Original Article

Mimosa pudica Modulates Neuroactive Ligand-Receptor Interaction in Parkinson's Disease

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ABSTRACT

Introduction: *Mimosa pudica* is scientifically reported for the enhancement of memory in multiple animal models including Parkinson's disease (PD); however, the probable molecular mechanism for this effect has not been explained yet. The present study demonstrates the probable molecular mechanism to improve memory via *in silico* techniques. **Materials and Methods:** Phytoconstituents present in *M. pudica* and their targets involved in Parkinson's disease were identified using open-source databases and published literature. Enrichment analysis of targeted proteins was identified using STRING, druglikeness of compounds was assessed using MolSoft and docking was carried using autodock4. **Results:** Out of twenty-seven phytoconstituents, seventeen modulated the proteins involved in the pathogenesis of PD. Norepinephrine was predicted to have the highest druglikeness score. The ADMET profiles revealed all phytoconstituents to be safe and are suitable for human consumption. Similarly, network analysis identified ADORA1 to be primarily targeted by phytoconstituents and luteolin was predicted to interact with maximum proteins. A docking study predicted quercetin and luteolin to possess the highest binding affinity with highly modulated protein ADORA1. **Conclusion:** *M. pudica* could primarily modulate neuroactive ligand receptor interaction followed by dopamine and serotonin synapses by regulating multiple proteins in PD.

Key words: Luteolin, *Mimosa pudica,* Network pharmacology, Parkinson's disease, Quercetin.

INTRODUCTION

Parkinson's disease, an extrapyramidal motor disorder; occurs due to the loss of dopaminergic neurons in the substantia nigra.[1] Progression of PD leads to complications including cognitive dysfunction, anxiety, depression, dementia[2] and some physical abnormalities i.e. tremors, rigidity, hypokinesia and impaired gait.[3] Multiple etiological factors have been reported for its progression including age, sex, oxidative stress, genetic and environmental factors leading to the formation of Lewy bodies.[1] Current pharmacotherapy of PD attempts to restore the dopaminergic activity in the neuronal cells by using dopamine precursor levodopa, dopamine receptor agonist like ropinirole, pramipexole, rotigotine, monoamine oxidase B (MAOB) inhibitors like rasagiline, safinamide, selegiline and catechol-O-methyltransferase (COMT) inhibitors like tolcapone, entacapone. Although these molecules are effective, the utilization of these agents is limited due to multiple side effects like postural hypotension, somnolence, hallucination and an increased incidence of impulse control disorders.[4,5] Further, PD is progressed due to the involvement of multiple proteins generating a complex network among them[6] which can be evaluated using a network pharmacology approach.[7] Hence, the therapeutic approach could utilize the neutralization of this network by targeting different molecules via multiple compounds which can be achieved by the traditional medicines.

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Traditional medicines have been used since ages to maintain health and improve various diseases. These agents comprise various plant sources and are associated with minimal side effects[8,9] show synergistic effect by interacting with multiple proteins and modulate multiple pathways.[10] About 25% of modern medicines are developed from the traditionally used medicines; however, there is a paucity of scientific evidence for the molecular mechanism of multicomponent treatments.[11] The network pharmacology approach helps to reveal the basis of multifaceted illnesses and drug impacts; thus helps to discover the probable molecular mechanism of the medicinal plants.[7]

Mimosa pudica belonging to family Fabaceae is a creeping annual plant that has been investigated for multiple pharmacological activities such as anti-depressant, anti-anxiety, anti-convulsant, hepatoprotective, diuretics, anti-inflammatory, anti-oxidant, analgesic, anti-epileptic and anti-diabetes including anti-parkinsonian.[12-14] However, the interaction of multiple phytoconstituents with their respective targets has not been understood yet. Therefore, the current study intended to investigate the interaction between phytoconstituents from *M. pudica* with their respective targets including modulated pathways via network pharmacology approach.

