ANTI-*ACANTHAMOEBA* EFFICACY OF PHENDIONE-LINKED METALLOCOMPLEXES AS AN EXCELLENT ALTERNATIVE FOR THE TREATMENT OF SEVERE AMOEBIC KERATITIS

GABRIELLA DA ROSA MONTE MACHADO[1], DAYARA CORRÊA MATIOLA[2], GABRIELI EDUARDA ISRAEL[2], MARINA ARAÚJO[1,2], VITORIA MANOELA DAMBRÓS[3], MÁRIO LETTIERI TEIXEIRA[3], LUIS GABRIEL WAGNER[4], CHRISTIANE FERNANDES HORN[4], KARIN SILVA CAUMO[1,2]

[1]POSTGRADUATE PROGRAM IN PHARMACY; FEDERAL UNIVERSITY OF SANTA CATARINA; FLORIANÓPOLIS, SC.
[2]LABORATORY OF APPLIED RESEARCH ON EMERGING PROTOZOANS; FEDERAL UNIVERSITY OF SANTA CATARINA; FLORIANÓPOLIS, SC.
[3]LABORATORY OF PHARMACOLOGY, INSTITUTO FEDERAL CATARINENSE; CONCÓRDIA SANTA CATARINA
[4]INTERDISCIPLINARY LABORATORY OF MEDICINAL INORGANIC CHEMISTRY AND CATALYSIS; FEDERAL UNIVERSITY OF SANTA CATARINA; FLORIANÓPOLIS, SANTA CATARINA

Amoebic keratitis is a serious infection that affects the human cornea and can lead to loss of visual acuity and the need for corneal transplantation. *Acanthamoeba* genus is among its main causative agents. The use of contact lenses and lack of proper hygiene are major factors in contracting the infection. Available clinical therapies are scarce, ineffective, and present toxicity to the cornea. Therefore, the need for new, effective therapeutic targets is urgent. This study evaluated the efficacy of Ag(I), Cu(II), and Zn(II) metallocomplexes bound to phendione against *A. castellanii* ATCC 50492 - genotype T4, and a clinical isolate (R40), as well as the irritant potential of these compounds in an ex vivo model. The metallocomplexes and the phendione ligand were successfully synthesized in the interdisciplinary laboratory of medicinal inorganic chemistry and catalysis using synthetic routes described in the literature. The metallocomplexes were tested at concentrations ranging from 200 to 10 µM for 48 hours at 30°C against *Acanthamoeba* spp. trophozoites ($8x10^5$ cells/mL). Alamar Blue® was used as a viability dye, and fluorescence was read at 535 nm (emission) and 690 nm (excitation). The irritant potential was determined using the hen egg chorioallantoic membrane assay (HET-CAM). At 200 µM, Cu phen, Ag phen, and Zn phen showed high efficacy, inhibiting approximately 90% and 80% of the *A. castellanii* strain and R40 isolate trophozoites, respectively, after 48 hours. Better IC50 values were found against the ATCC strain: Cu phen (IC50 4.35 µM), Ag phen (IC50 12.2 µM), Zn phen (IC50 17.56 µM), compared to the R40 isolate: Cu phen (IC50 6.96 µM), Ag phen (IC50 22.4 µM), Zn phen (IC50 61.7 µM). At 200 µM, none of the metallocomplexes showed irritant potential, with an irritation score (IS < 5). Thus, the metallocomplexes linked to phendione represent excellent alternatives for the development of new ophthalmic formulations for the treatment of severe amoebic keratitis.

Supported by: FAPESC, CNPq, UFSC.
Keywords: phendione metallocomplexes, *Acanthamoeba*; amoebic keratitis