### **C**[**haracterization of novel tellurium-functionalized fused heterocyclic systems with antimalarial activity in vitro.**](http://dspace.nwu.ac.za/handle/10394/12243)

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Malaria causes millions of victims every year around the world. In Brazil, since 2017, the number of malaria cases has increased significantly and thus attracting the crescent attention of the authorities to control this disease[1]. Among the considered druggable targets to develop new malaria chemotherapy agents, proteolytic enzymes are very attractive due to their critical roles in the life cycle of malaria parasites[2]. During the erythrocytic stage of infection, *Plasmodium* proteases process host´s hemoglobin and also facilitates parasite invasion and evasion from erythrocytes. Thus, protease inhibitors are promising therapeutical agents for malaria treatment. Organotelluranes are a class of selective and potent cysteine protease inhibitors as demonstrated previously for cathepsins[3] and caspases[4]. As part of a program to explore biological activities of organotelluranes, the action of a set of related organotelluranes in malaria model was assessed[5].Herein, we evaluated a group of heterocyclic organotelluranes against a 3D7 strain of *Plasmodium falciparum* *in vitro*, the inhibition of recombinant Falcipain-2 and intracellular proteolytic activity of isolated parasites and the effect on isolated erythrocytes and HUVEC cells as an approach to study compounds toxicity. All compounds were able to decrease parasitemia at 72 hours significantly accompanied by significant intracellular proteolysis inhibition (IC50 values up to 10 μM). These compounds did not lead to considerable cytotoxicity or hemolysis at concentrations close to the EC50 or IC50. The group of compounds analyzed was also able to inhibit Falcipain II with Ki values about 1 μM. Despite there is some apprehension about the use of tellurium compounds as chemotherapeutics, some compounds have shown negligible acute toxicities. Thus, our results demonstrate the importance of the organic moieties of organotelluranes to modulate their activities. Collectively, our results suggest that these compounds have a potential to be further improved and strengthen the potential of tellurium-based antimalarial drugs.

**References**:[1]Ministério da Saúde – Brazil, 2018. [2]I. Macreadie, et al, Antimalarial Drug Development and New Targets, Parasitology Today, 2000, 438-444. [3]R.L.O.R. Cunha, et al, Irreversible inhibition of human cathepsins B, L, S and K by hypervalent tellurium compounds, Biological Chemistry, 2009. [4]D. Persike, et al, Protective effect of the organotelluroxetane RF-07 in pilocarpine-induced status epilepticus, Neurobiology of Disease, 2008, 120-126. [5]S. El Chamy Maluf, et al, Hypervalent organotellurium compounds as inhibitors of P. falciparum calcium-dependent cysteine proteases, Parasitology International, 2016, 20-22.

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