Antileishmanial andantitrypanosomal activity of different Brazilian plant extracts

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Currently, over one billion people, about a sixth of the world population, are infected with one or more types of neglected tropical diseases (NTDs). The major NTDs are leishmaniasis, sleeping sickness, Chagas disease and malaria, which together account for about 50% of annual deaths caused by NTDs. The chemotherapy used against these diseases has several drawbacksand the appearing of resistances makes the development of new drugs of fundamental importance. So there is an urgent need to develop new, safe and cost-effective drugs against tropical disease. The aim of this study was investigate the inhibitory activity of three plant extracts (namely DA, DB and DC) on cellular viability of *Leishmania amanonensis*, *L. infantum* and *Trypanosomacruzi* Y. In order to determinate the IC_{50} and minimum inhibitory concentration (MIC), different concentrations of the extracts were added in the culture media containing 10^6 cells/ml. To evaluate the inhibitory activity DC extract on *Leishmania* and *T. cruzi* peptidases, intracellular peptidases were treated with the extract DC and analyzed by zymography. The mechanism of cell death induced by DC was preliminarily evaluated by flow cytometry. DA extract was not able to inhibit cell growth of *L. amazonensis* and *T. cruzi* and reduced cell viability of *L. infantum*to less than 40%. DB extract was active against *Leishmania* sp*.,* itinhibited 100% of the growth in concentrations between 250-500 µg/ml, showing IC_{50} values of 113.4 and 95.1 µg/ml for *L. amazonensis* and *L. infantum*, respectively. However, this extract did not affect the growth of *T. cruzi* . The extract DC inhibited completely the paratites with a IC_{50} values of 3.9µg/ml, 73.8 µg/ml and 115.2 µg/ml for *L. infantum*, *L. amazoenesis*, and *T. cruzi*, respectively. Moreover, the zymographic analyzes showed that DC extract was able to completely inhibit the cysteine peptidases of theses parasites. The results of flow cytometry using annexin and propidium iodide suggested the loss of cell membrane integrity. The *in vitro* evaluation of cytotoxicity in RAW 264.7 cell line showed CC_{50} value of 24.21 µg/ml. The DC extract is an interesting source of antiparasitic agent and the purification of the fraction with anti-parasitic activity is being conducted to increase the selectivity and reduce the cytotoxicity of the drug. Additionally, the mechanism of action of these isolated compounds will also be investigated.

Keywords: Natural products, antileishmanial activity, antitrypanosomal activity and peptidase inhibitor

Support: MCTI/CNPq, FAPERJ, CAPES, CEPEG-UFRJ