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Possibilities of Using Microalgea Varieties in Beekeeping Research

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Abstract

In medicine, microalgae are used to produce food supplements and medicines. In particular, algae such as spirulina and chlorella with their high content of proteins, vitamins, minerals and omega-3 fatty acids have positive effects on health. In addition, some types of microalgae have antimicrobial and antiviral properties and are being studied in the treatment of cancer and cardiovascular diseases. In animal husbandry, microalgae are used as a feed additive to improve animal nutrition. Microalgae can accelerate the growth of animals, strengthen their immune system and reduce environmental pollution. In particular, algae used in feed for ruminants can reduce methane emissions. In beekeeping, microalgae are used as food supplements for bees. Food supplements with microalgae can strengthen the bees' immune system and increase their survival rate in winter. In addition, microalgae can promote the production of compounds that increase propolis production. In summary, microalgae offer important health, productivity and environmental benefits in areas such as medicine, animal husbandry and beekeeping. Research in this field continues to provide solutions to support the sustainable and efficient use of microalgae.

Key Words: *Microalgea, Eco-frendly beekeeping, Study, Bee health, Sustainable*

Introduction

Algae comprise about 25,000-50,000 species of different sizes, shapes, pigments and functional compounds (Guiry, 2018). They are generally divided into prokaryotic unicellular cyanobacterial microalgae (blue-green algae) and eukaryotic unicellularand multicellular algae (green algae, red algae and brown algae) (Yaakob et al., 2014; Pereira, 2021; Ullmann and Grimm, 2021). Algae species have been known for centuries and are used in almost all areas of industry. Especially in the countries of the Far East and South Asia, algae species, which are widely used as food, in the medical, pharmaceutical and cosmetic industries and in the production of fertilizers in agriculture, are not only collected in their natural habitats, but also cultivated in the oceans and grown like plants on land (Atay, 1984). They are classified according to the ecosystem in which they occur, their size, their pigments and whether they are prokaryotic or eukaryotic. Algae that do not have true roots, stems and leaves are divided into microalgae and macroalgae according to their size.

Macroalgae are plant organisms that are between 1-2 cm and 40-50 m in size, depending on the species, and provide aquatic organisms with food, protection and reproduction. Macroalgae species have been used in the past as food, fertilizer, animal feed, dye, thickener, soap, glass raw material, gelling agent and to produce biofuels (Jensen, 1966). Microalgae are heterogeneous microorganisms that do not belong to a specific taxonomic group. They can be unicellular, colonial or filamentous. From an ecological point of view, they form a community of unicellular algae belonging to different large groups. Microalgae are widely distributed in freshwater, brackish, and marine ecosystems, although certain species are also capable of thriving in terrestrial environments such as rocks and soils. These microorganisms are the focus of research in botany, phycology, and microbiology. Cyanobacteria, which possess a prokaryotic structure, are not only studied within the fields of botany and phycology but also extensively researched in microbiology. From an ecological perspective, cyanobacteria, unicellular green and red algae, euglenoids (*Euglenophyta*), chrysophytes (*Chrysophyta*), and dinoflagellates (*Dinoflagellata*) collectively constitute the group of microalgae.

As photosynthetic organisms, microalgae play a crucial role in sustaining life on Earth. They contribute significantly to atmospheric oxygen production while simultaneously utilizing carbon dioxide for photoautotrophic growth. Their exceptional biodiversity enables them to inhabit diverse regions across the biosphere. Furthermore, microalgae exhibit remarkable resilience to environmental stressors, allowing them to withstand conditions such as temperature fluctuations, drought, salinity, photo-oxidative stress, anaerobic environments, osmotic pressure, and UV radiation (Minhas et al., 2016).

Numerous algal species have the ability to synthesize bioactive compounds with allelopathic properties. Allelopathy refers to a biological phenomenon in which an organism releases specific biochemical substances that influence the germination, growth, survival, and reproduction of other organisms within its environment. These compounds, classified as allelochemicals, belong to the category of secondary metabolites and can exert either beneficial (positive allelopathy) or detrimental (negative allelopathy) effects on target organisms and ecosystems. The allelopathic potential of microalgae has been explored as a biological strategy for controlling algal blooms and mitigating microbial contamination caused by bacteria, fungi, and protozoa.

Microalgae are also recognized for their ability to produce a wide range of biologically active compounds (BACs) with applications in biotechnology and clinical research. The emergence of antibiotic resistance among bacteria and other microorganisms poses a significant threat to both human and animal health. In this context, microalgae are considered promising candidates for the discovery of novel antibacterial agents that may circumvent resistance mechanisms. Notably, large-scale cultivation of microalgae in photobioreactors can be conducted under controlled conditions, facilitating the production of high or even ultra-high-density cultures (Richmond, 2004; Gordon and Polle, 2007; Sun et al., 2019; Wang et al., 2019; Jin et al., 2020).

