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Research Article

COMPUTATIONAL ANALYSIS OF PHYTOCOMPOUNDS PRESENT IN *LEUCAS ASPERA* TO TARGET PARKINSON'S DISEASE-CAUSING ALPHA-SYNUCLEIN

ASHTON MENEZES*

Department of Biotechnology, N.M.A.M. Institute of Technology, Nitte, Karnataka, India. Email: ashtonmenezes92309@gmail.com

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ABSTRACT

Objective: Parkinson's disorder is the second most prevalent neurodegenerative disorder in the world that manifests in both the motor and non-motor systems. The pathogenesis of the disorder involves alpha-synuclein in a variety of ways, and therefore, this protein can be appraised as a therapeutic target. In the present study, the bioactive phytocompounds from *Leucas aspera* were examined to establish their inhibitory activity against alpha-synuclein protein.

Methods: In this study, ten phytocompounds were selected from *L. aspera* and their efficacy to counteract Parkinson's disease (PD)-causing alpha-synuclein was evaluated. The study was done computationally using Indian medicinal plants, phytochemistry, and therapeutics and PubChem to source information and molecular structures of the phytocompounds. Several other tools were used for pharmacological assessment of these compounds under ADME properties and ProTox-II was used for toxicity prediction.

Results: Molecular docking using PyRx and BIOVIA revealed that Baicalein and Leucasperones A were the best antagonists for 3Q25 Parkinson's causing alpha-synuclein. Hence, these compounds can be used as potential candidates to produce drugs which help prevent PD.

Conclusion: Since ancient times, plants have been used to cure several maladies. The phytochemical Baicalein and Leucasperones A present in *L. aspera*, bind to disease causing alpha-synuclein, and help in disease management.

Keywords: Phytocompounds, *Leucas aspera*, Alpha-synuclein, Parkinson's disease, Antagonists.

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INTRODUCTION

The second-most prevalent neurodegenerative ailment worldwide is Parkinson's disease (PD). PD is a nerve system disorder with unexplained causes that manifest in both the motor and non-motor systems. PD is a chronic and progressive condition that typically affects older people, while it can also affect younger patients [1]. Cell loss in the substantia nigra, particularly in the ventral region of the pars compacta, is a pathological sign of PD. In comparison to the same region in those who are not afflicted, this region of the brain has lost 50–70% of its neurons by the time of death [2]. PD is typically identified by its initial motor signs. An additional symptom, such as muscle rigidity, resting tremor, or postural instability, is required for the diagnosis of bradykinesia, which is characterized by slowness of the start of voluntary movements and a progressive reduction in speed and amplitude of repetitive movements. Patients may have a range of pre-motor symptoms before the onset of motor symptoms and the confirmation of the diagnosis. These may begin up to a decade or more before the diagnosis. Up to 60–70% of patients may experience apathy, sleeplessness, insomnia, and constipation before receiving a diagnosis [3].

After an alpha-synuclein fragment was isolated from amyloid plaques in Alzheimer's disease (AD), the involvement of alpha-synuclein in neurodegenerative illnesses was initially suspected. Alpha-synuclein's importance in the etiology of PD was, however, confirmed by the finding that it is a key component of Lewy bodies and Lewy neurites, the pathological hallmarks of PD [4]. The pathogenesis of PD may involve alpha-synuclein in a variety of ways, but it is generally accepted that its toxic protofibrils in aberrant soluble oligomeric conformations are what cause cellular homeostasis to be disrupted and neuronal death by affecting a variety of intracellular targets, such as synaptic function. Furthermore, released alpha-synuclein may have negative effects on nearby cells, including the seeding of aggregation, thereby accelerating the spread of the disease [5].

Leucas aspera, as seen in Fig. 2, is found all over India and belongs to the family Labiatae. Almost all parts of the plant are known to contain medicinal compounds [6]. Thumbai is said to have anti-oxidative activity [7], anti-microbial activity [8], anti-fungal activity [9], antinociceptive activity [10], anti-cancer activity [11], and cytotoxic activity [12].

L. aspera (also known as Thumbai) (Fig. 1) has several phytocompounds, a few of which are known to help prevent PD. These phytocompounds can bind to alpha-synuclein and be used to synthesize drugs against PD. To select these antagonists, pharmacological screening must be done to ensure that the compound is suitable, which is achieved using adsorption, distribution, metabolism, excretion, and toxicity (ADMET) filters. Molecular docking is also performed to simulate the interaction between the compound and alpha-synuclein, and potential drug candidates are selected.

METHODS

Compilation of data and preparation of ligands

The phytocompounds present in *L. aspera* were collected from Indian medicinal plants, phytochemistry, and therapeutics (IMPPAT) (https://cb.imsc.res.in/imppat/) based on their pharmacological properties as corroborated by the previous research investigations [13]. Ten compounds were selected, and PubChem (https://pubchem.ncbi.nlm.nih.gov/) [14] was used to obtain the canonical SMILES and three-dimensional (3D) models of these compounds in standard data format.

