

Leishmanicidal effects of polyalthic acid derivatives on promastigote and amastigote forms of *Leishmania (Leishmania) infantum chagasi*

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Leishmaniasis is a chronic disease, with visceral and cutaneous manifestation caused by protozoa *Leishmania sp.* Drugs used frequently to treat are antimonial pentavalent and Amphotericin B. However, several side effects are observed using these drugs. Therefore, it is imperative the search of new compounds that could have leishmanicidal activity and minor side effects. The copaiba oil is one of the most used natural medicines in the Amazon for the treatment of several diseases including leishmaniasis, and effects of copaiba oil on *Leishmania (L.) amazonensis* have been confirmed in vitro. The polyalthic acid is a naturally occurring found in copaiba oil, reported in literature as an antitumor, gastroprotective and antimutagenic. In the search for a natural leishmanicidal agent, the polyalthic acid is an interesting compound to be tested. In this study, polyalthic acid derivatives will be tested against promastigote and amastigote forms of *Leishmania (L.) infantum chagasi*. Promastigotes of *Leishmania (L.) infantum chagasi* was growth at 26°C in Schneider pH 7,2 supplemented with 10% fetal bovine serum (FBS). Screening of compounds (100 µM) was performed against to 2.0 x 10⁵ parasites, to 72 hours in 26° C. Compounds with high leishmanicidal activity was submitted to MIC test, ranging from 0,78 µM to 200 µM, and cell viability was measured by absorbance at 530 nm using MTT assay. Reactive species of oxygen (ROS) was quantified using 2,7,-dichlorodihydrofluorescein diacetate (H₂DCFDA) against 2.0 x 10⁶ parasites incubated in present of compounds to 1 hour in 24° C. H₂DCFDA (5 µM) was added and the emission intensities were recovered after 15 minutes of incubation using an excitation wavelength of 485 nm and emission wavelength of 520 nm. Toxicity of these compounds was verified in mammals cells lines Vero and RAW 264.7 in DMEM supplemented with 10% FBS and incubated at 37°C and atmosphere of 5% CO₂ for 48 hours. Polyalthic acid derivatives which showed a higher leishmanicidal activity and low toxicity in mammals cells lines will be tested in intracellular amastigote form, using mammal cell RAW 264.7, in DMEM supplemented with 10% FBS and incubated at 37°C and atmosphere of 5% CO₂ for 48 hours. At present moment, ten from sixteen polyalthic acid derivatives tested presented leishmanicidal activity against promastigotes forms, and seven compounds showed IC₅₀ below 50 µM. These polyalthic acid derivatives does not showed production of reactive species of oxygen (ROS) and exhibited low toxicity in Vero and RAW cells and are being tested in amastigote forms. In conclusion, some compounds showed leishmanicidal activity against *Leishmania (L.) infantum chagasi* in promastigote form. Further experiments are necessary to prove leshmanicidal activity of these polyalthic acid derivatives.