This mini-review presents findings related to the utilization of selected microalgae species in various ecosystems and explores their potential applications in beekeeping. Additionally, the discussion addresses their contributions to sustainability and environmental conservation.

Sustainability and environmental benefits: Use of microalgae in beekeeping and impact on the environment

In recent years, microalgae have attracted attention as an important alternative in agriculture and animal husbandry due to their rapid biomass production potential, low environmental footprint and sustainable production methods. Considering the limitations and environmental impact of conventional feeds, microalgae represent a nutritionally and environmentally beneficial option for beekeeping.

Ecological advantages of microalgae production

Microalgae can produce large amounts of biomass through photosynthesis and contribute to the fight against climate change by absorbing carbon dioxide (CO_2) from the atmosphere during this process (Chisti, 2007). In contrast to traditional agricultural practices, the cultivation of microalgae does not cause any expansion of agricultural land or the loss of habitat (Wijffels et al., 2010). In addition, the use of saltwater or recycled wastewater instead of freshwater for microalgae cultivation enables efficient use of water resources (Pittman et al., 2011). This characteristic makes microalgae an attractive alternative in areas with water scarcity.

Sustainability of the use of microalgae in bee nutrition

Sugar syrup and pollen substitute commonly used in beekeeping may not be sufficient in terms of nutritional value and environmental sustainability. Microalgae can contribute to bee nutrition with their high content of proteins, essential amino acids, omega-3 fatty acids and antioxidants (Becker, 2007). These nutrients can boost bee immunity, improve colony health and reduce losses. In addition, the use of microalgae-based feeds can reduce the environmental impact of beekeeping. The production of sugar syrup usually requires large agricultural areas and large amounts of water. The use of microalgae-based feeds offers an environmentally friendly approach by ensuring a more efficient consumption of these resources (Barsanti and Gualtieri, 2014).

Prospects

For microalgae to be widely used in beekeeping, it is of great importance to reduce production costs and develop scalable production techniques. In addition, the long-term effects of microalgae-based feed on bees should be studied in more detail. Scientific studies in this area can accelerate the acceptance of microalgae as a sustainable option for beekeeping. Therefore, microalgae have significant potential as a sustainable feed source that minimizes environmental impact and improves bee health. Research on this topic can make a valuable contribution to both beekeeping and ecosystem conservation.

Effects and use as food

Although honeybee colony losses are thought to be due to a combination of stress factors, research shows that malnutrition is one of the main causes of these losses. Commercial beekeepers are increasingly turning to artificial pollen substitutes to support their colonies in times of food shortages and to increase bee populations prior to pollination. Nevertheless, these artificial diets are known to lack essential macronutrients, including proteins, lipids, prebiotic fibers, as well as vital micronutrients such as vitamins, minerals, and antioxidants. Consequently, enhancing the nutritional profile of pollen substitutes has become a crucial aspect of contemporary beekeeping practices. Microalgae offer considerable potential for plant nutrition as their biochemical composition is similar to that of natural pollen. Although there are few studies on honeybees, microalgae have been extensively studied in insect nutrition (Qiu et al., 2019), aquaculture (Guedes et al., 2015), animal husbandry (Madeira et al., 2017) and human nutrition (Caporgno & Mathys, 2018). The nutritional content of microalgae has been extensively characterized, and it has been shown that they can be evaluated both as a sole source of protein and as a feed additive for various organisms (Guedes et al., 2015; Madeira et al., 2017). Microalgae are rich sources of carotenoid pigments, particularly lutein, zeaxanthin, and astaxanthin, which have been shown to improve survival rates in various organisms when incorporated into their diet (Merchie et al., 1998; Babin et al., 2010). The most promising microalgae species in terms of beekeeping are Arthrospira and Chlorella. Arthrospira (known as Spirulina) consists of 60-70% of its dry weight in protein and is a highly bioavailable protein source. About half of the proteins contain essential amino acids (EAA) (Soni et al., 2017). Similarly, chlorella species have a protein content of 50-60% and offer a complete EAA profile (Kotrbáček et al., 2015). Arginine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, threonine, tryptophan and valine are among the essential amino acids required by honeybees, and these amino acids must be obtained from the diet. When worker bees consume pollen, these amino acids are incorporated into the vitellogenin lipoprotein in the fat body and form the precursor of the proteins of the hypopharyngeal glands that are secreted to feed the larvae (Crailsheim, 1990). A recent study has shown that Chlorella sorokiniana has positive effects on the growth and individual nutritional physiology of honey bee colonies. According to the results of the study, bees fed with this microalga showed an increase in fat body protein content, vitellogenin mRNA levels and hypopharyngeal gland size. These results suggest that chlorella is promising as a pollen substitute or dietary supplement (Jehlík et al., 2019).

