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IN SILICO HOMOLOGY MODELING AND VALIDATION OF A-GLUCOSIDASE ENZYME

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ABSTRACT

In this research work we have derived three dimensional (3D) structure of α-glucosidase enzyme through homology modeling and the predicted structure was validated with the help of PROCHECK analysis in the form of Ramachandran plot. According to Ramachandran plot statistics the derived model was found to be of good quality.

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INTRODUCTION:

Diabetes mellitus type 2, include 90% of all cases of diabetes mellitus is increasing considerably and affecting about 5% of the world population. The burden of diabetes is driven by vascular complications such as cardiovascular disease, stroke, nephropathy, retinopathy and renal failure. Type 2 diabetes mellitus is often associated with abnormalities in plasma lipid and lipoprotein profiles, and postprandial hyperlipidemia has been shown to be an independent risk factor and predictor of atherosclerosis[1-2]. α-glucosidase inhibitors delay carbohydrate digestion and prolong overall carbohydrate digestion time, causing a reduction in the rate of glucose absorption and consequently blunting the postprandial plasma glucose rise. Thus inhibition of enzyme α-glucosidase is a new and promising approach for the treatment of diabetes mellitus.

MATERIAL AND METHODS:

As the crystal structure of α-glucosidase enzyme is not available in the protein data bank (PDB), therefore the 3D structure of α-glucosidase was derived through homology modeling. The protein sequence (FASTA sequence) of enzyme α-glucosidase was retrieved from Uniprot/Swissprot database. The sequence was submitted to modweb[3] web server to find a suitable template with sufficient query sequence coverage and sequence identity. The model derived through modweb web server was selected on the basis of maximum sequence similarity (46.00 %) with the template (crystal structure of Human intestinal maltase-glucoamylase; PDB code: 2qmjA)[4].

RESULT AND DISCUSSION:

Structure of modeled enzyme (Figure 1) was validated through PROCHECK analysis. For this analysis, the PDB format file of modeled α-glucosidase enzyme was submitted to PDB SUM web server of European Bioinformatics Institute. The results of PROCHECK analysis was obtained in the form of Ramachandran plot (Figure 2) which resolve stereo chemical aspects along with main chain and side chain parameters with widespread analysis. The Ramachandran plot (PROCHECK) statistics are summarized in Table 1.

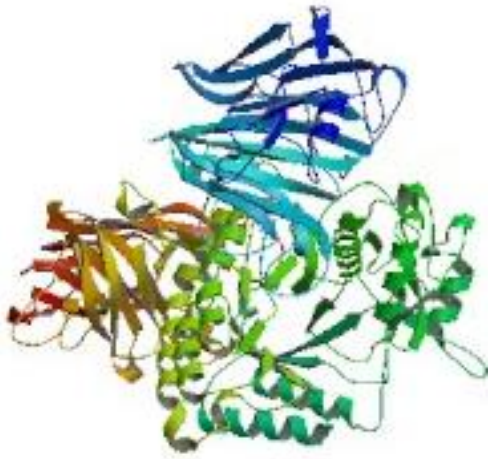

Figure 1: 3D structure of derived model of α-glucosidase enzyme

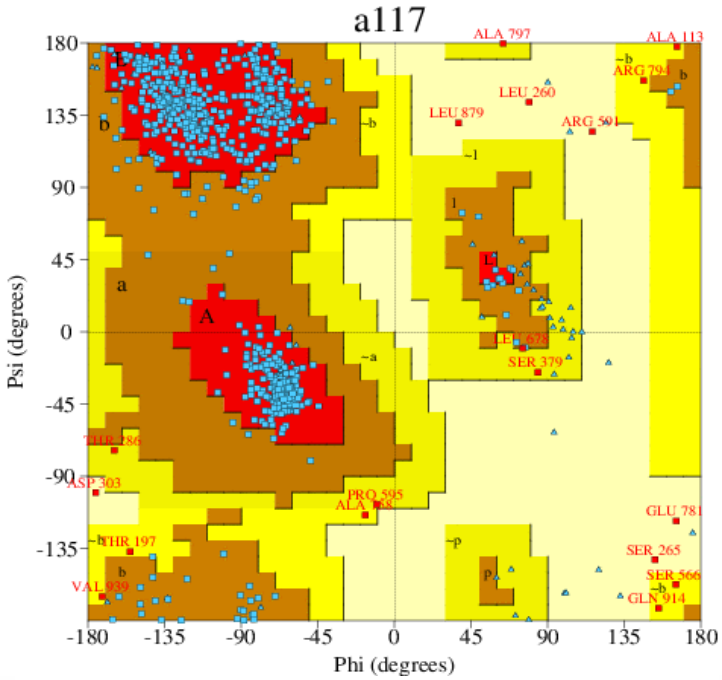

Figure 2: Ramachandran plot of homology modeled α-glucosidase enzyme

Table 1: Ramachandran plot (PROCHECK) Statistics of homology modeled α-glucosidase enzyme

Residue	No. of residues	Percentage
Most favoured regions [A,B,L]	631	87.0%
Additional allowed regions [a,b,l,p]	77	10.6%
Generously allowed regions [~a,~b,~l,~p]	11	1.5%
Disallowed regions	6	0.8%
Non-glycine and non-proline residues	725	100.0%
End-residues (excl. Gly and Pro)	2	
Glycine residues	67	
Proline residues	69	
Total number of residues	**863**	

CONCLUSION:

In this research work we have successfully derived the 3D structure of enzyme α-glucosidase. The modeled enzyme was validated through PROCHECK analysis (Ramachandran plot). The Ramachandran plot indicated that phi (φ) and psi(ψ) angles to contribute in conformations of amino acids excluding glycine and proline with 87.0 % residues in most favored region, 10.6 % in additional allowed region, 1.5 % in generously allowed region and 0.8 % residues in disallowed region. The above statistics of Ramachandran plot indicated that derived model was found to be of good quality and can be used for further molecular modeling study.

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