***IN VITRO* EVALUATION OF ARYLSUBSTITUTED IMIDAZOLES AS ANTIPROTOZOAL AGENTS AND DOCKING STUDIES ON STEROL 14α-DEMETHYLASE (CYP51) FROM *T. CRUZI*, *L. INFANTUM* AND *T. BRUCEI*.**

**MSc Julio A. Rojas Vargas1**, PhD América García López1, Lic. Yulier Perez1, Prof. PhD Paul Cos3, Prof. PhD Matheus Froeyen2

1Chemistry Department, Exact and Natural Science Faculty, Oriente University, Santiago de Cuba, Cuba,

jarojas@uo.edu.cu america@uo.edu.cu

2Medicinal Chemistry, Department of Pharmacy, Rega Institute, KU Leuven, Leuven, Belgium, mathy.froeyen@kuleuven.be

3Laboratory of Microbiology, Parasitology and Hygiene (LMPH), S7, Faculty of Pharmaceutical, Biomedical and Veterinary Sciences, University of Antwerp, Wilrijk, Belgium, paul.cos@uantwerpen.be

**Abstract.**

There is an urgent need to discover and develop new drugs to combat parasitic diseases as Chagas disease (*Trypanosoma cruzi*), Sleeping sickness (*Trypanosoma brucei*) and Leishmaniasis (*Leishmania ssp*). These diseases are considered among the thirteen most unattended diseases worldwide according to the WHO. In the present work, the synthesis of 14 arylsubstituted imidazoles and its molecular docking onto sterol 14α-demethylase (CYP51) was executed. In addition, the compounds, antiprotozoal activity against *T. brucei*, *T. cruzi*, *Tb. rhod* and *L.inf* was evaluated. *In vitro* antiparasitic results of the arylsubstituted imidazoles against *T. brucei*, *T. cruzi*, *Tb. rhod*, *L.inf* indicated that all samples from arylsubstituted imidazole compounds presented interesting antiparasitic activity to various extent. The ligands **5a**, **5c**, **5e**, **5f**, **5g**, **5i** and **5j** exhibited strong activity against *T. brucei*, *T. cruzi*, *Tb. rhod* and *L.inf* with IC50 values ranging from 0.88 to 4.98 μM. Most samples were cytotoxic against MRC-5 cell lines (1.17 < CC50 < 52.03 μM) and only ligand **5c** showed a good selectivity against all tested parasites. According to the results of the molecular docking, the aromatic substituents in positions 1, 4 and 5 have mainly stabilizing hydrophobic interactions with the enzyme matrix, while the oxygen from NO2, SO3H and OH groups interacts with the Fe2+ ion of the Heme group.

**Keywords.**

arylsusbtituted imidazoles, *Trypanosoma cruzi, Trypanosoma brucei*, *Trypanosoma b. rhodesiense, Leishmania infantum, in vitro* evaluation, molecular docking