In another study, a pollen substitute formulation containing Arthrospira was found to increase the performance of bee colonies compared to unfed control colonies (Kumar et al., 2013). However, the exact effects of Arthrospira on the health of individual bees and colony dynamics are not yet fully known. Two essential polyunsaturated fatty acids (PUFAs) that are important for honeybees are linoleic acid and α-linolenic acid (Arien et al., 2015). Studies have shown that dietary PUFA content is related to vitellogenin expression in the fat body (Wegener et al., 2018). 10-20% of the dry weight of Chlorella sorokiniana consists of lipids and studies have shown that this microalga increases fat storage in bees (Jehlík et al., 2019). However, species such as Botryococcus (25-75%), Nanochloropsis (31-68%) and Schizochytrium (50-77%) are known to have a much higher lipid content (Demirbaş and Demirbaş, 2011). Microalgae also contain valuable sources of vitamins such as tocopherols, ascorbic acid and B vitamins, as well as essential minerals such as sodium, potassium, calcium and magnesium (Fábregas and Herrero, 1990). Studies have shown that in worker bees fed with Chlorella vulgaris and Arthrospira platensis, growth rates increase, antioxidant defenses are strengthened, and the expression of heat shock proteins increases (Ricigliano et al., 2022). A significant increase in vitellogenin mRNA expression levels was observed in bees fed spirulina (Ricigliano et al., 2021). In addition, hypopharyngeal gland development, an increase in amino acid content and an increase in vitellogenin mRNA levels were observed in bees whose diet was supplemented with 0.5-10% Chlorella sorokiniana (Jang et al., 2022). In another study, it was reported that bee colonies fed with feed containing 25% spirulina produced more brood compared to the control group (McMenamin et al., 2023). Similarly, the positive effects of feeds containing chlorella (2%) on worker bees and colony health are highlighted (Jang et al., 2023). In addition, spirulina (2 g) was found to have positive effects on vitellogenin expression, abdominal lipid ratio and hypopharyngeal gland development (Güneşdoğdu et al., 2024). Experimental hives fed with Spirulina platensis, Scenedesmus quadricauda, Scenedesmus apiculatus, and Oocystis borgei Snow showed a 2.7% increase in hygienic behavior compared to control hives fed with honey and powdered sugar (Toderas et al., 2017). These results suggest that microalgae can be considered an important food source for honeybees and have the potential to be used as a pollen substitute or food supplement.

Table 1. Nutritional Content and Potential Benefits of Microalgae for Honey Bees

Microalgae	Nutritional Content and Benefits	References
Spirulina platensis	60-70% protein, high bioavailability amino acids, Vitamin and mineral source, Increases bee development and nutritional value, Increases vitellogenin level.	Soni et al., (2017) Becker (2007) Kumar et al., (2013) Güneşdoğdu et al., (2024)
Chlorella spp.	50-60% protein, full essential amino acid profile, High chlorophyll and antioxidant content.	Kotrbáček et al., (2015) Fábregas ve Herrero (1990)
Chlorella sorokiniana	Increases vitellogenin level.	Jehlík et al., (2019)
Chlorella vulgaris	It strengthens bee immunity and increases vitellogenin level.	Ricigliano et al., (2022)
Dunaliella salina	It is rich in beta-carotene.	Caporgno and Mathys (2018)

Antibacterial effect

The antimicrobial properties of microalgae have been associated with various bioactive compounds spanning multiple chemical classes, such as indoles, terpenes, acetogenins, phenols, fatty acids, and volatile halogenated hydrocarbons (Mayer and Hamann, 2005; Cardozo et al., 2007). For instance, the antimicrobial potential of supercritical extracts derived from the microalga *Chaetoceros muelleri* has been attributed to its lipid composition (Mendiola et al., 2007). Similarly, the antimicrobial effects observed in different pressurized extracts of *Dunaliella salina* are not solely linked to fatty acids but are also influenced by other bioactive compounds, including α- and β-ionone, β-cyclocitral, neophytadiene, and phytol (Herrero et al., 2006). As antibacterial agents, microalgae can prevent the occurrence of bacterial diseases. It has been shown that algae-derived long-chain polyunsaturated fatty acids (LC-PUFAs) and algal sterols, such as eicosapentaenoic acid (EPA), have antibacterial properties and can be effective against both Gram-positive and Gram-negative bacteria (Benkendorff et al., 2005; Desbois et al., 2009). A microalgae homogenate obtained from Tetraselmis suecica showed good in vitro antibacterial activity against various Vibrio species, including important shrimp pathogens such as Vibrio alginolyticus, Vibrio anguillarum, Vibrio parahaemolyticus and Vibrio vulnificus (Austin and Day, 1990). Honeybees infected with *Nosema ceranae* and provided with extracts from *Porphyridium marinum* and *Porphyridium purpureum* exhibited a reduced parasite load compared to the control group. Experimental bees experienced up to a 30% decrease in *Nosema* infection levels relative to untreated controls, and the parasite burden was approximately half that observed in fumagillin-treated individuals (Roussel et al., 2015). Additionally, extracts of *Chlorella sorokiniana* demonstrated antimicrobial activity against plate cultures of *Paenibacillus larvae* (Vránová, 2017), while similar inhibitory effects were noted when *Chlorella vulgaris* extracts were applied to spores and vegetative cultures of *Paenibacillus larvae* (Dostálková et al., 2021).

