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Research Article

Uncovering Gene Targets Modulated by *Withania somnifera* Phytochemicals for Alzheimer's Disease Intervention Using Network Pharmacology Approaches

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Abstract

Alzheimer's disease (AD) is a neurological disorder characterized by progressive memory loss, cognitive decline, and neuronal degeneration. The pathophysiology of Alzheimer's disease (AD) involves amyloid-beta buildup, tau hyperphosphorylation, oxidative stress, making the development of effective therapies challenging. This highlights the need for multi-target neuroprotective medicines. As a result, it is very important to quickly find natural bioactive compounds. *Withania somnifera* (Ashwagandha), has exhibited notable antioxidant, anti-inflammatory, and neuroprotective effects. We collected 65 phytochemicals and examined 49 of them based on ADMET characteristics. We collected gene targets for these chemicals (8,964) and AD-related genes (15,293) from separate databases. A comparison investigation revealed 920 overlapping genes. We detected 13 hub genes using Cytoscape for topological analysis: TP53, SRC, AKT1, HSP90AA1, EGFR, IL6, MAPK1, MAPK3, JUN, ESR1, BCL2, HSP90AB1, and GNAI1. After then, STRING was used to create networks of protein-protein interactions (PPIs). Network pharmacology demonstrated that the 13 hub genes are significantly associated with the regulation of apoptosis, MAPK signaling, PI3K-AKT signaling, and neuroinflammation. Docking studies revealed that significant phytochemicals like as Somniferine, Withaferin A, and Withanolide O have considerable binding affinity to hub proteins including AKT1, JUN, and HSP90AA1. This research on integrative network pharmacology and molecular docking demonstrates the potential application of W. Somnifera phytochemicals for the treatment of Alzheimer's disease.

Keywords

Alzheimer's Disease, *Withania somnifera*, Network Pharmacology, Molecular Docking, Hub Genes, Neuroprotection

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1. Introduction

Alzheimer's disease (AD) is a neurological disorder that progressively deteriorates. The most prevalent clinical indications of Alzheimer's disease (AD) are memory issues, aphasia, agnosia, apraxia, visuospatial ability impairment, executive dysfunction, personality and behavior changes, and other signs of dementia [1]. In the U.S., there are about 5.8 million persons with AD, and that figure is anticipated to go up in the next few years [2]. The pathological features of Alzheimer's Disease (AD) include amyloid-beta (Aβ) plaques, tau protein tangles, cholinergic dysfunction, senile plaques, glial cell activation, mitochondrial dysfunction, vascular abnormalities, calcium homeostasis, and neuronal degradation, all associated with increased oxidative stress and synaptic loss [3, 4]. Early-onset Alzheimer's disease results from infrequent mutations in the Amyloid beta precursor protein (APP), Presenilin 1 (PSEN 1), and Presenilin 2 (PSEN 2) genes [5, 6]. Dysregulation of signaling pathways including as PI3K/Akt, MAPK, JNK, and mTOR, which affect apoptosis, neural plasticity, and inflammatory responses, exacerbates the disease [7].

Natural compounds have emerged as promising multi-target therapeutic agents that focus on a single mechanism due to their antioxidant, anti-inflammatory, anti-amyloidogenic, and neurogenic properties such as polyphenols, flavonoids, alkaloids, and terpenoids which provide neuroprotection by neutralizing reactive oxygen species (ROS), maintaining mitochondrial balance, and regulating inflammatory pathways [8, 9]. *Withania somnifera*, (Ashwagandgha) is a plant that is often used in Ayurveda to help with neurological problems. The bioactive chemicals withanolides, alkaloids, and sitoindosides are found in its leaves, stems, and roots [10, 11]. Withanolide-rich extracts may facilitate the clearance of Aβ, reduce oxidative stress associated with Aβ, and prevent neuronal apoptosis, all mediated by insulin-degrading enzyme (IDE) and antioxidant mechanisms [12].

Network pharmacology integrates network biology and polypharmacology [13]. It is primarily utilized to examine multi-target medications linked to disease-related genes and to clarify their complex mechanisms [14]. It also demonstrates the interactions between bioactive substances and molecular networks, enabling a comprehensive examination of diverse compounds and their effects on targets and pathways [15, 16]. Gene ontology, KEGG, and networks of protein-protein interactions pathway enrichment analyses enable the methodical examination of molecular mechanisms and essential regulatory nodes [17, 18]. Expression study of hub genes clarifies regional relevance in Alzheimer's disease pathology, whereas molecular docking simulations validate the binding affinity of phytochemicals to target proteins [19]. This research examined 65 phytochemicals and identified 49 that complied with ADMET criteria [11]. We identified 13 hub genes (TP53, SRC, AKT1, HSP90AA1, EGFR, IL6, MAPK1, MAPK3, JUN, ESR1, BCL2, HSP90AB1, GNAI1) associated with AD by a protein network analysis [20]. Functional assignment in KEGG is the process of linking a collection of genes in the genome to a network of molecules in the cell that work together, like a pathway or a complex. This signifies a superior biological function [21].

Numerous in silico research have been conducted on Alzheimer's disease, and the therapeutic attributes of W. somnifera have been thoroughly examined. Nevertheless, there is a scarcity of research explicitly examining the effects of compounds derived from W. Somnifera influence particular genes associated with Alzheimer's disease. Examining these connections may clarify their possible role in Alzheimer's disease treatment.

