Research Article

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MOLECULAR DOCKING ANALYSIS OF JATAMANSONE WITH MONOAMINE OXIDASE-A RECEPTOR: EXPLORING ITS POTENTIAL NEUROPROTECTIVE ACTIVITY

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ABSTRACT

Background: Neurodegenerative and neuropsychiatric disorders are closely associated with oxidative stress, mitochondrial dysfunction, neuroinflammation, and altered monoamine neurotransmission. Monoamine Oxidase-A (MAO-A), a mitochondrial enzyme responsible for the oxidative deamination of serotonin, dopamine, and norepinephrine, contributes to neuronal damage when overactivated. Herbal phytocompounds have emerged as promising neuroprotective agents due to their multitarget actions and favourable safety profiles. Aim: To evaluate the neuroprotective potential of Jatamansone from *Nardostachys jatamansi* through molecular docking interaction with the MAO-A receptor. Materials and Methods: This *in silico* molecular docking study used the three-dimensional structure of Jatamansone obtained from the PubChem database and the crystal structure of MAO-A retrieved from the Protein Data Bank. Ligand and receptor structures were prepared and converted into PDBQT format. Molecular docking was performed using AutoDock Vina via the Webina platform. Binding affinity, docking conformations, and Root Mean Square Deviation (RMSD) values were analysed to assess interaction stability. Results: Jatamansone exhibited significant binding with the MAO-A receptor. The best docking pose showed a binding affinity of −8.351 kcal/mol, indicating strong ligand–receptor interaction. RMSD values below 2 Å for major docking poses suggested stable and reliable binding. The interaction profile supports the potential inhibitory activity of Jatamansone against MAO-A. Conclusion: Jatamansone demonstrated promising neuroprotective potential through stable interaction with the MAO-A receptor. These findings provide computational evidence supporting its possible therapeutic role in neurodegenerative and neuropsychiatric disorders, warranting further experimental validation.

Keywords: Jatamansone, Neuroprotection, Molecular Docking, MAO-A, Phytocompound, *Nardostachys jatamansi*

INTRODUCTION

Neurological disorders represent a major global burden on healthcare systems[1]. The term "Neurotransmitter disorders" refers to a broad and increasingly complex group of neurological conditions resulting from abnormalities in the synthesis, transport, release, and reuptake of various chemical mediators involved in neural communication[2]. Among the various molecular targets implicated in neuronal degeneration, Monoamine Oxidase-A (MAO-A) plays a critical role in regulating neurotransmitter metabolism.

Monoamine oxidases (MAOs) are outer mitochondrial membrane-bound flavoprotein enzymes responsible for the oxidative deamination of endogenous biogenic amines and exogenous xenobiotic amines[3]. Monoamine oxidase-A (MAO-A) and monoamine oxidase-B (MAO-B) inhibitors are widely utilised in clinical practice for the management of psychiatric and neurological disorders, respectively[4]. Therefore, MAO-A inhibition has emerged as an important therapeutic strategy in the management of neurodegenerative and neuropsychiatric disorders.

Currently available synthetic MAO inhibitors are associated with several adverse effects, including hepatotoxicity, cardiovascular complications, dependency, and dietary interactions. Consequently, natural phytocompounds with neuroprotective and antioxidant activities have attracted considerable scientific interest because of their multitarget therapeutic mechanisms and improved tolerability.

Nardostachys jatamansi is an important medicinal herb traditionally used in Siddha and Ayurvedic systems for neurological disorders, mental stress, epilepsy, insomnia, cognitive dysfunction, and psychiatric disturbances. It is widely recognised for its beneficial effects on neurological and cognitive functions[5]. Jatamansone, one of the major sesquiterpene constituents of *Nardostachys jatamansi*, has been reported to possess antioxidant, anxiolytic, antidepressant, anti-inflammatory, and neuroprotective properties[6]. However, molecular evidence regarding its interaction with the Monoamine Oxidase-A receptor remains limited.

Molecular docking has become an important computational approach in modern drug discovery for predicting ligand-receptor interactions, binding affinity, and molecular stability. Docking studies help identify potential pharmacological activity and facilitate preliminary screening of bioactive compounds before experimental validation.

