Antimicrobial activities of microalgae: an invited review

Helena M. Amaro¹, A. Catarina Guedes¹, F. Xavier Malcata¹,²*

¹CIMAR/CIIMAR – Centro Interdisciplinar de Investigação Marinha e Ambiental, Rua dos Bragas nº 289, P-4050-123 Porto, Portugal
²ISMAI – Instituto Superior da Maia, Avenida Carlos Oliveira Campos, Castelo da Maia, P-4475-690 Avioso S. Pedro, Portugal
*Corresponding author

Microalgae exhibit a huge genetic diversity; they may indeed appear as individual cells, colonies or extended filaments. Ubiquitously distributed throughout the biosphere, they can grow essentially under all types of environmental conditions. Microalgae are thus some of the most promising stakeholders in blue biotechnology: besides their notable metabolic versatility, they require only low cost inorganic N- and P-sources, sequester CO₂ as base nutrient, and rely on sunlight to fulfill energy requirements. They are known as well for their richness in bioactive compounds, with promising applications in pharmaceutical formulations; some are rather active against unwanted bacteria found in aquaculture and food processing, whereas others exhibit antiviral, antifungal and antialgal features. Their cell-free extracts have accordingly been tested as additives for food and feed formulation, in attempts to circumvent use of antimicrobial compounds of synthetic origin, or subtherapeutical doses of regular antibiotics. Recall, in this regard, the growing resistance of some bacterial strains, owing to the widespread and almost unrestricted use of antibiotics in cattle handling and by consumers at large. This chapter tackles all such items; for methodological reasons, it is divided into five sections: (1) introduction; (2) antibacterial action; (3) antiviral action; (4) antifungal action; and (5) antimicroalgal action.

Keywords: antibacterial, antifungal, antiviral, antimicroalgal

1. Introduction

Microalgae exhibit a notable biodiversity; they can in fact be found as individual cells, colonies or extended filaments. These microorganisms account for the basis of the food chain in aquatic ecosystems; they posses the intrinsic ability to take up H₂O and CO₂ that, with the aid of solar energy, are used to synthesize complex organic compounds, which are subsequently accumulated and/or secreted as primary or secondary metabolites. They are ubiquitously distributed throughout the biosphere, where they have adapted to survival under a large spectrum of environmental stresses – e.g. heat, cold, drought, salinity, photo-oxidation, anaerobiosis, osmotic pressure and UV exposure [1]; hence, they may grow essentially under all environmental conditions available, ranging from freshwater to extreme salinity, and can survive in moist, black earth and even desert sands – and they have as well been found in clouds, being in addition essential components of coral reefs. This wide span of ecosystems contributes to the myriad of chemical compounds that they are able to synthesize, thus accounting for their unique potential as stakeholders in blue biotechnology.

Almost 18,500 new compounds have been isolated from marine sources between 1965 and 2006, yet one estimates that ca. 97% of all existing marine compounds have not yet been obtained nor characterized [2]. Therefore, microalgae (especially those from marine origin) represent a unique opportunity to discover novel metabolites, or to produce known metabolites at lower costs. The rate of rediscovery – i.e. finding metabolites which were already obtained from other biological sources, is expected to be far lower (i.e. <5%) in microalgae than in more conventional microorganisms (i.e. > 90%) [3]. Microalgae possess the extra advantage of a substantial metabolic plasticity, dependent on their physiological state (i.e. stressed vs. nonstressed); likewise, their secondary metabolism can easily be triggered by most forms of externally applied stress (e.g. lack of a nitrogen source) [4].

Microalgae have for long been used with therapeutic purposes; their systematic screening for biologically active principles began in the 1950s. However, in the last decade microalgae have become the focus of extensive research efforts, aimed at finding novel compounds that might lead to therapeutically useful agents [5-7]. Microalgae have meanwhile been found to produce antibiotics: a large number of microalgal extracts and/or extracellular products have proven antibacterial, antifungal, antiprotozoal and antiplasmodial [8-11].

