CRYSTAL STRUCTURE OF THE ENZYME PURINE NUCLEOSIDE PHOSPHORYLASE FROM *SCHISTOSOMA MANSONI* IN COMPLEX WITH A MONOCYCLIC INHIBITOR

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The development of high affinity compounds against PNPs has always been based on purine-like compounds and the possibility of using monocyclic inhibitors against this enzyme has been largely ignored. We performed a Virtual Screen of the SmPNP structure to identify new potential ligands. Approximately 30,000 compounds with a MW ~280Da were tested, and as a result, 22 compounds were selected for enzyme inhibition assays. Eight compounds showed measurable inhibition of the enzyme in a single point assay. The most active compound, AT2328, fully inhibited the enzyme. This compound has a novel monocyclic structure never previously described in PNP inhibitors. The structure of the complex between PNP and AT2328 was obtained by soaking. The X ray diffraction data were collected on PX14.2 of the SRS, up to a resolution of 1,9Å using 0.98Å radiation. Data reduction resulting in an overall completeness of 94,8% with an R_{sym} of 7,1% for a total of 54047 unique reflections. The structure was solved by rigid body refinement. One non-protein peak corresponding to the AT2328 was found in each active site. The values of R and R_{free} are 18.5 and 24.8% respectively. AT2328 makes 6 H-bonds with both key residues and water molecules of the active site which could explain its marked inhibitory activity.