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Enzyme inhibition in trypanosomatids: a therapeutic target for crude extracts and fractions of natural products

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Introduction: Infections caused by trypanosomatids of *Leishmania* genus represent one of the largest global public health problems, currently with high endemicity especially in developing countries. The drugs of choice for the treatment of leishmaniasis are the pentavalent antimonials, which cause renal and cardiac toxicity, and induce resistance in the parasite. **Objective:** As part of our research aiming at the development of new drugs with leishmanicidal activity, were evaluated as to the inhibitory activity of proteases from amastigotes of *Leishmania (Leishmania) amanzonensis*, crude extracts and fractions (hexanic, ethyl-acetate, butanolic and aqueous), *in vitro*, obtained from *Arrabidaea brachypoda*, a native plant typical of the Cerrado biome. **Methods:** The amastigotes of *L. (L.) amazonensis* were isolated from infected mice, washed with PBS and lysates by ultrasound. After centrifugation, the supernatant (proteases) was collected and used in the ratings. For evaluation of the inhibitory activity of proteases, used the substrate fluorogenic Z-FR-AMC and the extract and fractions dissolved in DMSO. The solutions were incubated for 30 minutes after the addition of substances to be tested. Then, the substrate was added, followed by espectrofluorimetric analysis every 0.5 seconds, with a wavelength of excitation from 380 nm and emission of 460 nm. Each experiment was conducted in triplicate on three separate occasions, and the percentage inhibition calculated in relation to the control only with DMSO. **Results:** The crude extract and fractions, hexanic, ethyl-acetate, butanolic and aqueous presented IC_{50} of 136.3 ± 36.2, 132.1 ± 6.1, 65.3 ± 15.5, 116.7 ± 8.5 e >200 ug/mL, respectively. **Conclusion:** These results suggest that the ethyl-acetate fraction is the most efficient and a potent inhibitor of proteases from *L. (L.) amazonensis*, providing new perspectives for the development of more effective and less toxic drugs to assess their tripanocidal activity from the Brazilian Cerrado, targeting the proteases of the parasite.

Keywords: Trypanosomatids, *Leishmania*, *Arrabidaea brachypoda*, enzyme inhibition.

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