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Original Article

A NETWORK PHARMACOLOGY-BASED DRUG REPURPOSING STUDY OF LEVETIRACETAM UNCOVERS ITS INTERACTION WITH MULTI-DRUG TARGETS IN PARKINSON'S DISEASE

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ABSTRACT

Objective: The current study utilized network pharmacology to examine how Levetiracetam interacts with specific drug targets associated with Parkinson's Disease (PD) treatment.

Methods: We used information from Kyoto Encyclopedia of Genes and Genome (KEGG) studies and Protein-Protein Interaction (PPI) pathway analysis to create a network that depicts the relationships between Levetiracetam and PD targets. Further investigation involved PPI analysis, molecular docking, and Molecular Dynamics (MD) simulation studies, ultimately pinpointing five protein targets. Their participation in pathways such as Ribonucleic acid Polymerase II-specific Deoxyribonucleic acid binding Transcription Factor Binding (Gene Ontology [GO]:0061629), Axon (GO: 0030424), and Excitatory Postsynaptic Potential was emphasized by GO and KEGG pathway enrichment. Additionally, Dopamine Receptor D2 (DRD2), Solute Carrier Family 6 Member 3 (SLC6A3), Glycogen Synthase Kinase 3 Beta (GSK3B), Poly (ADP-ribose) Polymerase 1 (PARP1) and Myeloperoxidase (MPO) were identified as protein targets through PPI and molecular docking analysis.

Results: The results of molecular docking showed that protein targets, SLC6A3, have highest binding affinity with Levetiracetam. The MD Simulation result of Levetiracetam-SLC6A3 docked complex represented the complex to be quite stable with few conformational changes in the SLC6A3 structure. DRD2, SLC6A3, GSK3B, PARP1, MPO were recognized as the likely protein targets of Levetiracetam for treating PD. SLC6A3 was considered as a target of Levetiracetam in PD.

Conclusion: Our study revealed the mechanism of Levetiracetam in the treatment of PD and can contribute to more effective treatment for the same. By identifying key protein targets, this research lays the groundwork for future studies that could further explore Levetiracetam's efficacy.

Keywords: Parkinson's diseases, Levetiracetam, Network pharmacology, Molecular docking, MD simulation, SLC6A3

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INTRODUCTION

Parkinson's Disease (PD) is a complex and progressive neurodegenerative disorder characterized by symptoms such as tremors, bradykinesia and postural instability [1]. Despite being the second most prevalent neurodegenerative disease after Alzheimer's [2], PD remains incurable, with treatments focused primarily on symptom management [3]. The diagnosis of PD relies on clinical criteria and is often confirmed by histopathological findings of α-synuclein-containing Lewy [4].

Current research has explored various therapeutic avenues that include the repurposing of existing drugs. Levetiracetam-an, an anti-convulsant agent-has, shown potential in PD treatment [5]; however, its specific molecular targets and mechanisms of action in PD remain unidentified. Previous studies have primarily focused on its efficacy in epilepsy, with limited exploration in neurodegenerative contexts [6].

Utilizing network pharmacology, molecular docking and Molecular Dynamics (MD) simulations, we systematically investigated the interactions between Levetiracetam and specific protein targets associated with PD. These techniques offer a comprehensive framework for understanding the multi-target effects of Levetiracetam, potentially uncovering novel therapeutic pathways and mechanisms. Our approach integrates data from Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway studies, Protein-Protein Interaction (PPI pathway analysis) and Gene Ontology (GO) enrichment to construct a detailed interaction network, highlighting the significance of identified targets in PD pathology.

While Levetiracetam has shown promise in treating mild cognitive impairment in PD-particularly in reducing hippocampal hyperactivity and improving memory function-its specific molecular targets and broader mechanisms of action within the context of PD remain underexplored. The study by [7] primarily focuses on cognitive aspects and does not delve into the detailed molecular interactions of Levetiracetam with critical PD-related proteins such Dopamine Receptor D2 (DRD2), Solute Carrier Family 6 Member 3 (SLC6A3), Glycogen Synthase Kinase 3 Beta (GSK3B), Poly (ADP-ribose) Polymerase 1 (PARP1) and Myeloperoxidase (MPO) [8] conducted a systematic review and meta-analysis that highlighted the efficacy of Levetiracetam in improving cognitive function across various conditions, including epilepsy, amnestic mild cognitive impairment, schizophrenia and Alzheimer's disease. However, they noted that the specific cognitive domains affected by Levetiracetam and the robustness of the evidence supporting these effects are still not fully clear [9] have examined the differential prescribing patterns of Levetiracetam and highlighted potential biases in its use across various neuropsychiatric conditions. However, these studies do not address the detailed molecular interactions of Levetiracetam with critical PD-related proteins such as DRD2, SLC6A3, GSK3B, PARP1 and MPO. Molecular docking, despite being a powerful tool for drug design, often encounters challenges related to receptor flexibility and scoring accuracy. As demonstrated by [10], ensemble docking can sometimes enhance database enrichments, though it may not always be suitable for virtual screening applications, highlighting the need for further optimization in specific contexts. The methodologies used in our study-particularly the use of molecular docking and preclinical models are well-established in the field of antiepileptic drug discovery. Similar approaches have been outlined by [11], who reviewed the various models of epilepsy used to identify and characterize new chemical entities. These models are not only crucial for antiepileptic drug discovery but also provide a relevant framework for exploring Levetiracetam's potential in treating neurodegenerative conditions such as PD. Our study employs molecular docking and pharmacophore modeling techniques to explore the potential therapeutic effects of

Levetiracetam in PD, similar to the approach used by Mahfudin *et al.* (2023) in evaluating Kaempferol [12]. These computational methods have proven effective in identifying promising compounds for further investigation in neurodegenerative diseases.

This study aims to identify and characterize the molecular interactions of Levetiracetam in PD treatment, identify its potential repurposing and to offer insights into its application beyond epilepsy. By addressing the gaps in current research and providing a thorough analysis of Levetiracetam's targets, the study aims to contribute to the development of more effective PD therapies.

MATERIALS AND METHODS

Levetiracetam's drug target identification

The pharmacological targets of levetiracetam were found using the Swiss Target Prediction database (http://www.swisstargetprediction.ch/) [13]. Utilizing the Levetiracetam Simplified Molecular Input Line Entry System (SMILES) string (Compound Chemical Identifier [CID]: 5284583) that was acquired from the National Center for Biotechnology Information (NCBI) PubChem database (https://pubchem.ncbi.nlm.nih.gov/compound/5284583) [14] as the search term, related protein target sets were retrieved via default filter parameters.