MATERIALS AND METHODS

Bioactives and their targets

The reported phytoconstituents from *M. pudica* were retrieved from ChEBI (https://www.ebi.ac.uk/chebi/) and PCIDB database (https://www.genome.jp/db/pcidb) using the keyword "*Mimosa pudica*". Canonical SMILES of each compound along with their molecular weight and the molecular formula were recorded from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The targets of each compound were queried using BindingDB[15] at the percentage similarity of 70%. The gene code of each target was identified using UniProt (https://www.uniprot.org/). Similarly, targets for PD were identified with reference to the Therapeutic Target Database (TTD).[16]

Druglikeness and ADMET profile

Druglikeness score for each compound targeting proteins related to PD was predicted using MolSoft (https://molsoft.com/) based on *"Lipinski's Rule of Five"* model. Similarly ADMET profile of each phytoconstituent was predicted using admetSAR 2.0[17] using multiple regression models.

Gene set enrichment analysis

The list of protein/target(s) involved in the pathogenesis of PD was predicted using STRING (https://string-db.org/) and the respective pathways were predicted with reference to the KEGG pathway database.[18]

Network construction

Cytoscape version 3.5.1[19] was used to assemble the network among phytoconstituents, their targets and modulated pathways. The network was analyzed using "*edge count*" under "*network analyzer*" tool. The size of nodes indicates the degree of expression of phytoconstituents, proteins and pathways.

Docking study

The homology modeling of protein ADORA1 was prepared using accession number EAW91465.1 (query sequence) and PDB: 6D9H (template) using SWISS-MODEL (https://swissmodel.expasy.org/). To avoid the docking interference, water molecules and hetero atoms were removed using Discovery Studio 2019. The ligand molecules were retrieved from the PubChem and the energy was minimized using mmff94[20] force field. Docking was performed using autodock4[21] and the conformation scoring minimum binding energy was preferred to visualize the ligand-protein interaction in Discovery studio 2019.

RESULTS AND DISCUSSION

Bioactives and their targets

Twenty-seven compounds were identified from *M. pudica* in which seventeen modulated the proteins involved in the pathogenesis of PD; five were not predicted to modulate PD proteins whereas five were not predicted to any target.

Drug likeness and ADMET profile

Out of seventeen compounds, eleven and six compounds were predicted to score positive and negative druglikeness hit respectively. Norepinephrine was predicted to score the highest druglikeness score of 1.41. The list of phytoconstituents their types and druglikeness score is summarized in Table 1. Similarly, the ADMET profile of each phytoconstituent is represented in heat map (Figure 1).

Enrichment/network analysis

Gene set enrichment analysis identified thirty-two modulated pathways. The predicted pathway in PD having the highest count of the gene set was

Table 1: Compounds from *Mimosa pudica* targeting PD proteins.

Compound Name	Compound type	Molecular formula	Molecular mass (g/mol)	NHBA	NHBD	MolLogP	DLS
10H-phenothiazine	Organic compound	$C_{12}H_9NS$	199.05	1	1	3.91	-0.94
5,3'-di-O-methylluteolin	Flavonoid	$C_{17}H_{14}O_6$	314.08	6	2	3.38	0.78
Myricetin-3-O-arabinofuranoside	Flavonoid	$C_{20}H_{18}O_{12}$	450.08	12	8	0.33	0.78
Quercetin-3-O-β-D-xylopyranoside	Flavonoid	$C_{20}H_{18}O_{11}$	434.08	11	7	0.01	1.20
Myricetin-3-O-β-D-xylopyranoside	Flavonoid	$C_{20}H_{18}O_{12}$	450.08	12	8	0.37	0.9
Hernancorizin	Flavonoid	$C_{18}H_{16}O_7$	344.09	7	2	3.35	-0.03
Diplotasin	Flavonoid	$C_{19}H_{16}O_7$	356.09	7	1	2.16	-0.03
7,3',4'-trihydroxy-3,8-dimethoxyflavone	Flavonoid	$C_{17}H_{14}O_7$	330.07	7	3	2.69	0.30
2'-hydroxy-3,7,8,4',5'-pentamethoxyflavone	Flavonoid	$C_{20}H_{20}O_8$	388.12	8	1	3.36	-0.11
Diplotrin A	Flavonoid	$C_{19}H_{18}O_8$	374.10	8	2	3.01	-0.11
Diplotrin B	Flavonoid	$C_{19}H_{18}O_7$	358.11	7	1	3.39	0.24
Diplotrin C	Flavonoid	$C_{18}H_{16}O_6$	328.09	6	1	3.73	-0.02
Quercetin-3-O-α-D-arabinofuranoside	Tetrahydroxyflavone	$C_{20}H_{18}O_{11}$	434.08	11	7	0.04	0.81
Quercetin	Pentahydroxyflavone	$C_{15}H_{10}O_7$	302.04	7	5	2.11	0.93
Luteolin	Tetrahydroxyflavone	$C_{15}H_{10}O_6$	286.05	6	4	2.68	0.86
2''-O-α-L-Rhamnosyl-6-C-fucosyl-luteolin	Tetrahydroxyflavone	$C_{27}H_{30}O_{14}$	578.16	14	9	0.42	1.02
Norepinephrine	Catecholamine	$C_8H_{11}NO_3$	169.07	4	5	0.65	1.41
Co-careldopa*	Amine	$C_{10}H_{14}N_2O_4 \cdot C_9H_{11}NO_4$	423.16	11	11	-1.8	1.18

