CHARACTERIZATION OF CYCLOPALLADATE COMPOUNDS AS INHIBITORS OF CYSTEINE PROTEASES OF TRYPANOSOMATIDS

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Cysteine proteases are regarded as essential for the survival of several trypanosomatids parasitic protozoa. The CPB genes encode stage-regulated cathepsin L-like cysteine proteases considerably greater in the mammalian amastigote form, and CPs exist as multiple isoenzymes encoded by a tandem array of 19 genes in L. mexicana. Cruzipain, is a papain-like protease, which shares biochemical characteristics with both cathepsin-L and cathepsin-B, and it is a member of a large multigene family composed of polymorphic genes with stage regulated expression in the T. cruzi. Both enzymes, CPB and cruzipain are important virulence factors of leishmaniasis and Chagas’ Diseases. Our goal was study the effect of cyclepalladate compounds as inhibitors of rCPB2.8, and isoenzymes rCPB3 and rH84Y of L. Mexicana and cruzain of T. cruzi. The enzyme inhibition assays were carried out in 100mM sodium acetate pH-5.5, 2.5mM DTT at 35°C and Z-FR-MCA as fluorogenic probe in a spectrofluorimeter F-2500-Hitachi. The data were analyzed in Grafit-5.0 software and the IC50 determined. The results show the IC50s ranging between 0.27-93.12µM for rCPB2.8, and 0.69-29.93µM for rCPB3, and 1.88-21.33µM for rH84Y. The IC50 values of cruzain ranged between 1.57-240.38µM.

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