2. Materials and Methods

2.1. Prediction of Target Genes for Ashwagandha Phytochemicals and Alzheimer’s Disease

The present studies catalog the known phytocompounds derived from the roots of *Withania somnifera*, obtained from the PubChem (https://pubchem.ncbi.nlm.nih.gov/) [22], ChEBI (https://www.ebi.ac.uk/chebi/) [23], and IMPPat databases (https://cb.imsc.res.in/imppat/) (accessed on 8 December 2025) [24]. We used SwissADME, pkCSM, and ADMETlab 2.0 to look at the drug-likeness and ADMET profiles. We got rid of any compounds that didn't fulfill more than two Lipinski criteria, leaving us with 49 for the next study. We used SwissTargetPrediction (https://www.swisstargetprediction.ch/), STITCH (https://bio.tools/stitch), and other tools to find the projected gene targets for these active chemicals. We got genes connected to Alzheimer's disease from the DisGeNET (https://disgenet.com/) (accessed on December 15, 2025), OMIM (https://www.omim.org/) (accessed on December 19, 2025), and GeneCards (https://www.genecards.org/) (accessed on December 22, 2025) databases. We used Venny 2.1.0 (https://bioinfogp.cnb.csic.es/tools/venny/) (accessed on 23 December 2025) to find the genes that were the same in both sets.

2.2. Chromosomal Location and Tissue Distribution of Targets

To determine the functional context of the overlapping genes, their chromosomal locations were determined using ShinyGO v0.75 (https://bioinformatics.sdstate.edu/go75/) (accessed on 26 March 2026) [25, 26]. The Pa-GenBase dataset, obtained on 27 March 2026, via Metascape v3.5.2023.05.01 (https://metascape.org/), offered tissue-specific expression profiles, aiding in the identification of genes markedly expressed in brain regions associated with Alzheimer’s pathology [26].

2.3. Functional Enrichment and Pathway Analysis

Gene Ontology (GO) was examined to comprehend cellular components, biological processes, and molecular functions. After that, we performed KEGG pathway analysis to uncover signaling pathways that could be linked to kidney cancer and inflammation of the kidneys. We created enrichment plots that displayed the percentage of differentially expressed genes in each pathway using both p-values and corrected p-values [26]. We utilized the Protein Analysis Through Evolutionary Relationships (PANTHER) program v18.0 (https://pantherdb.org/) (accessed on 28 December 2025) for gene ontology and pathway analyses. This helped us understand how these genes that are commonly linked together affect the signaling pathways as a whole [27].

2.4. Construction of Protein–Protein Interaction (PPI) Networks

We used STRING using NetworkAnalyst v3.0 (https://string-db.org/) (accessed on March 30, 2026) to look at how proteins interact with each other. We used CytoHubba v0.1 (https://cytoscape.org/) (accessed on March 31, 2026) to create subnetworks in Cytoscape v3.10.1. This helped us locate hub genes based on degree centrality, closeness centrality, and based on RNA Expression. The top 20% of nodes were shown to be important hub genes [28, 29].

2.5. Physiochemical and ADMET Profiling of Phytochemicals

The hit compounds were subjected to in silico physicochemical investigation. We used the SwissADME (https://www.swissadme.ch/) (accessed on 2-12 April 2026) [30], ADMETlab2.0 (https://admetmesh.scbdd.com/) (accessed on 2-12 April 2026) [31], pkCSM (https://biosig.lab.uq.edu.au/pkcsm/) (accessed on 2-12 April 2026) [32], and Protox-II (https://tox.charite.de/) (accessed on 2-12 January 2026) [33] to look at the predicted ADMET properties. We used the canonical SMILES of the metabolites from the PubChem Database to make educated guesses on their ADMET features (absorption, distribution, metabolism, excretion, and toxicity). Finally, we rejected the protein targets associated with Lipinski's rule of five (LO5) metabolites that violated more than two of its criteria [34].

2.6. Hub Gene Expression Validation

The Human Protein Atlas v23.0 (https://www.proteinatlas.org/) (accessed on 16 April 2026) [35] verified the expression of hub genes in certain tissues, particularly in brain regions closely associated with Alzheimer's disease.

2.7. Protein and Ligand Preparation for Docking

On April 15, 2026, we acquired the crystal structures of hub proteins from the RCSB Protein Data Bank (https://www.rcsb.org/) [36]. We utilized AutoDock Tools v4 to get rid of water molecules, cofactors, and metal ions from proteins, add polar hydrogens, and figure out Gasteiger charges. We got ligand structures in SDF format from PubChem (https://pubchem.ncbi.nlm.nih.gov/) (accessed from April 28 to May 4, 2026) [37].

2.8. Binding Site Identification and Grid Box Generation

We identified binding sites by examining pockets derived from established protein-ligand interactions. PDB and CASTp [38] were used to find the known and undiscovered active sites of the protein structures, and BIOVIA Discovery Studio Visualizer v19.1 (BIOVIA) was used to look at the proteins' binding sites [39]. We generated the receptor grid with molecular docking and retrieved the binding sites from the complex structure with the PyRx—Python Prescription 0.8 virtual screening program [40].

2.9. Molecular Docking Simulation

We utilized PyRx v0.8 to undertake molecular docking and identified the chemicals that function well with the target proteins [40]. This platform has AutoDock Vina and AutoDock v4, which let us virtually test huge groups of chemicals against macromolecules. We utilized the default settings for the AutoDock Vina Wizard to execute docking simulations [41]. We put the compounds in order depending on how much binding energy they had (kcal/mol), how many hydrogen bonds they made, and how many hydrophobic contacts they made. The chemicals that bound the strongest were determined to be viable therapies for Alzheimer's disease that could work on more than one target.