NHBA: Number of hydrogen bond acceptor, NHBD: Number of hydrogen bond donor, DLS: Druglikeness score, *Gold standard molecule for PD

Figure 1: Heat map of ADMET profile of Phytoconstituents.

Lane 1:10H-phenothiazine, 2:5,3'-di-O-methylluteolin, 3:myricetin-3-O-arabinofuranoside, 4:quercetin-3-O-β-D-xylopyranoside, 5:myricetin-3-O-β-D-xylopyranoside, 6:hernancorizin, 7:diplotasin, 8:7,3',4'-trihydroxy-3,8-dimethoxyflavone, 9:2'-hydroxy-3,7,8,4',5'-pentamethoxyflavone, 10:diplotrin A, 11:diplotrin B, 12:diplotrin C, 13:quercetin-3-O-α-D-arabinofuranoside, 14:quercetin, 15:luteolin, 16:2''-O-α-L-Rhamnosyl-6-C-fucosyl-luteolin, 17:Norepinephrine and 18:co-careldopa

neuroactive ligand-receptor interaction with the lowest false discovery rate (Table 2). Similarly, the constructed network reflects luteolin to interact with a majority of proteins i.e. AChE, ADORA1, ADORA2A, MAOA, MAOB, PTGS1, PTGS2, GSK3B, OPRM1, HTR1A, HTR4, HTR2A and SLC6A3. Further, ADORA1 was identified to be targeted by the majority of phytoconstituents (Figure 2).

Docking study

Docking study predicted quercetin and luteolin to possess the highest binding affinity with protein ADORA1 i.e. -8.4 kcal/mol. However, quercetin was observed to have a higher number of hydrogen bond interactions with THR91 and ALA66 amino acids compared to luteolin. The binding affinity of each compound with ADORA1 is summarized in Table 3. Further, the interaction of quercetin and luteolin with ADORA1 is represented in Figure 3.

The current study aimed to predict the interaction of phytoconstituents from *M. pudica* with targets involved in the pathogenesis of PD along with the modulated pathways via network pharmacology approach. Network pharmacology is widely used to predict the plausible

Table 2: Enrichment analysis of proteins involved in PD.