Procurement, structural analysis, and purification of PD causing alpha-synuclein

The crystal structure of human alpha-synuclein with a resolution of 1.96 Å was downloaded from RCSB Protein Data Bank (https://www.rcsb.org/) [14] in protein data bank (PDB) format. The file was

used to obtain the Ramachandran plot and other secondary structure information using PDB sum (http://www.ebi.ac.uk/pdbsum/) [15], PROCHECK [16], EMBOSS pepstats (https://www.ebi.ac.uk/Tools/seqstats/emboss_pepstats/) [17], and EMBOSS pepwindow (https://www.ebi.ac.uk/Tools/seqstats/emboss_pepwindow/) [18]. The structure was, then, analyzed using Dassault Systems BIOVIA Discovery Studio Visualizer [19] and the protein purification was achieved by implementing the following steps: The free energy of the water molecule does not match the crystallographic structure. Since water molecules can affect docking scores, they were eliminated before docking. To facilitate binding with the ligands chosen for the inquiry, the prebound ligands are removed from the crystal structures. Chain A was left intact for analysis, while further chains were removed to simplify the protein structures. Polar hydrogen atoms are added to purified structures to enhance their quality.

Fig. 1: Leucas aspera also knows as "Thumbai"

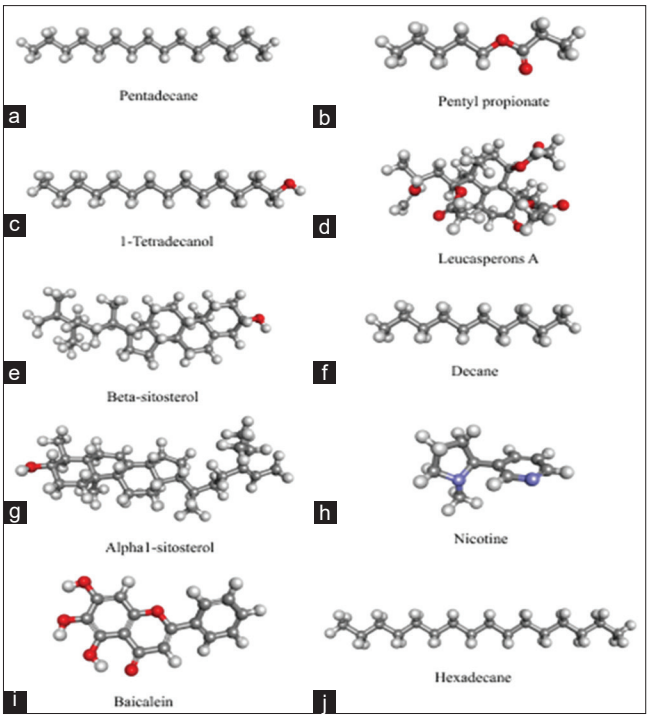

Fig. 2: (a-j) 3D models of selected phytocompounds from *Leucas aspera*

Drug likeliness of ligands

The primary factors that determine whether a chemical is a potential candidate for therapeutic development are its ADMET qualities. The basic physical and chemical qualities of a compound are known as its physicochemical properties which include molecular weight, topological polar surface area (TPSA), and lipophilicity. With the use of ADMETlab 2.0 (https://admetmesh.scbdd.com/) [20] and Swiss ADME (http://www.swissadme.ch/) [18], these attributes were examined. ProTox-II (https://tox-new.charite.de/protox_II/index.php?site=compound_input) [21] was used to predict the toxicity, and Chem AGG (https://admetmesh.scbdd.com/) [22] to conduct aggregation studies on these phytocompounds. The Lipinski rule of 5 was also analyzed using the Swiss ADME webserver.

Molecular docking studies

PyRx is a virtual docking tool that helps in simulating the binding of a ligand to a protein to better understand the features of the binding. In PyRx [23], the purified protein was loaded as the macromolecule and was converted to AutoDock. pdbqt format, whereas the phytocompounds were loaded as sdf files. Energy minimization was performed by applying the universal force field and the ligands were converted to pdbqt format. The grid was generated (Center X:3.3753 Y:29.9201 Z:10.4072; and Dimensions X:59.5072 Y:56.9185 Z:72.8138) and the ligands were appraised for docking. By default, parameters PyR× assumes the three-dimensional structures of the macromolecules as rigid and the ligands as flexible which takes up nine different conformations to attain the best optimal fit with the protein. The interaction data obtained were used to select compounds with the least binding affinities.

RESULTS

Phytocompounds selected

Ten phytocompounds present in *L. aspera* were selected from IMPPAT and their 3D structure was obtained from PubChem. The structures were viewed using BIOVIA, as shown in Fig. 2.

Protein structure procurement and purification

The crystal structure for human alpha-synuclein (http://doi.org/10.2210/pdb3Q25/pdb), as shown in Fig. 3a, was downloaded from RCSB Protein Data Bank and was purified using BIOVIA, as shown in Fig. 3b. The purification was done by removing ligand groups and water molecules. This is done to simplify the computational process as these molecules are not significant for the current research.

