ELSEVIER
Biochemistry and Biophysics Reports **24 (2020) 100837**
https://doi.org/10.1016/j.bcab.2019.101298

Exploring the Binding Interactions of Structurally Diverse dichalcogenoimidodiphosphinate Ligands with α-amylase: Spectroscopic Approach Coupled with Molecular Docking

Oghenetega J. Avwioroko, Temidayo T. Oyetunde , Francis O. Atanu , Chiagoziem A. Otuechere, Akpovwehwee A. Anigboro , Oluropo F. Dairo, Akpoyovware S. Ejoh , Sunday O. Ajibade , Martins O. Omorogie

Abstract: Postprandial hyperglycemia has orchestrated untimely death among diabetic patients over the decades and regulation of α-amylase activity is now becoming a promising management option for type 2 diabetes. The present study investigated the binding interactions of three structurally diverse dichalcogenoimidodiphosphinate ligands with α-amylase to ascertain the affinity of the ligands for α-amylase using spectroscopic and molecular docking methods. The ligands were characterized using 1 H and 31P NMR spectroscopy and CHN analysis. Diselenoimidodiphosphinate ligand (DY300), dithioimidodiphosphinate ligand (DY301), and thioselenoimidodiphosphinate ligand (DY302) quenched the intrinsic fluorescence intensity of α-amylase via a static quenching mechanism with bimolecular quenching constant (Kq) values in the order of x1011 M-1s -1, indicating formation of enzyme-ligand complexes. A binding stoichiometry of n≈1 was observed for α-amylase, with high binding constants (Ka). α-Amylase inhibition was as follow: Acarbose > DY301>DY300>DY302. Values of thermodynamic parameters obtained at temperatures investigated (298, 304 and 310 K) revealed spontaneous complex formation (ΔG<0) between the ligands and α-amylase; the main driving forces were hydrophobic interactions (with DY300, DY301, except DY302). UV–visible spectroscopy and Forster ¨ resonance energy transfer (FRET) affirmed change in enzyme conformation and binding occurrence. Molecular docking revealed ligands interaction with α-amylase via some key catalytic site amino acid residues (Asp197, Glu233 and Asp300). DY301 perhaps showed highest α-amylase inhibition (IC50, 268.11 ± 0.74 μM) due to its moderately high affinity and composition of two sulphide bonds unlike the others. This study might provide theoretical basis for development of novel α-amylase inhibitors from dichalcogenoimidodiphosphinate ligands for management of postprandial hyperglycemia.

Keywords: α-Amylase inhibition, Ligand-protein binding, Spectroscopy, Hyperglycemia, Anti-diabetic agents