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IN SILICO EVALUATION OF PHYTOCONSTITUENTS FROM *NARDOSTACHYS JATAMANSI* AGAINST NMDA RECEPTOR AS POTENTIAL ANTIEPILEPTIC AGENTS

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ABSTRACT

Epilepsy is a chronic neurological disorder affecting nearly 50 million people worldwide, and nearly one-third of patients remain refractory to existing antiepileptic drugs, which are also associated with significant adverse effects. Glutamate-induced excitotoxicity, mediated primarily through overactivation of the NMDA receptor, plays a central role in seizure initiation and progression, making it a promising target for novel anticonvulsant agents. Nardostachysjatamansi (Family: Valerianaceae), a traditional Ayurvedic herb, has long been used for neurological disorders including epilepsy, and its major bioactive constituent, jatamansone, was selected for computational evaluation against this target. In this study, the crystal structure of the NMDA receptor (PDB ID: 7E0S) was retrieved from the RCSB Protein Data Bank and prepared by removing water molecules and heteroatoms, followed by addition of polar hydrogens. The ligand, jatamansone, was optimized and energy-minimized prior to docking. Molecular docking was performed using AutoDockVina in the PyRx interface, and the resulting protein–ligand complex was analyzed using Discovery Studio Visualizer and PyMOL. The best docking pose (Run 4) showed a binding affinity of −6.13 kcal/mol and an estimated inhibition constant (Ki) of 32.18 µM, forming stable hydrogen bond and electrostatic interactions with key active-site residues ARG329, GLU330, ASP333, LYS401, and LYS697. These findings indicate that jatamansone can be accommodated within

the NMDA receptor binding pocket with favorable affinity, supporting its traditional use and suggesting its potential as a lead molecule for antiepileptic drug development, warranting further validation through molecular dynamics and in vitro/in vivo studies.

KEYWORDS: EPILEPSY; Nardostachysjatamansi; Jatamansone; NMDA receptor; Molecular docking; AutoDockVina; PyRx; Discovery Studio Visualizer.

1. INTRODUCTION

Epilepsy is a chronic neurological disorder characterized by recurrent, unprovoked seizures resulting from abnormal and excessive neuronal activity in the brain. It affects nearly 50 million people worldwide and remains a major public health concern. Although numerous antiepileptic drugs (AEDs) are available, approximately one-third of patients continue to experience uncontrolled seizures due to drug resistance. Moreover, long-term use of conventional AEDs is often associated with adverse effects, including cognitive impairment, dizziness, hepatotoxicity, and teratogenicity. These limitations highlight the need for the development of safer and more effective therapeutic agents.

Epilepsy is a multifactorial neurological disorder with significant medical, social, and economic consequences. Recurrent seizures adversely affect cognitive function, psychological well-being, education, employment, and overall quality of life. Despite continuous advances in pharmacotherapy, epilepsy remains inadequately controlled in a substantial proportion of patients, highlighting the need for the identification of novel therapeutic targets and treatment strategies.

Current antiepileptic drugs primarily act by enhancing γ-aminobutyric acid (GABA)-mediated inhibitory neurotransmission, blocking voltage-gated sodium or calcium channels, or suppressing glutamate-mediated excitatory neurotransmission. Although these drugs effectively control seizures in many patients, their long-term use is often associated with adverse effects such as sedation, dizziness, cognitive impairment, hepatic toxicity, tolerance, and teratogenicity. Moreover, nearly 30% of patients develop drug-resistant epilepsy, emphasizing the urgent need for safer and more effective therapeutic agents.

Among the molecular mechanisms involved in epilepsy, glutamate-induced excitotoxicity plays a central role in seizure initiation and progression. Excessive stimulation of ionotropic glutamate receptors, particularly the N-methyl-D-aspartate (NMDA) receptor, increases intracellular calcium concentration, leading to oxidative stress, mitochondrial dysfunction, neuronal injury, and persistent neuronal hyperexcitability. Consequently, modulation of

NMDA receptor activity has emerged as a promising strategy for the development of novel anticonvulsant drugs.

