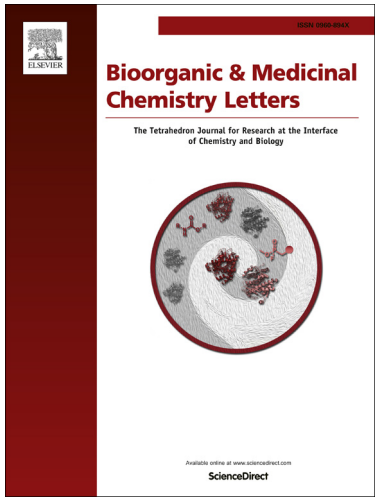

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Synthesis and biological characterization of new aryloxyindole-4,9-diones as potent trypanosomicidal agents

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Abstract

A new indole-4,9-dione and their phenoxy derivatives were synthesized and evaluated *in vitro* against the epimastigote form of *Trypanosoma cruzi*, Y strain. All of these novel compounds were found to be extremely potent and selective that the standard drug nifurtimox. Interestingly, phenoxyindole-4,9-dione **9d** displayed excellent nanomolar inhibitory activity, IC_{50}=20 nM, and high selectivity index, SI = 625. *In silico* studies using MOE program were performed to generate a preliminary pharmacophore model.

Keywords: Indolequinones, anti-*T. cruzi*, cytotoxicity, pharmacophore model.

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Chagas disease, or American tripanosomiasis, is a neglected tropical disease caused by the protozoan *Trypanosoma cruzi*, which affects 16-18 million people in many rural areas of Latin America.[1] There are two main drugs used for the treatment of this disease, nifurtimox (Nfx) and benznidazole, but both are toxic and present severe side effects.[2,3] Therefore, there is a need for more effective drugs and many efforts have been done in the search for new compounds with potential clinical utility.[4] Taking into account the anti-trypanosomal activity of natural naphthoquinones, the preparation of many compounds