Protein structure analysis

Secondary structure

PDBsum was used to analyze the secondary structure of alpha-synuclein. This tool shows the molecules making up the 3D structure and the schematic interactions between them. As per the data obtained

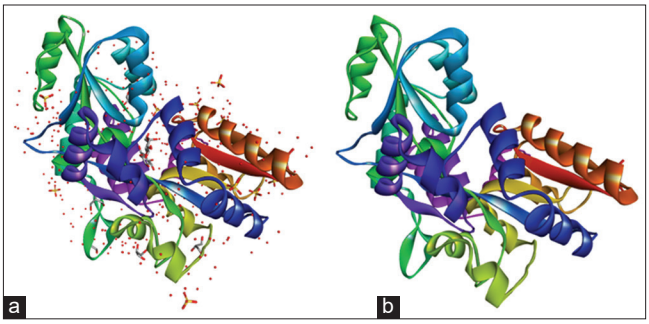

Fig. 3: 3D models of alpha-synuclein obtained using BIOVIA. (a) 3D structure of alpha-synuclein and (b) 3D structure of purified Alpha-synuclein

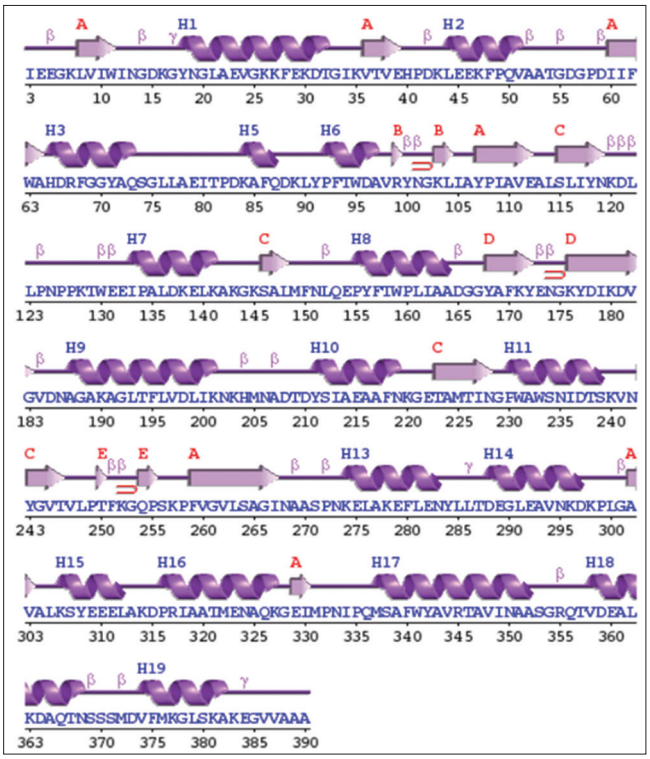

Fig. 4: Secondary structure of alpha-synuclein

in Fig. 4, the secondary structure of alpha-synuclein has five sheets, one beta-alpha-beta unit, three beta hairpins, one psi loop, three beta bulges, 17 strands, 19 helices, 21 helix-helix interactions, 29 beta turns, and three gamma turns. The structure has a total of 388 residues.

Ramachandran plot

The Ramachandran plot is a way to visualize energetically allowed regions for the torsions angle ψ against ϕ of amino acid in a protein structure. PROCHECK was used to produce the Ramachandran plot of alpha-synuclein, as shown in Fig. 5. The red regions on the graph are considered the sterically allowed regions, for which the conformation of peptides is stable. For *in silico* studies, more than 88% of the amino acids need to be in the sterically allowed region. About 92.5%, that is, 309 residues of the amino acid residues fall in the allowed region, whereas 0.3%, that is, one residue falls in the disallowed region. The remaining 7.2% falls in the sub-regions. Out of the 388 residues, 31 are glycine residues, 21 are proline residues, two are end-residues, and 334 are non-proline and non-glycine residues.

Hydropathy plot

The hydropathy plot, as shown in Fig. 6, is sketched for the amino acid residue on the X-axis and hydrophobicity/hydrophilicity on the Y-axis. It indicates the degree to which a protein's amino acids are hydrophobic or hydrophilic. EMBOSS pepwindow was used for this purpose. For a stable protein structure *in vivo*, hydrophobic residues align on the inside, whereas hydrophilic ones align on the outside.

Protein statistics

Protein statistics as shown in is the frequency of each amino acid residue in the protein sequence under a certain property. To collect statistical data on the amino acids under different characteristics such as size, charge, and pH, EMBOSS peptstats were used. The average molecular weight of the protein was found to be 42390.2 and the average residue weight was 109.253. In Table 1, it is seen that the protein has several small and non-polar residues, whereas the number of aromatic and basic residues is less.

