identifying promising compounds in the treatment of visceral leishmaniasis: antileishmanial activity and cytotoxicity of tetraoxane derivatives in the *in vitro* model

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leishmaniasis is a neglected tropical disease endemic in 98 countries, posing as a risk to 350 million people, with an incidence of 1.5 million new cases every year. although this disease was discovered more than 100 years ago, the currently available drugs for treatment of leishmaniasis are almost the same as the ones used 50 years ago. the efficacy of the treatment based on these drugs is limited due to their toxicity, the presence of resistant strains in several *leishmania* species, the length of treatment and its high cost. thus, the continuous search for a new, cheaper, effective and less toxic treatment for this disease is still necessary. tetraoxanes are compounds characterized by the presence of peroxidic bonds within its structure. the synthesis of these compounds has been widely studied because of its great antimalarial potential. in this study, we evaluated the potential of 4 asymmetrical 1,2,4,5-tetraoxane compounds to inhibit the intracellular growth of *Leishmania amazonensis* amastigotes parasitizing canine macrophages (dh82), in vitro. the elisa test was employed to measure the inhibitory activity of these compounds on intracellular parasites. the cytotoxicity of the active compounds was evaluated by metabolic activity using mtt assay. the tested compounds rc3, rc29, rc47 and rc73 were able to inhibit the intracellular amastigote proliferation with the respective ic50 values: 0.6, 19.7, 99.5 and 22.6 μμ. with the exception of compound rc47, all compounds presented better results than the positive control antimony salt iii (80 μμ) and low toxicity against canine macrophage (dh82), african green monkey kidney cells (bgm) and human hepatocytes-like cells (hepg2). moreover, the compound rc3 showed excellent antileishmanial activity at micromolar level and high selectivity index of 157. here, the present results denote the potential of 1,2,4,5-tetraoxane, in special the compound rc3, as promising candidate for the treatment against leishmaniasis.

keywords: antileishmanial, tetraoxane, *Leishmania amazonensis*