PD drug target screening

To find targets for PD, three databases were used: Disease Gene Network (DisGeNET) (https://www.disgenet.org/search) [15], Pharmacogenomics Knowledgebase (PharmGKB) database (https://www.pharmgkb.org/) [16], and GeneCards (http://www.genecards.org/) [17]. Using "Parkinson's Disease" as the search term, these databases predicted protein targets. It was thought that the genes that were extracted from these sources might be used as PD treatment targets. Subsequently, the overlapping genes among the three databases were recognized as the final drug targets for PD, earmarked for further investigation.

GO and KEGG pathway enrichment analysis

The Enrich online tool (https://maayanlab.cloud/Enrichr/) [18] was utilized for GO analysis, while R Studio software (version 4.0.2) was used for KEGG pathway enrichment analysis [19]. Statistically significant GO and KEGG pathways were identified with a value of ≤0.05. The top 10 GO terms encompassing molecular function, cell components, and biological processes, along with the 20 most relevant KEGG pathways, were selected for detailed analysis.

Drug-targets-pathway network construction

To delve deeper into exploring the relationship between levetiracetam, its targets and the pathways relevant to treating PD, we conducted an analysis using KEGG pathway enrichment to uncover how protein targets interact with associated pathways. Employing Cystoscope (version 3.10.0), an open-access bioinformatics tool renowned for visualizing molecular interactions [20], we constructed a network depicting the connections between drugs, targets and the disease.

PPI study was performed on previously identified protein targets using the Search Tool for Retrieval of Interacting Genes/Proteins (STRING) database [21], available at https://string-db.org/. The threshold for interaction was established at a minimum score of ≥0.4, while default settings were maintained for other parameters. The resulting PPI network was saved in a network file format for further analysis to pinpoint hub genes. The Cytohubba package within Cystoscope software [22] was then employed to identify these crucial hub genes within the PPI network.

Molecular docking analysis

To study the affinity and interactions between identified key drug targets and Levetiracetam, molecular docking emerged as a crucial tool. Utilizing AutoDock Vina software [23], the process commenced by acquiring the 3D structure of Levetiracetam (compound CID: 5284583) from NCBI PubChem. This structure underwent conversion through Open Babel software [24], to accommodate necessary modifications, including the addition of hydrogen atoms at pH = 7.2, incorporation of the Merck Molecular Force Field 1994 Online Mendelian Inheritance in Man (OMIM) force field for charge, and subsequent energy minimization before docking. Simultaneously, the protein data library provided the crystal structures of the therapeutic targets for levetiracetam [25]. The docking parameters were set to correspond with the active site residues of the protein structures, determining the x, y and z coordinates accordingly.

The resultant docked complexes were analyzed based on binding affinity, measured as the minimum binding energy in kcal/mol. Subsequently, Discovery Studio Client 2021 software [26] was employed to scrutinize 3D ligand-protein interactions and generate two-dimensional interaction figures. In-depth analysis encompassed the evaluation of hydrogen bonds, hydrophobic bonds and pi-alkyl interactions within the docked complexes.

MD simulation analysis

The molecular interactions of Levetiracetam with SLC6A3 were assessed through MD simulations using Desmond 2023.2 software [27]. The simulations focused on evaluating binding affinities following the identification of high affinity in molecular docking studies, employing the Optimized Potentials for Liquid Simulations 2005 (OPLS2005) force field. A Three-Site Transferable Intermolecular Potential (TIP3P) water model was used to prepare the system at a distance of 10 Ångströms (Å), with orthorhombic periodic boundary conditions. To neutralize the complex charge, sodium (Na^+) and chloride (Cl^-) particles were adjusted, followed by energy minimization through heating and equilibrium using the steepest descent method at 300 Kelvin (K) with annealing steps of 2000 and 0.001 Picoseconds (ps) time. The system underwent normalization at 1000 steps of equilibrium at a time step of 0.001 ps. Lastly, the Nosé-Hoover method with Isothermal-Isobaric (NPT) ensemble parameters was used to run a 100 Nanosecond (ns) production simulation at 300 Kelvin (K) temperature and 1 Atmosphere (Atm) pressure.

RESULTS

Screening the key drug targets of levetiracetam for treating pd through network pharmacology method

The Swiss Target Prediction database was employed to identify Levetiracetam's crucial targets for addressing PD. Initially, 101 protein targets were sourced (see Supplementary table 1). Removing targets with a probability score of 0 narrowed the field to 61 potential targets. Subsequently, PD-associated targets were gathered from GeneCards, PharmGKB and Disgenet databases-yielding a total of 339 from OMIM; 11,230 from GeneCards and 2,078 from Disgenet (refer to Supplementary Tables 2, 3, 4). Comparing these databases revealed 5 shared protein targets (DRD2, SLC6A3, GSK3B, PARP1, MPO) among the 143 PD targets and the 56 levetiracetam targets (fig. 1).

GO and KEGG pathway enrichments of predicted targets for treating PD by using levetiracetam

The investigation involved analyzing GO terms and KEGG pathways, with the results summarized in supplementary table 5. The top 10 GO terms related to biological process, cellular component and molecular function are shown in fig. 2B. Excitatory postsynaptic potential (GO: 0060079), Chemical synaptic transmission, postsynaptic (GO: 0099565), Regulation of postsynaptic membrane potential (GO: 0060078), Axon (GO: 0030424), Glutamatergic Synapse (GO: 0098978) and Neuron Projection (GO: 0043005), Flotillin Complex (GO: 0016600), Dendrite (GO: 0030425), Deoxyribonucleic acid-binding Transcription Factor Binding (GO: 0140297), Protein Serine Kinase Activity (GO: 0106310), Monoamine Transmembrane Transporter Activity (GO: 0008504) and Dynactin Binding. Additionally, fig. 2C displays the top 20 KEGG pathways, highlighting that the top 4 pathways Base excision repair, Hedgehog signaling pathway, Dopaminergic synapse and Drug metabolism—demonstrated significant correlation PD.