Pathway	Description	Count in Gene Set	Gene code	False Discovery Rate
hsa04080	Neuroactive ligand-receptor interaction	12	HTR4, ADORA2B, ADORA1, OPRM1, DRD1, DRD2, DRD3, CHRM2, HTR1A, CHRM5, HTR2A, HRH1	3.78e-14
hsa04726	Serotonergic synapse	8	PTGS1, PTGS2, HTR4, MAOB, SLC6A4, HTR1A, MAOA, HTR2A	9.77e-11
hsa04728	Dopaminergic synapse	7	GSK3B, DRD1, DRD2, DRD3, SLC6A3, MAOB, MAOA	1.15e-08
hsa04020	Calcium signaling pathway	7	HTR4, ADORA2B, DRD1, CHRM2, CHRM5, HTR2A, HRH1	8.14e-08
hsa05030	Cocaine addiction	5	DRD1, DRD2, SLC6A3, MAOB, MAOA	1.69e-07
hsa05034	Alcoholism	6	ADORA2B, DRD1, DRD2, SLC6A3, MAOB, MAOA	5.55e-07
hsa04024	cAMP signaling pathway	6	HTR4, DRD1, DRD2, ADORA1, CHRM2, HTR1A	2.93e-06
hsa04725	Cholinergic synapse	5	ACHE, CHRM5, CHRM2, KCNQ2, KCNQ1	5.08e-06
hsa05031	Amphetamine addiction	4	DRD1, SLC6A3, MAOB, MAOA	2.36e-05
hsa05012	Parkinson's disease	4	SNCA, DRD1, DRD2, SLC6A3	0.00042
hsa04923	Regulation of lipolysis in adipocytes	3	PTGS1, PTGS2, ADORA1	0.00056
hsa04540	Gap junction	3	DRD1, DRD2, HTR2A	0.0021
hsa05032	Morphine addiction	3	DRD1, ADORA1, OPRM1	0.0022
hsa04657	IL-17 signaling pathway	3	PTGS2, TNF, GSK3B	0.0022
hsa00360	Phenylalanine metabolism	2	MAOA, MAOB	0.0022
hsa00340	Histidine metabolism	2	MAOA, MAOB	0.0036
hsa00350	Tyrosine metabolism	2	MAOA, MAOB	0.0079
hsa05010	Alzheimer's disease	3	TNF, GSK3B, SNCA	0.0087
hsa00380	Tryptophan metabolism	2	MAOA, MAOB	0.0087
hsa00260	Glycine, serine and threonine metabolism	2	MAOA, MAOB	0.0087
hsa00330	Arginine and proline metabolism	2	MAOA, MAOB	0.0111
hsa00590	Arachidonic acid metabolism	2	PTGS1, PTGS2	0.0167
hsa00982	Drug metabolism - cytochrome P450	2	MAOA, MAOB	0.0185
hsa05140	Leishmaniasis	2	PTGS2, TNF	0.0199
hsa04750	Inflammatory mediator regulation of TRP channels	2	HTR2A, HRH1	0.0321
hsa04064	NF-kappa B signalling pathway	2	PTGS2, TNF	0.0321
hsa04660	T cell receptor signalling pathway	2	GSK3B, TNF	0.0341
hsa05165	Human papillomavirus infection	3	GSK3B, TNF, PTGS2	0.0342
hsa04931	Insulin resistance	2	GSK3B, TNF	0.0368
hsa04668	TNF signaling pathway	2	TNF, PTGS2	0.0368
hsa04071	Sphingolipid signalling pathway	2	TNF, ADORA1	0.0401
hsa05160	Hepatitis C	2	GSK3B, TNF	0.0488

molecular mechanism of folk medicines to manage multiple diseases. In addition, this approach also helps to identify the probable lead molecule from medicinal plants.[7]

PD is a movement disorder resulting due to the disturbance in neurotransmitter dopamine in the nigrostriatal dopaminergic neuron.[1] The treatment includes dopamine precursor which increases the brain dopamine level, dopamine agonist which mimics the effect of dopamine in the brain and inhibition of enzymes such as MAOB, COMT which are responsible for the degradation of dopamine.[4,5] In the present study, network analysis predicted the modulation of twenty five proteins i.e. TNF, AChE, ADORA1, ADORA2A, ADORA2B, CHRM2, CHRM5, DRD1, DRD2, DRD3, GSK3B, HRH1, HTR1A, HTR2A, HTR4, KCNQ1, KCNQ2, MAOA, MAOB, OPRM1, PTGS1, PTGS2, SLC6A3, SLC6A4 and SNCA by seventeen

