

Cytotoxic Evaluation of Secondary Metabolites Produced by an Endophytic Fungus of *Croton blanchetianus*

Naum, B.V.C.¹, Silva, M.G.L.¹, Silva, J.L.², Braga, R.M.³, Allard, P-M.⁴, Onuki, J.¹, Maria, D.A.¹, Melo, I.S.², Berlinck, R.G.S.⁴, Araújo, W. L.³, De Souza, A.O.¹

¹Laboratório de Biofísica e Bioquímica, Instituto Butantan, São Paulo, Brazil; ²EMBRAPA Meio Ambiente, Laboratório de Microbiologia Ambiental, São Paulo, Brazil; ³Instituto de Ciências Biomédicas, Universidade de São Paulo, São Paulo, Brazil. ⁴Instituto de Química de São Carlos, Universidade de São Paulo, São Paulo, Brazil.

Introduction: The semi-arid region of Brazil, named Caatinga, is an ecosystem with great biodiversity. Endophytic fungi from plant species endemic to this region have been poorly investigated for the production of new molecules for pharmaceutical applications. **Objectives:** The aim of this study was to evaluate the cytotoxic effect of two secondary metabolites produced by an endophytic fungus isolated from the plant *Croton blanchetianus*. **Material and Methods:** The fungus was cultivated in potato dextrose broth for 15 days. The culture medium was extracted with organic solvents. The medium extract was purified by reversed phase high performance liquid chromatography (RP-HPLC). For taxonomical identification of the fungus, beta-tubulin gene and the internal transcribed spacer of rDNA were analyzed. Two major compounds isolated from the culture medium were evaluated by MTT assay on endothelial (Huvec) and leukemic human (K562) cells. Cells were incubated in a microplate at 2×10^5 cells/mL, and treated with compounds 1 and 2 in the range of 0.4 to 214.22 mM, for 24 h. Supernatants of the cell cultures used for the colorimetric MTT assay were collected and maintained under refrigeration at -20°C for determination of lipid peroxidation products (TBARs). **Results and Discussion:** Taxonomic identification indicated that the fungus had compatibility with *Exserohilum rostratum*. The medium extract was purified resulting in compounds 1 and 2, which are under physical-chemical characterization. In leukemic cells, no significant cytotoxic effect was observed for both compounds, which increased the proliferation on endothelial cells, by 2x and 5x, respectively. Both compounds have not induced lipidic peroxidation. Data were obtained in comparison with the untreated cells (control). **Conclusion:** The data indicated no cytotoxicity for the compounds on tumoral or normal cells, but both of them induced cell proliferation of normal endothelial cells disclosing new perspectives for further studies on tissue remodeling.

Key words: Cytotoxicity, Secondary Metabolites, Fungus
Supported by PIBIC/CNPq, EMBRAPA and FAPESP