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In Silico Study of Usnic Acid Binding Affinity with Cell Wall Associated Protein of *Staphylococcus epidermidis*

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Abstract : *Lichens a unique group of fungus which associates with photobiont and forms a new entity and is well known for their biological activities. Usnic acid is a characteristic compound produced particularly by the lichen genera Usnea. Usnic acid was known for its antimicrobial activity against various human pathogens. Staphylococcus epidermidis, colonizes on clinical equipments and causes the infection in patients. Cell wall associated accumulation-associated protein (Aap) mediates the biofilm formation and intercellular adhesions. In present study, the binding affinity of usnic acid into the binding sites of Aap protein was investigated. In silico binding affinities was analyzed through Autodock Vina and the docked files were visualized via Chimera. The successful binding of usnic acid into the binding sites of Aap protein provides the insight into the capability of usnic acid into biofilm degradation and bacterial cell lysis. Although the oral administration of usnic acid is not safe as it causes hepatotoxicity but use of usnic acid as a disinfectant can be promoted and commercialized.*

Keywords: *Biofilm, Lichen, Staphylococcus epidermidis, usnic acid, Usnea*

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I. INTRODUCTION

Lichens, a consortium of two independent groups viz. mycobiont and photobiont forming an entirely new entity [1]. About 1050 compounds have been reported so far from the lichens and known for various biological activities [2,3]. Usnic acid is one of them produced by several genera of lichens but usnic acid is a characteristic compound produced by the genera *Usnea* [4]. Usnic acid is already known for its broad spectrum antimicrobial activity against human pathogens. *Staphylococcus epidermidis*, an opportunistic pathogen causes the contamination of clinical devices [5,6]. Recently a study on usnic acid obtained from *U. steineri* exhibited the strong in vitro antibacterial activity against *S. epidermidis* (MIC 3.12µg/mL) [7]. Cell wall associated accumulation-associated protein (Aap) of *S. epidermidis* is responsible for the intercellular adhesion and biofilm formation [8]. In present study the interaction between the Aap protein and usnic acid was investigated.

II. MATERIAL AND METHODS

II.I Accession of Target Protein and Ligand Selection Three dimensional structure of protein was downloaded from RCSB: Aap (PDB ID: 5TU9) [9]. Usnic acid structure was downloaded from PubChem compound database [10]. Three dimensional structure was prepared using CADD Group Chemoinformatics Tools and User Services [11]. Structure energy was minimized and hydrogen's were added and charges were assigned using Gasteiger [12].

II.II Molecular Docking Analysis The active binding sites of aforementioned protein were analyzed via Metapocket 2.0 [13]. Ligand-Protein docking was used to analyzed the binding affinity of Methyl-beta-orcinol with the 'aforementioned protein's structure. The PDB file were analyzed before docking solvents were deleted and hydrogens and other parameters was set [14]. Docking was performed via AutoDock Vina [15]. The docked files were visualized via UCSF Chimera 1.11.2 developed by Resource for Biocomputing, Visualization, and Informatics (RBVI) [16, 17]