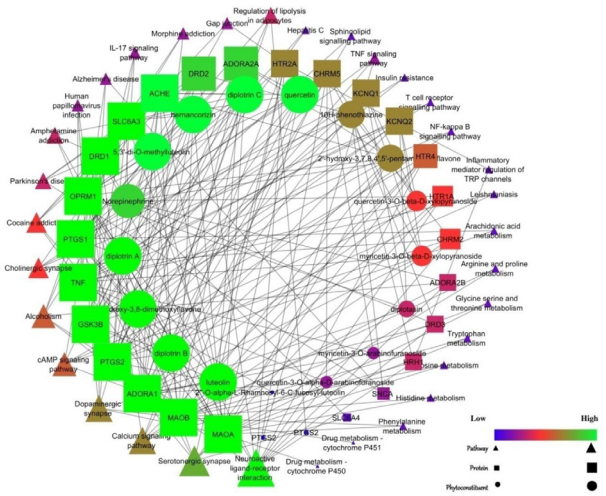

Figure 2: Interaction of phytoconstituents with their targets and respective modulated pathways.

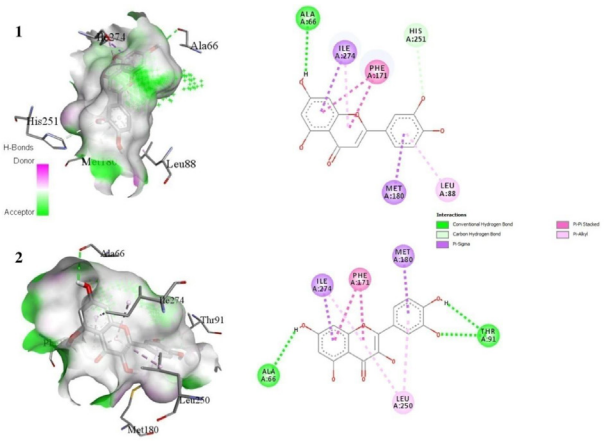

Figure 3: 3D and 2D Interaction of (1) luteolin and (2) quercetin with ADORA1.

Table 3: Binding affinity of compounds with ADORA1.

Compound	Binding affinity (kcal/mol)	NHB	NHBR
2'-hydroxy-3,7,8,4',5'-pentamethoxyflavone	-6	-	-
5,3'-di-O-methylluteolin	-6.4	3	SER235, VAL287
7,3',4'-trihydroxy-3,8-dimethoxyflavone	-8.1	2	ALA66, THR91
Diplotasin	-6.8	1	ARG105
Diplotrin A	-5.9	-	-
Diplotrin B	-6.2	3	GLN293
Diplotrin C	-7.6	-	-
Hernancorizin	-7.6	1	SER267
Luteolin	-8.4	1	ALA66
Myricetin-3-O-arabinofuranoside	-7	3	SER235, ARG291
Myricetin-3-O-β-D-xylopyranoside	-7	3	SER235, ARG291
Quercetin	-8.4	3	THR91, ALA66
Quercetin-3-O-α-D-arabinofuranoside	-7.1	4	LYS231, THR44, SER235
Quercetin-3-O-β-D-xylopyranoside	-6.9	2	VAL287, SER235
2"-O-α-L-Rhamnosyl-6-C-fucosyl-luteolin	-7	6	PRO261, HIS264, LYS265, ILE175, ASN148
10-H-phenothiazine	-7.3	-	-
Norepinephrine	-5.8	2	TYR12, GLU172

NHB: Number of Hydrogen Bonds, NHBR: Number of Hydrogen bond residues

phytoconstituents i.e. 2"-O-α-L-Rhamnosyl-6-C-fucosyl-luteolin, Norepinephrine, 10H-phenothiazine, 5,3'-di-O-methylluteolin, myricetin-3-O-arabinofuranoside, quercetin-3-O-β-D-xylopyranoside, myricetin-3-O-β-D-xylopyranoside, hernancorizin, diplotasin, 7,3',4'-trihydroxy-3,8-dimethoxyflavone, 2'-hydroxy-3,7,8,4',5'-pentamethoxyflavone, diplotrin A, diplotrin B, diplotrin C, quercetin-3-O-α-D-arabinofuranoside, quercetin and luteolin which suggests multiple compound and protein interactions. ADORA1 encodes the receptor called adenosine A1 receptor. Activation of adenosine A1 receptor shows inhibitory action in the brain; leads to suppress the presynaptic neuronal activity and its inhibition results in the availability of neurotransmitter dopamine, thus improving the condition.[22] In the present study, the majority of compounds from *M. pudica* were predicted to inhibit ADORA1 reflecting its role in PD. Further, MAOB, OPRM1, ADORA2A, PTGS1, PTGS2, GSK3B and AChE were also targeted by multiple phytoconstituents from *M. pudica*. MAOB is responsible for the metabolism of dopamine; inhibition of this enzyme increases the concentration of dopamine in the neuronal cell thus making its availability for neurotransmission; adding a beneficial effect in the management of PD.[23]