Microalgae cultures of Chlorella minutissima, Tetraselmis chui, Nannochloropsis species, Arthrospira platensis, and Isochrysis species have been shown to inhibit the growth of bacteria (Vibrio parahaemolyticus, V. anguillarum, V. splendidus, V. scophthalmi, V. alginolyticus, and V. lentus) (Kokou et al., 2012). The first antibacterial compound isolated in history (chlorellin) is believed to have been obtained from the microalgae Chlorella, which showed inhibitory activity against Gram-positive and Gram-negative bacteria (Pratt et al., 1944).

Some microalgae species exhibit antimicrobial activity via various mechanisms. For instance, *Fischerella ambigua*, a cyanobacterium isolated from a soil sample, produces parsiguine, a bioactive compound with antibacterial and antifungal properties (Ghasemi et al., 2004). Parsiguine exhibits antimicrobial activity against *Staphylococcus epidermidis* PTCC 1114 and *Candida krusei* ATCC 44507. Additionally, the marine diatom *Phaeodactylum tricornutum* has been found to contain antibacterial compounds effective against various bacterial species (Desbois et al., 2009). The primary bioactive molecule identified in this microalga is eicosapentaenoic acid (EPA), which has demonstrated potent activity against multidrug-resistant *Staphylococcus aureus* (MRSA) strains 16a and 252, along with other *S. aureus* strains, *Staphylococcus epidermidis*, *Bacillus weihenstephanensis*, and *Bacillus cereus*. Furthermore, EPA has been reported to be effective against *Vibrio (Listonella) anguillarum*, a pathogen responsible for hemorrhagic septicemia in fish, as well as *Micrococcus luteus*, *Photobacterium* species, and *Planococcus citreus*. Notably, eicosapentaenoic acid has also been described as toxic to herbivorous organisms (Jüttner, 2001). Another bioactive compound isolated from *P. tricornutum*, hexadecatrienoic acid, has shown antibacterial effects against *S. aureus* (Amaro et al., 2011). On the other hand, ethanol extracts from the red stage of Haematococcus pluvialis were found to have antimicrobial activity against Escherichia coli and S. aureus. This effect is most likely due to the presence of the short-chain fatty acids butanoic acid and methyl lactic acid (Santoyo et al., 2009). Polyunsaturated aldehydes are of particular importance among the bioactive compounds of algal origin. These compounds are synthesized by diatoms and have been found in species such as Skeletonema marinoi (formerly Skeletonema costatum) (Vidoudez et al., 2008; Sarno et al., 2005), Pseudonitzschia delicatissima and Thalassiosira rotula (Miralto et al., 1999). Decadienal, one of the most important compounds in this group, shows strong antibacterial activity against important human pathogens such as methicillin-resistant strains of Staphylococcus aureus (MRSA) and Haemophilus influenzae as well as bacteria such as Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Staphylococcus epidermidis. It is thought that decadienal is probably derived from arachidonic acid. This compound has also been reported to inhibit the growth of various Gram-negative bacteria, including *Aeromonas hydrophila*, *Vibrio anguillarum*, *Alteromonas haloplanktis*, *Photobacterium phosphoreum*, and *Psychrobacter immobilis*, as well as Gram-positive species such as *Planococcus citreus* and *Micrococcus luteus* (Smith et al., 2010). Furthermore, extracellular metabolites secreted by *Skeletonema costatum* during its mid-growth phase have demonstrated antibacterial activity against *Listeria monocytogenes* (Terekhova et al., 2009). Organic extracts from *S. costatum* have also exhibited inhibitory effects on several *Vibrio* species (Naviner et al., 1999), specifically suppressing the growth of *Vibrio mytili* T, *Vibrio* sp. S322 (a pathogen affecting Japanese oyster larvae), *Vibrio* sp. VRP (a pathogen of mussel larvae), and *Vibrio anguillarum*.

Additionally, strains of *Chroococcus dispersus*, *Chlorella vulgaris*, and *Chlamydomonas reinhardtii* have shown considerable antibacterial effects against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Escherichia coli*, and *Salmonella typhi* (Ghasemi et al., 2007). In the same study, *C. dispersus* strains were also found to inhibit the growth of *Pseudomonas aeruginosa*. Moreover, organic extracts obtained from *Euglena viridis* have demonstrated inhibitory effects on a range of bacterial species, including *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas fluorescens*, *Aeromonas hydrophila*, *Edwardsiella tarda*, *Vibrio alginolyticus*, *Vibrio anguillarum*, *Vibrio fluvialis*, *Vibrio parahaemolyticus*, *Vibrio harveyi*, and *Escherichia coli* (Das et al., 2005).

