Chagas112- **2-Iminothiazolidin-4-ones arrest *Trypanosoma cruzi* growth and impair trypomastigote development in macrophages**

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Chagas disease, caused by the flagellate protozoan *Trypanosoma cruzi*, affects about 18 million people in the Americas. Current chemotherapy of Chagas disease is based on benznidazole, which is toxic and has limited efficacy. Therefore, new chemotherapeutic agents need to be developed. In this work, we describe the identification of eight *Trypanosoma cruzi* inhibitors through a combination of thiazoles and hydrazones chemistry. The trypanocidal effect against *T. cruzi* was first evaluated by light microscopy through the determination of IC_{50} values for the replicative form epimastigote and bloodstream trypomastigotes of Y strain. Cytotoxicity was determined by incorporation of [^{3}H]- thymidine by splenocytes obtained from normal mice. The trypanocidal activity of the iminothiazolidin-4-ones was tested in a model of infection *in vitro* of macrophage cultures. All compounds showed activity for the replicative form epimastigote and the infective form trypomastigote, showing IC_{50} values ranging from 0.5 to 51.5 µM and 1.2 to 48.2 µM, respectively. In terms of cytotoxicity, compounds TS-40 and TS-59 showed the best profiles. The compounds had IC_{50} values of 9 µM and 1.2 µM, respectively, for trypomastigotes and IC_{50} values of 5.1 and 0.5 µM, respectively, for epimastigotes. All the values smaller than the IC_{50} of the standard drug (benznidazole IC_{50} = 11.2 µM for trypomastigotes and 7.5 µM for epimastigotes). In splenocyte cultures, all the compounds showed no or moderate cytotoxicity, demonstrating a selective toxicity of these compounds, especially compound TS-59, which is over 180 times more cytotoxic to trypomastigote than for mammalian cells. In the model of macrophage infection with *Trypanosoma cruzi*, all the iminothiazolidin-4-ones were able to reduce the percentage of macrophages infected and the relative number of amastigotes per cell. The compounds TS-40 and TS-59 showed the best activity. The IC_{50} of these compounds were 10.11± 0.09 µM for TS-40, and of 5.20±0.54 µM for TS-59, while benznidazole had an IC_{50} of 13.99±0.39 µM. Our results with iminothiazolidin-4-ones TS-40 and TS-59 argue for the evaluation of these compounds in the *in vivo* infection model in mice. **E-mail:** calcio0303@hotmail.com