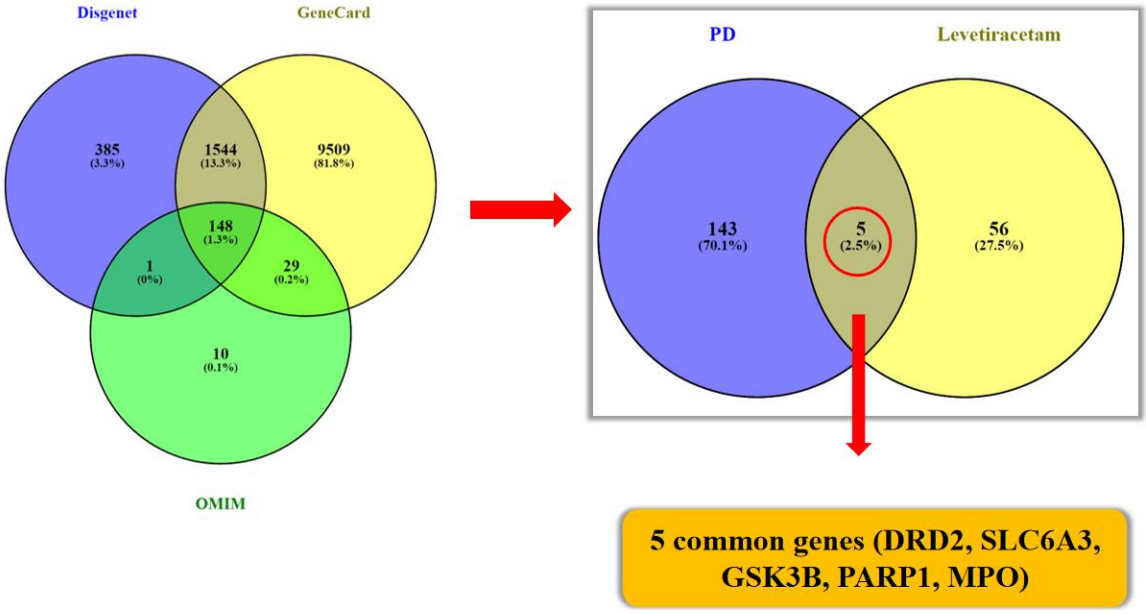


Fig. 1: Five common genes are depicted by the venn diagram's overlapping set: DRD2, SLC6A3, GSK3B, PARP1 and MPO. These genes are identified as common targets associated with both PD and the effects of Levetiracetam

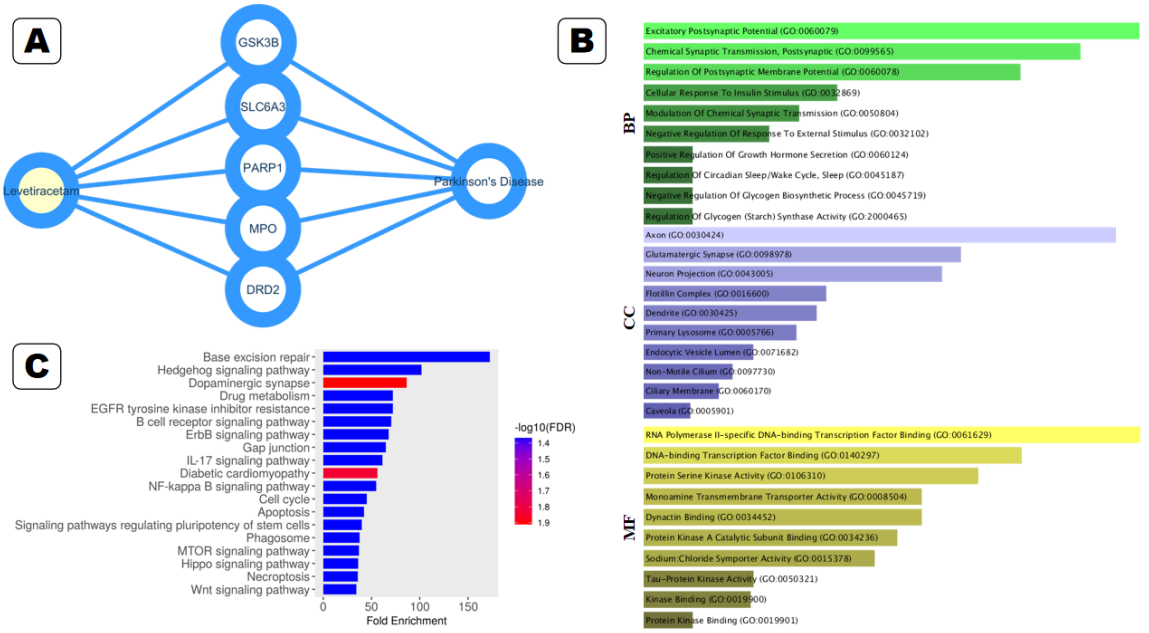


Fig. 2: Analyzing the five predicted protein targets, conducted GO and KEGG enrichment analyses. (A) The network diagram illustrates the connections between Levetiracetam and PD, focusing on the common targets and associated pathways. (B) The shared targets' GO enrichment study reveals different biological processes (green plot), cellular components (blue plot) and molecular functions (yellow plot). Notably, "Excitatory Postsynaptic Potential" (GO: 0060079), "Axon" (GO: 0030424) and the most important annotations in biological processes, cellular components and molecular activities, respectively, are " Ribonucleic acid Polymerase II-specific Deoxyribonucleic acid-binding transcription factor binding" (GO: 0061629). (C) For KEGG pathway enrichment analysis, we explored the commonly predicted five targets of Levetiracetam in treating PD, represented by bar charts where the bar size indicates the number of genes annotated in the respective KEGG pathways

Molecular docking analysis

Levetiracetam's interactions with predicted targets underwent assessment using AutoDock Vina software. The precision of molecular docking got gauged via Root mean Square Deviation (RMSD) and table 1 displays the AutoDock scores for potential protein targets. Lower minimum binding energy values signify stronger binding affinities with Levetiracetam. Among the top three targets demonstrating the least binding energy were SLC6A3 (-6.4 kcal/mol), GSK3B (-6.3 kcal/mol) and MPO (-6.3 kcal/mol). Molecular docking analysis was conducted on the commonly identified protein targets (DRD2, SLC6A3, GSK3B, PARP1, and MPO). Fig. 3A-4E illustrate the 3D molecular interaction diagrams of these five common targets with Levetiracetam. Moreover, table 2 provides a summary of the amino acid residues from targets involved in hydrogen bonds and hydrophobic interactions with Levetiracetam.