Therefore, the present study was undertaken to investigate the neuroprotective potential of Jatamansone, a major phytoconstituent of *Nardostachys jatamansi*, through molecular docking interaction with Monoamine Oxidase-A (MAO-A) receptor. The study aimed to evaluate the ligand–receptor binding affinity, analyse docking stability using RMSD values, and explore the possible inhibitory interaction of Jatamansone with MAO-A as a potential therapeutic target in neurological and neuropsychiatric disorders.

MATERIALS AND METHODS

Study Design

The present study was conducted as an *in silico* molecular docking analysis to evaluate the interaction between Jatamansone and the Monoamine Oxidase-A receptor.

Software and Databases Used

Table 1: Software and Databases Used in the Study

Category	Software/Database	Purpose
Chemical Database	PubChem	Ligand retrieval
Protein Database	Protein Data Bank (PDB)	Receptor retrieval
Docking Software	AutoDock Vina (Webina)	Molecular docking
File Conversion Tool	Open Babel	Format conversion
Visualization Tool	Discovery Studio / PyMOL	Interaction visualization

Ligand Preparation

The three-dimensional structure of Jatamansone was retrieved from the PubChem database in Structure Data File (SDF) format. The ligand structure was converted into Protein Data Bank (PDB) format and subsequently converted into PDBQT format using Open Babel software for docking compatibility.

The ligand was maintained in its three-dimensional conformational state to preserve molecular geometry during docking analysis.

Table 2: Ligand Details[7]

Parameter	Description
Ligand Name	Jatamansone
Source Plant	*Nardostachys jatamansi*
Chemical Class	Sesquiterpene
Molecular Weight	222.37 g/mol
Molecular Formula	$C_{15}H_{26}O$
H-Bond Donor Count	0
H-Bond Acceptor Count	1
Rotatable Bonds	1
Database	PubChem
Input Format	SDF
Docking Format	PDBQT

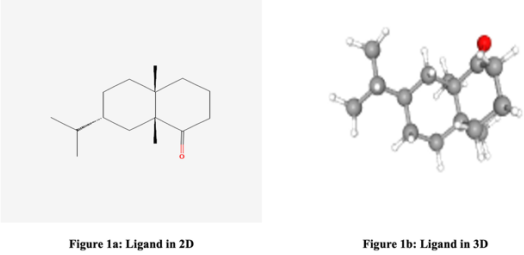

Figure 1a: Ligand in 2D Figure 1b: Ligand in 3D

Figure 1: Two-dimensional (2D) and three-dimensional (3D) chemical structures of Jatamansone retrieved from the PubChem database and utilised for molecular docking analysis.

Receptor Preparation

The crystal structure of the Monoamine Oxidase-A receptor was obtained from the Protein Data Bank. The receptor structure was converted into docking-compatible PDBQT format.

The receptor was retained in its native crystallographic conformation to preserve structural integrity and conserved molecular interactions during docking analysis.

Table 3: Receptor Details[8]

Parameter	Details
Protein Name	Monoamine Oxidase A (MAO-A)
PDB ID	2Z5X
Organism	Homo sapiens (Human)
Classification	Oxidoreductase
Experimental Method	X-ray Diffraction
Resolution	2.20 Å
Database	RCSB Protein Data Bank
Enzyme Type	Flavoprotein enzyme
Cellular Location	Outer mitochondrial membrane

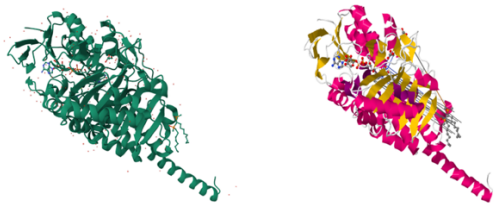

Figure 2a. Mol*(WebGL) Figure 2b. JSmol (JavaScript)

Figure 2: Three-dimensional crystal structure of human Monoamine Oxidase-A (MAO-A) receptor (PDB ID: 2Z5X) retrieved from the Protein Data Bank for molecular docking analysis.

