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Molecular Docking Studies of Alkaloids from *Desmodium triflorum* against Bacterial Proteins

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Abstract

Considering the current increase of antibiotic resistance, as alternatives to try the alkaloids from *D. triflorum* as antimicrobial compounds by molecular docking studies. The bacterial proteins were downloaded from Protein Data Bank with PDB id: 1UAG, 2X5O, 3UDI and 3TYE. The 2D structures of the ligands were drawn using Chemdraw 8.0. Docking was carried out using the softwares Pyrex, Chimarh, and Discovery. Among all the compounds indole-3-acetic acid and hypaphorine showed very good scores with the proteins 1UAG, 2X5O, 3UDI and 3TYE bacterial proteins. The proteins are involved in the cell wall synthesis, protein and nucleic acid synthesis. This shows that the antibacterial activity of the compounds of *D. triflorum* may be due to the inhibition of cell wall synthesis as well as protein and nucleic acid synthesis of the bacteria.

Key words *Desmodium triflorum;* Leguminosae; docking; bacterial proteins.

INTRODUCTION

Desmodium triflorum (L.) DC (Fabaceae/Leguminosae) a medicinal plant is a very small terrestrial, annual, prostrate herb, found in tropical countries including India, Srilanka, Philippines and Taiwan. The leaves are used in diarrhea, convulsions and as a galactagogue [1]. The fresh juice of the plant is also recommended for use in dysentery and as a laxative [2]. Dried powder of whole plant was taken on empty stomach is useful in curing bone fracture [3]. *Desmodium triflorum* contains chemical constituents Ursolic acid, Vitexin, Genistin, Fucosterol and rare diholosylflavane, 2-Glucosylvitexin. Leaves contains alkaloids like Phenethylamine(major alkaloid), Indole-3-acetic acid, Tyrumine, Trigonelline, Hypaphorine and Choline. Root contains Hypaphorine (major alkaloid), N, NDimethyl tryptophan betaine and Choline [8]. It was reported for its antibacterial activity also. The inhibition of cell wall synthesis, inhibition of protein synthesis, inhibition of nucleic acids synthesis and antimetabolites [12] are the mechanisms followed by the antimicrobial agents.

Considering the current increase of antibiotic resistance, the requirement of novel compounds to treat infections with lower side effects becomes important. In this regard, the alkaloids from *D. triflorum* were tried as antimicrobial compounds although their mechanisms of action are not known. Herein, we intended to extend the knowledge on possible interactions between these compounds and target proteins that would allow understanding and describing the mechanism of action.

MATERIALS AND METHODS

Molecular docking studies being carried out using 8 compounds which have been reported already in previous works. Four different bacterial proteins are used for docking studies, namely 1UAG, 2X5O, 3UDI involved in cell wall synthesis and 3TYE which is involved in the synthesis of dihydrofolic acid. The softwares used are Chemdraw, Pyrx, Chimera, and Discovery.

Preperation of the protein

The bacterial proteins were downloaded from Protein Data Bank with PDB id: 1UAG, 2X5O, 3UDI and 3TYE.

Structure of the ligands

The 2D structures of the ligands were drawn using Chemdraw 8.0

Molecular Docking

Docking was carried out using the softwares Pyrex, Chimarh, and Discovery.

RESULTS AND DISCUSSION

In the present work, the knowledge on target proteins of standard antibiotics is extended to the phytoconstituents identified from *D. triflorum*. Docking studies are performed for all the eight compounds present in order to evaluate their affinity to bacterial proteins that are known targets for some antibiotics with different mechanism of action. The compounds present in *D. triflorum* prove to be particularly interesting sources of bioactive compounds. The docking results of the eight compounds reported from *D. triflorum* and the corresponding 3-D figures are presented below. Among all the eight compounds indole-3-acetic acid and hypaphorine showed very good scores with the proteins 1UAG and 2X5O bacterial proteins. Thus the results were give in the below (Table 1).