Table 1: Molecular docking results

Genes name	PDB/Alpha fold ID	Minimum binding energy (kcal/mol)	Docking center		
			X	Y	Z
Dopamine receptor D2	7JVR	-5.7	60	60	60
Solute Carrier Family 6 Member 3	Q01959	-6.4	60	60	60
Glycogen Synthase Kinase 3 Beta	1JIB	-6.3	60	60	60
Poly(ADP-ribose) polymerase 1	3GJW	-5.8	60	60	60
Myeloperoxidase	6BMT	-6.3	60	60	60

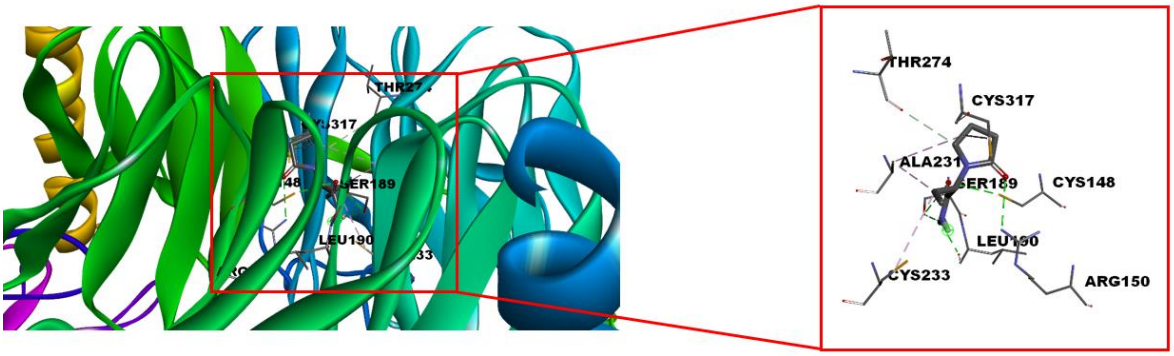


Fig. 3A: Docked complex of DRD2 (PDB ID: 7JVR) with levetiracetam. Green line: hydrogen bond interaction; purple line: Pi-alkyl interaction

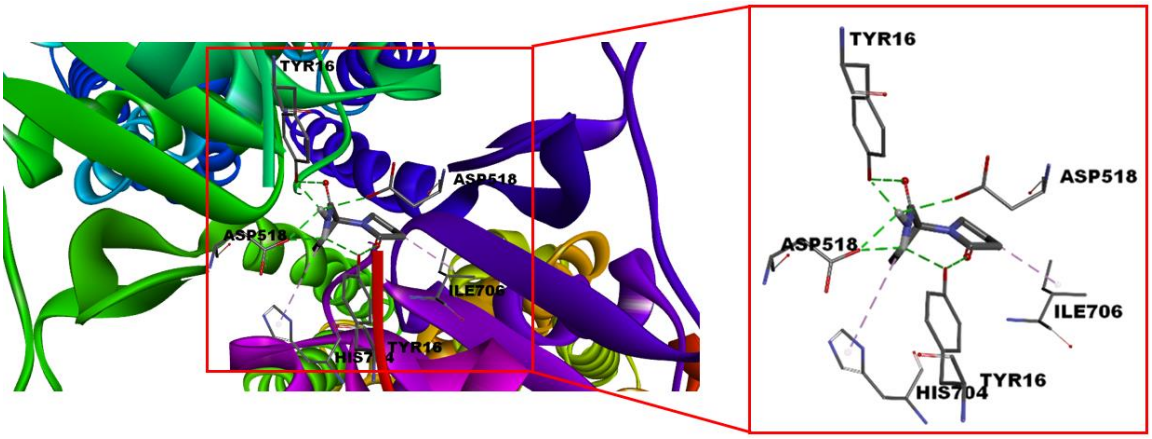


Fig. 3B: Docked complex of SLC6A3 (PDB ID: Q01959) with levetiracetam, green line: hydrogen bond interaction; purple line: Pi-alkyl interaction

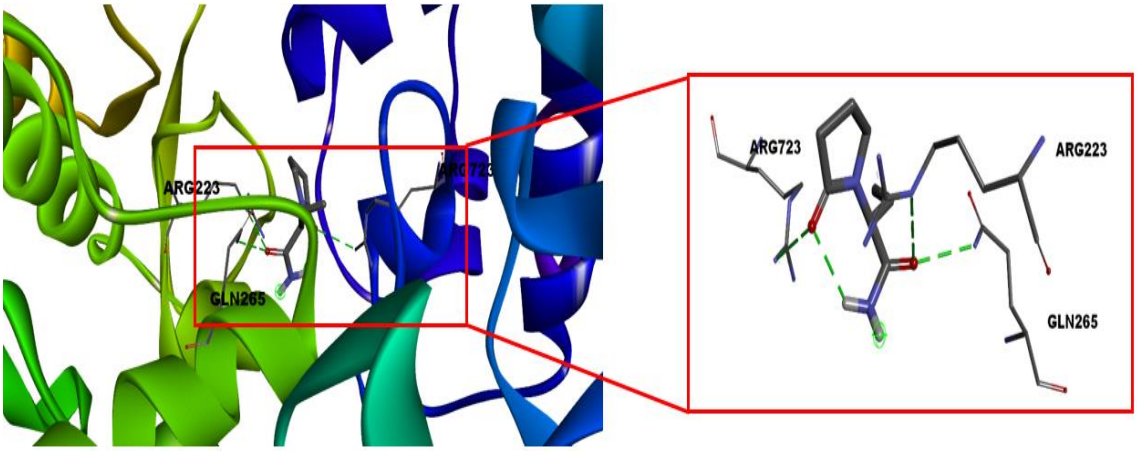


Fig. 3C: Docked complex of GSK3B (PDB ID: 1JIB) with levetiracetam. Green line: Hydrogen bond interaction; Purple line: Pi-alkyl interaction