Advances in computer-aided drug design (CADD) have significantly accelerated the early stages of drug discovery. Molecular docking is one of the most widely used computational techniques for predicting the binding orientation, binding affinity, and molecular interactions between a ligand and a target protein. The method enables rapid virtual screening of compounds, identification of key amino acid interactions, and prediction of possible mechanisms of action while reducing the cost and time required for experimental studies.

Molecular docking has become an indispensable tool in natural product research because it provides mechanistic evidence supporting the biological activity of phytoconstituents. The integration of computational studies with pharmacological investigations facilitates the identification of potential lead molecules for further preclinical and clinical development.

Therefore, the present study employed molecular docking to evaluate the interaction of the selected phytoconstituent with the NMDA receptor (PDB ID: 7E0S). Binding affinity, interaction patterns, and key amino acid residues involved in ligand binding were analysed to predict its potential antiepileptic activity and provide a computational basis for subsequent pharmacological evaluation.

2. PLANT PROFILE

Fig :1 Nardostachys jatamansi.

Nardostachys jatamansi DC. (Family: Valerianaceae), commonly known as Indian Spikenard or Jatamansi, is a perennial aromatic medicinal herb widely used in Ayurvedic, Unani, and

Tibetan systems of medicine for the management of neurological disorders. The plant is native to the alpine Himalayan regions of India, Nepal, Bhutan, and China, where it grows at altitudes of 3,000–5,000 m. The dried rhizomes and roots are the medicinally important parts and are valued for their rich content of bioactive phytoconstituents.

Phytochemical investigations have identified several biologically active compounds, including jatamansone (valeranone), nardostachone, nardosinone, sesquiterpenes, flavonoids, lignans, alkaloids, steroids, β-sitosterol, and essential oils. Among these, jatamansone is considered one of the major constituents responsible for the plant's pharmacological activities.

Traditionally, *N. jatamansi* has been used as a brain tonic and for the treatment of epilepsy, anxiety, insomnia, depression, memory impairment, headache, and other nervous system disorders. Recent pharmacological studies have demonstrated that the plant possesses antioxidant, anticonvulsant, neuroprotective, anxiolytic, antidepressant, anti-inflammatory, hepatoprotective, antimicrobial, and memory-enhancing activities. These therapeutic effects are primarily attributed to its diverse phytochemical constituents and their ability to modulate oxidative stress and neuronal signaling pathways.

Owing to its rich phytochemical composition and broad spectrum of neuropharmacological properties, *Nardostachysjatamansi* has attracted considerable attention as a potential source of lead molecules for the development of novel therapeutic agents against neurological disorders, particularly epilepsy.

3. MATERIALS AND METHODS:

3.1 Protein Preparation:

The three-dimensional crystal structure of the N-methyl-D-aspartate (NMDA) receptor (PDB ID: 7E0S) was retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/) in PDB format. The protein structure was prepared by removing water molecules, co-crystallized ligands, and other heteroatoms. Polar hydrogen atoms were added, and the prepared receptor was converted to PDBQT format using AutoDock Tools.

3.2 **Ligand:**

The ligand selected for the study was the phytoconstituent obtained from the ethanolic extract of Nardostachysjatamansi. The ligand structure was prepared in a suitable format for docking after geometry optimization and energy minimization.

3.3 Ligand Preparation

The selected phytoconstituent isolated from the ethanolic root extract of *Nardostachysjatamansi* was used as the ligand. The ligand structure was obtained in SDF/MOL format, subjected to geometry optimization and energy minimization, and subsequently converted into PDBQT format for docking analysis.

