The Essential Role of Ergosterol to Amastigote and Promastigote of *Leishmania (Leishmania) amazonensis*


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Leishmaniasis is an infectious disease caused by *Leishmania* protozoa and it is an important problem of public health. The treatment includes the use of pentavalent antimonials, but the toxic effects and drug resistance are frequently observed. Thus, the development of new treatment strategies is a challenge for many researchers. This work evaluated the effect of ketoconazole, an inhibitor of ergosterol biosynthesis, on *Leishmania (Leishmania) amazonensis* by in vitro and in vivo studies. Promastigotes cultured on presence of ketoconazole by 120 hours presented inhibition of growth ranging 40% to 69% at concentrations of 10nM to 1mM. Analysis by optical microscopy showed that 5nM of ketoconazole caused alterations on promastigote morphology. For *in vivo* studies, Balb/C mouse infected on footpad with promastigotes were submitted of treatment with ketoconazole 1mg/day for 9 weeks. Treated group presented decrease of 43% in lesion size and parasitic load reductions in footpad and lymph node. Histological analyses performed on footpad lesions of non-treated group showed severe tissue damage and macrophages infiltration containing large vacuoles filled with amastigotes. On the other hand, treated group showed macrophages infiltration containing lower number of vacuoles and amastigotes when compared with non-treated group and normal intact fibers of tissue were visualized indicating lower tissue damage. Taken together these data suggest an essential role for ergosterol on *L. (L.) amazonensis* for both, promastigote and amastigote. Therefore, more studies should be conducted in order to evaluate the use of Ketoconazole in association with drugs used on conventional therapy for leishmaniasis treatment.

Keywords: Ergosterol, ketoconazole, *Leishmania (Leishmania) amazonensis*

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