Pain is a prime non-motor symptom in PD patients; OPRM1 encodes opioid Mu 1 Receptor[24] which has been targeted by multiple phytoconstituents from *M. pudica* which could be one of the symptomatic reliefs in the PD. Further, the analgesic effect of *M. pudica*[13] could be due to the inhibition of this protein.

ADORA2A encodes the adenosine 2A receptor, which is also involved in the regulation of dopamine and glutamate release[22] thus it can be a potential target for PD and several other conditions such as depression,

insomnia, pain, etc. In the current study, PTGS2 is also targeted by various phytoconstituents of *M. pudica*. Increased release of arachidonic acid produces reactive oxygen species (ROS) to contribute in PD progression.[25] As per previous reports, PTGS2 inhibitors can be used in the pharmacotherapy for PD since they prevent the oxidation of dopamine.[26]

Flavonoids are widely known for their potential therapeutic effects against multiple diseases in the traditional medicine system.[27] In the present study, flavonoid particularly luteolin interacts with thirteen targets involved in PD i.e. AChE, ADORA1, ADORA2A, MAOA, MAOB, PTGS1, PTGS2, GSK3B, OPRM1, HTR1A, HTR4, HTR2A and SLC6A3. Hence, network analysis identified luteolin to interact with maximum proteins involved in PD.

Similarly, thirty-two pathways were identified to be associated with the proteins related to PD with reference to KEGG pathway analysis. Gene set enrichment analysis identified neuroactive ligand-receptor interaction to be highly expressed in PD with the highest number of gene count. The previous report suggests the association of neuroactive ligand-receptor interaction with α-synuclein which is involved in the dysregulation miRNAs in the brain.[28] Similarly, in the present study, we found the modulation of the neuroactive ligand-receptor interaction pathway which could regulate α-synuclein. In the present study, serotonergic synapse, dopaminergic synapse, calcium signaling pathway were also predicted to be modulated in PD. PD causes an imbalance in the production of serotonin, dopamine and norepinephrine. Dysfunction in serotonergic synapse leads to depression which is often associated with PD patients; results in increasing motor and cognitive symptoms in PD.[29] Aggregation of α-synuclein disturbs the calcium homeostasis which results in increased calcium influx inside the cell; causes excitotoxicity leading to cell death.[30]

Druglikeness character of each phytoconstituents from *M. pudica* was predicted based on *"Lipinski's Rule of Five"* which is a qualitative assessment to evaluate the drug-like property concerning factors like oral bioavailability.[31] In the present study, the majority of the compounds possess positive druglikeness scores reflecting their oral bioavailability. Similarly, ADMET of each phytoconstituents was predicted to assess the important pharmacokinetic parameters in the human body including probable toxicity of each molecule and was compared with co-careldopa. A docking study helps in the prediction of ligand molecules with their target. Previous studies utilized the *in silico* molecular docking to identify the hit molecules from multiple traditional medicines.[32-36] Similarly, in the present study quercetin and luteolin were predicted as hit molecules to have the highest binding affinity with ADORA1. Further, the druglikeness score of each phytoconstituent including their derivatives was also predicted. Hence, luteolin, quercetin and their derivatives could be the choice of lead molecules in PD for further investigations.