3.4 Molecular Docking

Molecular docking was performed using PyRx software employing the AutoDockVina docking engine. The prepared receptor and ligand were imported into the PyRx workspace, and the receptor binding site was defined using a grid box encompassing the active-site residues. Docking simulations were carried out using the default AutoDockVina parameters, and multiple binding conformations were generated. The best docking pose was selected based on the lowest binding free energy (kcal/mol) and favorable protein–ligand interactions.

3.5 Interaction Analysis

The docked protein–ligand complex was analyzed using Discovery Studio Visualizer and PyMOL. Binding affinity, hydrogen bonds, hydrophobic interactions, electrostatic interactions, and amino acid residues involved in ligand binding were evaluated to predict the stability and binding mode of the ligand within the active site of the NMDA receptor.

Table: 1 Interaction Analysis.

Software	Purpose
PyRx	Molecular docking
AutoDockVina	Docking engine
Discovery Studio Visualizer	Protein–ligand interaction analysis
PyMOL	Three-dimensional visualization
RCSB Protein Data Bank	Retrieval of protein structure

3.6 Statistical Analysis

As this investigation was an in silico molecular docking study, no statistical analysis was performed. The docking results were interpreted qualitatively based on the binding pose, interacting amino acid residues, and the docking score generated by the docking software.

3.7 Flow Chart of Methodology

Selection of Nardostachysjatamansi

↓

Preparation of Ethanolic Extract Phytoconstituent

↓

Retrieval of NMDA Receptor (PDB ID: 7E0S)

↓

Protein Preparation

Ligand Preparation
↓
Molecular Docking (AutoDockVina)
↓
Interaction Analysis (Discovery Studio)
↓
Result Interpretation
↓
Evaluation of Potential Anticonvulsant Activity

4. RESULTS

4.1 Molecular Docking Analysis:

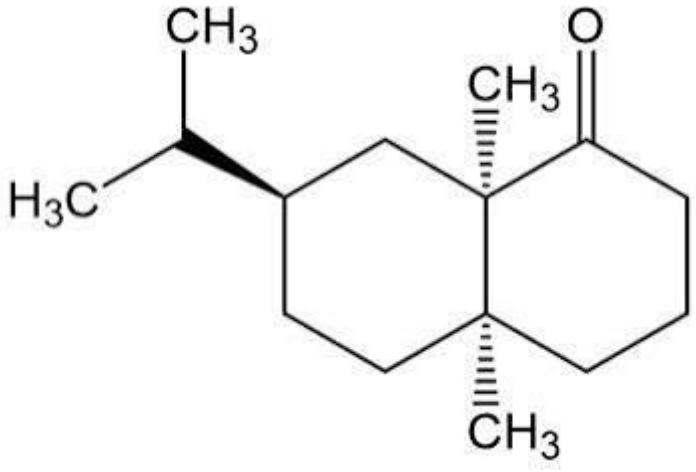

Fig: 2 ligand (jatamansone).

The molecular docking study was performed to evaluate the interaction of Jatamansone with the NMDA receptor (PDB ID: 7E0S). The docking analysis revealed that Jatamansone exhibited favorable binding within the active site of the receptor, with a **best binding affinity of −6.13 kcal/mol**. The ligand formed a stable protein–ligand complex through hydrogen bonding and electrostatic interactions with key amino acid residues, including **ARG329, GLU330, ASP333, LYS401, and LYS697**.

The best docking conformation (Run 4) showed an estimated inhibition constant (Ki) of **32.18 µM**, suggesting moderate binding affinity toward the NMDA receptor. The interaction profile indicated that hydrogen bonds and electrostatic interactions contributed significantly to ligand stabilization within the receptor binding pocket.

Table :1 Molecular Docking Results Of Jatamansone With The NMDA Receptor (PDB ID: 7E0S)

Parameter	Result
Target protein	NMDA receptor (PDB ID: 7E0S)
Ligand	Jatamansone
Docking software	AutoDockVina (PyRx)
Best docking pose	Run 4
Binding affinity	**−6.13 kcal/mol**
Estimated inhibition constant (Ki)	**32.18 µM**

Table :2 Key amino acid residues involved in ligand binding.