The antimicrobial activity of microalgae has been attributed to compounds belonging to several chemical classes – including indoles, terpenes, acetogenins, phenols, fatty acids and volatile halogenated hydrocarbons [6,7]; for instance, the antimicrobial activity of supercritical extracts obtained from the microalga Chaetoceros muelleri were related to its lipid composition [12]. However, the antimicrobial activity detected in several pressurized extracts from Dunaliella salina may be explained not only by several fatty acids, but also by such compounds as α- and β-ionone, β-cyclocitrinal, neophytadiene and phytol [10]. Efforts to identify the compounds directly responsible for those antimicrobial features – e.g. chlorellin [13], have been on the run, but are still relatively incipient owing the some new classes of compounds found.
Microalgal cell-free extracts are already being tested as additives for food and feed formulation, in attempts to replace antimicrobial compounds of synthetic origin currently in use – including subtherapeutical doses of antibiotics employed as prophylactic measure in animal breeding [14]. Recall, in this regard, the growing resistance of some bacterial strains arising from the widespread and essentially unrestricted use of antibiotics in cattle handling, and by domestic consumers use via self-prescription [15,16]. However, a key factor for their eventual economic feasibility is the possibility of operating large photobioreactors under aseptic conditions, which are able to produce biomass and metabolites to sufficiently high levels [17,18].

2. Antibacterial action

The past decade has witnessed a significant increase in the resistance of pathogenic bacteria to antibacterial agents – with direct implications in human morbidity and mortality. Hence, attention has been paid to a more detailed understanding of the mechanisms underlying antimicrobial resistance – as well as to improved methods to detect resistance, new antimicrobial options for treatment of infections caused by resistant microorganisms, and methods to prevent emergence and spreading of resistance in the first place. Most efforts were devoted to the study of antibiotic resistance in bacteria for several reasons: (i) bacterial infections are responsible for most community-acquired and nosocomial infections; (ii) the large and expanding number of antibacterial classes offers a more diverse range of resistance mechanisms; and (iii) the ability to move bacterial resistance determinants into standard, well-characterized bacterial strains facilitates more detailed studies of the underlying molecular mechanisms [19].

Pratt et al. [20] isolated the first antibacterial compound from a microalga, Chlorella; a mixture of fatty acids, viz. chlorellin, was found to be responsible for that inhibitory activity against both Gram+ and Gram- bacteria. Research aimed at identifying antibacterial active principles produced by microalgae has meanwhile boomed [11]. This realisation arose e.g. from the risk associated with several multidrug-resistant Staphylococcus aureus (MRSA) strains, which have been causing an increased concern in healthcare institutions worldwide – since they are not susceptible to most conventional antibiotics. Hence, discovery of novel antibacterial compounds following distinct biochemical mechanisms of action is urged. Although microalgae can synthesize a few useful products, search for novel antibiotics is still incipient; illustrative examples are tabulated in Table 1.
Antibiotics are typically less effective against Gram⁺ bacteria because of their complex, multilayered cell wall structure – which makes it more difficult for the active compound to penetrate them [31]; this justifies why the antibacterial activity of the supernatant (and methanolic extracts) is more potent against Gram + than Gram - bacteria [11,30]. The activity of cell lysates of *P. tricornutum* against both Gram⁺ and Gram⁻ bacteria (including MRSA) – even at micromole levels, was attributed to eicosapentaenoic acid, a compound synthesized de novo by diatoms [32]; this polyunsaturated fatty acid is found chiefly as a polar lipid species in structural cell components (e.g. membranes), and plays a role in microalgal defense – as it is toxic to grazers [33], as well as a precursor of aldehydes with deleterious effects upon such consumers as copepods [34]. Similarly, hexadecatrienoic acid isolated from *P. tricornutum* displays activity against (the Gram⁺ pathogen) *S. aureus*. High levels of palmitoleic acid and other bioactive fatty acids were also found in the fusiform morphotype of *P. tricornutum*, rather than in the oval morphs of this microalga; that fatty acid is active against various non-marine, Gram⁺ human pathogens at micromolar concentrations – and its lethal effects start immediately upon exposure [22]. Pressurized (liquid) ethanol extracts from *Haematococcus pluvialis* in its red stage possess antimicrobial activity against a Gram⁻ bacterium, *E. coli*, and a Gram⁺ bacterium, *S. aureus*; this was once again associated with the presence of short-chain fatty acids, namely butanoic and methyl lactic acids [24]. The exact mechanism of action of fatty acids remains unknown: they may act upon multiple cellular targets, even though cell membranes are the most probable ones – as membrane damage will likely lead to cell leakage and reduction of nutrient uptake, besides inhibiting cellular respiration; conversely, Desbois [21] claimed a peroxidative process.

