Structure Based Design of New Trypanocidal Drugs using Phosphoglycerate Mutase from *Trypanosoma brucei*

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Trypanosomiasis are Neglected Tropical Diseases that causes several health problems. The enzyme Phosphoglycerate mutase (PGAM, EC 5.4.2.1) participates in glycolysis and glyconeogenesis in Trypanosomatids, and was shown by RNA interference experiments to be important to the parasite survival. Our purpose is to identify lead compounds for PGAM using Structure-Based Virtual Screening and in-vitro High-Throughput Screening. The recombinant PGAM enzyme from *Trypanosoma brucei* (TbPGAM) was expressed in *Escherichia coli* BL21 and purified by chromatography methods using metal affinity resin and size exclusion cromatography. Coupled kinetics assays was standardized and the Michaelis-Menten constant from PGAM was confirmed at Km = 144 ± 6,8. The kinetics assays was adapted from the published data to be performed by an automatic Biomek 3000 (Beckman Coulter) system that uses 96 well-plates, allowing High-Throughput Screening of compounds. Furthermore virtual screening against a compound collection was implemented using the molecular database ZINC and PGAM homologue structure. Since the PGAM is an attractive molecular target for drug design, our results represents a preliminary effort for in-silico and in-vitro compound screening aiming to identify new TbPGAM inhibitors which may contribute to the international effort to develop effective novel drugs.

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Key words

Phosphoglycerate mutase; trypanosomiasis; Virtual Screening; Enzyme; *Trypanosnoma brucei*.