Amino acid residue	Interaction type
ARG329	Hydrogen bond / Electrostatic interaction
GLU330	Hydrogen bond
ASP333	Electrostatic interaction
LYS401	Hydrogen bond
LYS697	Electrostatic interaction

The docking results demonstrated that Jatamansone occupied the active binding pocket of the NMDA receptor and established multiple favorable interactions that may contribute to the stability of the protein–ligand complex. These findings suggest the potential of Jatamansone to modulate NMDA receptor activity, supporting its possible anticonvulsant mechanism.

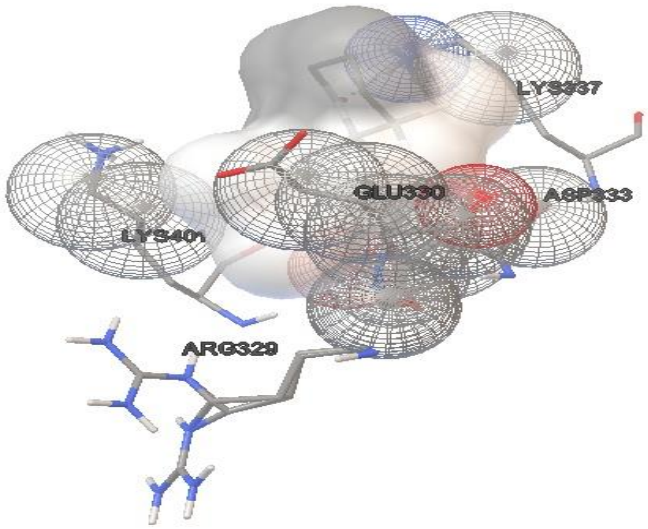

Fig: 3 Three-Dimensional Docking Pose OfThe Phyto-constituent FromThe Ethanolic Extract Of*NardostachysJatamansi* Within The Active Binding Site OfThe NMDA Receptor (PDB ID: 7E0S).

Table: 3 Docking Run Summary Table.

Run	Final Energy(kcal/mol)	Binding Energy(kcal/mol)	Ki(µM)	Intermolecular Energy(kcal/mol)	vdW + H-Bond + Desolvation (kcal/mol)	Electrostatic Energy(kcal/mol)	Internal Energy(kcal/mol)	Torsional Free Energy(kcal/mol)
1	-6.561	-5.97	42.22	-6.27	-5.91	-0.35	-0.29	+0.30
2	-6.567	-5.98	41.29	-6.28	-5.93	-0.35	-0.29	+0.30
3	-6.673	-6.12	32.42	-6.42	-6.44	+0.02	-0.25	+0.30
4	-6.680	-6.13	32.18	-6.43	-6.44	+0.01	-0.25	+0.30
5	-6.565	-5.98	41.40	-6.28	-5.92	-0.35	-0.29	+0.30
6	-6.539	-5.95	43.72	-6.25	-5.89	-0.35	-0.29	+0.30
7	-6.556	-5.97	41.98	-6.27	-5.91	-0.36	-0.29	+0.30
8	-6.606	-6.03	38.15	-6.33	-5.98	-0.35	-0.28	+0.30
9	-6.568	-5.98	41.25	-6.28	-5.93	-0.35	-0.29	+0.30
10	-6.603	-6.03	38.13	-6.33	-6.00	-0.32	-0.28	+0.30