<table>
<thead>
<tr>
<th>Microalga</th>
<th>Active compound</th>
<th>Target microorganism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Phaeodactylum tricornutum</em></td>
<td>Eicosapentaenoic acid</td>
<td>MRSA, <em>Listonella anguillarum</em>, <em>Lactococcus garvieae</em>, <em>Vibrio spp.</em></td>
<td>[21,22]</td>
</tr>
<tr>
<td></td>
<td>Short chain fatty acids</td>
<td></td>
<td>[23]</td>
</tr>
<tr>
<td><em>Haematococcus pluvialis</em></td>
<td>Short-chain fatty acids (butanoic acid and methyl lactate)</td>
<td><em>Escherichia coli</em>, <em>Staphylococcus aureus</em></td>
<td>[24]</td>
</tr>
<tr>
<td><em>Skeletonema costatum</em></td>
<td>Unsaturated, saturated long chain fatty acids</td>
<td><em>Vibrio spp.</em></td>
<td>[25]</td>
</tr>
<tr>
<td><em>Euglena viridis</em></td>
<td>Organic extracts</td>
<td><em>Pseudomonas</em>, <em>Aeromonas</em>, <em>Edwardsiella</em>, <em>Vibrio</em>, <em>E. coli</em></td>
<td>[26]</td>
</tr>
<tr>
<td><em>S. costatum</em></td>
<td>Extra-metabolites</td>
<td><em>Listeria monocytogenes</em></td>
<td>[27]</td>
</tr>
<tr>
<td><em>Staurastrum gracile</em></td>
<td>Methanolic extracts</td>
<td></td>
<td>[28]</td>
</tr>
<tr>
<td><em>Pleurastrum terrestre</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Dictyosphaerium pulchellum</em></td>
<td>Methanolic extracts</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Klebsormidium crenulatum</em></td>
<td>Aqueous extract</td>
<td></td>
<td>[28]</td>
</tr>
<tr>
<td><em>Chlorococccum sp.</em></td>
<td>α-Linolenic acid</td>
<td></td>
<td>[29]</td>
</tr>
<tr>
<td><em>Chlorococccum HS-101</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Chlorokybus atmophyticus</em></td>
<td>Acetone extract</td>
<td></td>
<td>[28]</td>
</tr>
<tr>
<td><em>Chlamydomonas reinhardtii</em></td>
<td>Methanolic and hexanolic extracts</td>
<td><em>S. aureus</em>, <em>Staphylococcus epidermidis</em>, <em>Bacillus subtilis</em>, <em>E. coli</em>, <em>Salmonella typhi</em></td>
<td>[30]</td>
</tr>
</tbody>
</table>

Antibiotics are typically less effective against Gram⁺ bacteria because of their complex, multilayered cell wall structure – which makes it more difficult for the active compound to penetrate them [31]; this justifies why the antibacterial activity of the supernatant (and methanolic extracts) is more potent against Gram⁺ than Gram⁻ bacteria [11,30].
Furthermore, compounds synthesized by *Scenedesmus costatum*, and partially purified from its organic extract, exhibited activity against aquaculture bacteria because of their fatty acids longer than 10 carbon atoms in chain length – which apparently induce lysis of bacterial protoplasts. The ability of fatty acids at large to interfere with bacterial growth and survival has been known for quite some time, but recent structure-function relationship studies suggest that said ability depends on both their chain length and degree of unsaturation. Such compounds as cholesterol can antagonize antimicrobial features [12], so both composition and concentration of free lipids should be taken into account [35].

Among microalgal-derived oxylipins, the antibacterial activities of polyunsaturated aldehydes deserve a special mention. Such compounds are synthesized by diatoms, e.g. *S. costatum* and *Thalassiosira rotula*. One illustrative example is decadienal – probably derived from (the polyunsaturated) arachidonic acid (C20:4 n-3), which exhibits a strong activity against such important human pathogens as MRSA and *Haemophilus influenza* – with MIC values of 7.8 and 1.9 μg/mL, respectively, and well as against *E. coli* and *Pseudomonas aeruginosa*, and *S. aureus* and *Staphylococcus epidermidis* (Gram’ and Gram’ bacteria, respectively). Furthermore, it impairs growth of diverse marine bacteria, such as (the Gram’) *Aeromonas hydrophila*, *L. anguillarum*, *Alteromonas haloplanktii*, *Photobacterium phosphoreum* and *Psychrobacter immobile*, and the (Gram’) *Planococcus citreus* and *Micrococcus luteus* [22].