Molecular Docking Procedure

Molecular docking analysis was performed using AutoDock[9] Vina implemented through the Webina platform[10]. A blind docking methodology was employed to evaluate possible ligand-binding conformations across the receptor surface.

The docking algorithm generated multiple binding poses based on ligand flexibility and receptor compatibility. Binding affinity values were expressed in kcal/mol.

Table 4: Docking Parameters

Parameter	Details
Docking Tool	AutoDock Vina
Platform	Webina
Docking Type	Blind Docking
Number of Modes Generated	6
Energy Unit	kcal/mol
Scoring Function	Vina Scoring Function

Docking Analysis

The generated docking conformations were analyzed based on:

- Binding affinity values
- RMSD lower and upper bound values
- Ligand orientation stability
- Conformational similarity
- Potential interaction stability

Binding affinity values with more negative scores were interpreted as stronger ligand-receptor interactions.

RESULTS

Molecular docking analysis was performed to evaluate the interaction between Jatamansone and the Monoamine Oxidase-A (MAO-A) receptor. A total of six docking conformations were generated using AutoDock Vina. The obtained docking poses exhibited binding affinities ranging from −8.351 to −5.376 kcal/mol, indicating favourable interactions between the ligand and the target receptor.

Among all conformations, Mode 1 demonstrated the highest binding affinity of −8.351 kcal/mol, suggesting the most energetically favourable and stable ligand–receptor complex. This docking pose was therefore considered the optimal binding conformation for further interpretation. The negative binding energy value reflects spontaneous interaction and strong binding potential of Jatamansone toward the active site of the MAO-A receptor.

The remaining docking poses also exhibited appreciable binding affinities, with values of −7.104 kcal/mol (Mode 2), −7.071 kcal/mol (Mode 3), −6.778 kcal/mol (Mode 4), −6.220 kcal/mol (Mode 5), and −5.376 kcal/mol (Mode 6). Although these values were lower than those of Mode 1, they indicate the presence of multiple energetically favourable orientations of Jatamansone within the receptor binding cavity.

Table 5: Docking Results of Jatamansone with MAO-A Receptor

Mode	Binding Affinity (kcal/mol)	RMSD L.B	RMSD U.B
1	**−8.351**	0	0
2	**−7.104**	1.719	4.281
3	**−7.071**	1.880	3.436
4	**−6.778**	1.984	4.248
5	**−6.220**	2.412	4.544
6	**−5.376**	1.561	2.821

Analysis of Root Mean Square Deviation (RMSD) values revealed satisfactory docking reliability. Mode 1 showed RMSD lower-bound (L.B.) and upper-bound (U.B.) values of 0.000 Å, indicating that it served as the reference conformation. Modes 2, 3, and 4 displayed RMSD lower-bound values below 2 Å, suggesting conformational similarity and stability relative to the best-ranked pose. Modes 5 and 6 showed slightly higher RMSD values; however, they remained within an acceptable range, indicating reasonable binding consistency and flexibility within the receptor pocket.

The docking results suggest that Jatamansone can effectively occupy the MAO-A binding cavity, demonstrating favourable structural compatibility with the receptor. The presence of multiple stable docking conformations further supports the ligand's adaptability within the active site environment. The strong binding affinity observed for the top-ranked pose indicates a potential inhibitory interaction with the MAO-A enzyme.

DISCUSSION

Monoamine oxidase A (MAO-A) is an enzyme encoded by the MAO-A gene located on the X chromosome in humans and certain primate species, and it plays a crucial role in the metabolism of monoamine neurotransmitters[11]. Monoamine Oxidase-A is an important mitochondrial enzyme involved in the oxidative metabolism of monoamine neurotransmitters. Elevated MAO-A activity has been strongly associated with depression, and MAO-A inhibitors have been reported to exhibit therapeutic efficacy in the management of depression and anxiety disorders[12]. Therefore, MAO-A inhibition has emerged as a major pharmacological target in neuroprotection and neuropsychiatric therapeutics.

Table 6: PDBQT structural coordinates and atomic configuration of Jatamansone used for molecular docking analysis.