III. RESULTS AND DISCUSSION

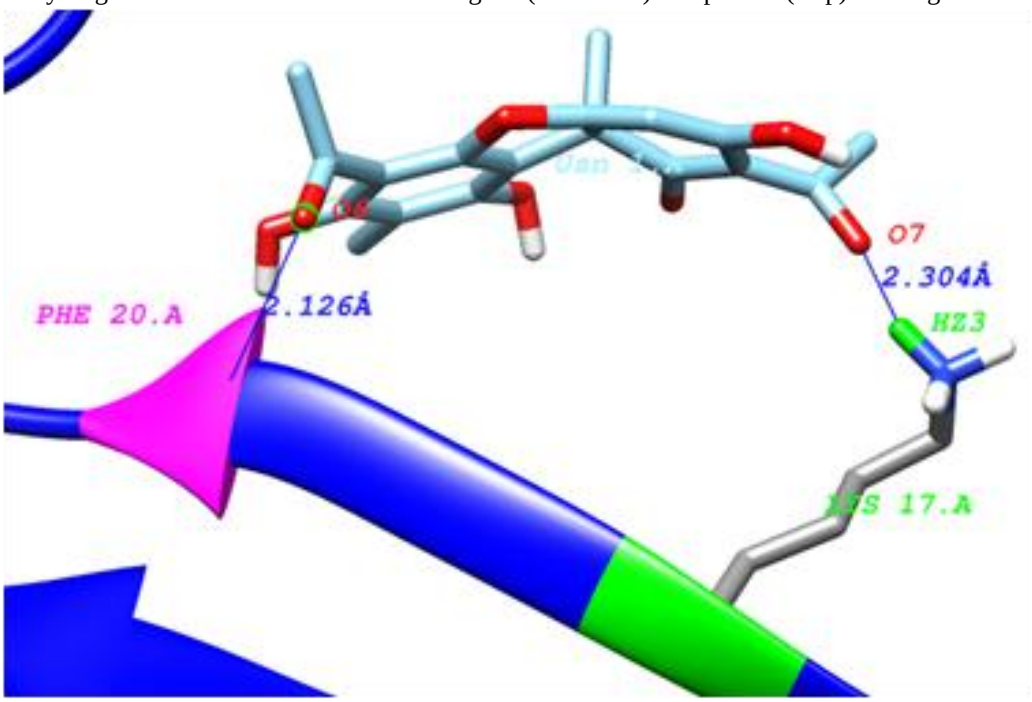
The binding affinity of usnic acid into the binding sites of Aap protein were tabulated in Table 1. The virtual docking of usnic acid (ligand) into the active binding sites of Aap protein was successful with several hydrogen bonds listed into the Table 1. The hydrogen bond of best fitted model with minimum score, RMSD l.b. and RMSD u.b. was represented in Fig 1. The successful binding of usnic acid provides the insight that it is effective against bacterial biofilm and cell lysis may takes place through Aap proteins. Usnic acid isolated from U. subfloridana are known for the rupturing of cell membrane of S. aureus [18]. Although the oral administration of usnic acid is not safe as it causes fluminant liver failure [19]. So, it might be used commercially as a disinfectant for clinical equipments or oral hygiene.

IV. FIGURE AND TABLE

TABLE 1: In silico binding affinity of usnic acid and Aap Protein.

S. No.	Binding site	State	Score	RMSD l.b.	RMSD u.b.	HBond (all)	HBond Ligand Atom	HBond Receptor Atom
1	1	V	-5.7	0.0	0.0	2	2	2
2	1	V	-5.3	1.691	1.812	3	3	3
3	1	V	-5.1	3.845	6.248	1	1	1
4	1	V	-5.1	2.259	6.637	1	1	1
5	1	V	-5.0	2.01	6.209	0	0	0
6	1	V	-4.9	2.338	6.89	1	1	1
7	1	V	-4.9	2.074	3.734	1	1	1
8	1	V	-4.9	2.632	6.349	1	1	1
9	1	V	-4.8	2.356	6.662	1	1	1
10	1	V	-4.7	1.298	6.813	2	2	2
11	2	V	-5.1	0.0	0.0	0	0	0
12	2	V	-5.0	0.985	1.033	0	0	0
13	2	V	-5.0	2.048	6.427	0	0	0
14	2	V	-4.8	2.532	6.678	1	1	1
15	2	V	-4.5	2.915	6.479	0	0	0
16	2	V	-4.4	2.185	6.785	0	0	0
17	2	V	-4.2	1.391	6.833	0	0	0
18	2	V	-4.2	2.883	5.939	0	0	0
19	2	V	-4.1	1.789	2.63	0	0	0
20	2	V	-3.9	2.634	5.173	0	0	0
21	3	V	-4.0	0.0	0.0	0	0	0
22	3	V	-1.8	2.388	6.988	3	3	3
23	3	V	-1.0	1.674	6.572	0	0	0

Fig.1: The hydrogen bonds of best fitted model of ligand (usnic acid) and protein (Aap) docking.



V. CONCLUSION

The successful in silico docking of ligand (usnic acid) and cell associated protein proves the potential of usnic acid as an disinfectant of commercial purpose.

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