### 3. Antiviral action

A number of infectious diseases caused by viruses have emerged (and re-emerged) in recent years. Although several antiviral drugs have been specifically developed, drug-resistant mutations are constantly occurring – so new antiviral active principles are necessary, especially those from sources that do not constitute (or are exposed to) viral pools. This is why microalgae have received a strong attention as potential suppliers of antiviral agents [36]; a few selected examples are listed in Table 2.

<table>
<thead>
<tr>
<th>Microalga</th>
<th>Active compound</th>
<th>Mechanism of action</th>
<th>Target virus</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Navicula directa</em></td>
<td>Polysaccharide</td>
<td>Inhibition of hyaluronidase</td>
<td>HSV1 &amp; 2, Influenza A virus</td>
<td>[37]</td>
</tr>
<tr>
<td><em>Gyrodinium impudicum</em></td>
<td>p-KG03 exopolysaccharide</td>
<td>Inhibition (or slowing down) of cytopathic effect</td>
<td>Encephalomyocarditis virus</td>
<td>[38]</td>
</tr>
<tr>
<td><em>Dunaliella primolecta</em></td>
<td>Phoehorhde α-, β-like compounds</td>
<td>Inhibition of cytopathic effect</td>
<td>HSV1</td>
<td>[39]</td>
</tr>
<tr>
<td><em>Chlorella autotrophica</em></td>
<td>Sulfated polysaccharides</td>
<td>Replication inhibition <em>C. autotrophica</em>: 47.4-67.4 % *Ellipsoidon sp.: up to 44 %</td>
<td>VHSV, ASFV</td>
<td>[40]</td>
</tr>
<tr>
<td><em>Ellipsoidon sp.</em></td>
<td>Allophycocyanin</td>
<td>Inhibition of cytopathic effect, delay in synthesis of viral RNA</td>
<td>Enterovirus 71</td>
<td>[41]</td>
</tr>
<tr>
<td>Cryptomonads</td>
<td>Extracellular sulfurated polysaccharides</td>
<td>Inhibition of cytopathic effect</td>
<td>Influenza virus A &amp; B, RSV A &amp; B, HSV-1</td>
<td>[42]</td>
</tr>
</tbody>
</table>

Viral growth is generally divided into three stages, and antiviral action may take place at a single or more stages: Stage I, which consists on adsorption and invasion of cells; Stage II, or eclipse phase, during which the cell is forced to synthesize multiple copies of said virus; and Stage III, or maturity and release of virus particles. For instance, the anti-HSV activity of the antiviral compound acyclovir® is expressed at stage II, but the anti-HSV factor from *Dunaliella* sp. inactivates the viral function at stage I [43,44]. Sulphated exopolysaccharides from marine microalgae have been claimed to interfere with Stage I of some enveloped viruses [45]; they offer competitive advantages because of their broad antiviral spectrum against e.g. HSV and HIV-1 [46]. Apparently, their inhibitory effect arises from interaction with the positive charges on the virus or on the cell surface – which prevents penetration of the former into the host cells [47,48]; they may also selectively inhibit reverse transcriptase in the case of HIV, thus hampering production of new viral particles after infection [49] – yet the exact step during viral replication when they act remains to be elucidated. Antiviral highly sulphated polysaccharides from several species of red microalgae consist mainly of xylose, glucose and galactose [49,50]; they are unusually stable when exposed to extreme pH and temperature [51].