CONCLUSION

The present study demonstrated the interaction of phytoconstituents from *M. pudica* with targets related to PD primarily modulating ADORA1 and neuroactive ligand receptor interaction. Further, quercetin and luteolin were predicted as a hit molecule in the constructed network.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATION

ADMET: Absorption, Distribution, Metabolism, Excretion and Toxicity; **BindingDB:** Binding database; **ChEBI:** Chemical Entities of Biological Interest; **COMT:** Catechol-O-methyltransferase; **KEGG:** Kyoto Encyclopedia of Genes and Genomes; **MAOB:** Monoamine oxidase B; **PCIDB:** PhytoChemical Interactions Data Base; **PD:** Parkinson's Diseases; **PDB:** Protein Data Bank; **SMILES:** Simplified molecular-input line-entry system; **STRING:** Search Tool for the Retrieval of Interacting Genes/Proteins.

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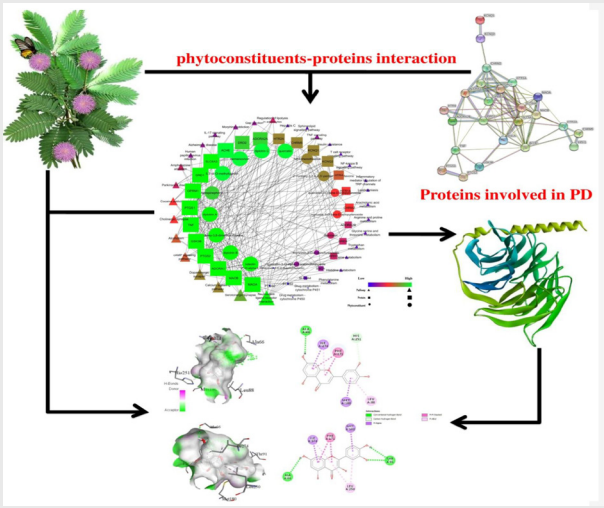
PICTORIAL ABSTRACT



SUMMARY

The present study proposed the probable molecular mechanism of *Mimosa pudica* to manage Parkinson's disease via the network pharmacology approach. Multiple phytoconstituents from *Mimosa pudica* and their respective targets were identified using open source databases and cheminformatic tools. Druglikeness score provides the concept if the organic molecules can behave like a drug if administered orally which identified norepinephrine; one of the endogenous neurotransmitters. Additionally, enrichment analysis revealed neuroactive ligand-receptor interaction via the incorporation of the highest number of gene count. Likewise, 2"-O-α-L-Rhamnosyl-6-C-fucosyl-luteolin was predicted to have the highest number of interactions with ADORA1 which is one of the majorly targeted protein molecules by the phytoconstituents from *Mimosa pudica*. Furthermore, 10-H-phenothiazine was predicted for highest probability to cross the blood-brain barrier. In brief, the study reflected the utilization of bioinformatic tools to provide the probable interactions of multiple phytoconstituents from *Mimosa pudica* with targets involved in the pathogenesis of Parkinson's disease by modulating multiple pathways to evoke the synergistic effect.

About Authors

Taaza Duyu Interests to assess the potential lead hits using knowledge-based study from folk medicines focusing over neurodegenerative pathogenesis and metabolic disorders. Further, she utilizes *in silico* tools to predict the probable targets of multiple phytochemicals and their experimental validation.

Pukar Khanal has been awarded the gold medal twice for his academic performance. His area of interest covers network pharmacology, ADMET profiling of lead hits from a natural source, gene set enrichment analysis, prediction and assessment of protein-protein network interaction, *in silico* molecular docking, protein modeling and utilizing Danio rerio as a preliminary animal model. Further, he interests to utilize regression models for the evaluation of PKPD profiles and data correlation with wet-lab protocols.

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Prof. Basanagouda M. Patil has served the KLE College of Pharmacy, Belagavi and Hubli as a Professor, Principal and Dean Faculty of Pharmacy, KAHER. Belagavi. He has been awarded with "Prof. M.L. Khorana Memorial award" for publishing best research paper in Indian Journal of Pharmaceutical Sciences. His interest of research area covers pathophysiology of insulin resistance induced endothelial dysfunction and neurodegenerative disease. He interests for *in silico* prediction and its experimental validation. Further, he also interests in utilizing Danio rerio as a preliminary animal model.

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