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In silico exploration and anticancer insights of isoaspartyl peptidase from *Arthrospira platensis*

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Abstract: Isoaspartyl peptidase is an enzyme widely distributed in plants, animals, and some bacterial species, where it contributes to protein maintenance by removing abnormal β-linked aspartyl residues from polypeptide N-termini. This repair mechanism has drawn increasing attention in biomedical fields, particularly in oncology. Despite this interest, isoaspartyl peptidases from cyanobacteria, including *Arthrospira platensis*, have not been extensively investigated. In this study, a detailed computational analysis of isoaspartyl peptidase from *A. platensis* was performed to explore its physicochemical characteristics, structural organization, and potential biological roles. The protein was predicted to exhibit good stability, resistance to temperature variations, hydrophilic properties, and an overall acidic nature. Secondary structure prediction indicated a predominance of random coils, followed by α-helices and a smaller proportion of β-strands.Three-dimensional structural models were generated using several bioinformatics platforms, including AlphaFold, LOMETS, SWISS-MODEL, Phyre2, and I-TASSER. Among these, the AlphaFold-derived model demonstrated superior quality according to validation analyses such as PROCHECK, ERRAT, and Verify3D. Domain investigation revealed the presence of a conserved Asparaginase_2 domain, suggesting functional conservation within this enzyme family. Functional domain analysis identified the presence of an Asparaginase_2 domain (E-value: 1.5×10^{-107}), indicating a conserved enzymatic function. Protein interaction analysis highlighted a probable association with cyanophycin, supported by a high confidence score. Furthermore, molecular docking analysis indicated potential anticancer activity, with asparagine showing the strongest binding affinity (Vina score: −5 kcal/mol). Overall, this study offers the first comprehensive computational insight into isoaspartyl peptidase from *Arthrospira platensis*, emphasizing its structural features and possible functional applications. These findings provide a foundation for future experimental validation and potential exploitation in biotechnology and medical research.

Keywords: Cyanobacteria, physicochemical properties, functional features, 3D protein model, Asparaginase, Anticancer potential

• Introduction

Isoaspartyl peptidase (EC 3.4.19.5) is a key enzyme catalyzing the specific cleavage of isoaspartyl residues at the N-terminal position of polypeptides. Produced by various organisms (bacteria, fungi, plants), it plays a critical role in the repair of damaged proteins. This mode of action could be particularly exploited in oncology for the treatment of various cancers, a promising alternative to bacterial asparaginases whose use is limited by immunogenic effects.

In this case , In this context, *Arthrospira platensis* (spirulina), a non-pathogenic and edible cyanobacterium widely recognized for its nutritional and pharmaceutical value, represents a promising source for the production of biocompatible asparaginase. , This study aims to determine the structure-function-interaction relationships of *A. platensis* isoaspartyl peptidase in order to optimize its anti-cancer applications.

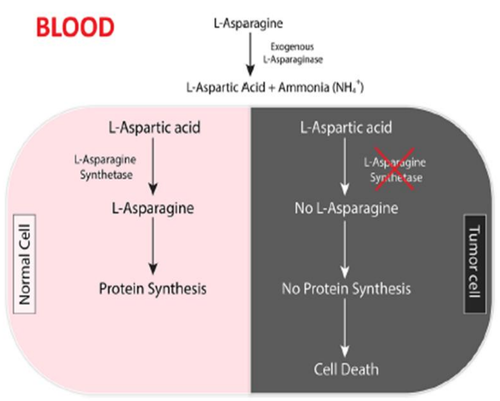


Fig. 1.Mechanism of action of asparaginase (Parashiva *et al.*, 2023)

