ml of the *P. cruentum* PE, respectively. Characteristic apoptotic features like nuclear shrinkage, condensed chromatin and membrane blebbing, as well as formation of apoptotic bodies and DNA fragmentation were observed in PE-treated tumor cells. At the same time, the algal pigment exerted a potent stimulatory effect on the proliferation of normal hamster bone marrow cells, thereby demonstrating bidirectional positive effects (Minkova et al., 2011).

Marennine is a water-soluble green pigment synthesised and excreted by the marine diatom *Haslea ostrearia*, known to be responsible for the phenomenon "greening of oysters". Purified intracellular marennine and extracellular marennine significantly inhibit the growth of marine bacteria (*Polaribacter irgensii*, *Pseudoalteromonas elyakowii* and the pathogenic *Vibrio aesturianus*). Both forms of marennine are active against five different adherent human cancer cell lines and also possess antiviral (HSV1) properties (Gastineau et al., 2012).

2.3.3.4. Other algal metabolites of pharmacological significance

Dolastatins (pseudopeptides) are an interesting group of biologically active metabolites, isolated from marine cyanoprokaryotes, mainly from the genera *Lyngbya*, *Oscillatoria* and *Symploca*. Curacins are a group of mixed polyketide synthase - nonribosomal peptide synthase derived compounds produced by and isolated from *Lyngbya majuscula*. Representatives of the two groups inhibit tubulin polymerization and microtubule assembly thereby having antiproliferative potential. Moreover, dolastatins and curacins are used as lead compounds for the development of synthetic drug analogues having better pharmacological and pharmacokinetic properties in the treatment of various cancer types. Curacin A, dolastatin 10 and dolastatin 15 and their analogues are in preclinical and/or clinical trials as potential anticancer drugs (Uzair et al., 2012). Microalgae are also sources of essential for life vitamins and vitamin precursors, most notably ascorbic acid, α- β- and γ-tocopherol, riboflavin, nicotinate, biotin, folic acid and pantothenic acid.

2.3.4. Cosmetics applications of microalgae

Due to their valuable biological properties and activities, microalgae-derived compounds such as polysaccharides, lipids, proteins (amino acids), carotenoids and phycobiliproteins are explored for cosmeceutical purposes. The polysaccharides from *Porphyridium* are bioactive cosmetic ingredients (Stolz and Obermayer, 2005). Lipid-based cosmetics, in the form of creams or lotions, provide both nourishing and protecting effects to the skin. Amino acids are important for skin hydration, elasticity and photoprotection (especially mycosporine-like amino acids) (Lebeau and Robert, 2003). Beta-carotene (provitamin A), the richest source of which is *Dunaliella salina*, stimulates cell regeneration at the level of the epidermis or dermal connective tissue, inhibits the production of melanin and has antioxidant activity. *Chlorella* and *Arthrospira* (*Spirulina*) are the main species established on the skin care, sun protection and hair care market (Stolz and Obermayer, 2005). "Dermochlorella", extracted from *Chlorella vulgaris*, stimulates collagen synthesis in the skin and thus supports tissue regeneration and wrinkle reduction (Codif, St. Malo, France). "Protulines" is a protein-rich extract from *Arthrospira*, which helps combat early skin aging, exerting a tightening effect and preventing stria formation (Exsymol S.A.M., Monaco). Two other products are also on the market: an ingredient from *Nannochloropsis oculata* with excellent skin-tightening properties ("Pepha-Tight") and an ingredient from *Dunaliella salina*, which markedly stimulates cell proliferation and turnover and positively influences the energy metabolism of skin ("Pepha-Ctive") (Stolz and Obermayer, 2005). "AstaReal Oil 50F" and "AstaTROL" (Fuji Chemical Industry Co., Ltd., Toyama, Japan) are products containing astaxanthin from *Haematococcus pluvialis* as an active ingredient. In human clinical studies, the combination of oral administration and topical application of these products results in improvements in skin wrinkle, age spot size, elasticity, skin texture and moisture content (Tominaga et al., 2012). Algobad, Roupi Shampoo, Algofem, etc are microalgae-derived cosmetic products, developed in Bulgaria (Fournadzhieva et al., 2003).

2.4. Other applications of microalgae

Because of their unique composition, structure and physico-chemical characteristics, microalgal highly sulphated polysaccharides are raw materials for food, pharmaceutical, cosmetic and textile industries as thickeners, stabilizers, emulsifiers, flocculants and moisturizers (referred in Arad and Levy-Ontman, 2010). They may also be used as biolubricants for bone joints and to mitigate degenerative joint disorders caused by arthritis, or even as drag-reducing substances for ships (De Jesus Raposo et al., 2013 and ref. therein).