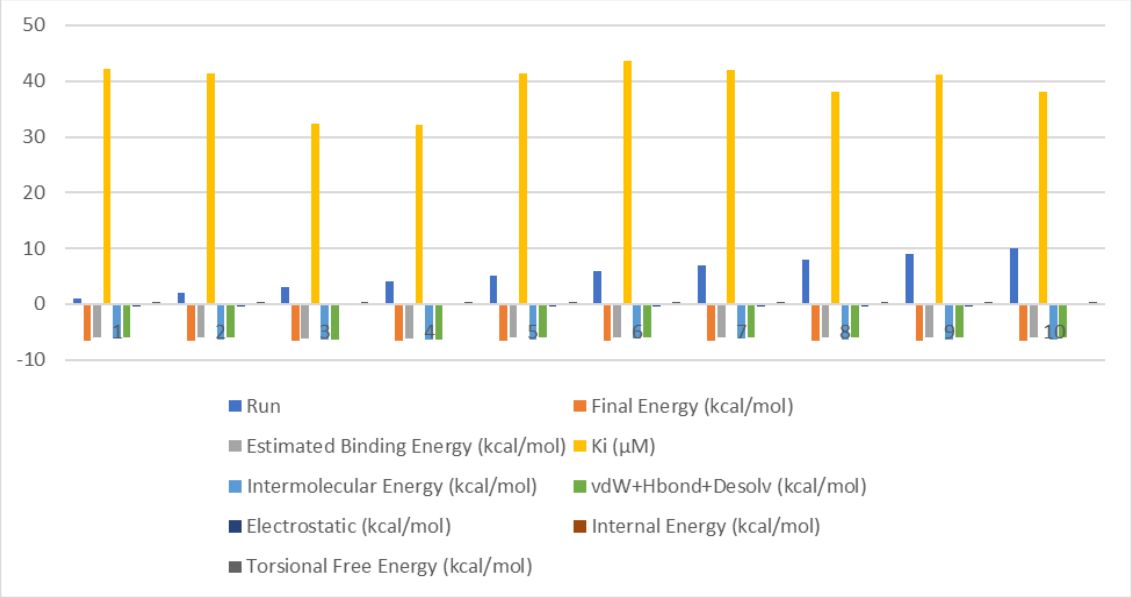

Fig: 4 Docking Run Summary.

Table: 4 Cluster Analysis Table.

Cluster Rank	Sub-Rank	Run No.	Binding Energy (kcal/mol)	Cluster RMSD (Å)	Reference RMSD (Å)
1	1	4	−6.13	0.00	4.92
1	2	3	−6.12	0.09	4.86
1	3	10	−6.03	1.67	4.61
1	4	8	−6.03	1.69	4.64
1	5	9	−5.98	1.69	6.02
1	6	2	−5.98	1.68	6.00
1	7	5	−5.98	1.69	6.01
1	8	7	−5.97	1.70	6.04
1	9	1	−5.97	1.70	5.99
1	10	6	−5.95	1.70	5.99

