IN SILICO EVALUATION OF EFFICIENCY OF COMPOUNDS FROM THE MEDICINAL PLANT PRUNUS PERSICA AGAINST ERYTHRASMA

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***Abstract* :** Bacterial infections are common among many medical complications and one such type is erythrasma, which affects the folds of the skin (intertriginous area). This chronic superficial infection was caused by the organism *Corynebacterium minutissimum*. The lesion initially appears to be pink, as it progresses quickly and becomes brown and scaly. The aim of the present study is to identify drugs from plant sources, specifically against tetrahydrodipicolinate *N*-succinyltransferase (DapD) protein involved in the biosynthesis of L-lysine (PDB ID: 53ER). The secondary metabolites from the medicinal plant *Prunus persica* was selected and analysed in the present study. The phytocompounds reported in the literature for its presence were retrieved from PubChem database and the docking studies were carried out to observe the binding efficiency with the target protein. Among the compounds, chlorogenic acid had the G-Score of -7.56 kcal/mol and interactions were observed with Ser-325, His-185, Lys-207 and Asp-322. The future perspective of the study is to evaluate the antibacterial efficiency of the plant extracts against *C. Minutissimum* through *in vitro* techniques.

KEYWORDS

Erythrasma, *Corynebacterium minutissimum*, Tetrahydrodipicolinate N-Succinyltransferase, *Prunus persica*, Molecular docking studies, Chlorogenic acid.

I. INTRODUCTION:

Erythrasma is a superficial chronic skin infection caused by *Corynebacterium minutissimum* results in the formation of brown, scaly skin patches. The organism is a Gram positive, non-spore forming facultatively anaerobic bacillus bacteria[1]. Based on the infection, the types of erythrasma are classified as generalized and interdigital erythrasma where the former affects the people affected with type 2 diabetes mellitus and obese. Generalized erythrasma also prevails among the population in warm climates and aggravate the worse situation when tight cloths are worn. In interdigital erythrasma the infection mostly affects the skin folds, feet and shows severe symptoms[3]. At early pink lesions emerge and progresses in the formation of brown and scaly patches. The erythrasmic patches are found in the interspaces of the toes and intertriginous areas like arm pits, groins, underbreast and areas where the skin rubs against each other. Erythrasma is often misdiagnosed and confused with dermatophytic infection, mycosis and tinea infections [4]. Human population from tropical and subtropical areas are mostly affected as well as the elderly people are more susceptible due to their weakened immune system. Though the causative organism was identified as *C. minutissimum*, very less information regarding its pathogenesis were observed. In addition, the organism were found in the formation of lesions, subcutaneous abscesses, cutaneous fistulas[5,6], baceteremia[7] among the patients affected with HIV, other immunodeficiency diseases, people undertaking cancer treatment and also patients of chronic, acute myeloid leukemia. Antimicrobial resistance is another consequences posed by the organism against the existing antibiotics[1]. Although the organism was identified as causative for erythrasma since in 1961, the complete knowledge on the organism was lacking. Bioinformatics an emerging field in analyzing the biological concepts using computer techniques aids in the study of genes, their products and genomes of *C. minusitissimum*. This would help in identifying significant, effective drug molecules against potent protein targets. One such vital component is the L-Lysine, which is synthesized only by the bacteria's and yeast would serve greater in the development of unique target drugs[8]. There are two different pathways for the biosynthesis: diaminopimelic acid (DAP) and aminoadipic acid (AAA) pathways. In the present study, enzyme tetrahydrodipicolinate *N*-succinyltranferase (DAPD) was selected as target[9]. In recent years, the scientific evaluation of plant's secondary metabolites is famous and the medicinal plant *Prunus persica* was studied for antibacterial activity against the target protein. The plant *Prunus persica* belongs to the family Rosaceae[10], in which the compound chlorogenic acid is predominantly present in the peel and pulp of the fruit, which showed significant antibacterial activity[11].

METHODS AND MATERIALS:

The 3D structure of the target protein tetrahydrodipicolinate *N*-succinyltranferase (DAPD) was retrieved from the Protein Data Bank (PDB) database of respective PDB ID: 53ER. The compounds of number 63 from the plant *Prunus persica* were retrieved from Pubchem database. First and foremost the plant compounds were predicted for its ADME (Absorption, Distribution, Metabolism, Excretion) using Qikprop module of Schrodinger software. The compounds were further analyzed for its binding efficiency with the target protein through molecular docking studies. The Glide module of Schrodinger was utilized, where the protein was first prepared by removing the water molecules, energy minimized and optimized. The compounds were as well prepared by defining the chirality and flexibility of rotatable bonds. The grid was generated with the predicted active site

residues for studying the binding efficiency with the selective residues. After the completion of docking process, the compound-target protein complex was observed using Pymol viewer software. The active sites were predicted using Ligsite, an online tool.

