MODE OF ACTION OF THE ANTIFUNGIC ITRACONAZOLE AGAINST *TOXOPLASMA GONDII* TACHYZOITES IN CELL CULTURE

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The antifungal agent itraconazole (ITZ) is an effective drug against systemic fungal infections inhibiting cytochrome P-450 mediated ergosterol synthesis. Previous studies of our group demonstrated the high susceptibility of *Toxoplasma gondii* to azasterols and quinuclidines, known inhibitors of the ergosterol biosynthetic pathway. In this work we present data of the activity of this azole as potential agent for the treatment of toxoplasmosis. LLC-MK2 cells infected with tachyzoites were incubated with different concentrations of ITZ for 24h and 48h. The IC_{50} values obtained were 114 nM and 53.6 nM respectively, demonstrating a selective effect against *T. gondii in vitro*. In addition ITZ also demonstrated a cidal effect, as this drug permanently abolished the infection of the cells. Transmission electron microscopy analysis provided evidence of the mode of action of ITZ. Intracellular tachyzoites after treatment with ITZ showed drastic morphological changes, suggesting that the parasites lost the bulk of their subpellicular microtubules. The drug also affected parasite endodyogeny producing tachyzoites containing many daughter cells still gathered. This observation was confirmed by fluorescence microscopy after incubation with DAPI and by three-dimensional reconstruction of serial thin sections examined by transmission electron microscopy of treated parasites. These data suggest that ITZ possibly affect the daughter cells scission from the maternal mass during budding process.

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