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Pathway for cyanotoxin valorization - Microscystin as case study

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The worldwide occurrence of hepatotoxic cyanobacterium *Microcystis aeruginosa* and the accumulation of its intracellular toxin microcystin, the most widespread cyanotoxin, have been commonly associated with water impairment causing several human deaths and various animal intoxication incidents. These findings led the World Health Organization and several national governments to establish guidelines and recommendation values for this toxin in water, which gave rise to an increasing demand for microcystin's analytical standards. These standards might be used either as laboratory standards for human and environmental risk assessment or as tools for molecular and cell biology studies. Also, recent research works highlighted the huge potential of cyanotoxins to be applied as anticancer/antitumor drugs or antimicrobial agents. However, the existing commercial microcystin solutions present prohibitive prices around 28000€/mg due to constraints found in up- and downstream processes.
Envisaging the need to decrease the production cost of such high added-value products the aim of our work was to i) evaluate the effect of environmental factors on *Microcystis aeruginosa* growth and toxin accumulation; ii) develop cultivation strategies to optimize cyanobacteria growth and maximize toxin productivity; iii) optimize downstream processing steps in order to obtain high yields of cyanotoxin.
Utilizing an innovative approach of combining and assessing the synergistic interactions of four different abiotic factors on growth kinetics and toxin production, it was possible to reach variations of approximately 2000-fold. Cultivation systems have shown to play a significant role on biomass productivity since the use of flat-panel photobioreactors resulted in similar maximum biomass concentrations in half of the time of the growth, when compared to bubble columns. The exposure of toxin-producer *M. aeruginosa* to extracts and filtrates of cultures of other microorganisms determined interesting effects on biomass growth. As example, extracts of non-toxic *M. aeruginosa* enhanced growth in 53% while extracts of *S. obliquus* had a negative impact decreasing growth in 19%. In biomass harvesting, despite all the four methods analysed presenting efficiencies above 90%, the addition of aluminium chloride has shown to be the fastest. Regarding cell disruption, amongst the methodologies studied, implementation of freeze-thaw cycles followed by sonication was found to be the best approach to promote intracellular organic matter release, resulting in approximately 100% of disruption efficiency. These results are a step forward in the path of implementing microcystin's industrial scale production in order to allow the development of innovative biotechnological products and approaches in distinct fields such as health and water quality.