Phycobiliproteins have deep and intense color, stability, a broad excitation spectrum and high fluorescence quantum yield and are without any toxic effect. These unique properties lead to extensive use of the phycobiliproteins as natural colorants in food and cosmetics, as fluorescent tags in diagnostic tests and in various research applications (Kuddus et al., 2015).

Diatoms biomineralize a mixture of silica, proteins and carbohydrates to form an inorganic silica shell that surpasses modern engineering capabilities. These intricately patterned silica structures are presently used as diatomaceous filters, but may prospectively be applied in nanotechnologies or computer chips (Bozarth et al., 2009).

3. CONCLUSION

As the need for more natural, safe, eco-friendly and renewable products increases, microalgae will continue to be explored for and used as a source of such products. In recent decades, science and industry mark a significant progress in the disclosure and utilization of the enormous biotechnological potential of microalgae, but there are still challenges to be solved. One of the biggest challenges is to achieve energy- and cost-effective production, which involves the attainment of higher productivity and exploiting more fully the produced biomass. Many scientists from around the world are looking for innovative solutions of this challenge. The production of valuable metabolites from microalgae can be more environmentally sustainable, cost-effective and profitable, if combined with processes such as wastewater and flue gas treatments. In fact, various studies demonstrate the complex use of microalgae for agricultural and/or industrial purposes and for environmental protection.

ACKNOWLEDGEMENTS

Research that was conducted on biological activities of selected microalgae in the author's and co-author's laboratories was supported by a research grant D002-299/2008 from the National Science Fund, Ministry of Education and Science, Bulgaria.

REFERENCES

Abdel-Raouf N, AA Al-Homaidan, IBM Ibraheem, 2012. Agricultural importance of algae. Afr J Biotechnol, 11(54): 11648–11658.

Adarme-Vega TC, DKY Lim, M Timmins, F Vernen, Y Li, PM Schenk, 2012. Microalgal biofactories: a promising approach towards sustainable omega-3 fatty acid production. Microb Cell Fact, 11: 96.

Ambati RR, SM Phang, S Ravi, RG Aswathanarayana, 2014. Astaxanthin: sources, extraction, stability, biological activities and its commercial applications-A Review. Mar Drugs, 12: 128–152.

Arad S (Malis), O Levy-Ontman, 2010. Red microalgal cell-wall polysaccharides: biotechnological aspects. Curr Opin Biotech (COBIOT), 21(3): 358–364.

Azarpira H, P Behdarvand, K Dhumal, G Pondhe, 2014. Potential use of cyanobacteria species in phycoremediation of municipal wastewater. Int J Biosci, 4(4): 105–111.

Batista AP, L Gouveia, NM Bandarra, JM Franco, A Raymundo, 2013. Comparison of microalgal biomass profiles as novel functional ingredient for food products. Algal Res 2: 164–173.

Becker EW, 2004. Microalgae in human and animal nutrition. In: Handbook of microalgal culture, Ed A Richmond, Oxford, Blackwell, 312–351.

Ben-Amotz A, 1999. *Dunaliella* β-carotene: from science to commerce. In: Enigmatic microorganisms and life in extreme environments, Ed J Seckbach, Kluwer, Netherlands, 401–410.

Bere T, JG Tundisi, 2010. Biological monitoring of lotic ecosystems: the role of diatoms. Braz J Biol, 70(3): 493–502.

Bhagavathy S, P Sumathi, I Jancy Sherene Bell, 2011. Green alga *Chlorococcum humicola* – a new source of bioactive compounds with antimicrobial activity. Asian Pac J Trop Biomed, S1–S7.

Bisova K, DM Krylov, JG Umen, 2005. Genome-wide annotation and expression profiling of cell cycle regulatory genes in *Chlamydomonas reinhardtii*. Plant Physiol, 137: 475–491.

Borowitzka MA, 1995. Microalgae as source of pharmaceuticals and other biologically active compounds. J Appl Algol, 7: 3–15.

Bozarth A, U-G Maier, S Zauner, 2009. Diatoms in biotechnology: modern tools and applications. Appl Microbiol Biotechnol, 82: 195–201.

Buono S, AL Langellotti, A Martello, F Rinna, V Fogliano, 2014. Functional ingredients from microalgae. Food Funct, 5: 1669–1685.