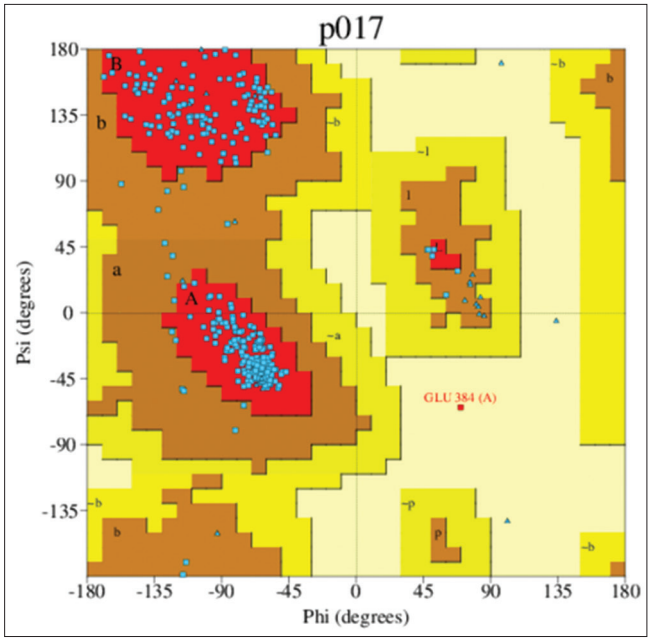

Fig. 5: Ramachandran plot of alpha-synuclein

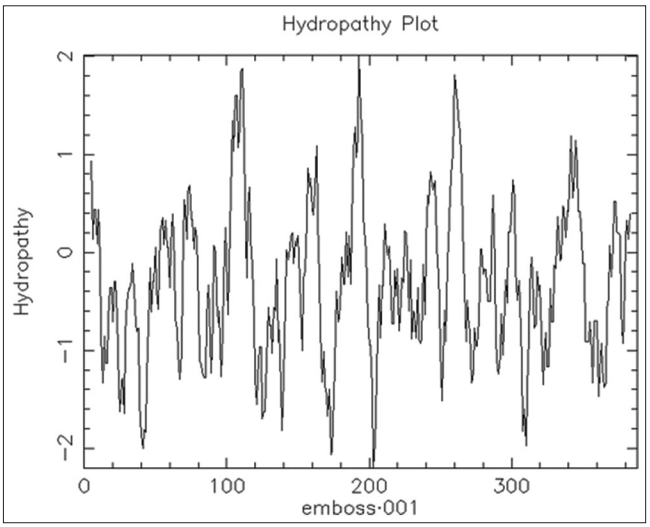

Fig. 6: Hydropathy plot of alpha-synuclein obtained using EMBOSS pepwindow

Table 1: Statistical information of alpha-synuclein obtained using EMBOSS pepstats

Property	Residues	Number	Mole%
Tiny	(A+C+G+S+T)	114	29.381
Small	(A+B+C+D+G+N+P+S+T+V)	205	52.835
Aliphatic	(A+I+L+V+)	124	31.959
Aromatic	(F+H+W+Y)	42	10.825
Non-polar	(A+C+F+G+I+L+M+P+V+W+Y)	223	57.474
Polar	(D+E+H+K+N+Q+R+S+T+Z)	165	42.526
Charged	(B+D+E+H+K+R+Z)	99	25.515
Basic	(H+K+R)	46	11.856
Acidic	(B+D+E+Z)	53	13.660

Drug likeliness analysis

The physicochemical properties, ADMET properties, and Lipinski rule of 5 are important criteria for a compound to be used in drug synthesis.

Aggregation data and toxicity prediction are also important for the synthesis of a drug with minimum side effects.

Pharmacological studies

The parameters for physicochemical properties are shown in Table 2.

For compounds in Table 3, it is observed that Decane, pentadecane, and hexadecane violate three of the parameters.

Lipinski Filter analysis

The Lipinski rule includes 5 parameters which are enlisted in Table 4.

The compounds highlighted in Table 5 are those which do not follow a minimum of four of the Lipinski rules. Hence, alpha1-sitosterol and beta-sitosterol cannot be used as candidates for drug synthesis.

ADME analysis

ADME analysis includes four major properties. Blood brain barrier (BBB) restricts the penetration of the compound into the brain. This information is of utmost importance for the synthesis of a drug. Gastrointestinal (GI) adsorption should be high to improve the drug's efficacy. The compound should be easily soluble as well. Hence, less negative solubility values are accepted. The screening of the compounds based on ADME properties is enlisted in Table 6.

Toxicity prediction

LD_{50} is a way to measure the short-term poisoning potential of a material. It is the amount of substance, administered all at once, that causes the death of 50% of test animals. LD_{50} values <500 mg/kg are given as highly toxic. The toxicity categorization as per ProTox-II is given in Table 7.

The compounds highlighted in red in Table 8, that is, nicotine and leucasperones A are considered to be highly toxic and should be used in very less quantities.

Aggregation properties

Aggregation is one of the main reasons for false positives in high throughput screening. Chem AGG is a web server that classifies compounds as aggregators and non-aggregators. The non-aggregators are potential lead molecules. Compounds with a probability score of zero are impossible to aggregate. In Table 9, it is seen that all compounds have a probability score of 0 and, therefore, are impossible to aggregate, that is, they are potential drug candidates.

