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P177: Cytotoxic activity of marine cyanobacteria against cancer cell lines

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Marine cyanobacteria possess an extensive capacity to produce compounds that were found to induce biological activities against cell lines and organisms [1]. Many of the marine cyanobacteria compounds already described were found to induce toxicity against cancer cells [2]. Nearly all of these compounds derive from strains of the genera Lyngbya and Leptolyngbya. Nevertheless, there are other genera that have been largely overlooked, mainly because, under natural conditions they occur at low densities. Here we present the results of a screening work that aimed to evaluate the anti-cancer potential of five cyanobacterial strains from the genera *Cyanobium, Leptolyngbya, Romeria* and *Synechocystis*, isolated from the Portuguese coast. Crude extracts obtained by dichloromethane and methanol extractions and three fractions obtained using Si column chromatography with a gradient from 100% hexane, to 100% ethyl acetate to 100% methanol were tested for cytotoxicity against the human cancer cell lines colon adenocarcinoma (HT29 and RKO), hepatocellular carcinoma (HepG2), neuroblastoma (SH-SY5Y) and osteosarcoma (MG63). (Growth inhibition/proliferation was evaluated by the MTT assay at 24, 48 and 72 hours. The results show controversial effects of the cyanobacteria extracts, since both inhibitory and stimulatory effects on cell growth within the same strain were observed.

[1] Nagarajan, M., Maruthanayagam, V., and Sundararaman, M. (2012). A review of pharmacological and toxicological potentials of marine cyanobacterial metabolites. J Appl Toxicol 32, 153-185; [2] Sithranga Boopathy, N., and Kathiresan, K. (2010). Anticancer drugs from marine flora: an overview. J Oncol 2010, 214186.
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P178: The response of different human and murine cell lines to crude extracts and pure chemical constituents of cyanobacteria

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The toxicity of cyanobacteria and the occurrence of the cyanobacterial water blooms is permanent problem in water management, agriculture and in recreation areas in most of the countries. The ability of cyanobacteria to produce broad spectrum of secondary metabolites, including substances toxic to human, is well known for last three decades. Beside traditionally monitored hepatotoxins and neurotoxins, there exists a large group of cyanobacterial compounds that target basic mechanisms required for a single cell survival. Such compounds are usually grouped into an artificial class of cytotoxins. Up till now around 80 cyanobacterial cytotoxins have been known. Most of them are general cytotoxins which can affect human health, moreover, majority of cyanobacterial compounds and their effect on human remains unknown. Thus methodology for determination of toxicity (cytotoxicity) of cyanobacterial metabolites and their mixtures is needed. In order to test cytotoxicity of cyanobacterial compounds, the selected cyanobacterial extracts have been tested for the cytotoxicity to four cell lines of human (HeLa and HepG2) and murine (YAC-1, Sp2) origin. These data were compared with the standard cytotoxicity assay performed on murine fibroblasts (BALB/c). Finally a subset of the extracts was tested for its toxicity to the cultured hepatocytes as one of the *in vitro* model in human toxicological studies. Roughly one third of cyanobacterial extracts has been found to cause cytotoxicity to the cell lines *in vitro*. Although higher sensitivity to crude cyanobacterial extracts has been found in some cell lines (mainly for murine lymphoid cell lines YAC-1 and Sp/2). The strong correlation in cytotoxic effects (over 70%, p=0.0001) has been found among the effects caused by cyanobacterial extracts to the cell lines of HeLa, HepG2 and the standard assay using BALB/c. This result suggests that most of cyanobacterial metabolites can be generally cytotoxic with low organ targeted specificity. In present contribution we discuss possible development of standard method for cytotoxicity testing and estimation of possible threat of cyanobacterial metabolites to human. The isolation of new cytotoxins (puwainaphycin F and muscotoxin) is presented and their cytotoxicity in pure state and in crude extract is compared.