Cardol P, D González-Halphen, A Reyes-Prieto, D Baurain, RF Matagne, C Remacle, 2005. The mitochondrial oxidative phosphorylation proteome of *Chlamydomonas reinhardtii* deduced from the genome sequencing project. Plant Physiol, 137: 447–459.

Cha KH, SY Koo, DU Lee, 2008. Antiproliferative effects of carotenoids extracted from *Chlorella ellipsoidea* and *Chlorella vulgaris* on human colon cancer cells. J Agric Food Chem, 56: 10521–10526.

Chacón-Lee TL, GE González-Mariño, 2010. Microalgae for “healthy” foods—possibilities and challenges. Compr Rev Food Sc Food Saf, 9: 655–675.

Day JG, EE Benson, RA Fleck, 1999. In vitro culture and conservation of microalgae: applications for aquaculture, biotechnology and environmental research. In Vitro Cell Dev–Plant, 35: 127–136.

De Caire GZ, MS de Cano, MCZ de Mulé, RM Palma, K Colombo, 1997. Exopolysaccharide of *Nostoc muscorum* (cyanobacteria) in the aggregation of soil particles. J Appl Phycol, 9: 249–253.

De Jesus Raposo MF, RMSC de Morais, AMMB de Morais, 2013. Bioactivity and applications of sulphated polysaccharides from marine microalgae, Review. Mar Drugs, 11: 233–252.

Desbois AP, A Meams-Spragg, VJ Smith, 2009. A fatty acid from the diatom *Phaeodactylum tricornutum* is antibacterial against diverse bacteria including multi-resistant *Staphylococcus aureus* (MRSA). Mar Biotechnol, 11: 45–52.

Dismukes GC, D Carrieri, N Bennette, GM Ananyev, MC Posewitz, 2008. Aquatic phototrophs: efficient alternatives to land-based crops for biofuels. Curr Opin Biotechnol, 19: 235–240.

El Semary NA, SM Ghazi, MM Abd El Nabi, 2009. Investigating the taxonomy and bioactivity of an Egyptian *Chlorococcum* isolate. Austr J Basic Appl Sci, 3: 1540–1551.

Falkowski PG, JA Raven, 1997. Aquatic Photosynthesis, Blackwell Science, Oxford.

Fernández-Rojas B, J Hernández-Juárez, J Pedraza-Chaverri, 2014. Nutraceutical properties of phycocyanin. J Funct Foods, 11: 375–392.

Fournadzhieva S, K Bojadgieva, P Pilarski, 2003. Bulgarian experience in aquaculture (microalgae) - cultivation, production and development. European Geothermal Conference 2003. URL: https://pangea.stanford.edu/ERE/db/IGAstandard/record_detail.php?id=667

Gardeva E, R Toshkova, L Yossifova, K Minkova, N Ivanova, L Gigova, 2014. Antitumor activity of C-phycocyanin from *Arthronema africanum* (Cyanophyceae). Braz Arch Biol Technol, 57(5): 675–684.

Gastineau R, JB Pouvreau, C Hellio, M Morançais, J Fleurence, P Gaudin, N Bourgougnon, JL Mouget, 2012. Biological activities of purified marennine, the blue pigment responsible for the greening of oysters. J Agric Food Chem, 60: 3599–3605.

Gigova L, R Toshkova, E Gardeva, G Gacheva, N Ivanova, L Yossifova, G Petkov, 2011. Growth inhibitory activity of selected microalgae and cyanobacteria towards human cervical carcinoma cells (HeLa). J Pharm Res, 4: 4702–4707.

Gol'din E, 2012. Biologically active microalgae and cyanobacteria in nature and marine biotechnology. Turk J Fish Aquat Sci, 12: 423–427.

Gouveia L, AP Batista, I Sousa, A Raymundo, NM Banderra, 2008. Microalgae in novel food products. In: Food chemistry research developments, Ed NK Papadopoulos, Nova Science Publishers, Inc., New York, 75–111.

Guedes AC, FX Malcata, 2012. Nutritional value and uses of microalgae in aquaculture. Aquaculture, Ed Z Muchlisin, ISBN: 978-953-307-974-5, InTech, Available from: http://www.intechopen.com/books/aquaculture/nutritional-value-and-uses-of-microalgae-in-aquaculture

Guedes AC, CR Barbosa, HM Amaro, CI Pereira, FX Malcata, 2011. Microalgal and cyanobacterial cell extracts for use as natural antibacterial additives against food pathogens. Int J Food Sci Tech, 46(4): 862–870.