Table 2: Parameters for physicochemical properties

Properties		Optimal range
Lipophilicity	xLogP	−0.7–+5.0
Size	Molecular weight	150–500 g/mol
Polarity	Topological polar surface area	20–130
Saturation	Sp3 hybridization	Not <0.25
Flexibility	Rotatable bonds	Not more than 9

Brain or intestinal estimated permeation method (BOILED-egg) assessment

BOILED-Egg gives the diagrammatic representation of ADME properties. The ligands in the white region have high gastrointestinal absorption whereas, those present in the yellow region have high potential to pass the blood brain barrier. In Fig. 7, the compounds marked in blue are said to be effectively fluxed by permeability glycoprotein (PGP^+), and the ones marked in red are said to be non-substrate of PGP. Alpha1-sitosterol and beta-sitosterol are out of range and, hence, are not considered potential drug candidates.

Molecular docking analysis

As per Table 10, alpha1-sitosterol and beta-sitosterol have the least binding affinity, but these compounds were ruled out as they violate Lipinski's rule. Hence, Leucasperones A and Baicalein were chosen for further analysis. In general, compounds with a binding affinity < −5.0 can be used for further analysis.

Docking of protein with selected compounds

PyRx was used to analyze the compounds' inhibitory activity and determine the binding affinity and docking score. When a protein and ligand are docked, a scoring formula called the "docking score" is used to forecast how well they will bind. Once the docking results were obtained, suitable compounds with the most negative binding affinity, that is, Baicalein and Leucasperones A were chosen for further analysis. Visualization was done using Dassault Systems BIOVIA Discovery Studio Visualizer and the Two-dimensional (2D) as well as 3D models were obtained, as seen in Figs. 8 and 9. Furthermore, Tables 11 and 12 contain information about the category and type of interaction along with the bond distance for the corresponding amino acid residues in the ligand.

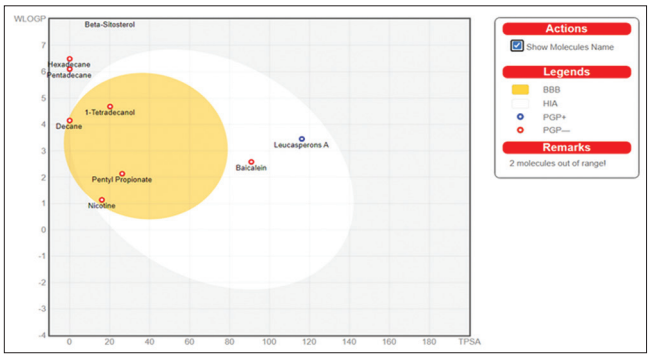

Fig. 7: Brain or intestinal estimated permeation method diagram obtained using Swiss ADME

Table 3: Physicochemical properties

Ligand	Molecular weight	Fraction Csp3	Rotatable bonds	Topological polar surface area	Lipophilicity
Nicotine	162.23	0.5	1	16.13	1.17
Alpha1-Sitosterol	426.72	0.87	5	20.23	9.03
Leucasperones A	478.58	0.69	11	116.2	1.89
Beta-sitosterol	414.71	0.93	6	20.23	9.34
Hexadecane	226.44	1	13	0	8.28
Decane	142.28	1	7	0	5.01
Baicalein	270.24	0	1	90.9	3.16
1-Tetradecanol	214.39	1	12	20.23	6.03
Pentyl propionate	144.21	0.88	6	26.3	2.77
Pentadecane	212.41	1	12	0	7.74

Visualization of the molecular interaction of the baicalein with alpha-synuclein

The compounds alpha-1-sitosterol and beta-sitosterol were not visualized despite their best exhibiting best binding affinities as they didn't fulfil admet properties and Lipinski Rule of 5. Therefore, the ligands Baicalein and Leucasperones were appraised as lead drugs. The ligand Baicalein demonstrated strong interactions with amino acids ASN12, ASP15, ARG67, GLU125, TRP231, TYR156, TRP63, ALA64 and PRO155 (Fig. 8 and Table 11).

Leucasperones A

The ligand Leucasperone A established a strng interaction with the A chain amino acids with a bimding affinity of -8.8. The ligand was interacting wth LYS43, ASN13, TYR211, ASP15, ARG67, TRP63, GLU45, ASP42, LYS16 and GLU112 amino acids.

DISCUSSION

The earliest therapeutic intervention of Parkinson's disease dates back to 1877 wherein belladonna alkaloids were employed as anticholinergic agents. The first detailed description was provided by James Parkinson in 1817. Anticholinergic medications were used to treat PD as early as the 19th century, and early treatments were empirical observation based. The first levodopa clinical studies on humans followed the identification of dopaminergic deficiencies in PD and the dopamine synthesis pathway. Additional historically significant anatomical, biochemical, and physiological studies have revealed additional pharmacological and surgical targets for PD, enabling contemporary clinicians to provide a range of treatments aimed at enhancing function in this still incurable condition [24].

Table 4: Lipinski rule parameters

Property	Optimal range
Molecular weight	150–500 Daltons
MlogP	<4.15
H Donors	<5
H acceptors	<10
Molecular refractivity	40–130

After the separation of an alpha-synuclein fragment from amyloid plaques in AD, the role of alpha-synuclein in neurodegenerative illnesses was initially suspected. Later, but only in a small number of families, it was discovered that two distinct alpha-synuclein mutations were linked to autosomal-dominant PD. However, the revelation that alpha-synuclein is a significant component of Lewy bodies and Lewy neurites, the pathological hallmarks of PD, validated its participation in the pathogenesis of PD.

