

CRYSTAL STRUCTURE OF *TRYPANOSOMA CRUZIDIHYDROOROTATE*
DEHYDROGENASE

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Dihydroorotate dehydrogenase (DHODH) catalyzes the oxidation of dihydroorotate to orotate, the first aromatic intermediate in the biosynthetic pathway toward pyrimidine nucleotides. At present, there is a great interest in inhibitors of DHODH as therapeutic agents for the treatment of cancer, rheumatoid arthritis and parasitic disease. *Trypanosoma cruzi* is a protozoan parasite responsible for Chagas' Disease that according to the World Health Organization affects 16 to 18 million people in Latin America and causes around 21,000 deaths a year. Here we present the crystallization and X-ray structure of *Tc*DHODH. Crystals of the *Tc*DHODH in fusion with 6xHis tag at the N-terminal were grown at 25°C by the hanging drop vapour-diffusion technique using ammonium sulfate as a precipitant. Crystals of *Tc*DHODH have been cryofrozen in presence of glycerol and synchrotron radiation data were collected at the MX-1 beam line (LNLS). *Tc*DHODH crystals belong to the orthorhombic space group $P2_12_12_1$, with unit-cell parameters $a=82.39$, $b=123.92$, $c=128.89$ Å. The crystal structure of *Tc*DHODH has been solved by molecular replacement and refined to 2.2Å resolution with 4 molecules in A.U. The three-dimensional structure of *Tc*DHODH can further be used for the design of highly specific inhibitors of *Tc*DHODH through the technology of structure-based drug design as a tool against Chagas' Disease.

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