Antiviral effect

Several viral diseases have emerged or re-emerged in recent years. Although there are some antiviral drugs specifically designed to combat these diseases, the constant emergence of drug-resistant mutations in viruses is a major problem. Therefore, microalgae are of great interest as potential sources of antiviral compounds (Borowitzka, 1995). According to Amaro et al. (2011), the viral infection process is divided into three phases: Initial phase: adsorption of the virus to the host cell and invasion of the cell; Mid-phase: the phase in which the cell is forced to synthesize numerous copies of the virus; Final phase: the maturation of the new virus particles and their release from the cell. The effect of the antiviral drug acyclovir on the herpes simplex virus (HSV), for example, is observed in mid-phase of the viral infection (Elion et al., 1977). In contrast, antiviral factors derived from Dunaliella species neutralize the function of the virus in initial phase (Ohta et al., 1998). *Dunaliella primolecta* extract was found to have the highest antiviral activity against *HSV-1*. Three of these antiviral compounds were purified by chromatographic methods and NMR and MS analyzes showed that these compounds are phophorbide-like structures.

Sulfated polysaccharides from the cell wall of the red microalgae Porphyridium sp. have shown strong antiviral activity against the herpes simplex virus type 1 and 2 (HSV-1, HSV-2) and the varicella zoster virus (VZV) (Huleihel et al., 2001). These sulfated polysaccharides also inhibit the replication of two economically important viruses, viral hemorrhagic septicemia virus of salmonids (VHSV) and African swine fever virus (ASFV) (Fabregas et al., 1999). On the other hand, *allophycocyanin* extracted from *Spirulina platensis* has been observed to mitigate the cytopathic effects in cells infected with *enterovirus 71*. This viral infection poses a significant health risk, particularly in children, as it is associated with high morbidity and mortality rates. The discovery of the antiviral activity of *allophycocyanin* represents a noteworthy advancement in this field. Its mechanism of action has been linked to delaying viral RNA synthesis within infected cells while simultaneously reducing apoptosis in *enterovirus 71*-infected rhabdomyosarcoma cells (Shih et al., 2003).

Several polysaccharides derived from marine algae have also demonstrated substantial antiviral properties (Ahmadi et al., 2015). Among these is *naviculan*, a sulfated polysaccharide isolated from the diatom *Navicula directa* (Lee et al., 2006). Research findings indicate that *naviculan* exhibits strong antiviral effects against *HSV-1* and *HSV-2* (IC_{50}: 7–14 µg/mL) and plays a crucial role in inhibiting the early replication stages of the influenza virus. Notably, *naviculan* has also shown inhibitory activity against *HIV* by interfering with viral attachment and penetration processes. Additionally, it has been reported to prevent the fusion of *CD4*-expressing cells with *HeLa* cells expressing the *HIV* glycoprotein gp160.

Moreover, *p-KG03*, a sulfated exopolysaccharide extracted from *Gyrodinium impudicum*, has displayed significant antiviral activity against *encephalomyocarditis virus (EMCV)* in vitro (EC_{50} = 26.9 µg/mL) (Yim et al., 2004). Similarly, *Cochlodinium polykrikoides* produces polysaccharides (A1 and A2) capable of inhibiting the cytopathic effects of *influenza virus types A and B*, *respiratory syncytial virus types A and B*, and *HIV-1* (Hasui et al., 1995). In another study, *calcium spirulan* extracted from *Arthrospira platensis* demonstrated selective inhibition against multiple viruses, including *HSV-1* (in *HeLa* cells), *HCMV* (in *HEL* cells), *influenza A* (in *MDCK* cells), *Coxsackie virus* (in *Vero* cells), *measles* (in *Vero* cells), *HIV-1* (in *MT-4* cells), *poliovirus* (in *Vero* cells), and *mumps virus* (in *Vero* cells) (Hayashi et al., 1996).

Table 2. Antibacterial Effects of Microalgae on Various Bacteria

Microalgae	Bacteria It Affects	References
Chlorella minutissima	*Vibrio parahaemolyticus, V. anguillarum, V. splendidus, V. scophthalmi, V. alginolyticus,* and *V. lentus*	Kokou et al., (2012)
Tetraselmis chui		
Nannochloropsis spp.		
Arthrospira platensis		
Isochrysis spp.		
Chlorella spp.	*Gram-positive and Gram-negative bacteria*	Pratt et al., (1944)
Fischerella ambigua	*Staphylococcus epidermidis* and *Candida krusei*	Ghasemi et al., (2004)
Phaeodactylum tricornutum	*Staphylococcus aureus (MRSA), S. epidermidis, Bacillus cereus, Vibrio anguillarum, Micrococcus luteus,* and *Photobacterium* spp.	Desbois et al., (2009)
Haematococcus pluvialis	*Escherichia coli* and *Staphylococcus aureus*	Santoyo et al., (2009)
Skeletonema marinoi	*Listeria monocytogenes*	Terekhova et al., (2009)
Chroococcus dispersus	*Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Escherichia coli,* and *Salmonella typhi*	Ghasemi et al., (2007)
Euglena viridis	*Pseudomonas aeruginosa, Vibrio alginolyticus, Vibrio parahaemolyticus,* and *Escherichia coli*	Das et al., (2005)
Chlorella sorokiniana	*Paenibacillus larvae*	Vránová (2017)
Chlorella vulgaris	*Paenibacillus larvae* (spore-forming and vejetatif-forming)	Dostálková et al., (2021)
Porphyridium marinum	*Nosema ceranae*	Roussel et al., 2015
Porphyridium purpureum		