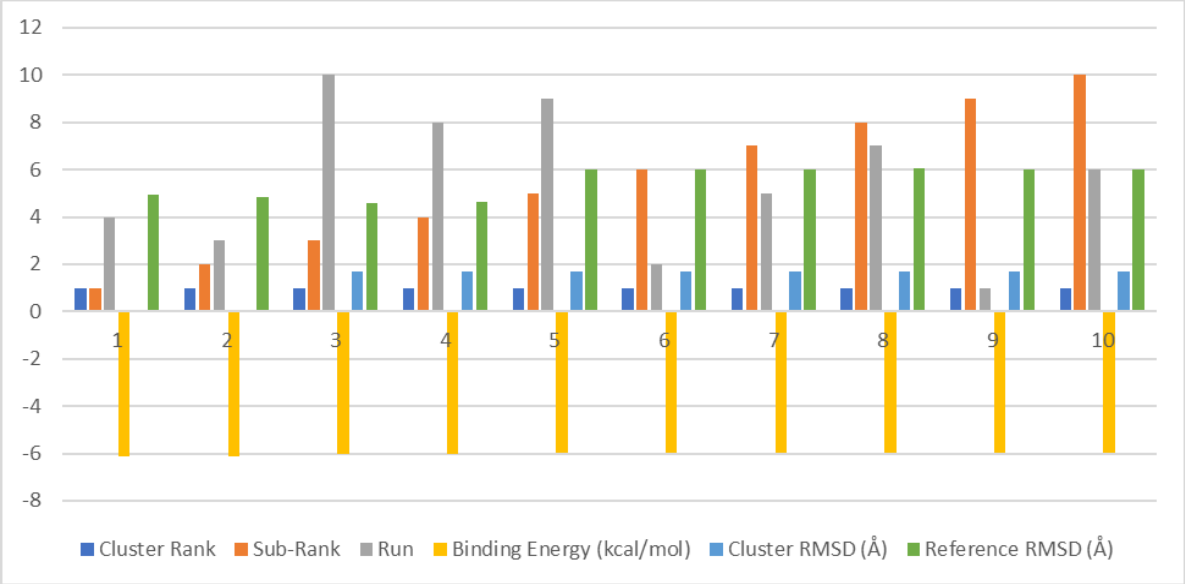

Fig: 5 Cluster Analysis.

Table: 5 Molecular Docking Result of Jatamansone with NMDA Receptor.

Parameter	**Result**
Protein	NMDA Receptor (PDB ID: 7E0S)
Ligand	Jatamansone
Docking Software	AutoDock 4.2.6
Number of Docking Runs	10
Best Binding Energy	−6.13 kcal/mol
Estimated Inhibition Constant (Ki)	32.18 µM
Best Docking Pose	Run 4
Grid Size	60 × 60 × 60
Grid Spacing	0.375 Å

Table: 6 Statistical Analysis Summary.

Parameter	**Value**
Number of Docking Conformations	10
Number of Clusters	1
RMSD Tolerance	2.0 Å
Lowest Binding Energy	−6.13 kcal/mol
Mean Binding Energy	−6.01 kcal/mol
Information Entropy	0.00
Partition Function (Q)	10.10
Free Energy (A)	−1370.25 kcal/mol
Internal Energy (U)	−6.01 kcal/mol
Entropy (S)	4.58 kcal/mol/K
Temperature	298.15 K

Table: 7 Run 4 - Best Binding Conformation. (-6.13 kcal/mol)

Parameter	Value
Translation (X, Y, Z)	(−0.309, 3.334, −4.551) Å
Quaternion (X, Y, Z, W)	(−0.161, 0.537, 0.729, 0.394)
Torsion Angle	68.72°
Intermolecular Energy	−6.43 kcal/mol
van der Waals + Hydrogen Bond + Desolvation Energy	−6.44 kcal/mol
Electrostatic Energy	+0.01 kcal/mol
Internal Energy	−0.25 kcal/mol
Torsional Free Energy	+0.30 kcal/mol
Estimated Inhibition Constant (Ki)	32.18 µM

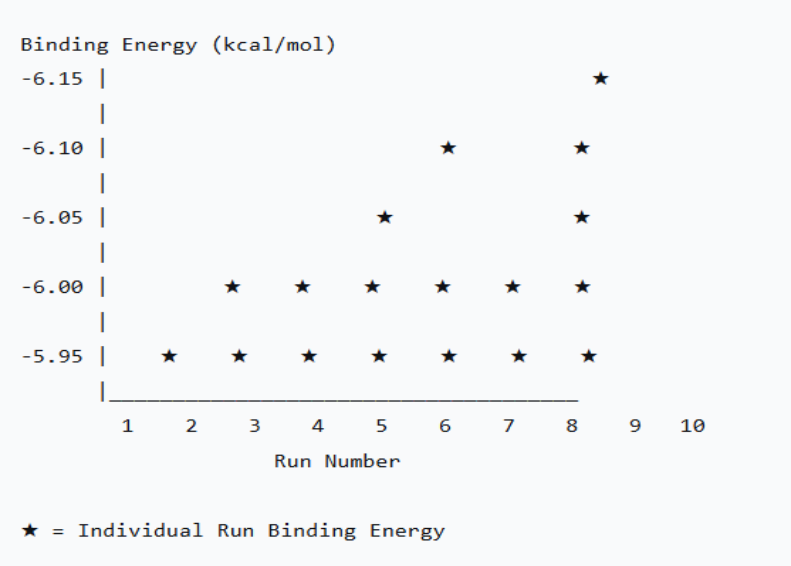

Fig : 6 Graph 1: Binding Energy Distribution Across Runs.