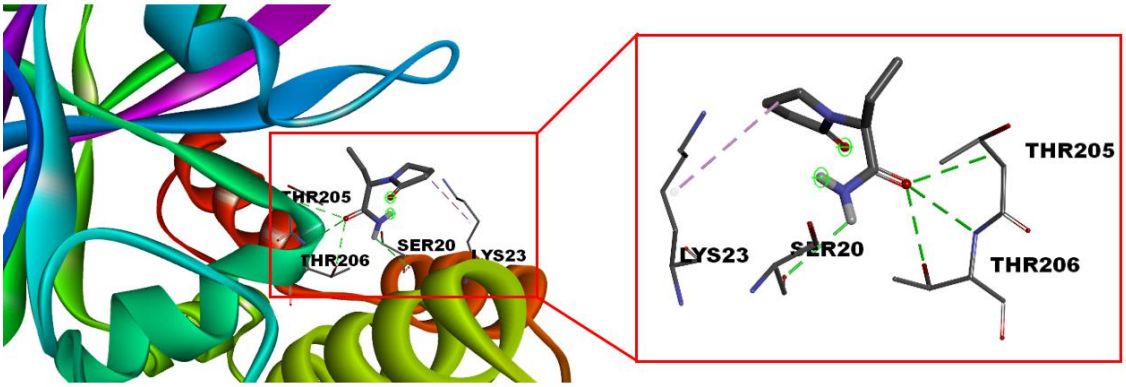


Fig. 3D: Docked complex of PARP1 (PDB ID: 3GJW) with levetiracetam. Green line: hydrogen bond interaction; purple line: Pi-alkyl interaction

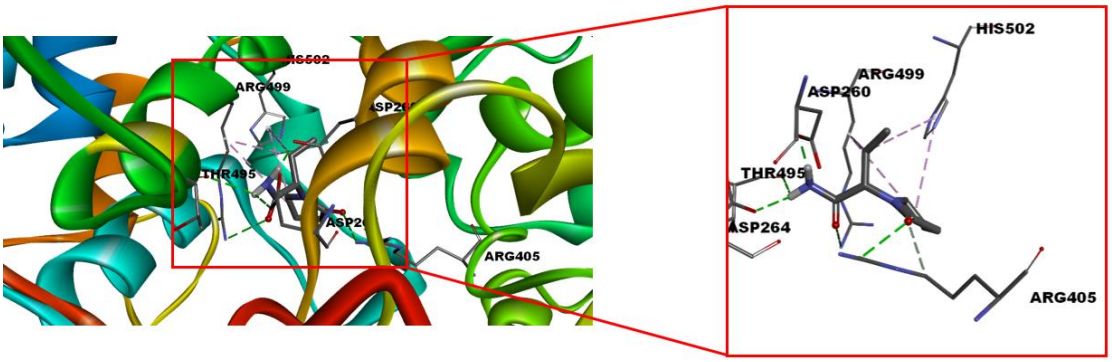
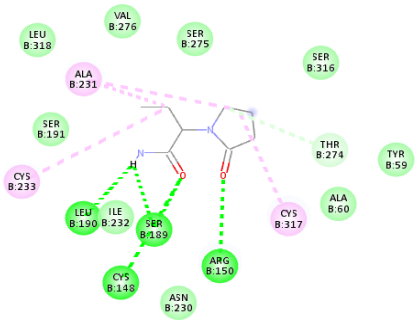
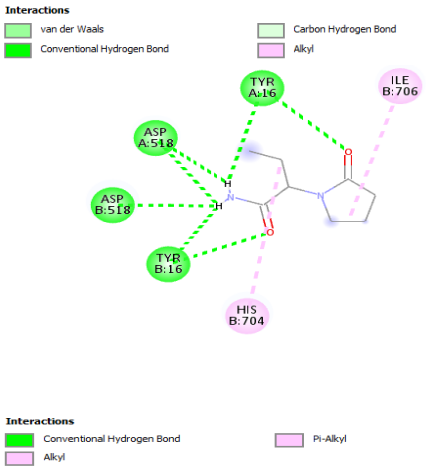
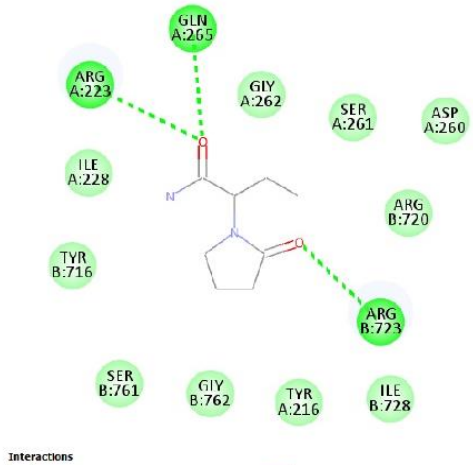
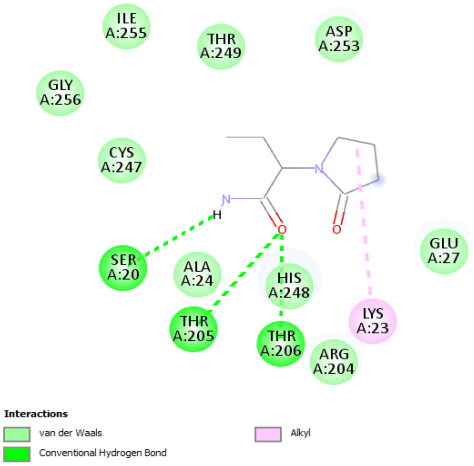
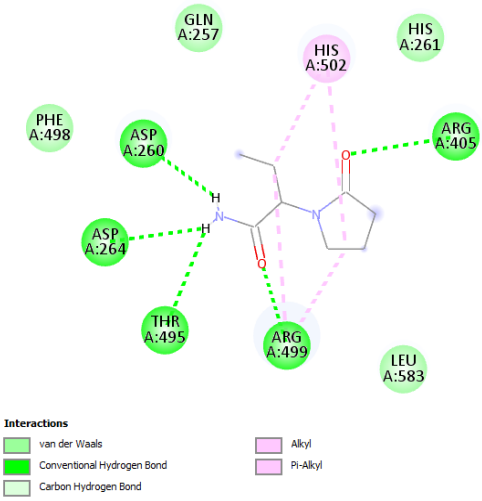


Fig. 3E: Docked complex of 3GJW (PDB ID: 6BMT) with levetiracetam. Green line: hydrogen bond interaction; Purple line: Pi-alkyl interaction

Table 2: 2D interactions of all docked complexes with levetiracetam

Gene	Hydrogen bond interactions	Hydrophobic contacts	2D interaction plot
DRD2	CYS B: 148, ARG B: 150, SER B: 189, LEU B: 190	ALA B: 231, CYS B: 233, CYS B: 317	
SLC6A3	TYR A: 16, ASP A: 518, TYR B: 16, ASP B: 518	HIS B: 704, ILE B: 706	