Another important antiviral action associated with sulphated polysaccharides is against two enveloped rhabdoviruses bearing significant economic importance: the viral hemorrhagic septicemia virus (VHSV) of salmonid fish and the...
African swine fever virus (ASFV) – see Table 2. Extracts from marine microalgae can find a prophylactic usefulness in hatcheries against VHSV, and perhaps also against other fish-contaminating enveloped viruses in addition to mammalian viral diseases [40]. Consequently, application of such compounds appears to be a particularly attractive option in anti-viral therapy, because their pleiotrophic mode of action is less likely to lead to development of resistant mutants than other compounds that exhibit only one target throughout the viral life cycle. NMR and MS analyses of the antiviral compounds synthesized by D. primolecta [39] revealed structures not yet found in nature; in particular, the pheophorbide-like substances found had the proton at position 21 replaced by a hydroxyl group, which might be the key for the observed unique antiviral activity.

A homopolysaccharide of galactose with uronic acid (3.0 %, w/w) and sulfate groups (10.3 %, w/w) from Gyrodinium impudicum strain KG03 [38] exhibited an impressive activity in vitro (EC₅₀=26.9 µg/mL) against swine encephalomyocarditis virus, which is widespread at the subclinical level; its acute form leads to sudden death in piglets, as well as reproductive failure in adult animals [52].

Despite their successful antiviral performance, the metabolic pathways leading to sulfated polysaccharides are still poorly known. Their secretion by unicellular red algae was originally characterized via radiolabeling – which showed biosynthesis of the carbon chain, and sulfation of the resulting polysaccharide to occur in the Golgi apparatus [53]; these findings were confirmed in Porphyridium sp. [54] and other red microalgae [55]. More recently, Keidan et al. [56] used ¹⁴C pulse-chase experiments and ultrastructural microscopy to conclude that brefeldin A – a membrane-traffic inhibitor of the Golgi apparatus, decreases the contents of the bound and the soluble forms of polysaccharides, while inhibiting cell-wall binding of polysaccharides to a greater extent than its soluble counterpart (in both actively growing and resting cells).

Discovery of small molecules that can specifically disrupt a particular protein-protein interface remains a challenge – but is of a particular interest in virology, since the antiviral drugs currently available target only viral proteins.

4. Antifungal action

The study of resistance to antifungal agents has lagged for behind that of antibacterial resistance – likely because fungi were not recognized as important pathogens until several years ago [57,58]. For instance, the annual death rate caused by candidiasis remained steady between 1950 and 1970, but increased significantly ever since in association with several changes in medical practice – including more widespread use of therapies that depress the immune system, frequent and often indiscriminate use of broad-spectrum antibacterial agents, common use of indwelling intravenous devices, and advent of chronic immunosuppressive viral infections (e.g. AIDS). The associated increase in fungal infections prompted search for newer and safer agents to combat fungal infections [19] – and a few noteworthy results encompassing microalgae are listed in Table 3.
### Table 3: Antifungal features of selected compounds from microalgae.

<table>
<thead>
<tr>
<th>Microalga source</th>
<th>Active compound</th>
<th>Target microorganism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydomonas reinhardtii</em></td>
<td>Methanolic extracts</td>
<td><em>Candida kefyr,</em> <em>Aspergillus niger,</em> <em>Aspergillus fumigatus</em></td>
<td>[30]</td>
</tr>
<tr>
<td><em>Chlorella vulgaris</em></td>
<td>Methanolic extracts</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Oocystis sp.</em></td>
<td>Karatungiols</td>
<td><em>A. niger,</em> <em>Trichomonas foetus</em></td>
<td>[59]</td>
</tr>
<tr>
<td><em>Scenedesmus obliquus</em></td>
<td>Methanolic extracts</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Amphidinium sp.</em></td>
<td>Karatungiols</td>
<td><em>A. niger,</em> <em>Trichomonas foetus</em></td>
<td>[59]</td>
</tr>
<tr>
<td><em>Goniodoma pseudogoniaulax</em></td>
<td>Goniodomin A</td>
<td></td>
<td>[28,60]</td>
</tr>
<tr>
<td><em>Gambierdiscus toxicus</em></td>
<td>Polyether compounds</td>
<td></td>
<td>[28,61]</td>
</tr>
<tr>
<td><em>Prorocentrum lima</em></td>
<td>Polyether compounds</td>
<td></td>
<td>[28]</td>
</tr>
<tr>
<td><em>Dinophysis fortii</em></td>
<td>Polyether compounds</td>
<td></td>
<td>[28]</td>
</tr>
<tr>
<td><em>Haematococcus pluvialis</em></td>
<td>Butanoic acid and methyl lactate</td>
<td><em>Candida albicans</em></td>
<td>[24]</td>
</tr>
<tr>
<td><em>Chlorella pyrenoidosa,</em></td>
<td>Methanolic extracts</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Scenedesmus quadricauda</em></td>
<td>Methanolic extracts</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Katircioglu et al. [63] studied 10 microalgal strains, previously isolated from distinct freshwater reservoirs in Turkey, for their antifungal performance upon three yeasts (*S. cerevisiae, C. albicans* and *Candida tropicalis*); *Oscillatoria* sp. and *Chlorococcus* sp. were found to perform best.

