Investigation of origin of the aromatic portion of prenylquinones in *Plasmodium falciparum*

Gabriel Cândido Moura [1]; Liviah Andreassa La Pastina [1]; Juliana Tonine Mesquita [1]; Marcelo José Pena Ferreira [2]; Alejandro Miguel Katzin [1].

[1] University of São Paulo, São Paulo, Brazil. Department of Parasitology, Institute of Biomedical Sciences;

[2] University of São Paulo, São Paulo, Brazil. Department of Botany, Institute of Biosciences.

Malaria is a disease that impacting the tropical regions of the planet, caused by protozoan parasites of the phylum *Apicomplexa* of the genus *Plasmodium*, the most severe cases are caused by *P. falciparum*. The arising of drug resistance in different endemic regions inspires effort in the search for new targets for disease treatment, causing less impact on the host. After observing the inhibition of proliferation of *P. falciparum* by glyphosate, a widely known herbicide, there was uncertainty in regards of the presence of the shikimate pathway in these parasites, this pathway has been identified in plants, bacteria and fungi, but is absent in mammals. Therefore, it is considered a good target for new antimalarials drugs. Composed of seven enzymatic steps, the shikimate pathway results in the formation of chorismate, which in turn, is considered a "metabolic node" and also an important substrate in several parts of metabolism, such as the biosynthesis of folates and prenylquinones. This work aims investigate the origin of the aromatic portion of prenylquinones in *P. falciparum*, looking for derivative products of the shikimate pathway in parasite cultures. In **t**his work used *P. falciparum* 3D7 parasites in culture that were incubated with D-[^{14}C(U)]-glucose or [3-^{3}H] shikimic acid. After extracting the metabolites of interest, the samples were submitted to RP-HPLC system with the intention of separating intermediates and products (shikimate, chorismate, P-aminobenzoate, P-hydroxybenzoate) of the shikimate pathway. Culture plates containing parasites were used, cultured at different concentrations of compounds to determine the inhibitory concentration 50%, then we evaluated the proliferation of the parasite. Incorporation assays using [3-^{3}H] shikimic acid demonstrated its absorption by the parasites. Through the metabolic markings using radioactive compounds, it was possible to observe C.P.M levels in the fractions corresponding to the output of shikimate, chorismate, P-aminobenzoate, P-hydroxybenzoate in the shikimate metabolic pathway. Inhibition tests showed a decrease in the proliferation of parasites against the compounds used, mainly chlorogenic acid and its derivatives. After looking over the results obtained, we concluded that the parasites in culture are able to incorporate the radioactive materials used, hence being able to metabolize them, producing intermediates and products with retention times equal to those of shikimate pathway intermediates. Furthermore, compounds that were suggested as inhibitors of the shikimate metabolic pathway inhibited parasite proliferation.