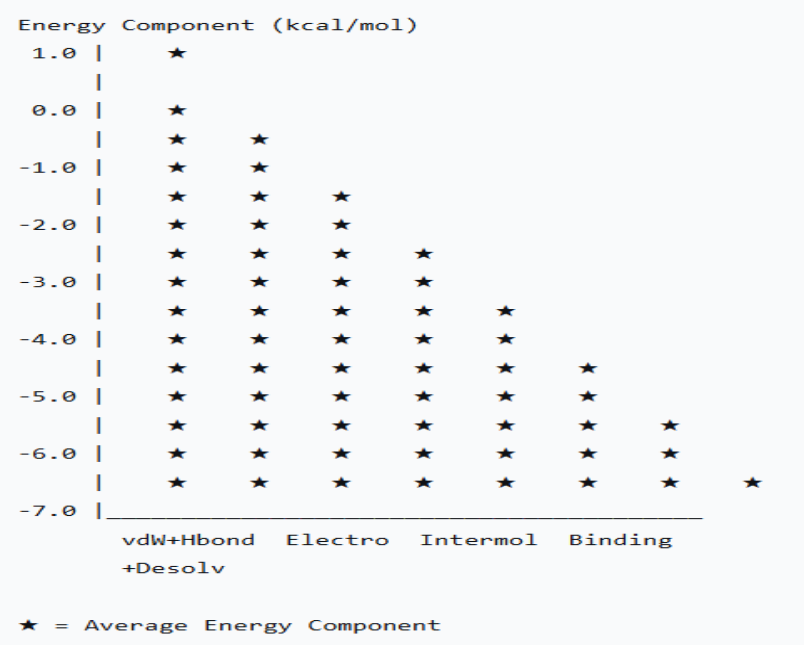

Fig: 7 Graph 2: Energy Components Comparison.

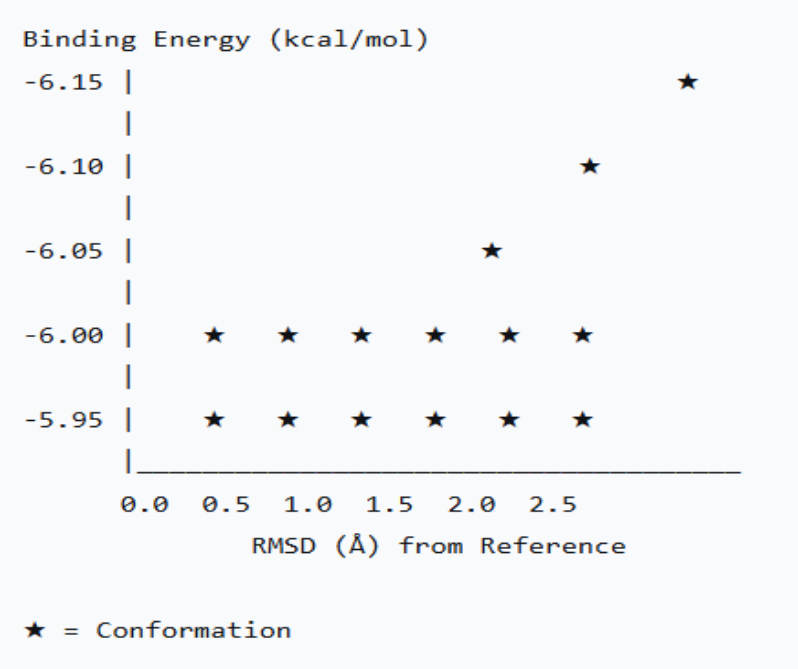

Fig: 8 Graph 3: Energy vs RMSD Analysis.