• Materials and methods

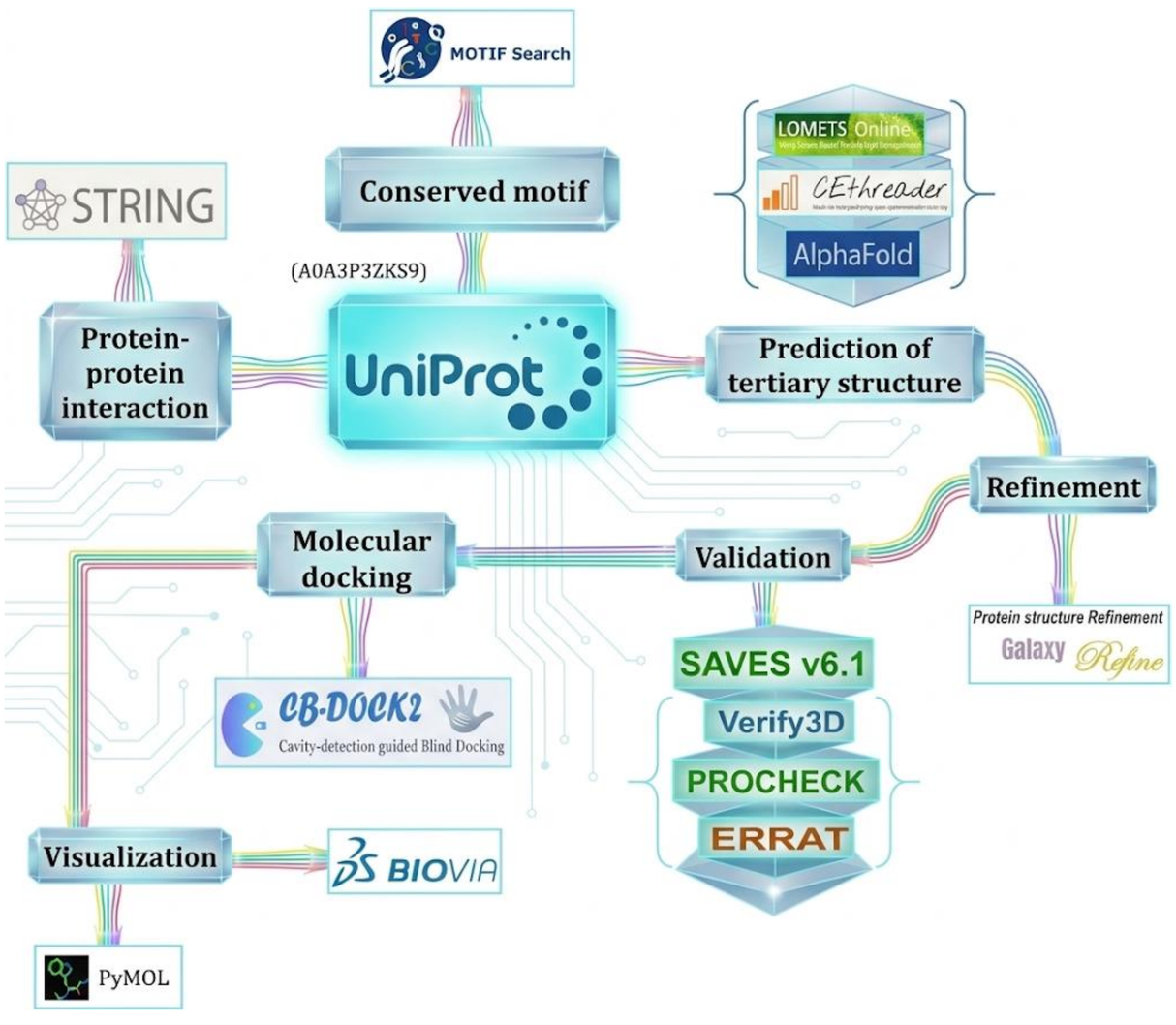


Fig 2. Bioinformatics Workflow for functional analysis of *Arthrospira platensis* Isoaspartyl peptidase.

Table 1. Ligands used for molecular docking with the *A. platensis isoaspartyl* peptidase.

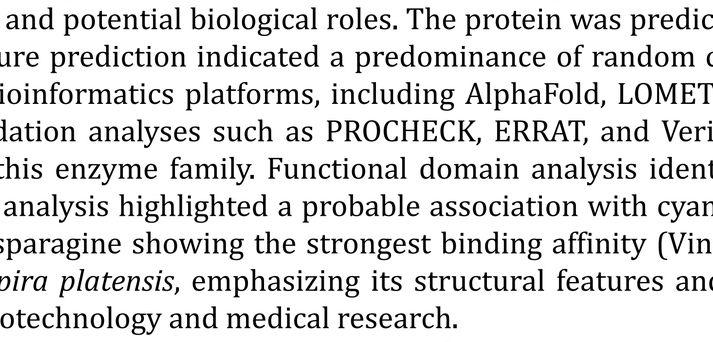
Ligand	Pubchem CID	Molecular formula	Nature
Estradiol	5757	C18H24O2	Estrogenic hormone
Estriol	5756	C18H24O3	Œstrogène faible
Asparagine	6267	C4H8N2O3	Amino acid
Citrulline	9750	C6H13N3O3	Non-proteinogenic amino acid
Chloroquine	2719	C18H26ClN3	Antimalarial
Thiorphan	3132	C12H15NO3S	Neprilysin enzyme inhibitor
Darunavir	213039	C27H37N3O7S	Antiretroviral protease inhibitor

• Results and discussions

Pfam (1 motif)

Pfam	Position(Independent E-value)		Description
Asparaginase_2	7..304(1.5e-107)	Detail	PF01112, Asparaginase

Fig. 3.MOTIF Finder analysis revealing the functional motif of Isoaspartyl Peptidase from *Arthrospira platensis*.