Gurbuz F, H Ciftci, A Akcil, 2009. Biodegradation of cyanide containing effluents by *Scenedesmus obliquus*. J Hazard Mater, 162: 74–79.

Hanikenne M, U Krämer, V Demoulin, D Baurain, 2005. A comparative inventory of metal transporters in the green alga *Chlamydomonas reinhardtii* and the red alga *Cyanidioschizon merolae*. Plant Physiol, 137: 428–446.

Harel M, D Clayton, 2004. Feed formulation for terrestrial and aquatic animals. US Patent 20070082008 (WO/2004/080196).

Herrero M, E Ibañez, A Cifuentes, G Reglero, S Santoyo, 2006. *Dunaliella salina* microalga pressurized liquid extracts as potential antimicrobials. J Food Protection, 69: 2471–2477.

Kuddus M, P Singh, G Thomas, A Ali, 2015. Production of C-phycocyanin and its potential applications. In: Biotechnology of Bioactive Compounds: Sources and Applications, Eds VK Gupta, MG Tuohy, M Lohani, A O'Donovan, John Wiley & Sons Ltd, Chichester, UK, 283–300.

Kumar SR, M Hosokawa, K Miyashita, 2013. Fucoxanthin: a marine carotenoid exerting anti-cancer effects by affecting multiple mechanisms. Mar Drugs, 11: 5130–5147.

Lagarde D, L Beuf, W Varmaas, 2000. Increased production of zeaxanthin and other pigments by application of genetic engineering techniques to *Synechocystis* sp. strain PCC 6803. Appl Environ Microbiol, 66(1): 64–72.

Lebeau T, J-M Robert, 2003. Diatom cultivation and biotechnological relevant products. Part II: Current and putative products. Appl Microbiol Biotechnol, 60: 624–632.

Lika K, IA Papadakis, 2009. Modeling the biodegradation of phenolic compounds by microalgae. J Sea Res, 62: 135–146.

Marin K, M Stirnberg, M Eisenhut, R Krämer, M Hagemann, 2006. Osmotic stress in *Synechocystis* sp. PCC 6803: low tolerance towards non-ionic osmotic stress results from lacking activation of glucosylglycerol accumulation. Microbiol, 152: 2023–2030.

Markou G, D Georgakakis, 2011. Cultivation of filamentous cyanobacteria (blue-green algae) in agro-industrial wastes and wastewaters: A review. Appl Energ, 88: 3389–3401.

Minkova KM, RA Toshkova, EG Gardeva, MI Tchorbadjieva, NJ Ivanova, LS Yossifova, L Gigova, 2011. Antitumor activity of B-phycoerythrin from *Porphyridium cruentum*. J Pharm Res, 4: 1480–1482.

Mittag M, S Kiaulehn, CH Johnson, 2005. The circadian clock in *Chlamydomonas reinhardtii*. What is it for? What is it similar to? Plant Physiol, 137: 399–409.

Moheimani NR, MA Borowitzka, 2006. The long-term culture of the coccolithophore *Pleurochrysis carterae* (Haptophyta) in outdoor raceway ponds. J Appl Phycol, 18: 703–712.

Moore RE, 1996. Cyclic peptides and depsipeptides from cyanobacteria: a review. J Ind Microbiol, 16: 134–143.

Munoz R, B Guieysse, 2006. Algal-bacterial processes for the treatment of hazardous contaminants: A review. Water Res, 40: 2799–2815.

Najdenski H, L Gigova, I Iliev, P Pilarski, J Lukavský, I Tsvetkova, M Ninova, V Kussovski, 2013. Antibacterial and antifungal activity of selected microalgae and cyanobacteria. Int J Food Sci Tech, 48(7): 1533–1540.

Nakao H, S Kuwazuka, 1991. Microbes

in the soil and effects of hot water-extract of *Chlorella* on the growth of plants. Absts Papers, Jpn Soc Soil & Fertilizer, 37: 43.

Nakashima Y, I Ohsawa, F Konishi, T Hasegawa, S Kumamoto, Y Suzuki, S Ohta, 2009. Preventive effects of *Chlorella* on cognitive decline in age-dependent dementia model mice. Neur Lett, 464: 193–198.

Not F, R Siano, WHCF Kooistra, N Simon, D Vaulot, I Probert, 2012. Diversity and ecology of eukaryotic marine phytoplankton. Adv Bot Res, 64: 1–53.

