Synthetic derivatives of gibbilimbol B are *in vitro* effective against intracellular amastigotes of *Trypanosoma cruzi*

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Chagas disease is a neglected parasitic disease caused by *Trypanosoma cruzi* parasites. It is an important public health problem and account for more than 8 million people infected worldwide. New chemotherapies remain a priority, as the only available treatment is inefficient and highly toxic. Our previous studies demonstrated the antitrypanossomal activity of the gibbilimbol B, an alkenylphenol isolated from the leaves of the Brazilian plant *Piper malacophyllum* (Piperaceae). In this work, we investigated the *in vitro* anti-*T. cruzi* activity and the mammalian cytotoxicity of five new synthetic analogues of gibbilimbol B. The activity against the intracellular amastigotes was determined using peritoneal macrophages as host cells and the 50% effective concentration (EC_{50}) was determined by light microscopy counting. The 50% cytotoxic concentration (CC_{50}) of the compounds was determined using L-929 mammalian cells by the colorimetric MTT assay. Our results demonstrated that all compounds presented activity against *T. cruzi* amastigotes, with EC_{50} values in a range between 1 to 36 µM; the compounds demonstrated low to moderate mammalian cytotoxicity with CC_{50} values in a range between 120 to >200 µM. The selectivity index, given by relation between the mammalian toxicity and the antiparasitic activity, ranged from >5 to 24. Benznidazole was used as standard drug and resulted in an EC_{50} value of 6 µM and a CC_{50} >200 µM. These new gibbilimbol B derivatives have been shown promising selectivity against *T. cruzi* intracellular parasites and may be selected as new hit compounds for drug design studies.

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