RESULT AND DISCUSSION:

The compounds retrieved were tabulated (Table 1) along with the pubchem ID of respective chemical molecules, ADME properties predicted. Among 63, only 51 compounds obeyed the Lipinski's rule of five or thumb rule, i.e the drug like molecules should possess molecular weight of 500dalton, hydrogen bond donor, acceptor of 5, 10 respectively and the water/octanol coefficient should be less or equal to 5. Therefore, these fifty one compounds were docked, from which thirty seven compounds showed efficient binding. The compound chlorogenic acid had least G-SCORE of-7.56 Kcal/mol, which formed 4 hydrogen bond each interacted with the amino acid residues ser325, his185, lys207 and asp322 with the respective bond length 2.1, 1.9, 1.8 and 1.5Å (Table 2). The compound structure as well as the interactions of ligand with target protein was shown in Figure1 (Fig. 1A adn 1B).

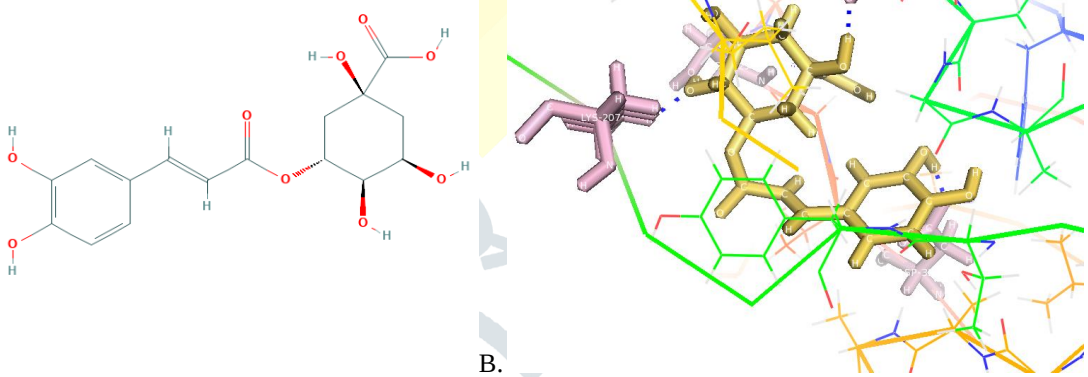
Table 1: ADME Properties of Plant compounds of *Prunus persica*