C

Ligand	Pubchem CID	Molecular formula	Molecular weight (g/mol)	Vina Score (Kcal/mol)	Cavity volume (Å3)
Asparagine	6267	$C_4H_8N_2O_3$	132.12	-5	1078

Fig. 4.Analysis of the molecular interaction between the ligand asparagine and the enzyme receptor of *Arthrospira platensis* isoaspartyl peptidase. A. The cavity illustration shows the area of the protein receptor's surface where the ligand-receptor interaction occurs. **B.** 2D diagram illustrating the different types of interactions between receptor residues and ligand, as observed in BIOVIA Discovery Studio Visualizer.**C.** Minimum Binding Energy and Predicted Cavity Size for Using Vina Scores from the CB-DOCK Web Interface.

Table2. Physicochemical parameters of the A. platensis isoaspartyl peptidase as determined by ExPASy ProtParam.

Property	Value
Number of amino acids	314
Molecular weight (Da)	33310.68
Theoretical pI	5.07
negatively charged residues (Asp + Glu)	39
positively charged residues (Arg + Lys)	31
Extinction coefficient (EC)	1845
Instability index (II)	37.2 (Stable)
Aliphatic index (AI)	94.78
GRAVY	-0.082

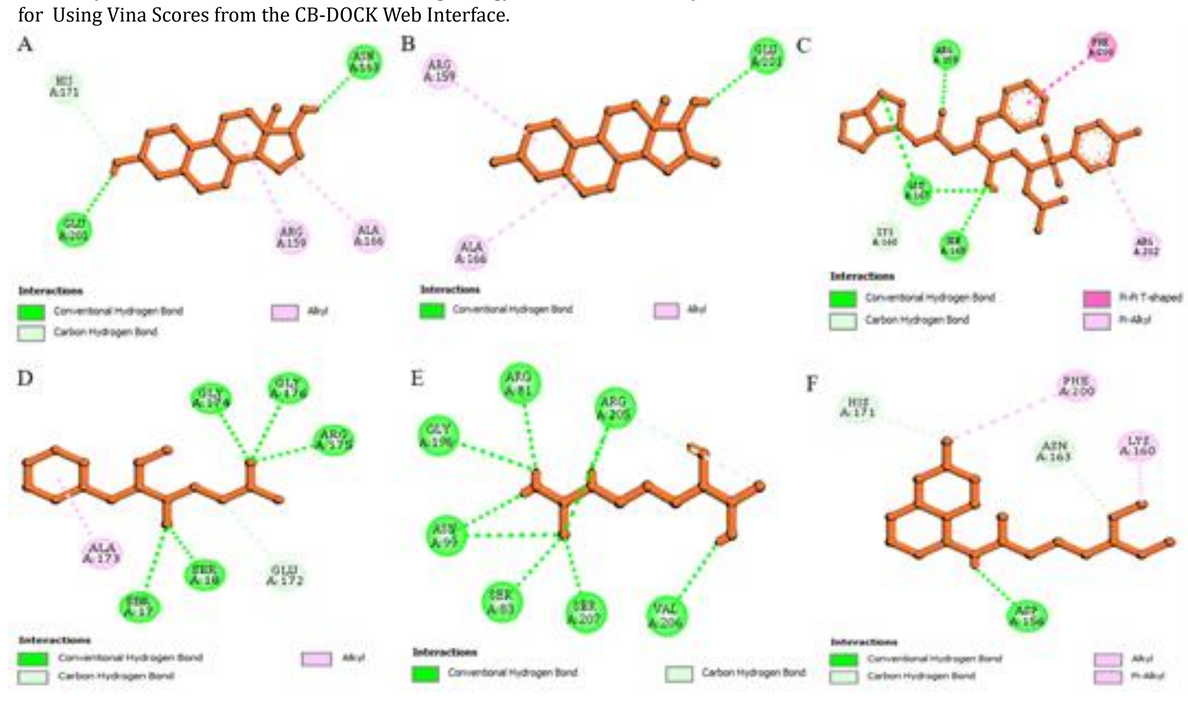


Fig.5. Two-dimensional interaction profiles of *A. platensis* isoaspartyl peptidase residues with selected ligands (BIOVIA Discovery Studio). A) Estradiol, B) Estriol, C) Darunavir, D) Thiorphan, E) Citrulline, F) Chloroquine (CID identifiers provided).

Conclusions

The results of this study reveal that isoaspartyl peptidase from *Arthrospira platensis* possesses a conserved structural motif characteristic of asparaginases, confirmed by molecular docking analyses demonstrating a high affinity for asparagine (score of -5 kcal/mol). These structural data open promising perspectives for the rational engineering of this enzyme, particularly in the field of therapeutic applications. In-depth knowledge of its molecular configuration will allow the optimization of its catalytic properties for targeted biotechnological developments.

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