3. Results

3.1. Identification of Common Target Genes

A total of 65 phytochemicals were isolated from *W. somnifera*. The ADMET characteristics indicated that 49 compounds satisfied the criteria for further investigation. Target prediction found 8,964 genes that are linked to compounds, while Alzheimer's disease (AD)-related targets found 15,293 genes. DisGeNET, OMIM, and GeneCards all have these. A comparative analysis identified 920 common gene targets considered as potential treatment possibilities for Alzheimer's disease (AD) (Figure 1).

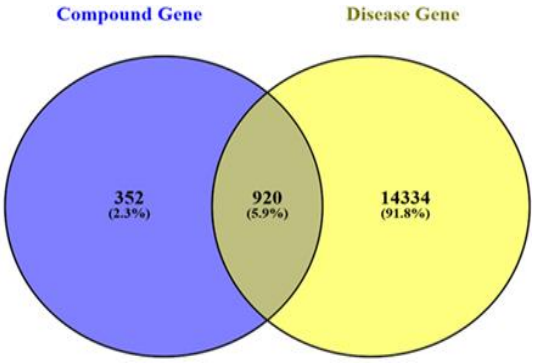


Figure 1. *Venn diagram showing the overlapping genes between Ashwagandha-derived compounds and AD-related target genes.*

3.2. Protein-Protein Interaction (PPI) Network Analysis

You can utilize PPI data to build computer models of networks of diseases. You can use these models to guess how illnesses will spread over the planet. The STRING database brought in the 920 targets that were overlapped (confidence score ≥ 0.75). This produced a PPI network with 4,312 edges that are very well connected. Cytoscape visualization revealed numerous dense interaction clusters, indicating that these targets probably have strong functional linkages (Figure 2).

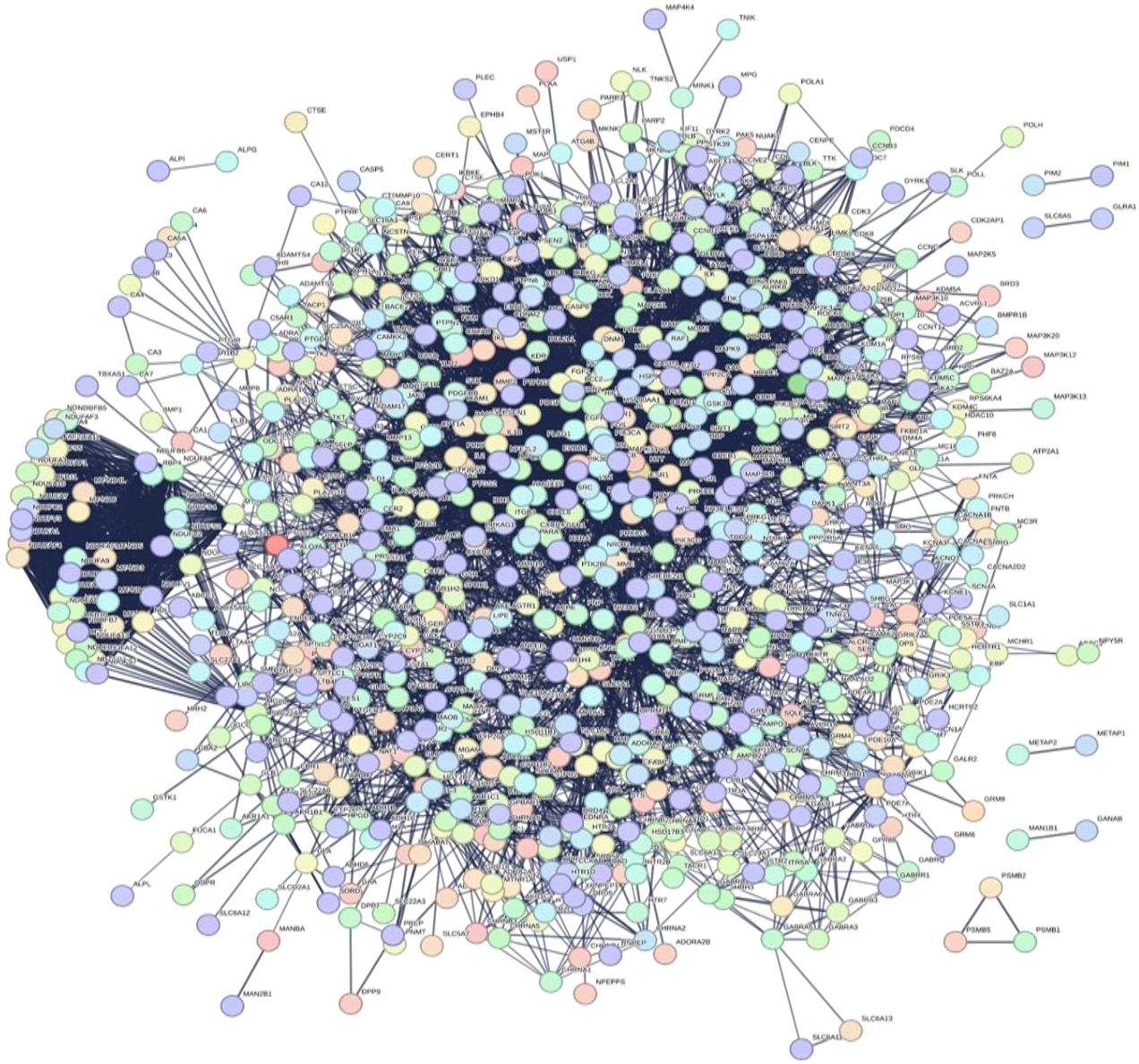


Figure 2. *PPI network of overlapping targets generated by STRING and visualized in Cytoscape.*