Padhi SB, S Behera, P Swain, S Behura, G Behera, M Panigrahi, S Baidya, A Mishra, S Beza, H Panigrahi, N Dash, S Pradhan, N Ratha, 2010. Computational biology and protein modeling of cyanobacteria using bioinformatics tools and techniques. Int J Bioinf Res, 2(2): 88–95.

Pasquet V, P Morisset, S Ihammouine, A Chepied, L Aumailley, J-B Berard, B Serive, R Kaas, I Lanneluc, V Thiery, M Lafferriere, J-M Piot, T Patrice, J-P Cadoret, L Picot, 2011. Antiproliferative activity of violaxanthin isolated from bioguided fractionation of *Dunaliella tertiolecta* extracts. Mar Drugs, 9: 819–831.

Perales-Vela HV, JM Pena-Castro, RO Canizares-Villanueva, 2006. Heavy metal detoxification in eukaryotic microalgae. Chemosphere, 64: 1-10.

Plaza M, M Herrero, A Cifuentes, E Ibáñez, 2009. Innovative natural functional ingredients from microalgae. J Agric Food Chem, 57: 7159–7170.

Pouneva ID, KM Minkova, 2010. Review: Antarctic algae – a model system for oxidative stress resistance. Gen Appl Plant Physiol, 36(3-4): 115–123.

Pratt R, TC Daniels, JB Eiler, JB Gunnison, WD Kumler, JF Oneto, LA Strait, HA Spoehr, GJ Hardin, HW Milner, JH Smith, HH Strain, 1944. Chlorellin, an antibacterial substance from Chlorella. Science, 99: 351–352.

Reboud X, N Majerus, J Gasquez, S Powles, 2007. *Chlamydomonas reinhardtii* as a model system for pro-active herbicide resistance evolution research. Biol J Linnean Soc, 91: 257–266.

Rochaix JD, 2004. Genetics of the biogenesis and dynamics of the photosynthetic machinery in eukaryotes. Plant Cell, 16: 1650–1660.

Santoyo S, L Jaime, M Plaza, M Herrero, I Rodriguez-Meizoso, E Ibañez, G Reglero, 2012. Antiviral compounds obtained from microalgae commonly used as carotenoid sources. J Appl Phycol, 24: 731–741.

Schuchardt JP, M Huss, M Stauss-Grabo, A Hahn, 2010. Significance of long-chain polyunsaturated fatty acids (PUFAs) for the development and behaviour of children. Eur J Pediatr, 169: 149–164.

Singh H, JS Khattar, AS Ahluwalia, 2014. Cyanobacteria and agricultural crops. Vegetos, 27(1): 37–44.

Stolz P, B Obermayer, 2005. Manufacturing microalgae for skin care. Cosmet Toiletries, 120: 99–106.

Tominaga K, N Hongo, M Karato, E Yamashita, 2012. Cosmetic benefits of astaxanthin on humans subjects. Acta Biohim Pol, 59(1): 43–47.

Uzair B, S Tabassum, M Rasheed, SF Rehman, 2012. Exploring marine cyanobacteria for lead compounds of pharmaceutical importance. ScientificWorldJournal, DOI: 10.1100/2012/179782

Vassilakaki M, S Pflugmacher, 2008. Oxidative response of *Synechocystis* sp. (PCC 6803) due to exposure to microcystin-LR and cell-free cyanobacterial crude extract containing microcystin-LR. J Appl Phycol, 20: 219–225.

Wen R, Z Sui, X Zhang, S Zhang, S Qin, 2007. Expression of the phycoerythrin gene of *Gracilaria lemaneiformis* (Rhodophyta) in *E. coli* and evaluation of the bioactivity of recombinant PE. J Ocean Univ China, 6: 373–377.

Wiegand C, S Pflugmacher, 2005. Ecotoxicological effects of selected cyanobacterial secondary metabolites: a short review. Toxicol Appl Pharmacol, 203: 201–218.

Williams PJB, LML Laurens, 2010. Microalgae as biodiesel & biomass feedstocks: Review & analysis of the biochemistry, energetics & economics. Energy Environ Sci, 3: 554–590.

Wu GF, QY Wu, ZY Shen, 2001. Accumulation of poly-β-hydroxybutyrate in cyanobacterium *Synechocystis* sp. PCC6803. Bioresour Technol, 76: 85–90.

Zhang J, Z Sun, P Sun, T Chen, F Chen, 2014. Microalgal carotenoids: beneficial effects and potential in human health. Food Funct, 5: 413–425.