Indole-3-acetic acid showed very good interactions with the 1UAG, 2X5O, 3UDI and 3TYE and have a binding score of -5.8, -5.8, -6.0 and -5.7 K cal/mole respectively. It showed hydrogen bonding with SER 264 of 1UAG, with ASN:268 and SER:264 of 2X5O, with GLN285 and ILE 241 of 3UDI and with ASN147 and ALA190 of 3TYE. In addition to this this also showed alkyl-pi alkyl interactions, pi-pi stacked and pi-cation interactions with the proteins (Fig 1). Likewise hypaphorine showed binding scores of -6.9, -5.9, -6.3 and -6.0 K cal/mole with 1UAG, 2X5O, 3UDI and 3TYE proteins respectively. It exhibited hydrogen bonding with THR270 of 1UAG, LEU199 of 2X5O, TRP123 of 3TYE. Further here there are more hydrophobic interactions (Fig 2). Both the proteins are

involved in the cell wall synthesis. This shows that the antibacterial activity of the compounds of *D. triflorum* may be due to the inhibition of cell wall synthesis of the bacteria.

Table 1. Molecular docking studies of the compounds from *D. triflorum* against the proteins 1UAG, 2X5O, 3UDI and 3TYE.

Ligands	Docking Details	1UAG	2X5O	3UDI	3TYE
β-phenethylamine	Binding score (K cal/mol)	-3.9	-4.8	-4.9	-4.9
	Conventional H-bond	THR:321	-	GLU:281	GLY:188
	Alkyl and pi-alkyl	ALA:414	-	-	-
	Others	PHE:422 (Pi-Pi T-shaped)	PHE:303 (Pi-Pi stacked)	GLU:281	PHE:71 (Pi-Pi stacked)
S-(-)-Stachydrine ,	Binding score (K cal/mol)	-4.2	-4.1	-5.1	-4.2
	Conventional H-bond	SER:264, HIS:267	ALA:328 ASN:331	ASN:416	ARG:254
	Alkyl and pi-alkyl	LEU:333 PHE:303	PHE:303 HIS:267	PRO:243	LYS:220 PRO:69
	Others	-	-	-	THR:67
Tyramine	Binding score (K cal/mol)	-4.1	-4.1	-4.3	-4.5
	Conventional H-bond	LEU:330,333 VAL:335	ASN:113, 271 HIS:267	VAL:391,389	THR:67
	Alkyl and pi-alkyl	-	-	-	-
	Others	-	-	-	-
Indole-3-Acetic acid	Binding score (K cal/mol)	-5.8	-5.8	-6	-5.7
	Conventional H-bond	SER:264	ASN:268 SER:264	GLN:285 ILE:241	ASN:147 ALA:190
	Alkyl and pi-alkyl	-	PHE:303	-	-
	Others	PHE:303(Pi-Pi stacked) HIS:267(Pi- cation)	-	GLU:281	PHE:71 (Pi-Pi stacked) PHE:189
Hypaphorine	Binding score (K cal/mol)	-6.1	-5.9	-6.3	-6.0
	Conventional H-bond	THR:270	LEU:199	-	TRP:123
	Alkyl and pi-alkyl	-	-ILE:220	LYS:137 LEU:141	-
	Others	ASP:213, ASN:211 (C-H Bond)	ARG:221 (C-H Bond)	ALA:181	PHE:71
DMT-N-oxide	Binding score (K cal/mol)	-4.7	-5.1	-5.0	-5.6
	Conventional H-bond	VAL:335	LEU:330,333 ASN:360, GLY:332	-	TRP:123
	Alkyl and pi-alkyl	LEU:333,339	LEU:333,339 VAL:335,364	-	-
	Others	VAL:335, LEU:330 (C-H bond)	-	PHE:422 TRP:429	PHE:71 TYR:103 PHE:189
Hordenine	Binding score (K cal/mol)	-4.4	-4.9	-5.6	-5.3
	Conventional H-bond	-	THR:270, HIS:267	-	-
	Alkyl and pi-alkyl	ALA:328	ALA:328	ALA:66 PRO:184	PRO:184 ALA:66
	Others	ASN:331 (Pi Donor H bond)	GLY:324(C-H Bond) HIS:267(Pi-Pi T shaped)	LYS:137	LYE:137
Trigonelline	Binding score (K cal/mol)	-4.7	-4.7	-4.8	-4.8
	Conventional H-bond	LEU:333	LEU:333	-	-
	Alkyl and pi-alkyl	LEU:333,339	LEU:333,339, 330	-	-
	Others	LEU:330(C-H Bond)	LEU:330	PRO:243	PRO:243