3.3. Identification of Hub Genes

We used the Cytoscape plug-in CytoHubba to look at the PPI network. We assessed the three methodologies: Degree, Closeness, and RNA expression. The 13 hub genes we detected include TP53, SRC, AKT1, HSP90AA1, EGFR, IL6, MAPK1, MAPK3, JUN, ESR1, BCL2, HSP90AB1, and GNAI1.The bar charts shows the RNA expression levels in their brain regions which is measured in nTPM. We can see HSP90AA1, MAPK1, MAPK3, and HSP90AB1 shows very high expression level. Genes like TP53, AKT1, and EGFR shows the moderate expression and on the other hand, SRC, IL6, and ESR1 shows the low expression level. These genes are the most important regulatory nodes that connect. (Figure 3) shows that chemicals in *Withania somnifera* are connected to AD pathways.

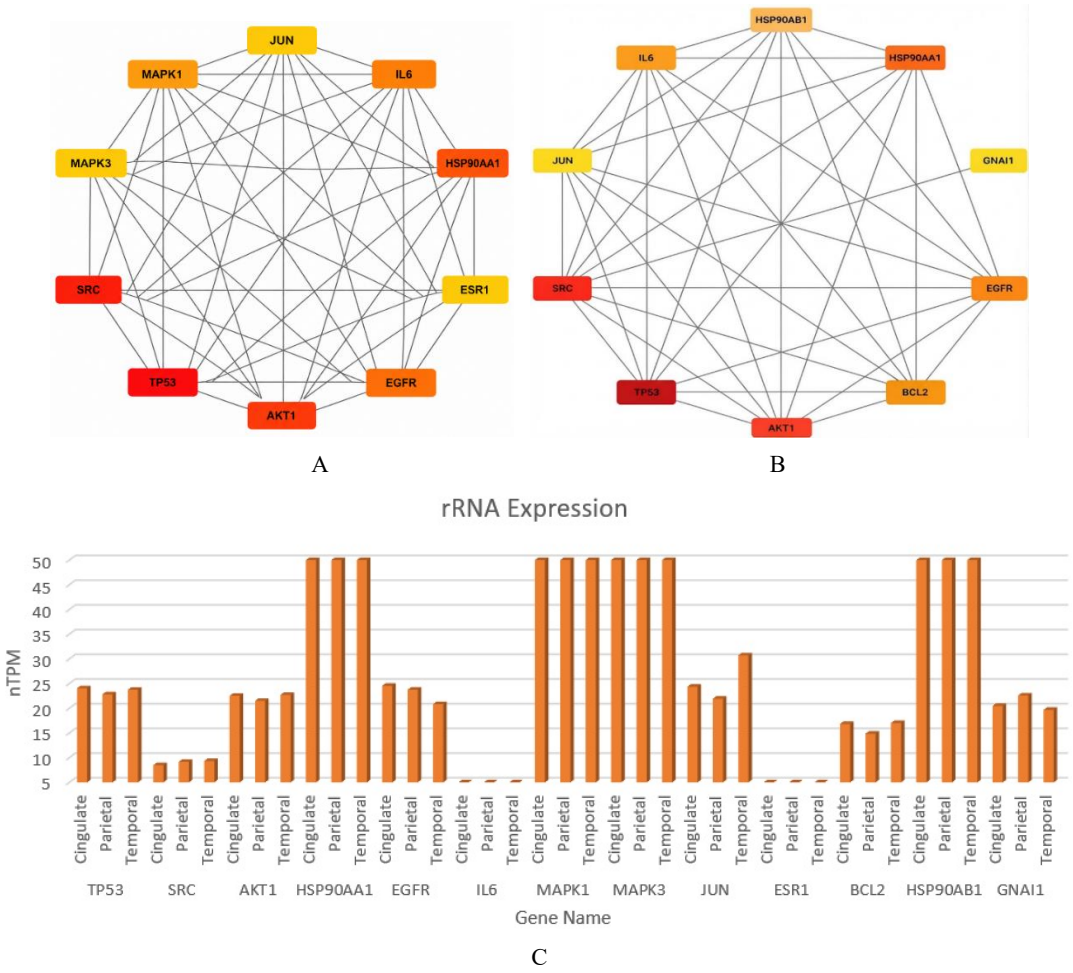


Figure 3. *(A) shows the genes identified in the cytoscape according to the Degree methods, (B) shows the genes identified in the cytoscape according to the Closeness methods, and (C) shows the gene identification through RNA Expression by Human Protein Atlas.*

3.4. Functional Enrichment (GO) Analysis

We ran a Gene Ontology (GO) enrichment analysis on the 920 targets that were the same. The results showed a lot of growth in:

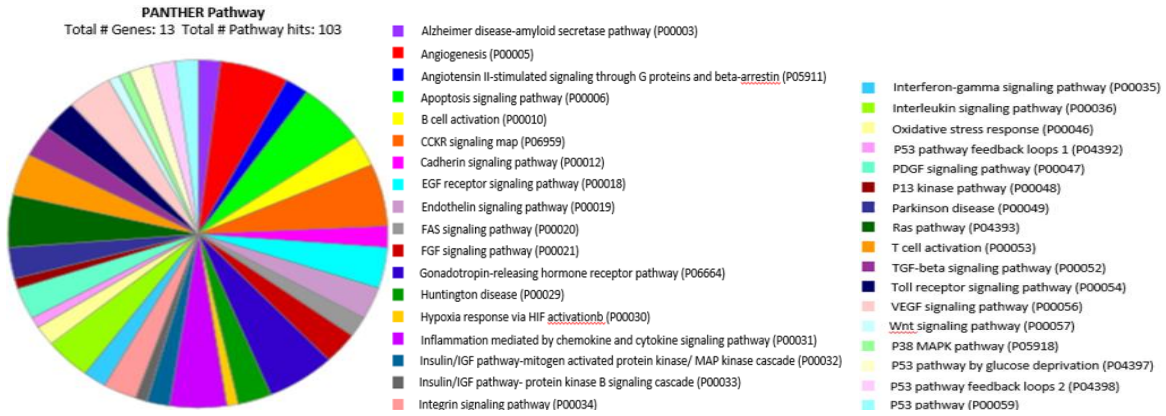
The targets were largely related to managing apoptosis, the inflammatory response, and synaptic transmission when it came to Biological Processes (BP). These activities are essential for neuronal survival, neuroinflammation, and inter-neuronal communication, all of which are critical to the progression of Alzheimer's disease (AD). Some of the more specific terminology for Molecular Functions (MF) were transcription factor binding and protein kinase activity. This suggests that a significant number of these genes are probably implicated in intracellular signaling pathways and gene regulatory mechanisms. Most of the targets were discovered in the cytoplasm, nucleus, and plasma membrane complexes when it came to Cellular Components (CC). This distribution reveals that the genes that were discovered are involved in both signaling events that happen inside cells and activities that happen on membranes. These results indicate that the overlapping genes are primarily involved in processes that are highly relevant to Alzheimer's disease pathology (Figure 4).

Figure 4. *GO enrichment analysis of overlapping targets. (A) Biological process, (B) Molecular function, and (C) Cellular components.*

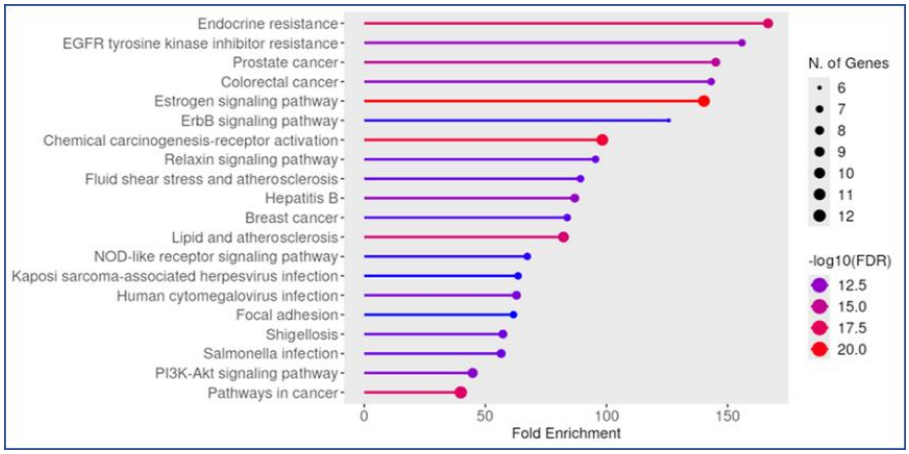
3.5. KEGG Pathway Enrichment Analysis

A KEGG pathway enrichment study revealed that 65 signaling pathways were significantly enriched ($p < 0.05$). The PI3K–Akt signaling pathway, the MAPK signaling route, signaling pathways associated to neuroinflammation, and pathways connected to the processing and metabolism of amyloid-beta were all very important to Alzheimer's disease (AD).

These signaling pathways are particularly important for the survival of neurons, the function of synapses, the body's reaction to inflammation, and the production of amyloid plaques. All of these things are critical for how AD develops. The enhancement of these routes signifies that *W. somnifera* Phytochemicals may function as therapeutics by simultaneously influencing multiple molecular mechanisms that induce neurodegeneration (Figure 5).



A



B

Figure 5. *KEGG pathway enrichment of overlapping targets (A-B).*

3.6. ADMET Properties of *Withania Somnifera* (Ashwagandha) Phytochemicals

Using programs like SwissADME, pkCSM, and ADMETlab 2.0, we found that 49 of the 65 phytochemicals we first found matched the ADMET evolution criterion. The chemicals that were chosen had good pharmacokinetic features, namely good oral bioavailability, good solubility, and low anticipated toxicity levels. Table 1 shows the most important ADMET characteristics for these chemicals.

