AMEBICIDAL EFFECTS OF ADAMANTANE-AZOLE GOLD(I) COMPLEXES: A STUDY OF CELL DEATH PATHWAY IN *Acanthamoeba castellanii* AND TOXICITY PROFILE

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Acanthamoeba spp. are protozoa that belong to the group of free-living amoebae, responsible for *Acanthamoeba* keratitis (AK), an ocular infection commonly associated with contact lens users, and granulomatous amoebic encephalitis (GAE), a brain infection with a high mortality rate. The lack of selective and effective treatments highlights the need for new molecules with biological activity against *Acanthamoeba.* Studies have demonstrated that gold complexes are capable of inhibiting selenoenzymes such as thioredoxin reductase, which are involved in the redox balance of *Acanthamoeba*. Therefore, this study aims to evaluate the activity of adamantane-azole gold(I) complexes (C1-C4) against *Acanthamoeba castellanii* (ATCC 50492) T4 genotype. It investigates the cell death pathway through changes in the cell cycle, mitochondrial activity and phosphatidylserine (PS) exposure, cytotoxicity against rabbit corneal cells (SIRC ATCC CCL-60), irritation potential on chorioallantoic membrane (HET-CAM), and in vivo toxicity in *Tenebrio molito*r larvae. Thus, the compounds C2 and C4 demonstrated high amoebicidal activity with 50% inhibitory concentration (IC_{50}) values of 0.12 µM and 6.23 µM, respectively. C2, C3 and C4 caused changes in the cell cycle and induced PS exposure, while C4 also induced mitochondrial depolarization. In the cytotoxicity assay, C3 was the least toxic complex, with a 50% cytotoxic concentration (CC_{50}) of 32.3 µM. C2 and C4 maintained over 70% cell viability at concentrations ≤ 25 µM. None of the compounds showed irritability on the chorioallantoic membrane of the hen's egg (SI<5) at 200 µM. Moreover, after 48 h of exposure at 200 µM, all gold complexes maintained a high larval survival rate (60%). In conclusion, the gold(I) complexes showed excellent results against *A. castellanii,* likely through apoptosis induction, and demonstrated low or absent toxicity in the tested models. These findings support the potential development of a new treatment for AK and GAE.

Supported by: CNPq and FAPESC

Keywords: *Acanthamoeba spp.,* gold(I) metal complexes; amebicidal activity;