

2-Phenylaminonaphthoquinones and related compounds : synthesis, trypanocidal and cytotoxic activities

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Abstract

A series of new 2-aminonaphthoquinones and related compounds were synthesized and evaluated in vitro as trypanocidal and cytotoxic agents. Some tested compounds inhibited epimastigote growth and trypomastigote viability. Several compounds showed similar or higher activity and selectivity as compared with current trypanocidal drug, nifurtimox. Compound **4l** exhibit higher selectivity than nifurtimox against *Trypanosoma cruzi* in comparison with Vero cells. Some of the synthesized quinones were tested against cancer cells and normal fibroblasts, showing that certain chemical modifications on the naphthoquinone moiety induce and excellent increase the selectivity index of the cytotoxicity (**4g** and **10**). The results presented here show that the anti-*T. cruzi* activity of 2-aminonaphthoquinones derivatives can be improved by the replacement of the benzene ring by a pyridine moiety. Interestingly, the presence of a chlorine atom at C-3 and a highly lipophilic alkyl group or aromatic ring are newly observed elements that should lead to the discovery of more selective cytotoxic and trypanocidal compounds.