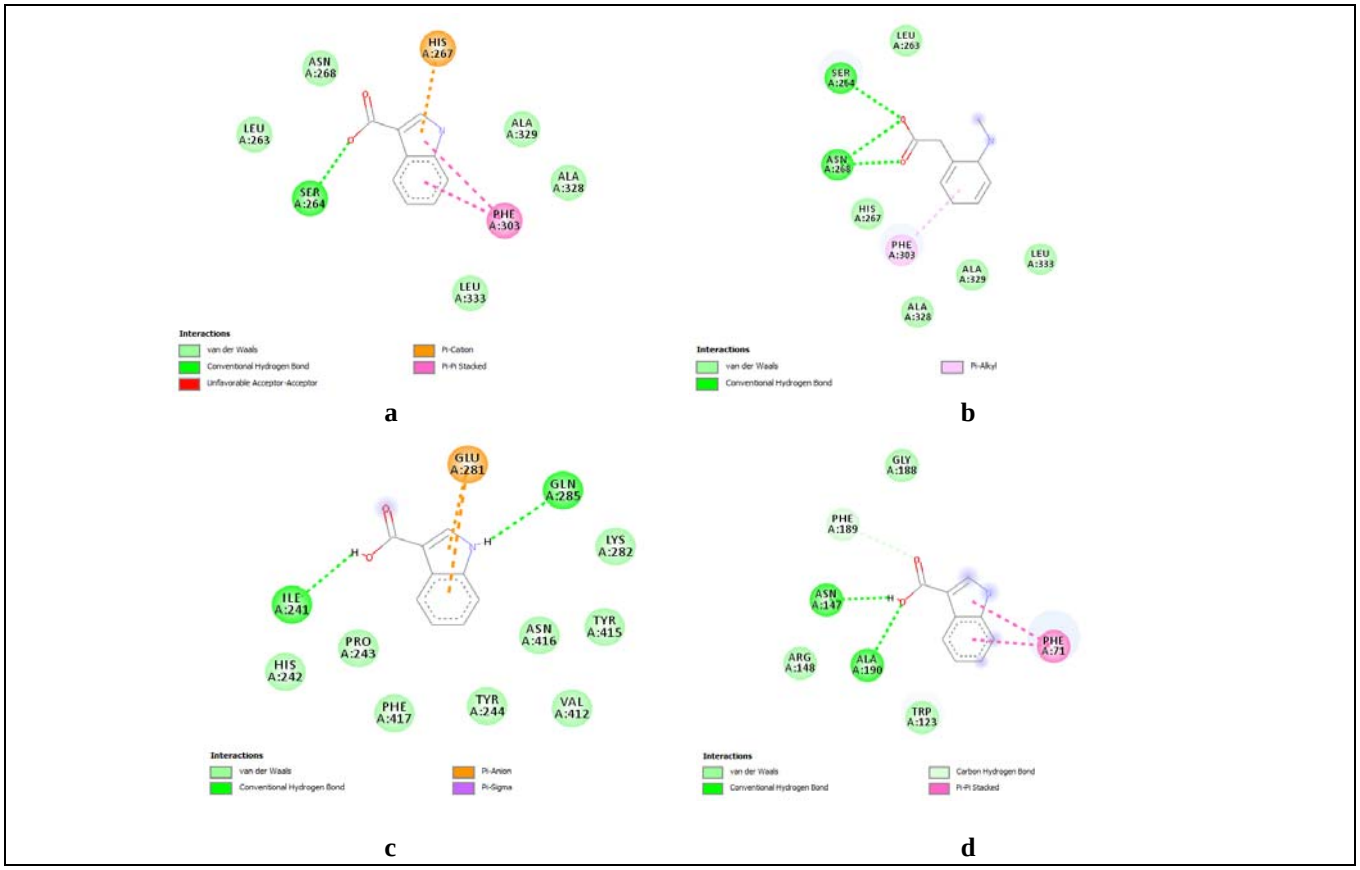

Figure 1. Molecular docking of Indole-3-Acetic acid against the bacterial proteins a. 1UAG, b. 2X5O, c. 3UDI and d. 3TYE.