Gene	Hydrogen bond interactions	Hydrophobic contacts	2D interaction plot
GSK3B	ARG A: 223, GLN A: 265, ARG B: 723	-	
PARP1	SER A: 20, THR A: 205, THR A: 206	LYS A: 23	
MPO	ASP A: 260, ASP A: 264, ARG A: 405, THR A: 495, ARG A: 499	HIS A: 502	

The molecular docking analysis shows that Levetiracetam exhibits strong binding affinities with several key protein targets-particularly SLC6A3-with a minimum binding energy of-6.4 kcal/mol. This interaction was characterized by the formation of hydrogen bonds with residues Tyrosine 16 (TYR16) and Aspartic Acid 51 (ASP51), as well as hydrophobic interactions involving Histidine 704 (HIS704) and Isoleucine 706 (ILE706) (table 2). The stability of the Levetiracetam-SLC6A3 complex was further confirmed by MD simulations-which showed minimal fluctuation in the RMSD values over a 100 ns period and indicates a stable interaction.

MD simulation analysis

The stability and structural alterations of Levetiracetam within the SLC6A3 drug binding site were examined. Numerous analyses were carried out, including Radius of Gyration (RoG), Molecular Surface Area (MolSA), Solvent Accessible Surface Area (SASA), Polar Surface Area (PSA) plots, Protein-ligand RMSD and Protein Root mean Square Fluctuation (RMSF). During a 100 ns molecular MD simulation, RMSD gauged the average displacement of atoms relative to a fixed frame, revealing an average deviation. The Molecular Mechanics Generalized Born Surface Area [MMPB(GB)SA] Energy calculation for the docked complex yielded-0.97 kcal/mol (refer to fig. 4). Notably, the

Levetiracetam-SLC6A3 complex (lig-fit-prot) achieved stability within the initial 50 ns, maintaining equilibrium throughout the simulations at distances of 3 and 7Å, respectively (see fig. 5A). Analyzing the RMSF revealed protein chain alterations during Levetiracetam interaction with SLC6A3, observing amino acid residue fluctuations within a 100 ns simulation, with a maximum fluctuation of 3 Å (depicted in fig. 5B).