Table 1. *ADMET properties of Withania Somnifera (Ashwagandha).*

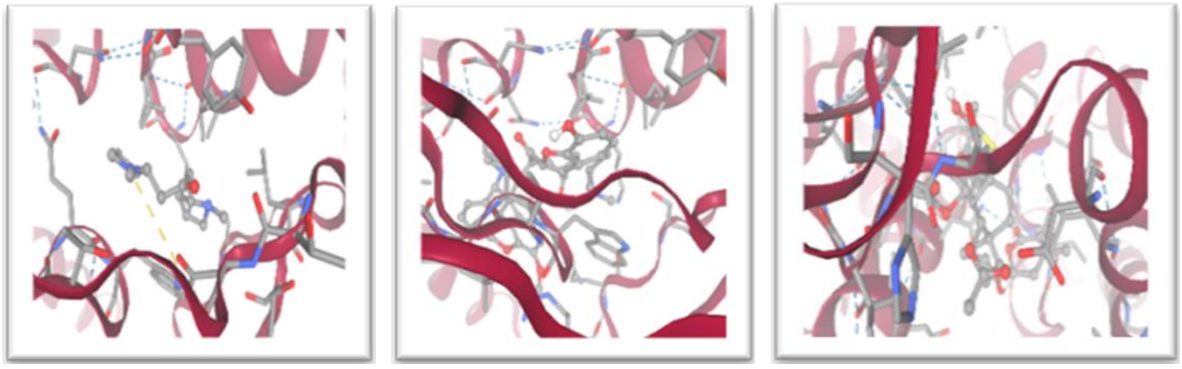
Compound	Molecular weight	Number of Rotatable Bonds	Number of hydrogen bond acceptors	Number of hydrogen bond donor	Lipinski	Bioavailability score	GI absorption
Cuscohygrine	224.34	4	3	0	Yes;0 violation	0.55	High
Somniferine	608.68	3	9	2	Yes;1 violation	0.55	High
Withanolide O	452.58	2	5	2	Yes;0 violation	0.55	High
Withaferin A	470.6	3	6	2	Yes;0 violation	0.55	High
withanolide A	470.60	2	6	2	Yes;0 violation	0.55	High
Pelletierine	141.21	2	2	1	Yes;0 violation	0.55	High

Compound	Molecular weight	Number of Rotatable Bonds	Number of hydrogen bond acceptors	Number of hydrogen bond donor	Lipinski	Bioavailability score	GI absorption
Myristic-acid	228.37	12	2	1	Yes;0 violation	0.85	High

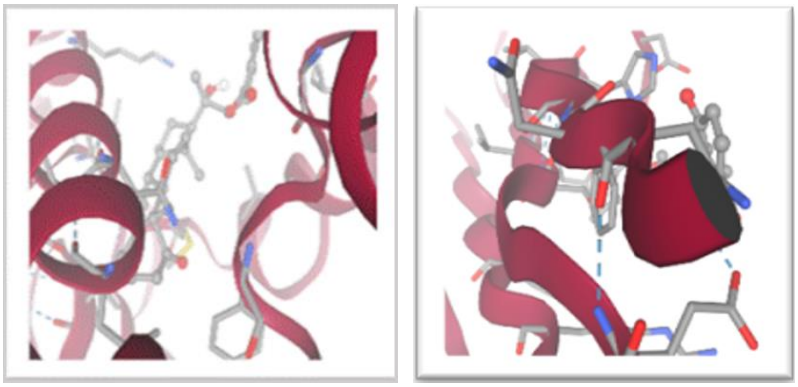
3.7. Molecular Docking Analysis

The interaction between a receptor molecule and a ligand molecule is made possible by predicting the appropriate physical arrangement and the docking process. We employed Molecular Docking research to investigate the interactions between the identified hub proteins and the active compounds derived from *W. somnifera*. We examined 37 compounds-protein complexes, whose binding energies varied from -5.6 to -10.2 kcal/mol, indicating usually substantial binding affinities. Somniferine had a substantial binding affinity for AKT1 (−9.402 kcal/mol), and it made three hydrogen bonds that kept the complex stable. Withaferin, A had a strong interaction with JUN (−7.958 kcal/mol), which was made easier by two hydrogen bonds. Also, Withanolide O had a strong bond with HSP90AA1 (-7.185 kcal/mol), which was largely due to hydrophobic interactions and we also compared it with the market available drug Memantine.

Overall, these data demonstrate that the phytochemicals in *W. somnifera* can bind to several AD-related hub proteins in a stable and effective way. This ability to bind to more than one target suggests that they could be suitable candidates for treating Alzheimer's Disease (AD) by modifying how complex cellular processes work. (See Table 2).



A: AKT1-Cuscohygrin B: AKT1-Somniferin C: HSP90AA1-Withanolide



D: JUN – Withaferin A E: HSP90AB1 – Withanolide A

Figure 6. *(A) shows the 3D representation of binding orientation and intramolecular in-teraction between the AKT1 and the ligand Cuscohygrin., (B) shows the 3D representation of intramolecular interaction between the AKT1 and the ligand Somniferin, (C) shows the 3D representation of intramolecular interaction between the HSP90AA1 and the ligand Withanolide O, (D) shows the 3D representation of intramolecular interaction between the JUN and the ligand Withaferin A, and (E) shows the 3D representation of intramolecular interaction between the HSP90AB1 and the ligand Withanolide A.*

Table 2. Molecular docking between targets and their associated compounds.

Gene	Protein target	Compound name	Docking score
AKT1	8UW9	Memantine (Control drug)	-6.9
		Cuscohygrin	-6.3
		Somniferine	-9.4
HSP90AA1	7S9F	Memantine (Control drug)	-6.0
		Withanolide O	-7.2
JUN	8SOS	Memantine (Control drug)	-7.5
		Withaferin A	-7.9
HSP90AB1	6N8Y	Memantine (Control drug)	-6.5
		Withanolide A	-7.1

4. Discussion

Alois Alzheimer was the first person to talk about Alzheimer's disease (AD), which is the most frequent kind of dementia. It is a slowly developing neurodegenerative condition characterized by neuron plaques and neurofibrillary tangles, predominantly originating from the buildup of amyloid-beta (Aβ) peptides in the medial temporal lobe and neocortical parts of the brain [42]. Consequently, innovative approaches like as network pharmacology have emerged to enhance our comprehension of the disease's complexities and identify medicines that address multiple targets. In this perspective, bioactive chemicals derived from *W. somnifera*, celebrated for its rich history in traditional medicine, present a promising avenue for the identification of novel medicines. Traditional drug development strategies that focus on inhibiting one target have typically failed in clinical trials. Network pharmacology is one of the best biology-based ways to do this. Network pharmacology is a discipline that integrates network biology and polypharmacology [13]. Network Pharmacology is mostly used to study multi-target medications linked to disease-related genes and to clarify how they act in detail [14]. *W. Somnifera* is a significant herb since it enhances the functionality of the brain and nerve system, hence improving memory and regulating the reproductive system [43].

