FUTURE PERSPECTIVES FOR THE TREATMENT OF CHAGAS DISEASE:
NITRO COMPOUNDS ACTION IN INFECTIVE FORMS OF *Trypanosoma cruzi*

Nascimento SB\(^1\), Pitombo MM\(^1\), Baldow QCS\(^1\), Rodrigues AEL\(^1\), Saraiva FMS\(^1\),
Costa DSS\(^2\), Cupello MP\(^1\), Domingos J\(^2\), Costa PRR\(^2\), Dias AG\(^2\), Nogueira
NPA\(^1\), Paes MC\(^1\).

\(^1\) Instituto de Biologia Roberto Alcantara Gomes - Departamento de Bioquímica

\(^2\) Departamento de Química Orgânica - Universidade do Estado do Rio de Janeiro- RJ - Brasil.

Chagas disease is a parasitic illness that persists without satisfactory chemotherapy or treatment protocols. The nitro compounds, nitrones, arise as an alternative, once they are stable and have low toxicity against mammalian cells. Therefore, we evaluated the effect of three structurally different nitrones against evolutive forms of *Trypanosoma cruzi*. Initially, bloodstream trypomastigotes were incubated for 24h with the nitrones LQB110, LQB302, LQB303 and the number of parasites was quantified in a Neubauer chamber. Among the drugs tested, only LQB303 promoted a significant increase in parasites lysis, with an IC\(_{50}\) 13.1µM. For this reason, we continued the experiments studying the effect of LQB303 upon infective and proliferative forms of *T. cruzi*. We tested the effect of the nitrone on the other infective form, the metacyclic trypomastigotes. The parasites were subjected to different concentrations of LQB303, and MTT analysis demonstrated a significant decrease in viability of metacyclic forms after 24, 48 and 72 hours. Once again, we observed a great increase in metacyclic lysis with an IC\(_{50}\) of 20.6µM. Next, we tested the effect of LQB303 upon a proliferative form, the epimastigotes. The cells were incubated with LQB303 and quantified after 48h. Even low concentrations of the nitrone decreased epimastigote proliferation (IC\(_{50}\)= 6 µM). Subsequently, the permeability of LQB303-treated epimastigotes or metacyclic trypomastigotes plasma membrane to PI was assessed by flow cytometry. We observed a great increase in PI fluorescence and a decrease in cell size, suggesting the loss of membrane integrity of both forms. Furthermore, peritoneal macrophages were infected with bloodstream trypomastigotes in the presence of LQB303 for 48h. After amastigote quantification, we observed a significant reduction in the number of infected cells, without reducing the viability of non-infected macrophages. In conclusion our results suggest that LQB303 greatly impaired *T cruzi* viability, possibly by disturbing the parasites plasma membrane selectivity.

Keywords: *Trypanosoma cruzi*, trypanocidal activity, LQB303