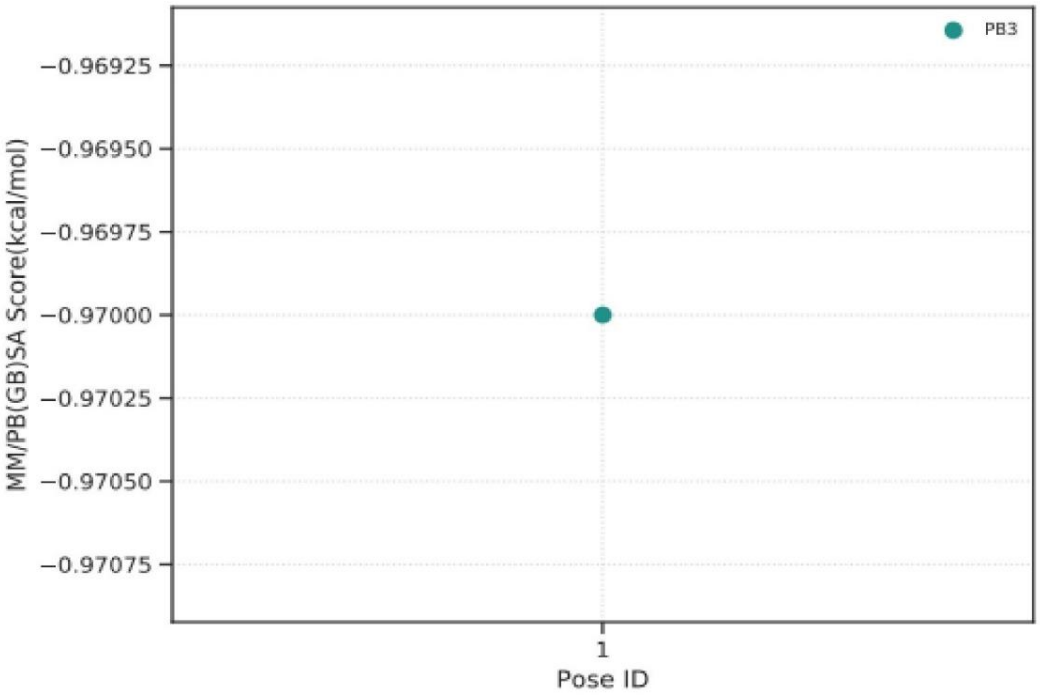


Fig. 4: MMPB (GB) SA energy calculation for docked complex

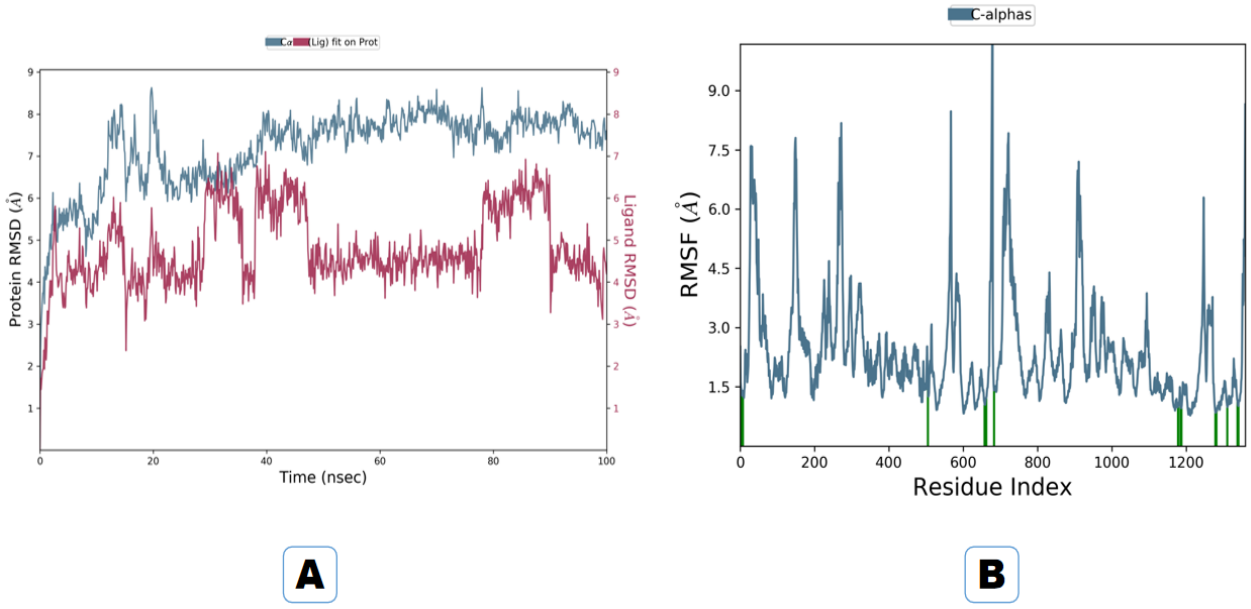


Fig. 5: Results of RMSD and RMSF plots

MD simulation of the top-scored protein target (SLC6A3) with Levetiracetam were represented the formation of Hydrogen bond and hydrophobic interactions in the active site region. Fig. 6 illustrates the representation of the Radius of Gyration (RoG), MolSA, Solvent Accessible Surface Area (SASA) and Polar Surface Area (PSA).

The timeline illustrates the several interactions that take place during the MD simulation, including H-bonds, hydrophobic, ionic and water bridges. The histogram shows the total number of distinct interactions that occurred between the ligand and the protein during the simulation. Additionally, it highlights the specific amino acid residues engaged with the ligand (levetiracetam) throughout the simulation. Notably, amino acids such as TYR 16, ASP 518, SER 705, ILE 706, HIS 707 demonstrate more pronounced interactions with the ligand, depicted by a distinct shade of orange on the plot, as indicated by the color scale on the side (fig. 7).