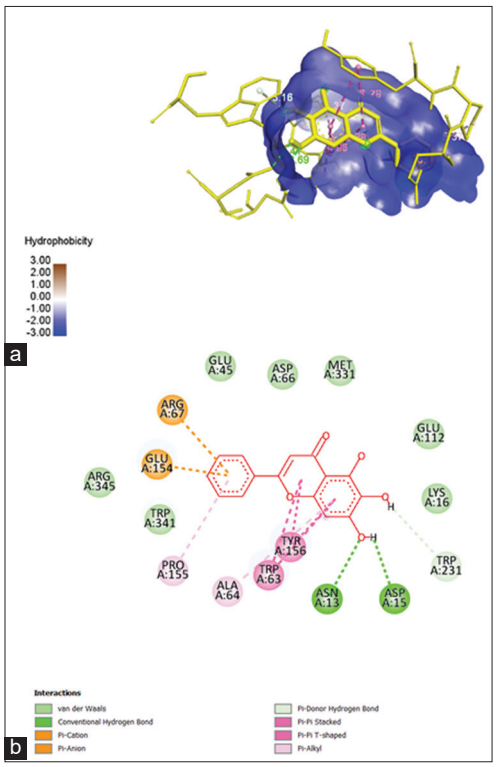

Fig. 8: Visualization of molecular interactions between baicalein and alpha-synuclein. (a) 3D interaction diagram and (b) 2D interaction diagram

Table 5: Data for the properties of the Lipinski rule obtained using Swiss ADME

Ligand	Molecular weight	MLogP	Hydrogen acceptors	Hydrogen donors	Molar refractivity
Nicotine	162.23	1.17	2	0	53.13
Alpha1-sitosterol	426.72	6.82	1	1	137.56
Leucasperones A	478.58	2.22	8	1	126.65
Beta-sitosterol	414.71	6.73	1	1	133.23
Hexadecane	226.44	6.44	0	0	79.03
Decane	142.28	4.82	0	0	50.18
Baicalein	270.24	0.52	5	3	73.99
1-Tetradecanol	214.39	3.95	1	1	70.57
Pentyl Propionate	144.21	1.96	2	0	41.85
Pentadecane	212.41	6.19	0	0	74.22

Table 6: ADME data obtained using Swiss ADME

Ligands	Blood Brain barrier penetration	GI absorption	PGP substrate	Solubility (LOGSw-SILICOS IT)
Nicotine	Yes	High	No	–2.62 (Soluble)
Alpha1-sitosterol	No	Low	No	–5.97 (Moderately soluble)
Leucasperones A	No	High	Yes	–4.43 (Moderately soluble)
Beta-sitosterol	No	Low	No	–6.19 (Poorly soluble)
Hexadecane	No	Low	No	–6.33 (Poorly soluble)
Decane	Yes	Low	No	–3.87 (Soluble)
Baicalein	No	High	No	–4.4 (Moderately soluble)
1-Tetradecanol	Yes	High	No	–4.96 (Moderately soluble)
Pentyl propionate	Yes	High	No	–2.34 (Soluble)
Pentadecant	No	Low	No	–5.92 (Moderately soluble)

Table 7: Toxicity categorization

Class	LD_{50} (mg/kg)
I	LD_{50} <5
II	5< LD_{50} <50
III	50< LD_{50} <300
IV	300< LD_{50} <2000
V	2000< LD_{50} <5000
VI	LD_{50} >5000

Table 8: Toxicity data obtained using ProTox-II

Compound	Predicted LD_{50} (mg/kg)	Predicted toxicity class
Nicotine	3	1
Alpha1-sitosterol	2000	4
Leucasperones A	452	4
Beta-sitosterol	890	4
Hexadecane	750	3
Decane	750	3
Baicalein	3919	5
1-tetradecanol	1000	4
Pentyl propionate	14000	6
Pentadecane	750	3

Table 9: Aggregation data obtained using Chem AGG

Compound	Aggregator class	Probability score
Nicotine	0	0.033
Alpha1-sitosterol	0	0.008
Leucasperones A	0	0.012
Beta-sitosterol	0	0.031
Hexadecane	0	0.024
Decane	0	0.024
Baicalein	0	0.119
1-Tetradecanol	0	0.011
Pentyl propionate	0	0.028
Pentadecane	0	0.024

Table 10: Binding affinity data obtained from PyRx

Ligand	Binding affinity
Nicotine	−6.2
Alpha1-sitosterol	−10.6
Leucasperones A	−8.8
Beta-sitosterol	−9.9
Hexadecane	−6.1
Decane	−4.9
Baicalein	−8.7
1-tetradecanol	−5.8
Pentyl propionate	−4.8
Pentadecane	−6.1

Neurodegeneration may be caused by aggregation of the pathological protein. Moreover, unlike the insoluble fibrils found in Lewy bodies, soluble oligomers of alpha-synuclein may be far more deadly. It has been demonstrated that a variety of conditions speed up the *in vitro* aggregation of alpha-synuclein. Therefore, it is planned to use of therapeutic methods to stop this aggregation. Alpha-synuclein appears to interact with a wide range of proteins and membrane phospholipids, suggesting that it may take part in several signaling pathways, even though little is known about its normal function. It may specifically affect dopaminergic neurotransmission, synaptic plasticity, cell survival, and cell differentiation. Hence, it is also feasible for pathogenic pathways based on disturbing normal function [4].