This study thoroughly incorporated phytochemical analysis, ADMET profiling, target identification, the development of protein-protein interaction (PPI) networks, and molecular docking to examine the efficacy of Ashwagandha's bioactive ingredients against Alzheimer's Disease. We obtained 65 chemicals from PubChem and additional sources. The ADMET characteristics and Lipinski screening led to the discovery of 49 compounds [30]. Using the SwissTargetPrediction, STITCH, and SEA databases, target prediction discovered 8,964 potential genes that could be connected to drugs [44]. There are 15,293 genes that are associated to AD in DisGeNet, OMIM, and GeneCards [45]. STRING analysis was performed on 920 overlapping genes, resulting in a highly interconnected protein-protein interaction (PPI) network with 4,312 edges [46]. The strong connections between these targets made it seem like they were working together, which fits with the fact that AD is caused by numerous genes. We discovered 13 hub genes with the help of Cytoscape and CytoHubba. TP53, SRC, AKT1, HSP90AA1, EGFR, IL6, MAPK1, MAPK3, JUN, ESR1, BCL2, HSP90AB1, and GNAI1 [47]. These hub genes provide substantial mechanistic evidence linking *W. Somnifera* phytochemicals are associated with significant pathways related to Alzheimer's disease (AD).

Gene Ontology (GO) research revealed that overlapping gene targets are common in the control of apoptosis, the inflammatory response, and synaptic signaling [48]. KEGG enrichment identified 65 pathways, with the most significant being the PI3K-Akt signaling pathway, which regulates neuronal survival and glucose metabolism; it is essential for synaptic plasticity but linked to apoptosis when dysregulated [49]. ADMET filters look at 65 phytochemicals and discover 49 that are easy for the GI tract to absorb, have a high oral bioavailability (0.55–0.85), and don't break Lipinski's rules too often. Withanolide A, Withaferin A, and Somniferine exhibited notably favorable profiles, characterized by reduced toxicity projections, suggesting improved safety relative to many synthetic neuropathics [50, 51]. Molecular docking verified stable connections with hub proteins. The binding capabilities are between -5.6 and -10.2 kcal/mol. Somniferine–AKT1 (−9.402 kcal/mol), Withaferin A–JUN (−7.958 kcal/mol), Withanolide O–HSP90AA1 (7.185 kcal/mol), Wthanolide A–HSP90AB1 (7.174 kcal/mol), and Cuscohygrin–AKT1 (6.337 kcal/mol) are the chemicals with the highest binding affinities. We also compared the binding affinities with the market available drug Memantine. In many cases compounds from W.Somniera showed better binding affinities than the marketed drug memantine. Thus, it can be preliminarily suggested that compounds from

W. Somnifera may be used as better therapeutic agents [52].

This work demonstrates that multi-target phytocompounds may serve as therapeutic agents by integrating computational pharmacology with empirical evidence of antioxidant activity. Compounds derived from *W. Somnifera* operates through many methods by reducing the likelihood of resistance formation and improving therapeutic effectiveness. The computational results provide a solid basis for drug development; however, in vivo studies are essential to confirm the safety and molecular mechanisms of these molecules. Preclinical animal models ought to be utilized to assess the bioavailability and toxicity of prominent candidates including Cuscohygrin, Somniferin, Withanolide A, Withanolide O, and Withaferin A. These investigations will be crucial in aligning computational predictions with therapeutic applications, thereby advancing the development of *W. Somnifera* phytochemicals provide innovative treatment prospects for Alzheimer's disease.

5. Conclusions

This research utilized an integrated network pharmacology and molecular docking approach to evaluate the therapeutic efficacy of *W. somnifera* in the treatment of Alzheimer's disease through a multi-target mechanism. After examining 65 phytochemicals, 49 of them were found to bind strongly to Hub genes such HSP90AB1, AKT1, JUN, and HSP90AA1. Withanolide A, Somniferine, Withaferin A, Withanolide O, and Cuscohygrin are some of these compounds. These compounds have an advantage over typical medicines that just target one thing because they affect critical pathways including P13K-Akt and amyloid-beta processing. While these computational findings are promising, experimental validation of in vitro and in vivo are essential to confirm these connections. In conclusion, *W. somnifera* serves as a potent natural reservoir for the creation of multi-target phytopharmaceuticals as useful adjuncts or alternatives for the management of Alzheimer's disease.

