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Abstract

Activity of 2-benzyl-1-(2-hydroxyethyl)-5-nitroindazolin-3-one on *Trypanosoma cruzi* Bloodstream Trypomastigotes (Y strain): In Vitro and In Vivo Studies †

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Benznidazole and nifurtimox, the currently available drugs for the specific treatment of Chagas disease, show limited effectiveness and high toxicity that prompt the identification of therapeutic alternatives. In this context, our group has proposed 5-nitroindazole derivatives as antichagasic prototypes, according to their activity in vitro and in vivo [1–5]. The lack of cytotoxicity and outstanding activity on the replicative forms of *Trypanosoma cruzi* (i.e., epimastigotes and intracellular amastigotes) previously shown by 2-benzyl-1-(2-hydroxyethyl)-5-nitroindazolin-3-one [5], encouraged assaying this compound in vitro on bloodstream trypomastigotes of Y strain (DTU TcII) and then, moved it to murine models of toxicity and infection. After confirming NOAEL >25 mg/kg and no signs of acute toxicity (i.e., normal weight, organs appearance, hemogram and biochemistry), infected mice were treated on the 5th and 8th dpi with doses of 25, 12.5 or 6.25 mg/kg/day. The results obtained in this acute model of *T. cruzi* infection in mice showed that this compound achieved ca. 30% of parasitemia reduction on the 8th dpi when administered either at 25 mg/kg/day p.o. or 6.25 mg/kg/day ip. Accordingly, new treatment schemes and molecule optimization are now considered for further analysis in vivo, aiming to contribute to the identification of novel alternative therapies for Chagas disease.

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