Fig: 9 Graph 4: Cluster Distribution.

5. CONCLUSION

The present in silico study demonstrated that Jatamansone, a major phytoconstituent of *Nardostachysjatamansi*, exhibited favorable binding interactions with the NMDA receptor (PDB ID: 7E0S), an important therapeutic target implicated in epileptogenesis. Molecular docking revealed a best binding affinity of **−6.13 kcal/mol**, with the ligand forming stable hydrogen bond and electrostatic interactions with key active-site residues, including

ARG329, GLU330, ASP333, LYS401, and LYS697. These interactions suggest that Jatamansone can be accommodated within the receptor binding pocket and may contribute to modulation of NMDA receptor activity.

The docking findings provide computational evidence supporting the potential antiepileptic activity of Jatamansone and are consistent with the traditional medicinal use of *Nardostachysjatamansi* in neurological disorders. Although the observed binding affinity indicates promising receptor interaction, molecular docking alone cannot confirm biological efficacy. Therefore, further validation through molecular dynamics simulations, in vitro receptor-based assays, and in vivo pharmacological studies is required to establish its mechanism of action and therapeutic potential.

Overall, the present study identifies Jatamansone as a promising lead phytoconstituent for the development of novel antiepileptic agents targeting the NMDA receptor and provides a scientific basis for future experimental investigations.

6. REFERENCES

1. Löscher W, Potschka H, Sisodiya SM, Vezzani A. Drug resistance in epilepsy: Clinical impact, potential mechanisms, and new therapeutic approaches. *Nat Rev Neurol.* 2020;16(12):661–676.
2. Rogawski MA, Löscher W, Rho JM. Mechanisms of action of antiseizure drugs and the ketogenic diet. *Cold Spring HarbPerspect Med.* 2016;6(5):a022780.
3. Traynelis SF, Wollmuth LP, McBain CJ, Menniti FS, Vance KM, Ogden KK, et al. Glutamate receptor ion channels: Structure, regulation, and function. *Pharmacol Rev.* 2010;62(3):405–496.
4. Paoletti P, Bellone C, Zhou Q. NMDA receptor subunit diversity: Impact on receptor properties, synaptic plasticity, and disease. *Nat Rev Neurosci.* 2013;14(6):383–400.
5. Trott O, Olson AJ. AutoDockVina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *J Comput Chem.* 2010;31(2):455–461.
6. Dallakyan S, Olson AJ. Small-molecule library screening by docking with PyRx. In: Hempel JE, Williams CH, Hong CC, editors. *Chemical Biology: Methods and Protocols*. Methods in Molecular Biology. Vol. 1263. New York: Humana Press; 2015. p. 243–250.
7. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, et al. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. *J Comput Chem.* 2009;30(16):2785–2791.

8. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, et al. The Protein Data Bank. *Nucleic Acids Res.* 2000;28(1):235–242.
9. Meng XY, Zhang HX, Mezei M, Cui M. Molecular docking: A powerful approach for structure-based drug discovery. *CurrComput Aided Drug Des.* 2011;7(2):146–157.
10. Singh A, Duggal S. Medicinal properties of *Nardostachysjatamansi* (DC.): A review. *Orient Pharm Exp Med.* 2009;9(3):173–182.
11. Rahman H, Eswaraiah MC, Dutta AM. In vitro and in vivo pharmacological activities of *Nardostachysjatamansi*: A review. *J Appl Pharm Sci.* 2011;1(5):60–63.
12. Sahu R, Dhongade HJ, Pandey A, Sahu P. Pharmacological and phytochemical review on *Nardostachysjatamansi*. *Pharmacogn Rev.* 2016;10(19):13–17.