Abbreviations

AD	Alzheimer's Disease
ADMET	Absorption, Distribution, Metabolism, Excretion, and Toxicity
APP	Amyloid Precursor Protein
PSEN1	Presenilin 1
PSEN2	Presenilin 2
PI3K	Phosphoinositide3-kinase
AKT	Protein Kinase B
MAPK	Mitogen-Activated Protein Kinase
JNK	c-JUN N-Terminal Kinase
GO	Gene Ontology
KEGG	Kyoto Encyclopedia of Genes and Genome
PPI	Protein Protein Interaction
PDB	Protein Data Bank
nTPM	Normalized Transcripts Per Million

Author Contributions

Md Sarowre Hossen: Conceptualization, Former Analysis, Methodology, Resources, Visualization, Writing – review & editing

Abdullah Al Nafiz: Conceptualization, Former Analysis, Methodology, Resources, Visualization, Writing – original draft, Writing – review & editing

Shakil Hossen: Methodology, Resources, Visualization, Writing – review & editing

Md Shahidul Islam: Writing – review & editing

Safia Iqbal: Investigation, Resources, Supervision, Validation, Visualization, Writing – review & editing

Md Rezaul Karim: Investigation, Resources, Supervision, Validation, Visualization, Writing – review & editing

Data Availability Statement

The data are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no conflicts of interest.

Appendix

Table 3. *ADMET profiling of the identified phytochemicals.*

Compound	Molecular weight	Number of Rotatable Bonds	Number of hydrogen bond acceptors	Number of hydrogen bond donor	Lipinski	Bioavailability score	GI absorption
Withanolide Q	470.60	3	6	3	Yes;0 violation	0.55	High

Compound	Molecular weight	Number of Rotatable Bonds	Number of hydrogen bond acceptors	Number of hydrogen bond donor	Lipinski	Bioavailability score	GI absorption
Withanolide R	470.6	2	6	2	Yes;0 violation	0.55	High
Withanolide M	468.58	2	6	2	Yes;0 violation	0.55	High
Hygrine	468.58	2	6	2	Yes;0 violation	0.55	High
Withanolide D	470.60	2	6	2	Yes;0 violation	0.55	High
Withaferin A	470.6	3	6	2	Yes;0 violation	0.55	High
Withasomnine	184.24	1	1	0	Yes;0 violation	0.55	High
Withanolide G	454.6	2	5	2	Yes;0 violation	0.55	High
Withanolide O	452.58	2	5	2	Yes;0 violation	0.55	High
27-Deoxy-14-hydroxywithaferin A	470.6	2	6	2	Yes;0 violation	0.55	High
Withanolide P	454.60	2	5	2	Yes;0 violation	0.55	High
27-Deoxywithaferin A	454.6	2	5	1	Yes;0 violation	0.55	High
Withanolide N	452.58	3	5	2	Yes;0 violation	0.55	High
Withanone	470.60	2	6	2	Yes;0 violation	0.55	High
17alpha-hydroxywithanolide D	486.60	2	7	3	Yes;0 violation	0.55	High
Pelletierine	141.21	2	2	1	Yes;0 violation	0.55	High
Withanolide C	523.06	2	7	4	Yes;1 violation	0.55	High
Withanolide L	452.58	2	5	2	Yes;0 violation	0.55	High
Withanolide H	470.6	3	6	3	Yes;0 violation	0.55	High
Withanolide I	454.6	2	5	2	Yes;0 violation	0.55	High
Withanolide K	470.60	2	6	3	Yes;0 violation	0.55	High
Withanolide J	470.60	2	6	3	Yes;0 violation	0.55	High
Cuscohygrine	224.34	4	3	0	Yes;0 violation	0.55	High
Withasomidienone	438.60	3	4	1	Yes;1 violation:	0.55	High
Somniferine	608.68	3	9	2	Yes;1 violation	0.55	High
Nicotine	162.23	1	2	0	Yes;0 violation	0.55	High
Anahygrine	224.34	4	3	1	Yes;0 violation	0.55	High
Tropine	141.21	0	2	1	Yes;0 violation	0.55	High
Myristic acid	228.37	12	2	1	Yes;0 violation	0.85	High
Stearic acid	284.48	16	2	1	Yes;1 violation	0.85	High
Palmitic acid	256.42	14	2	1	Yes;1 violation	0.85	High
Oleic acid	282.46	15	2	1	Yes;1 violation	0.85	High
Linoleic acid	280.45	14	2	1	Yes;1 violation	0.85	High
withanolide A	470.60	2	6	2	Yes;0 violation	0.55	High
Withasomidienone	438.60	3	4	1	Yes;1 violation	0.55	High
17-alpha-hydroxywithanolide D	488.61	2	7	4	Yes;0 violation	0.55	High

Compound	Molecular weight	Number of Rotatable Bonds	Number of hydrogen bond acceptors	Number of hydrogen bond donor	Lipinski	Bioavailability score	GI absorption
Withanolide B	454.6	2	5	1	Yes;0 violation	0.55	High
Solasodine	413.64	0	3	2	Yes;1 violation	0.55	High
17-Isowithanolide E	486.6	2	7	3	Yes;0 violation	0.55	High
(-)-Anaferine	224.34	4	3	2	Yes;0 violation	0.55	High
27-Deoxywithaferin A	454.6	2	5	1	Yes;0 violation	0.55	High
24,25-dihydrowith-anolide D	472.61	2	6	2	Yes;0 violation	0.55	High
Viscosalactone B	488.61	3	7	3	Yes;0 violation	0.55	High
2,3-Didehydrosomnifericin	488.61	3	7	4	Yes;0 violation	0.55	High
Sominone	458.63	3	5	3	Yes;0 violation	0.55	High
2,3-Dihydrowithaferin A	472.61	3	6	2	Yes;0 violation	0.55	High
Esculetin	178.14	0	4	2	Yes;0 violation	0.55	High
Scopoletin	192.17	1	4	1	Yes;0 violation	0.55	High
gamma-Aminobutyric acid	103.12	3	3	2	Yes;0 violation	0.55	High

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