L. aspera is found all over India. The plant has historically been employed as a pesticide and antipyretic. It has been demonstrated

Table 11: Interaction data between baicalein and alpha-synuclein

Name	Distance	Category	Types
A:ASN13:HD21-N: UNK1:O	2.69356	Hydrogen bond	Conventional hydrogen bond
N:UNK1:H-A: ASP15:OD1	2.41148	Hydrogen bond	Conventional hydrogen bond
A:ARG67:NH2-N: UNK1	3.90674	Electrostatic	Pi-cation
A:GLU154:OE1-N: UNK1	3.21051	Electrostatic	Pi-anion
N:UNK1:H-A: TRP231	3.15719	Hydrogen bond	Pi-donor hydrogen bond
A:TYR156-N: UNK1	4.78425	Hydrophobic	Pi-Pi stacked
A:TYR156-N: UNK1	4.7619	Hydrophobic	Pi-Pi stacked
A:TRP63-N: UNK1	5.29354	Hydrophobic	Pi-Pi T-shaped
A:TRP63-N: UNK1	5.3847	Hydrophobic	Pi-Pi T-shaped
A:TRP63-N: UNK1	4.96344	Hydrophobic	Pi-Pi T-shaped
N:UNK1-A: ALA64	5.3672	Hydrophobic	Pi-Alkyl
N:UNK1-A: PRO155	5.37409	Hydrophobic	Pi-Alkyl

Table 12: Interaction data between leucasperones A and alpha-synuclein

Name	Distance	Category	Types
A:LYS43:HN-N: UNK1:O	2.04021	Hydrogen bond	Conventional hydrogen bond
N:UNK1:C-A: ASN13:OD1	3.70748	Hydrogen bond	Carbon hydrogen bond
N:UNK1:C-A: TYR211	3.77098	Hydrophobic	Pi-sigma

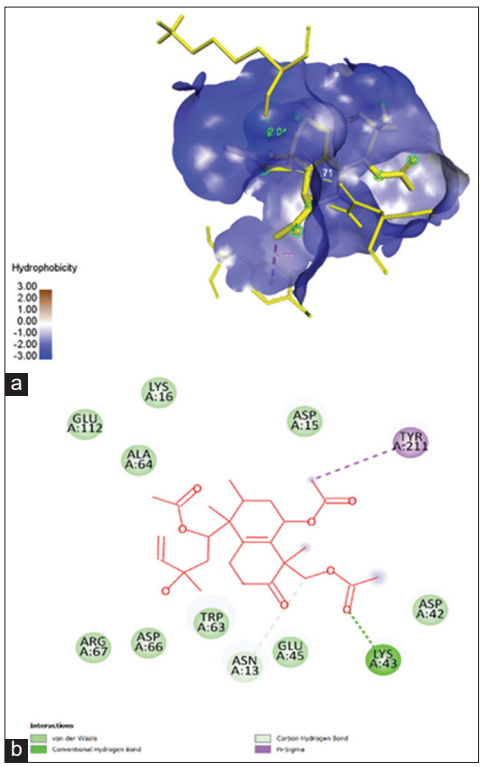

Fig. 9: Visualization of molecular interactions between Leucasperones A and alpha-synuclein. (a) 3D interaction diagram and (b) 2D interaction diagram

to have a variety of pharmacological effects in terms of medicine, including antifungal, antioxidant, antibacterial, antinociceptive, and cytotoxic activity. Numerous phytochemical components, including triterpenoids, oleanolic acid, ursolic acid, and b-sitosterol, as well as

nicotine, sterols, glucoside, diterpenes, and phenolic compounds, are also present, according to studies [6].

Considering these characteristics, this plant was chosen as a source to obtain chemicals to test their likelihood of being PD-resistant. Nicotine, alpha1-sitosterol, Leucasperones A, beta-sitosterol, hexadecane, decane, baicalein, 1-tetradecanol, and pentadecane were the ten compounds selected for analysis. Following the completion of pharmacological investigations to exclude relatively inappropriate compounds such as alpha1-sitosterol and beta-sitosterol as they violate the Lipinski rule, molecular docking was carried out, and two of the compounds with binding affinities <5.0, that is, Baicalein and Leucasperones A were selected. From their 2D interaction diagram of the protein-ligand complex, it can be inferred that several amino acids such as tyrosine, tryptophan, glutamic acid, lysine, and alanine are involved in hydrogen bonds, electrostatic interactions, and hydrophobic interactions. These substances are good candidates for the creation of a medicine that prevents PD by acting on human alpha-synuclein.