Pressurized liquid ethanol extracts of *H. pluvialis* were tested by Santoyo et al. [24] against *C. albicans* and *A. niger*; all extracts were active against the former, but not against *A. niger*. The main compounds responsible for such antifungal activity were claimed to be butanoic acid and methyl lactate, both of which had previously been described to possess antimicrobial activity [64,65].

Abedin and Taha [62], on the other hand, studied the antifungal activity of two green microalgae (*C. pyrenoidosa* and *S. quadricauda*) against 8 fungi (*A. niger, A. flavus, P. herquei, F. moniliforme, Helminthosporium sp., A. brassicaceae, S. cerevisiae* and *C. albicans*) – with favourable results for nearly all extracts; these data are consistent with those by Volk and Ferkert [66], who found microalgae to exhibit a high biological activity against *P. aeruginosa, C. tropicalis* and *S. cerevisiae*.

The supernatant (methanolic and hexane) extracts of several microalgae against four strains of fungi (*C. kefyr, C. albicans, A. niger* and *A. fumigatus*) were tested by Ghasemi et al. [30]; nine *Chlorella vulgaris* spp., *Chlamydomonas reinhardtii*, *Oocystis* sp. and *S. obliquus* proved active against *C. kefyr, A. niger* and *A. fumigatus*, but only marginally active against *C. albicans*; their results indicated that an antifungal activity was predominantly associated with *Chlorella* spp. Furthermore, several solvents were tested, but only methanolic extracts were found to possess a feasible antifungal activity.

### 5. Antimicroalgal action

Inhibitory phenomena between microalgal cells have been reported in the past; Bagchi et al. [67] originally proposed that natural algaeicides could effectively be applied in control of toxic algal blooms. However, Pratt [68] was the first to report that growth of *C. vulgaris* was depressed by a compound (chlorellin) that was produced and excreted into the medium – and several other extracellular metabolites able to inhibit their own growth and the growth of other species have meanwhile been reported [69]; some examples are listed in Table 4.
Table 4 Antimicroalgal features of selected compounds from microalgae.

<table>
<thead>
<tr>
<th>Microalga source</th>
<th>Active compound</th>
<th>Target microorganism</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Peridinium bipes</em></td>
<td>Water-soluble extract</td>
<td><em>Microcystis aeruginosa</em></td>
<td>[28,70]</td>
</tr>
<tr>
<td><em>Isochrysis galbana</em></td>
<td>C_{22}H_{38}O_{7} from cell-free filtrates</td>
<td><em>Dunaliella salina,</em> <em>Platymonas elliptica,</em> <em>C. vulgaris,</em> <em>Chaetoceros muelleri,</em> <em>Chlorella gracilis,</em> <em>Nitzschia closterium,</em> <em>P. tricornutum</em></td>
<td>[71]</td>
</tr>
</tbody>
</table>

Autoinhibition was also observed in *H. pluvialis* and *S. costatum* [72,73]. The antimicroalgal ability appears to derive either from interference with chlorophyll and protein syntheses [71] – as in the case of *I. galbana*, or because of changes in membrane permeability coupled with dissociation of phycobilin assemblages in the thylakoid membranes – thus leading to leakage across the cell wall [70].

Acknowledgements A PhD fellowship (ref. SFRH/BD/62121/2009), supervised by author F.X.M., was granted to author H.M.A., under the auspices of ESF (III Quadro Comunitário de Apoio) and the Portuguese State. A postdoctoral fellowship (ref. SFRH/BPD/72777/2010), supervised by author F.X.M., was granted to author A.C.G., also under the auspices of ESF (III Quadro Comunitário de Apoio) and the Portuguese State.

References


