EFFECT OF KETOCONAZOLE ON GROWTH, MORPHOLOGY AND INFECTIVITY OF *Leishmania (Viannia) braziliensis* PROMASTIGOTES

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Azole drugs are antifungal agents which cause inhibition of sterol biosynthesis. Previous work in our lab showed that sterol depletion on *Leishmania (Viannia) braziliensis* promastigotes membrane by methyl-ß-cyclodextrin causes a disruption of lipid rafts and a significant decrease of parasite infectivity (Yoneyama *et al*, 2006) confirming an important role of lipids and their organization on plasma membrane in parasite infectivity processes. In order to better characterize the role of ergosterol in parasite growth and development, different concentrations of ketoconazole were added in *L. (V.) braziliensis* cultures. Low ketoconazole concentration as 18nM inhibited about 75% of parasite growth and caused changes on morphology as truncated flagella and dilatation of flagellar membrane. It should be noted that these changes did not alter distribution of gp180 (a flagellar glycoprotein) on flagellar membrane. Other structural modifications observed included multiple nucleous and kinetoplasts, and deregulation in tubulin polymerization, suggesting that ketoconazole affects parasite cell cycle. A significant reduction (about 85%) of macrophage infectivity was observed when parasites were treated with 18nM of ketoconazole. Lower dose of ketoconazole (1.8nM) which does not affect parasite growth and cell cycle, inhibited in 41% the parasite infectivity, indicating that ketoconazole at 10^{-9}M may alter biochemical pathways resulting in decrease of *L. (V.) braziliensis* infectivity.
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