Table 3. Antiviral Effects of Microalgae on Various Bacteria

Microalgae	Viruses It Affects	References
Dunaliella primolecta	*Herpes simplex virus (HSV-1)*	Ohta et al. (1998)
Porphyridium sp.	*Herpes simplex virus (HSV-1, HSV-2), Varicella zoster virus (VZV), VHSV,* and *ASFV*	Huleihel et al. (2001); Fabregas et al. (1999)
Spirulina platensis	*Enterovirus 71*	Shih et al. (2003)
Navicula directa	*HSV-1, HSV-2, Influenza virus,* and *HIV*	Lee et al. (2006)
Gyrodinium impudicum	*Encephalomyocarditis virus (EMCV)*	Yim et al. (2004)
Cochlodinium polykrikoides	*Influenza A/B, Respiratory syncytial virus (RSV),* and *HIV-1*	Hasui et al. (1995)
Arthrospira platensis	*HSV-1, HCMV, Influenza A, Coxsackie, HIV-1, Polio, Measles,* and *Mumps*	Hayashi et al. (1996)
Nostoc flagelliforme	*HSV-1, HSV-2, Human cytomegalovirus,* and *Influenza A*	Kanekiyo et al. (2007)

Furthermore, *nostoflan*, an acidic polysaccharide produced by *Nostoc flagelliforme*, has been identified as an inhibitor of *HSV-1*, *HSV-2*, *human cytomegalovirus*, and *influenza A virus* (Kanekiyo et al., 2007). Studies suggest that its antiviral effect against *HSV* stems from its ability to block viral attachment to host cells.

Despite the significant advancements in this field, various challenges remain. Nevertheless, ongoing research continues to introduce promising new strategies for the sustainable treatment of viral infections, expanding the potential avenues for future scientific progress.

Antifungal effect

Fungal infections are known for their long-term persistence and pathogenic yeasts are a common source of transmission between humans and animals. Infections with Candida spp. are among the most resistant strains, especially in women, and can lead to infertility (Pellati et al., 2008), arthritis (Yordanov et al., 2004) and various organ damage if left untreated. Immunocompromised individuals are more susceptible to fungal diseases caused by yeast and mold spores. Parsiguine, a compound isolated from Fischerella ambigua, and known for its antibacterial properties, has been shown to be effective against the yeast Candida krusei ATCC 44507, and is considered an important antifungal agent (Ghasemi et al., 2004).

In recent studies, ten different strains of microalgae isolated from freshwater sources in Turkey were found to have antifungal activity against the yeast species Saccharomyces cerevisiae, Candida albicans and Candida tropicalis. Among these species, Oscillatoria sp. and Chlorococcus sp. stand out as microalgae with the strongest antifungal activity (Katircioglu et al., 2006). In addition, ethanol extracts of Haematococcus pluvialis were tested on Candida albicans and Aspergillus niger; all extracts were found to be effective against C. albicans but showed no inhibition against A. niger (Santoyo et al., 2009). The compounds responsible for this antifungal activity were butanoic acid and methyl lactate, which were previously known for their antimicrobial properties (Cherrington et al., 1991). In addition, Chlamydomonas reinhardtii, which has a broad spectrum of biological activities, exhibits both antibacterial and antifungal effects. In one study, this microalgae species was found to inhibit the growth of Candida kefyr, Aspergillus niger, and Aspergillus fumigatus (Ghasemi et al., 2007).

In addition, the antifungal effect of the extracts of Scenedesmus obliquus was investigated and in particular the diethyl ether extracts were tested against Aspergillus flavus, Aspergillus steinii, Aspergillus ochraceus, Aspergillus parasiticus, It was found to be effective against fungal species such as Aspergillus westerdijikia, Aspergillus carbonarius, Fusarium verticillioides, Fusarium proliferatum and Penicillium verrucosum (Marres et al., 2019). However, aqueous, methanol, ethanol, acetone and chloroform extract only showed antifungal activity in some fungal species. For example, the aqueous extract proved to be effective against A. flavus, A. steinii, A. westerdijikia and A. carbonarius. Caratungiols A and B isolated from the marine dinoflagellate Amphidinium sp. belong to the class of polyols and studies have shown that caratungiol A at a concentration of 12 µg/disk exhibits antifungal activity on Aspergillus niger (Washida et al., 2006).

