

## Chagas080- *In vitro* evaluation of anti-*Trypanosoma cruzi* activity of physalins purified from *Physalis angulata*

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*Physalis angulata* L., Solanaceae, is an annual herb commonly used in popular medicine in many tropical and subtropical countries, and its extracts contain a variety of substances, including a class of seco-steroids (physalins). We have previously demonstrated the immunomodulatory, antimalarial and antileishmanial activity of physalins purified from *P. angulata*. Here we investigated the trypanocidal activity of physalins B, D, F and G. The cytotoxicity of compounds was determined by incorporation of [<sup>3</sup>H]-thymidine, in cultures of splenocytes obtained from normal mice. The trypanocidal effect was first evaluated by light microscopy through the determination of IC<sub>50</sub> values for epimastigote and trypomastigote forms of *T. cruzi* (Y strain). We also evaluated the effects of the compounds in intracellular forms in cultures of macrophages infected with *T. cruzi* trypomastigotes. Transmission electron microscopy was performed to analyze the effects of physalin B in the ultrastructure of trypomastigotes. Our data demonstrated the high trypanocidal activity of the physalins against bloodstream trypomastigote and epimastigote forms. Physalins B and F had an IC<sub>50</sub> for trypomastigotes of 0.68 ± 0.007 µM and 0.84 ± 0.04 µM, respectively, whereas the positive control benznidazole presented an IC<sub>50</sub> of 11.3 ± 1.88 µM. Physalin B is approximately fifty times more cytotoxic for trypomastigotes than to mammalian cells. In the model of macrophage infection, all four physalins were able to reduce the percentage of infected cells and the intracellular parasite number at concentrations non-cytotoxic to macrophages. Transmission electron microscopy revealed that the treatment of trypomastigotes with physalin B at 0.68 µM induced kinetoplast disorganization, alterations in the Golgi apparatus cisternae and endoplasmatic reticulum, a light extraction of the cytoplasm of the parasite and the appearance of myelin figure that may indicate autophagy. Our results showed that the physalins tested were very active *in vitro* against both extracellular and intracellular forms of *Trypanosoma cruzi* and suggest their potential use in the development of new antichagasic chemotherapy. **E-mail:** calcio0303@hotmail.com