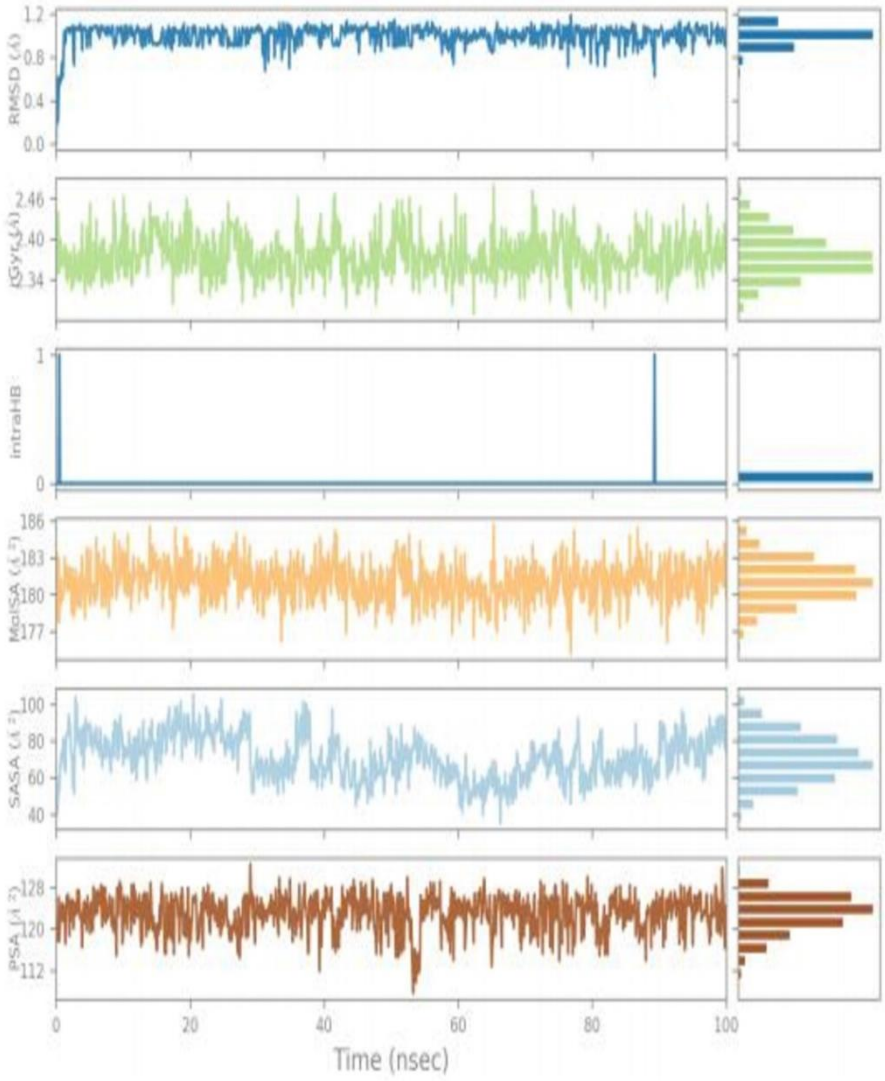


Fig. 6: RoG, MolSA, SASA and PSA of levetiracetam with SLC6A3

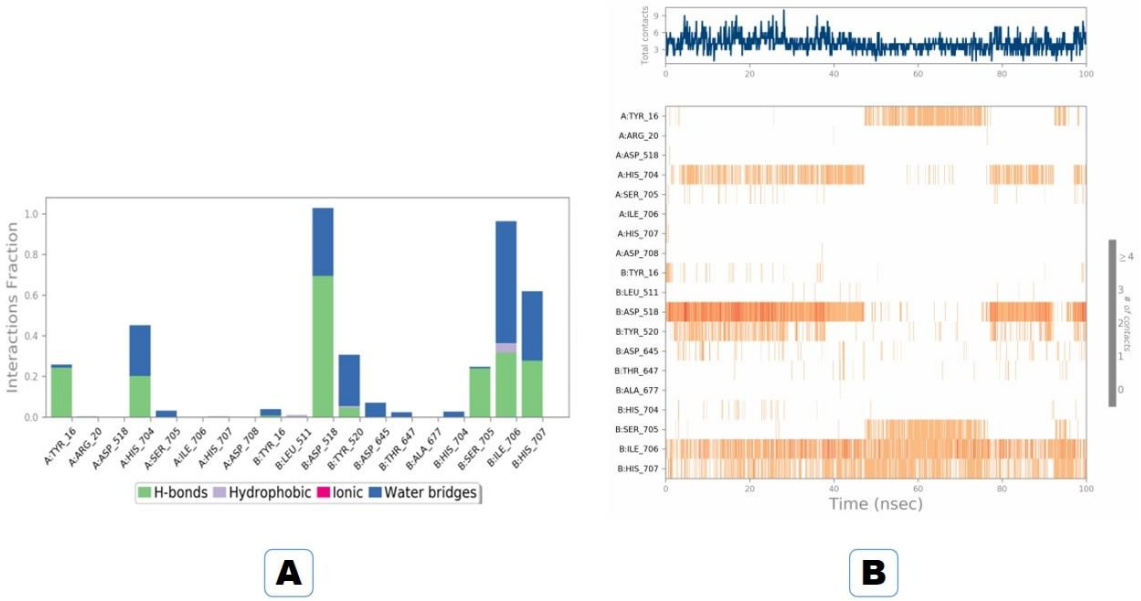


Fig. 7: Protein-ligand contact timeline plot

DISCUSSION

Network pharmacology stands out as a groundbreaking approach in pinpointing novel drug targets for PD notably focusing on multi-target interactions ('disease-gene-target-drug'). Levetiracetam, an antiepileptic medication, received Food and Drug Administration (FDA) approval in 2000 for adjunctive therapy in focal seizures, myoclonic seizures and primary generalized seizures. Its mechanism involves reducing abnormal brain excitation. Our study collated two sets of targets: 1) 143 PD targets from OMIM, GeneCards and Disgenet databases and 2) 56 levetiracetam targets from the Swiss Target Prediction database. Five potential common protein targets were identified. The protein target showing the highest binding affinity underwent further analysis through a 100 ns MD simulation study. Ultimately, SLC6A3 emerged as the primary Levetiracetam target for PD, supported by network pharmacology, molecular docking and MD simulation analyses. Our findings demonstrate the strong binding affinity of Levetiracetam to SLC6A3, suggesting a potential mechanism for its therapeutic effects in PD by enhancing dopaminergic signalling in the brain and potentially alleviating motor symptoms associated with dopamine deficiency in PD patients.

Within the family of sodium-and chloride-dependent neurotransmitter transporters, the gene SLC6A3 encodes a critical dopamine transporter [18]. Interestingly, a 40 bp Variable Number Tandem Repeat (VNTR) is present in its 3' Untranslated Region (UTR) associated with conditions like PD, idiopathic epilepsy and dependencies like alcohol, cocaine, nicotine and attention-deficit hyperactivity disorder [28, 29]. Functionally, SLC6A3 manages dopamine reuptake in the synapse, influencing dopaminergic neurotransmission [30] and its dysregulation is implicated in disorders such as parkinsonism [31]. Specific diseases linked to SLC6A3 include Parkinsonism-Dystonia 1 and tobacco addiction (ABUSE, 2014). In terms of routes, it's connected to the movement of amino acids and oligopeptides as well as inorganic cations and anions. Notably, a faulty SLC6A3 gene leads to Parkinsonism-Dystonia Infantile (PKDYS) [32]**.** Dopamine Transporter (DAT) inhibitors, like Levetiracetam, are considered in treating depression due to increased synaptic dopamine levels and as adjuncts in managing PD [33, 34].

In the context of PD treatment-managing L-DOPA-Induced Dyskinesia (LID) remains a challenge-as noted in the study by AlShimemeri, Fox, and Visanji (2020) [35]**.** They highlight that prolonged L-DOPA treatment, which is the standard therapy for PD, often leads to the development of uncontrolled movements known as LID. Currently the only approved treatment for LID is amantadine-an N-Methyl-D-Aspartate (NMDA) antagonist-which has limited efficacy and associated side effects. The strong binding affinity of Levetiracetam to SLC6A3, as demonstrated in our molecular docking and MD simulation analyses, suggests that this drug may also have a role in modulating dopaminergic transmission, which could indirectly impact dyskinesia.

By comparing these approaches, it becomes clear that Levetiracetam might serve as a multifaceted therapeutic option. Not only could it potentially mitigate motor symptoms associated with PD, as suggested by its binding to SLC6A3, but it might also offer a novel approach to managing LID, particularly in cases where existing treatments like amantadine are insufficient.

Our findings align with and expand upon existing research that highlights the critical role of SLC6A3 (DAT) in PD. Previous studies have established that SLC6A3 is integral to dopaminergic neurotransmission, with dysregulation implicated in various neuropsychiatric disorders, including Parkinsonism [18, 31]. Levetiracetam, traditionally used as an antiepileptic, has been suggested in literature as a potential modulator of dopamine levels due to its interaction with DAT [33]. However, the precise molecular mechanisms through which Levetiracetam affects SLC6A3 and its broader implications for PD treatment have not been fully explored. Our study provides the first detailed molecular characterization of Levetiracetam's interaction with SLC6A3, indicating a strong binding affinity. This suggests that Levetiracetam may inhibit SLC6A3, enhancing synaptic dopamine levels and potentially alleviating motor symptoms in PD patients. These findings support the hypothesis that DAT inhibitors, including Levetiracetam, could serve as adjunct therapies for PD by targeting dopamine reuptake pathways.

While our study provides strong evidence for Levetiracetam's potential as a PD therapy, several critical questions remain unanswered. The precise molecular mechanism by which Levetiracetam inhibits SLC6A3 is not yet fully understood and needs further investigation. The long-term effects of DAT inhibition by Levetiracetam in Parkinson's patients, particularly its impact on neuroplasticity and the progression of dopaminergic neuron degeneration, require thorough exploration. Future research should consider the role of genetic variations, such as the VNTR in the 3' UTR of SLC6A3, which may influence the drug's efficacy. Adopting personalized medicine approaches that account for these genetic differences could significantly enhance the therapeutic potential of Levetiracetam in the treatment of PD.

CONCLUSION

We identified DRD2, SLC6A3, GSK3B, PARP1 and MPO as potential targets of Levetiracetam in PD treatment. Among these-SLC6A3 emerged as a particularly significant target-as identified through comprehensive analyses involving network pharmacology, molecular docking and MD simulations. Our findings demonstrate the power of network pharmacology in uncovering novel drug targets and highlight Levetiracetam's potential to be repurposed as an anti-parkinsonian agent.

This study not only introduces a new therapeutic avenue for Levetiracetam but also offers a promising molecular target-SLC6A3-for future PD treatments. The implications of this research extend beyond basic science and potentially furthering the development of more targeted and effective therapies for PD. Further clinical studies are warranted to explore the therapeutic efficacy of Levetiracetam in Parkinson's patients-particularly in relation to its interaction with SLC6A3.

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CONFLICT OF INTERESTS

All the authors declared that there is no conflict of interest.

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