Although *in silico* studies are in favor of these two compounds, they can also have other drawbacks which overshine their potential as a drug candidate. Baicalein is known to cause stomach pain, constipation, and vomiting, whereas Leucasperones A can cause an allergic reaction. Hence, it is important to note that the results of *in silico* studies may differ from that *in vitro*.

CONCLUSION

According to the results of this study, the plant *L. aspera* contains the phytochemicals Baicalein in their flowers and Leucasperones A in their ariel parts, which can be used to create PD medications. The protein that causes PD has active sites that some substances can bind to, inhibiting its activities. In addition, it can be inferred that medicinal plants are crucial for the development of medications for both established and newly discovered diseases. It is possible to research other plants to find even more potent medication possibilities.

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REFERENCES

1. Beitz JM. Parkinson's disease: A review. Front Biosci (Schol Ed) 2014;6:65-74.
2. Davie CA. A review of Parkinson's disease. Br Med Bull 2008;86:109-27.
3. Sveinbjornsdottir S. The clinical symptoms of Parkinson's disease. J Neurochem 2016;139 Suppl 1:318-24.
4. Lücking CB, Brice A. Alpha-synuclein and Parkinson's disease. Cell Mol Life Sci 2000;57:1894-908.
5. Stefanis L. α-Synuclein in Parkinson's disease. Cold Spring Harb Perspect Med 2012;2:a009399.
6. Prajapati MS, Patel JB, Modi K, Shah MB. *Leucas aspera*: A review. Pharmacogn Rev 2010;4:85-7.
7. Chew AL, Jessica JJ, Sasidharan S. Antioxidant and antibacterial activity of different parts of *Leucas aspera*. Asian Pac J Trop Biomed 2012;2:176-80.
8. Mangathayaru K, Lakshmikant J, Sundar NS, Swapna R, Grace XF, Vasantha J. Antimicrobial activity of *Leucas aspera* flowers. Fitoterapia 2005;76:752-4.
9. Babu A, Mohamed MS, Jaikumar K, Anand D, Saravanan P. *In-vitro* antifungal activity of leaf extracts of *Leucas aspera* and *Leucas zeylanica*. Int J Pharm Sci Res 2016;7:752-6.
10. Rahman MS, Sadhu SK, Hasan CM. Preliminary antinociceptive, antioxidant and cytotoxic activities of *Leucas aspera* root. Fitoterapia 2007;78:552-5.
11. Mohan A, Nair SV, Lakshmanan VK. *Leucas aspera* nanomedicine shows superior toxicity and cell migration retarded in prostate cancer cells. Appl Biochem Biotechnol 2017;181:1388-400.
12. Islam AK, Ohno O, Suenaga K, Kato-Noguchi H. Two novel phytotoxic substances from *Leucas aspera*. J Plant Physiol 2014;171:877-83.
13. Mohanraj K, Karthikeyan BS, Vivek-Ananth RP, Chand RP, Aparna SR, Mangalapandi P, *et al*. IMPPAT: A curated database of Indian medicinal plants, phytochemistry and therapeutics. Sci Rep 2018;8:4329.
14. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, *et al*. PubChem in 2021: New data content and improved web interfaces. Nucleic Acids Res 2021;49:D1388-95.
15. De Beer TA, Berka K, Thornton JM, Laskowski RA. PDBsum additions. Nucleic Acids Res 2014;42:D292-6.
16. Laskowski RA, MacArthur MW, Moss DS, Thornton JM. PROCHECK: A program to check the stereochemical quality of protein structures. J Appl Crystallogr 1993;26:283-91.
17. Kim M, Kim H, Lee W, Lee Y, Kwon SW, Lee J. Quantitative shotgun proteomics analysis of rice anther proteins after exposure to high temperature. Int J Genomics 2015;2015:238704.
18. McWilliam H, Li W, Uludag M, Squizzato S, Park YM, Buso N, *et al*. Analysis tool web services from the EMBL-EBI. Nucleic Acids Res 2013;41:W597-600.
19. BIOVIA DS. BIOVIA Discovery Studio Visualizer. Vol. 20. California, United States: BIOVIA Software Version; 2017. p. 779.
20. Xiong G, Wu Z, Yi J, Fu L, Yang Z, Hsieh C, *et al*. ADMETlab 2.0: An integrated online platform for accurate and comprehensive predictions of ADMET properties. Nucleic Acids Res 2021;49:W5-14.
21. Banerjee P, Eckert AO, Schrey AK, Preissner R. ProTox-II: A webserver for the prediction of toxicity of chemicals. Nucleic Acids Res 2018;46:W257-63.
22. Yang ZY, Yang ZJ, Dong J, Wang LL, Zhang LX, Ding JJ, *et al*. Structural analysis and identification of colloidal aggregators in drug discovery. J Chem Inf Model 2019;59:3714-26.
23. Dallakyan S, Olson AJ. Small-molecule library screening by docking with PyRx. Methods Mol Biol 2015;1263:243-50.
24. Goetz CG. The history of Parkinson's disease: Early clinical descriptions and neurological therapies. Cold Spring Harb Perspect Med 2011;1:a008862.