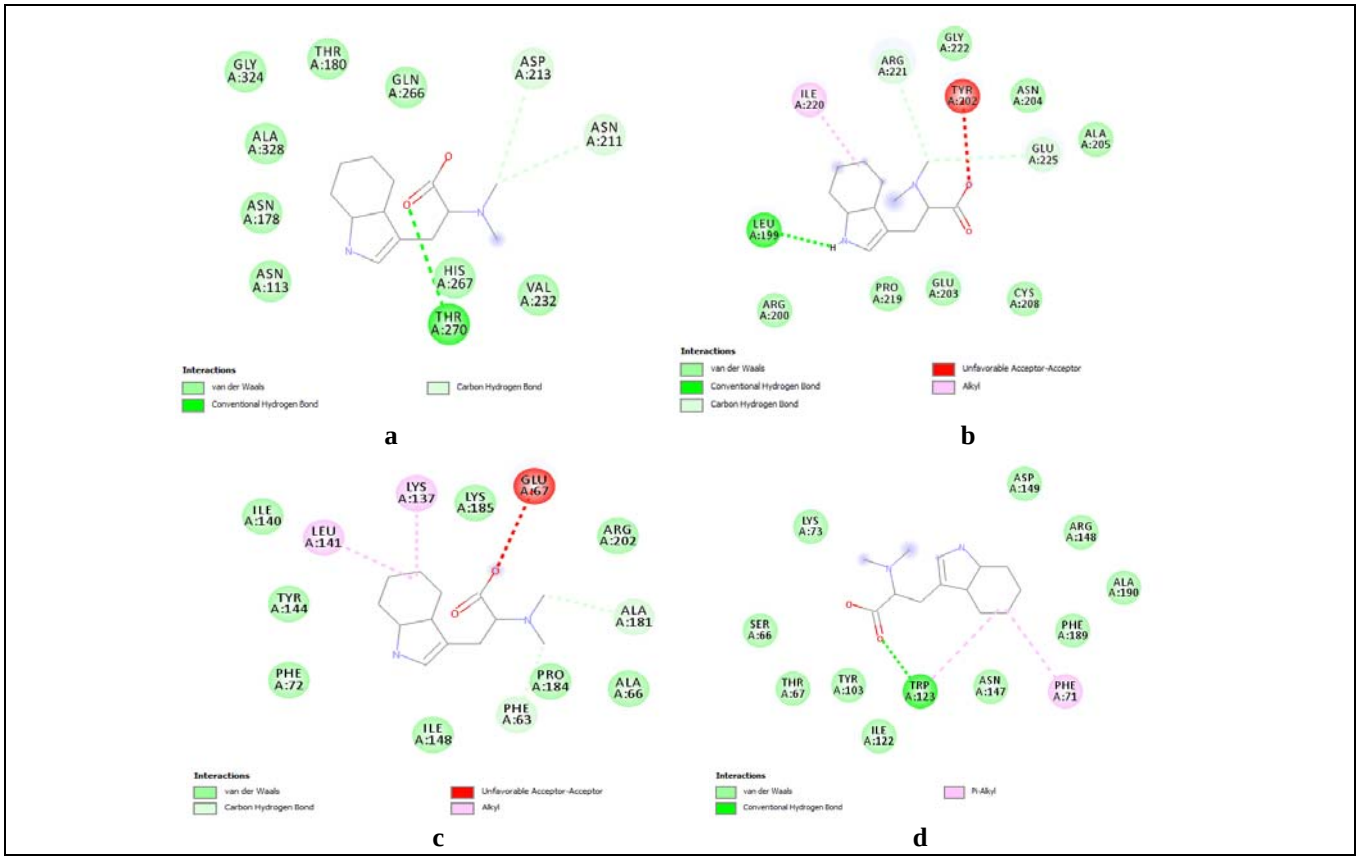

Figure 2. Molecular docking of Hypaphorine Indole-3-Acetic acid against the bacterial proteins a. 1UAG, b. 2X5O, c. 3UDI and d. 3TYE.

CONCLUSION

The compounds reported from *Desmodium triflorum* were subjected to molecular docking studies with bacterial proteins 1UAG, 2X5O, 3UDI and 3TYE. Among all the compounds indole-3-acetic acid and hypaphorine showed very good scores with the proteins 1UAG, 2X5O, 3UDI and 3TYE bacterial proteins. The proteins are involved in the cell wall synthesis, protein and nucleic acid synthesis. This shows that the antibacterial activity of the compounds of *D. triflorum* may be due to the inhibition of cell wall synthesis as well as protein and nucleic acid synthesis of the bacteria.

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