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First identification of marine diatoms with anti-tuberculosis activity

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Marine microalgae are considered a potentially new and valuable source of biologically active compounds for applications in several biotechnology sectors. They can be easily cultured, have short generation times and enable an environmentally-friendly approach to drug discovery by overcoming problems associated with the over-utilization of marine resources and the use of destructive collection practices. Considering the increasing rate of antibiotic-resistance bacteria and infections by fungi, 46 microalgae have been screened in this study for possible antibacterial and antifungal activities. Two different extraction methods have been used in order to increase the probability of finding positive hits. In particular, we screened microalgae in both control and nutrient stress conditions. We also tested different strains for 7 species in order to study potentially different bioactivities due to strain diversity. Results showed that extracts of two diatoms, *Skeletonema tropicum* and *Chaetoceros pseudocurvisetus*, had anti-tuberculosis activity and were active only when cultured in the control and phosphate-starvation conditions, while the nitrogen starvation condition showed no activity. In addition, we tested both the organic and water extracts and found that only the organic extracts for both diatoms were active. The organic extracts of these two diatom species were not toxic on normal human cell lines.

Microalgae are eukaryotic plants that contribute up to 25% of global productivity and 50% of all aquatic productivity[1,2]. They are the basis of aquatic food webs and have colonized almost all biotopes, from temperate to extremes environments (e.g. cold/hot environments, hydrothermal vents). The number and diversity of microalgal species offer a great reservoir of compounds with possible applications in various biotechnology sectors (i.e. food, energy, health, environment and biomaterials)[3–8].

Microalgae can be easily cultivated in photo-bioreactors (e.g. in 35,000 L bioreactors) to obtain huge biomass, have short generation times (doubling time = 5–8 h for some species) and represent a renewable and still poorly explored resource for drug discovery[4,9,10]. Their advantage is also their metabolic plasticity, dependent on their non-stressed or stressed status under different light, temperature and nutrient stress[11,12]. However, although a range of bioactivities have been observed from microalgal extracts, the active principles are often unknown[11–16]. Not much is known on the potential applications of microalgae as sources of anti-infective agents, but it has been suggested that they have evolved protection mechanisms against infections such as surface-fouling bacteria that are indigenous to ocean waters or because of competition for the same resources.

Extracts from different marine microalgae have shown the capability to inhibit bacterial growth with variable levels of activity. Lipophilic extracts of the diatom *Skeletonema costatum* showed significant antibacterial effects against *Listonella anguillarum*[17], while extracts of the diatom *Phaeodactylum tricornutum* were active against both *L. anguillarum* (Gram−) and *Staphylococcus aureus* (Gram+)[18]. Kokou *et al.*[19] screened extracts of the green algae *Tetraselmis chui* and *Nannochloropsis* sp. and the haptophyte *Isochrysis* sp. against six *Vibrio* bacterial strains and found that all the microalgae inhibited *Vibrio* growth. They also tested if light stress could change the antibacterial activity, but the activity was not influenced by the presence or absence of light. Sushanth and Rajashekhar[20] tested the activity of extracts of the diatoms *Chaetoceros calcitrans* and *Skeletonema costatum*, and green alga *Nannochloropsis oceanica* against *S. aureus*, *Streptococcus pyogenes*, *Bacillus subtilis*, *E. coli*, *Proteus vulgaris*, *Klebsiella pneumoniae* and *Salmonella typhi*. All microalgal extracts were only active against *S. aureus*,

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