ROOT					
ATOM 0.297 OA	1 O	UNL -	1	34.534	30.102 -18.664 0.00 0.00
ATOM +0.140 C	2 C	UNL	1	34.570	31.023 -17.845 0.00 0.00
ATOM +0.075 C	3 C	UNL	1	34.044	32.389 -18.229 0.00 0.00
ATOM +0.008 C	4 C	UNL	1	34.991	33.491 -17.793 0.00 0.00
ATOM +0.008 C	5 C	UNL	1	35.347	33.370 -16.315 0.00 0.00
ATOM 0.020 C	6 C	UNL -	1	35.980	31.996 -15.948 0.00 0.00
ATOM +0.012 C	7 C	UNL	1	37.370	31.905 -16.632 0.00 0.00
ATOM +0.008 C	8 C	UNL	1	36.230	31.958 -14.413 0.00 0.00
ATOM +0.004 C	9 C	UNL	1	34.958	31.864 -13.571 0.00 0.00
ATOM 0.007 C	10 C -	UNL	1	34.070	30.693 -13.996 0.00 0.00
ATOM +0.018 C	11 C	UNL	1	33.765	30.754 -15.500 0.00 0.00
ATOM +0.032 C	12 C	UNL	1	35.039	30.813 -16.387 0.00 0.00
ATOM +0.019 C	13 C	UNL	1	35.755	29.442 -16.312 0.00 0.00
ENDROOT					
BRANCH 10 14					
ATOM 0.014 C	14 C -	UNL	1	32.772	30.685 -13.187 0.00 0.00
ATOM +0.007 C	15 C	UNL	1	32.754	29.506 -12.219 0.00 0.00
ATOM +0.007 C	16 C	UNL	1	31.562	30.637 -14.117 0.00 0.00
ENDBRANCH 10 14					

The table represents atom types, atomic charges, spatial coordinates, and rotatable bond information of the ligand prepared for AutoDock Vina docking simulation.

The present molecular docking study demonstrated significant interaction between Jatamansone and MAO-A receptor with a binding affinity of −8.351 kcal/mol. Binding affinity values below −7 kcal/mol are generally considered indicative of strong ligand-receptor interaction in docking studies. The obtained docking score, therefore, suggests stable interaction and possible inhibitory potential of Jatamansone towards MAO-A enzyme.

The generated docking conformations further demonstrated stable ligand orientation and structural compatibility. RMSD values below 2 Å observed in major docking poses indicate reliable docking prediction and conformational consistency. These findings support the stability of the ligand-receptor complex.

Previous pharmacological investigations have reported antioxidant[13], anxiolytic[14], antidepressant[15], and neuroprotective activities[16] of *Nardostachys jatamansi*. Jatamansone has also been associated with the modulation of oxidative stress pathways and neuronal protection. The present docking findings provide additional computational evidence supporting its neurotherapeutic relevance.

The neuroprotective activity of Jatamansone may be associated with the modulation of monoamine neurotransmitter metabolism and the reduction of oxidative neuronal stress through interaction with the MAO-A receptor. Herbal phytocompounds generally possess multitarget pharmacological activity with relatively lower toxicity compared to synthetic neurotherapeutic agents.

Molecular docking studies provide insights into the binding interaction between a ligand and its target enzyme, including the amino acid residues involved, the nature of molecular interactions, and the binding affinity expressed in terms of binding energy values[17]. However, docking studies alone cannot establish definitive pharmacological efficacy. Further *in-vitro, in vivo*, and clinical investigations are required to validate the neuroprotective mechanism and therapeutic significance of Jatamansone.

CONCLUSION

The present *in silico* molecular docking study demonstrated strong and stable interaction between Jatamansone and Monoamine Oxidase-A receptor, suggesting promising neuroprotective potential. The significant binding affinity and stable docking conformations support the possible therapeutic relevance of Jatamansone in neurological and neuropsychiatric disorders.

The findings provide computational evidence supporting further pharmacological exploration of Jatamansone as a potential neuroprotective phytocompound. Additional experimental studies are necessary to validate its pharmacological efficacy and therapeutic application.

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