

# Glycosylated metal chelators as anti-protozoa agents with tunable selectivity.

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## Abstract

*Trypanosoma cruzi* and *Leishmania amazonensis* are the causative agents of Chagas' disease and leishmaniasis, respectively. These conditions affect millions of people worldwide, especially in developing countries. As such, there is an urgent need for novel, efficient and cost-effective treatments for these diseases, given the growing resistance and side-effects of current therapies. This work details the evaluation of the anti-parasitic activity of novel amino- and imino pyridyl metal chelators, their glycosylated derivatives and some of their metal complexes. Our results revealed the potent and metal-dependent activity for the amino pyridyl compounds: Cu(ii) complexes were most effective against *T. cruzi* trypomastigotes presenting an LD<sub>50</sub> value of 1.7 µM, while Zn(ii) complexes presented excellent activity against *L. amazonensis* promastigotes, with an IC<sub>50</sub> value of 1.3 µM. The treatment of trypomastigotes with the test compounds caused some significant morphological changes when compared to the typical appearance of non-treated parasites, including rounding in shape with reduced cell size, swelling of the cell body and shortening or loss of flagellum. In *L. amazonensis* promastigotes, the compounds induced the loss of flagellum and a reduced cell size. Further morphological alterations, such as a swelling and rounding of the cell, were also observed. In addition, the compounds showed excellent selectivity indexes and very low relative toxicity as judged by *in vitro* and *in vivo* studies, respectively, using RAW macrophages and *Galleria mellonella* larvae model.