S.no	molecule	mol_MW (Molecular weight)	donorHB (Donor - Hydrogen Bonds)	accptHB (Acceptor - Hydrogen Bonds)	QPlogPo/w	QPlogBB (Predicted brain/blood partition coefficient)	Human Oral Absorption	Percent Human Oral Absorption	Rule of Five	Rule of Three
	Compound ID (pubchem CID)	**130 - 725**	**0 - 6**	**2.0 - 20.0**	**–2.0 – 6.5**	**–3.0 – 1.2**	**1- Low, 2- Medium, 3- High**	**>80% is high <25% is poor**	**Maximum 4**	**Maximum 3**
1	311	192	3	5.8	0.2	-1.8	1	21.3	0	1
2	370	170	4	4.3	-0.6	-1.7	2	41.5	0	1
3	525	134	2	4.7	-0.4	-1.4	2	35	0	1
4	2355	216	0	3.8	1.5	-0.1	3	**94.9**	0	0
5	2519	194	0	5	-0.1	-0.3	3	**80.8**	0	0
6	2519	194	0	5	-0.1	-0.3	3	**81.1**	0	0
7	2543	310	1	1.5	5.6	-0.1	1	**100**	1	1
8	6199	186	0	3	1	0	3	**91.8**	0	0
9	6549	154	1	0.8	3.1	0.1	3	**100**	0	0
10	6755	174	0	6	-0.7	-0.6	2	68.2	0	0
11	6989	150	1	0.8	3.3	0.1	3	**100**	0	0
12	7461	136	0	0	4	0.9	3	**100**	0	0
13	9064	290	5	5.5	0.5	-1.8	2	61	0	1
14	10205	188	0	3.8	0.8	-0.6	3	**80.3**	0	0
15	10748	176	0	3.3	1.1	-0.1	3	**92.4**	0	0
16	16590	146	0	1	3.4	0.2	3	**100**	0	0
17	26229	187	1	2.8	1.9	-0.4	3	79.2	0	0
18	31253	136	0	0	4.6	0.9	3	**100**	0	0
19	61041	150	0	2	2	0.1	3	**100**	0	0
20	64971	457	2	3.7	6.1	-0.5	1	**93.4**	1	1
21	73145	427	1	1.7	7.1	0.2	1	**100**	1	1
22	86374	226	1	4	2.1	-0.6	3	**95.3**	0	0
23	93147	286	1	1.5	4.9	0	3	**100**	0	1
24	107905	442	7	8	0.4	-3.9	1	22.9	1	2
25	108058	541	0	10.2	3.6	-0.5	3	**91.1**	1	0
26	222757	377	1	4.2	5	-0.4	1	**100**	1	1
27	367617	344	0	8.4	0.8	-0.2	3	**87.5**	0	0
28	439378	174	4	5.5	-3	-1.1	1	22.2	0	1
29	445858	194	2	3.5	1.4	-1.2	3	67.2	0	0
30	969516	368	2	7	2.9	-2.1	3	**85.5**	0	0
31	1794427	354	6	9.7	-0.2	-3.1	1	20.3	1	1
32	5276618	374	0	7.5	1.3	-1.5	3	69.2	0	0
33	5280459	448	6	12.1	-0.5	-2.8	2	16.7	2	2
34	5280794	413	1	1.7	7.5	-0.3	1	**100**	1	1
35	5280863	286	3	4.5	1.1	-1.8	3	64.7	0	0
36	5281426	162	1	3.3	0.7	-0.5	3	**81.1**	0	0
37	5281553	136	0	0	4.6	0.9	3	**100**	0	0

38	5281764	474	6	11	0.8	-6	1	0	2	1
39	5281792	360	5	7	1.2	-3.4	1	40.6	0	1
40	5315472	308	2	5.5	2.6	-2	3	**81.2**	0	0
41	5316673	432	5	11.3	0.1	-2.3	2	40.6	1	0
42	5386591	234	0	5	2.6	0	3	**82.2**	0	0
43	5469789	244	1	1.7	5.1	-0.7	3	**100**	1	1
44	5742590	577	4	10.2	5	-2.3	1	70.7	2	1
45	6440397	312	4	8.2	-0.1	-3.6	1	12.1	0	1
46	6450930	328	2	4	5	-2.3	2	62.9	1	1
47	9881148	234	0	5	2.5	-0.1	3	**81.8**	0	0
48	11095734	204	0	0	5.2	1.1	3	**100**	1	1
49	11980944	368	2	7	2.9	-2.1	3	**85.5**	0	0
50	12305761	418	5	11.7	-0.6	-2.8	1	28.5	1	2
51	100978913	271	1	4.5	2.5	-0.5	3	**81.1**	0	0

Table 2: Interaction of Selected Plant Compound with tetrahydrodipicolinate *N*-succinyltranferase (DAPD)

S. No.	Ligand name	Interacting Residues	Bond Length (Å)	No. of Hydrogen Bonds	G-Score (Kcal/mol)
Prunus persica					
1	Chlorogenic acid	Ser-325 (H-O)	2.1	4	-7.56
		His-185 (O-H)	1.9		
		Lys-207 (H-O)	1.8		
		Asp-322 (O-H)	1.5		



A. B.

Fig.1: A. Structure of Chlorogenic acid from the plant Prunus persica, B. Pymol view of DAPD-chlorogenic acid complex

Note: The pink coloured molecules represent the amino acid residues, the yellow coloured molecule represents the ligand and blue dotted lines represent the hydrogen bond formation between the ligand and respective aminoacid residues.

Recently, the various secondary metabolites of *Withania somnifera* was analyzed for tetrahydrodipicolinate *N*-succinyltransferase protein indicated the efficiency of 4-B-hydroxywithanolide, 2-3 dihydowitaferin A, withanoloide E, Withanoloide D and withanoloide F in interacting the target protein and high probability towards the development of new drug[12]. The enzyme and the respective gene was targeted in the case of treating Mycobacterium tuberculosis[13].

CONCLUSION:

The study shows the efficient binding of the plant compound with the active amino acid residues of tetrahydrodipicolinate *N*-succinyltranferase (DAPD). The future perspective of this study is to provide this significant plant compound for treating erythrasma.

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