According to Abedin and Taha (2008), ethanol, acetone, diethyl ether, and methanol extracts of S. quadricauda exhibited antifungal properties against fungal species such as A. niger, A. flavus, P. herquei, and F. moniliforme. Similarly, Vehapi et al. (2018) found that extracts of Chlorella vulgaris and Chlorella minutissima showed strong antifungal activity against A. niger and Fusarium oxysporum when cultured in iroko tree sap. The study showed that the antifungal activity of these algae species varied when cultured in different media, with lower activity in BBM media and wastewater from Istanbul. In a study conducted by Ghasemi et al. (2007), the antifungal activity of the supernatants of 15 different algae strains was investigated and it was reported that Chlamydomonas reinhardtii, Chlorella dispersus, Chlorella vulgaris, Chlorella sp., Anacystis nidulans, Chlorella ellipsoidea, and Oocystis sp. showed moderate antifungal activity against fungi such as Candida kefyr, Aspergillus fumigatus, and A. niger. However, only the strain C. dispersus 039 proved to be effective against C. albicans, while the other algae extracts showed no activity against C. albicans. These results show that the antifungal activity of microalgae species can be optimized not only with growth media and cultivation techniques, but also with modern molecular biotechnological methods that allow the manipulation of intracellular and extracellular target metabolites.

Table 4. Antifungal Effects of Microalgae on Various Bacteria

Microalgae	Types of Fungi It Affects	References
Fischerella ambigua	*Candida krusei*	Ghasemi et al. (2004)
Oscillatoria sp. and *Chlorococcus sp.*	*Saccharomyces cerevisiae, Candida albicans, Candida tropicalis*	Katircioglu et al. (2006)
Haematococcus pluvialis	*Candida albicans*	Santoyo et al. (2009)
Chrococcus sp. Mogan, Chrococcus sp. Kurtbogazi, Oscillatoria sp.S.F., Oscillatoria sp. Burdur, Oscillatoria sp. Mogan, Oscillatoria limnosa 1966/1380, Anabaena sp.Burdur, Synechocystis aquatilis 1965/426, and *Chlorella vulgaris*	*Bacillus subtilis ATCC 6633,* *Bacillusthuringiensis RSKK 380,* *Bacillus cereus RSKK 863,* *Bacillus megaterium RSKK 578,* *Yersinia enterocolitica ATCC 1501,* *Escherichia coli ATCC 11230,* *Staphylococcus aureus ATCC 25923,* *Micrococcus luteus NRLL B-4375,* *Micrococcus flavus,* *Pseudomonas aeruginosa ATCC29212,* *Saccharomyces cerevisiae ATCC,* *Candida albicans,* *Candida tropicalis*	Katircioğlu et al. (2005)
Chlamydomonas reinhardtii	*Candida kefyr, Aspergillus niger, Aspergillus fumigatus*	Ghasemi et al. (2007)
Scenedesmus obliquus	*Aspergillus flavus, Aspergillus steinii, Aspergillus ochraceus, Aspergillus parasiticus, Fusarium verticillioides*	Marres et al. (2019)

Table 5. Antiprotozoal Effects of Microalgae on Various Bacteria

Microalgea	Protozoa It Affects	References
Amphidinium sp.	*Tritrichomonas foetus*	Washida et al. (2006)
Calothrix sp.	*Plasmodium falciparum*	Rickards et al. (1999)
Fischerella ambigua	*Plasmodium falciparum* and *Trypanosoma rhodesiense*	Perez et al. (1990)
Microcystis aeruginosa	*Plasmodium falciparum* and *Trypanosoma brucei rhodesiense*	Portmann et al. (2008b)
Nostoc sp.	*Plasmodium falciparum*	Barbaras et al. (2008)

Antiprotozoal effect

Protozoal infections are serious health problems that often affect people living in tropical regions. The people most affected by these diseases often live in the poorest parts of the world. Protozoa are single-celled organisms that, like their host cells, are eukaryotic in structure. This makes it difficult to develop effective drugs against protozoa, which have a low risk of toxicity due to their similar cell structure to their host cells. In addition, drug resistance of protozoa is an important issue that needs to be considered. Algae are an inexhaustible source of biologically active compounds (BACs) thanks to their unique physiological properties. For this reason, many researchers worldwide are focusing on the antiprotozoal potential of algae. Most of these studies focus on macroalgae species (Torres et al., 2014). For example, the marine dinoflagellate Amphidinium sp. also exhibits antiprotozoal properties. Caratungiol A from this alga was found to be effective against Tritrichomonas fetus at a concentration of 1 µg/ml (Washida et al., 2006). Another important species, Calothrix sp., synthesizes indole-[3,2-j] phenanthridine compounds called calothrixin A and B, which show antiplasmodial activity against Plasmodium falciparum FAF6 (Rickards et al., 1999). However, Ambigol C, a natural compound isolated from Fischerella ambigua, showed moderate antiprotozoal activity against P. falciparum clone KI (IC50 = 1.5 µg/mL) and NF54 (IC50 = 2.4 µg/mL) strains (Perez et al., 1990). It has also been reported to be moderately effective against Trypanosoma rhodesiense (Wright et al., 2005). Aeracylamides A and B (Portmann et al., 2008a) and compounds C and D were isolated from M. aeruginosa strain PCC 7806 (Portmann et al., 2008b). Of these compounds, aeracylamide B exhibited submicromolar IC50 values against P. falciparum, while aeracylamide C showed low micromolar activity against T. brucei rhodesiense (Portmann et al., 2008b). The β-carboline indole alkaloid nostocarboline, obtained from Nostoc sp. 78-12A, showed significant activity against the P. falciparum K1 strain (Barbaras et al., 2008). This compound showed growth inhibitory properties at nanomolar concentrations against Plasmodium sp.

Table 6. Antiparasitic Effects of Microalgae on Various Bacteria

Microalgea	Parasites It Affects	References
Cladophora crispata	*Echinococcus granulosus* (Hydatid cyst)	Athbi et al. (2014)
Chlorella vulgaris	*Steinernema feltiae* (Nematode)	Zielinsky et al. (2020)
Chroococcus minutus, *Calothrix parietina*, and *Gloeocapsa gigantea*	*Varroa destructor*	Hassan and Mahmoud (2006)

Antiparasitic effect

In addition to their antiprotozoal properties, compounds can also be isolated from algae and microalgae that are effective against multicellular parasitic organisms, especially parasitic animals. For example, alkaloid and ethyl acetate extracts from Cladophora crispata have been found to reduce the number and weight of hydatid cysts caused by Echinococcus granulosus (Athbi et al., 2014). In this study, the efficacy of these extracts was compared with the commonly used antiparasitic drug albendazole. Although the lowest number of cysts and the smallest cyst sizes after treatment were found in the albendazole-treated group, alkaloid and ethyl acetate extracts showed a similar effect.

Recent studies have shown that extracts of Chlorella vulgaris have a toxic effect on the nematode Steinernema feltiae (Zielinsky et al., 2020). These nematodes infect insects and kill their hosts through entomopathogenic bacteria. In the study, it was observed that hydrophilic extracts of C. vulgaris completely killed S. feltiae when applied at concentrations of 37.5, 75, and 150 mg/mL. Parasitic diseases are not only a major public health problem for humans, but also of great importance for domestic animals and agricultural production. Previous research shows that antiparasitic agents from the microalgae have been studied more than those from the microalgae. Therefore, further investigation of the antiparasitic potential of microalgae could contribute to the development of new treatment options in the future. Studies conducted mainly on honeybees (*Apis mellifera*) have shown that microalgae can be effective in controlling Varroa destructor mites. A lower infestation rate was found in hives fed with algae than in untreated hives. In colonies fed with the species Chroococcus minutus, Calothrix parietina, and Gloeocapsa gigantea, the average mite infestation rate was 2.7, compared to 26.26% in untreated control colonies. In the same study, a mite infestation rate of 2.9% was recorded in hives treated with oxalic acid (Hassan and Mahmoud, 2006). These data indicate that the antiparasitic potential of microalgae is considerable and that their effect against different parasite species should be investigated in more detail.

Conclusion

In recent years, parasitic, fungal, and bacterial pathogens threatening bee health have necessitated innovative solutions beyond conventional treatment methods. In this context, microalgae stand out as a multifaceted tool for bee health management, not only due to their nutritional value but also their antiparasitic, antifungal, and antibacterial properties. Studies reveal that microalgae species such as *Spirulina platensis*, *Chlorella vulgaris*, and *Nannochloropsis* exhibit inhibitory effects against common bee parasites like *Nosema ceranae*. Moreover, phenolic compounds, polysaccharides, and antimicrobial peptides in microalgal extracts demonstrate antifungal and antibacterial activity against pathogens such as *Ascosphaera apis* (chalkbrood) and *Paenibacillus larvae* (American foulbrood). These bioactive components may enhance individual and colony-level immunity by modulating bees' defense mechanisms. The therapeutic potential of microalgae could reduce reliance on chemical treatments, minimizing residue and resistance risks. However, further research is needed to elucidate their mechanisms of action, optimize dosages, and validate efficacy under field conditions. Investigating synergistic effects of different microalgae strains or their combination with probiotics represents a promising future direction. In conclusion, microalgae are not merely a nutritional supplement but also a natural bioprotective agent for beekeeping. Integrating microalgae-based strategies into sustainable apiculture could offer economic and ecological advantages. Advancing research in this field may revolutionize honeybee health management practices.

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