PROSPECTS
IN PHARMACEUTICAL SCIENCES

Prospects in Pharmaceutical Sciences, 23(4), 103-114
https://prospects.wum.edu.pl/

Original Article

ELUCIDATING NEUROPHARMACOLOGICAL IMPLICATIONS OF VINCETENE: A MULTI-TARGET COMPUTATIONAL STUDY ON ATAXIA, ENCEPHALITIS, AND MENINGITIS

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Received: 05.05.2025 / Revision: 24.06.2025 / Accepted: 25.06.2025 / Published online: 01.10.2025 / Published in final form: 23.12.2025

ABSTRACT

Ataxia, meningitis, and encephalitis are exemplars of acute neurological ailments that are convoluted and often fatal, with limited therapeutic options and multifactorial pathophysiology. The polypharmacological adeptness and outstanding safety profiles of plant-derived bioactive molecules make them intriguing candidates for neuroprotective drug research. Vincetene, an isoquinoline alkaloid identified in species of the genera *Vincetoxicum* and *Cynanchum*, was selected for this investigation and evaluated for its neurotherapeutic feasibility using a comprehensive *in silico* approach. Pharmacokinetic profiling using SwissADME anticipated guaranteed drug-likeness, blood-brain barrier permeability, high gastrointestinal absorption, and no interaction with P-glycoprotein. Vincetene justified multiple drug-likeness rules (Lipinski, Veber, Ghose, Egan, Muegge) and demonstrated a bioavailability score of 0.55. Toxicological evaluation via ProTox-II recommended non-carcinogenic, non-mutagenic, and non-cytotoxic properties, but implied potential hepatotoxicity, neurotoxicity, immunotoxicity, and respiratory toxicity. Network pharmacology assessment pinpointed 49 intersecting genes between vincetene targets and disease-related genes. Hub genes divulged through protein–protein interaction networks included PI3KCA, AKT2, AKT3, MTOR, and HSP90AA1. Gene ontology and pathway enrichment analysis signified the contribution of vincetene to PI3K-Akt, HIF-1, and ErbB signaling pathways, which are decisive for neuronal survival and stress response. Molecular docking established stable binding to target proteins 2Z83 (-7.6 kcal/mol), 5KTR (-6.1 kcal/mol), and 1Q5K (-8.8 kcal/mol). These findings suggest that vincetene exerts multi-targeted neuroprotective effects and holds promise as a neurotherapeutic lead compound. Overall, this study provides the tactical repositioning of vincetene for the management of complex neurological disorders, paving the way for future experimental research.

KEYWORDS: docking; *in silico*; isoquinoline alkaloid; neurodegeneration; neuroprotection; vincetene

1. Introduction

Alkaloids are a radically different class of secondary metabolites containing nitrogen. They are in general extracted from plants and biosynthesized from amino acids [1]. They account for on or about twenty percent of all recognized secondary metabolites produced by plants and are thought to exist in barely discernible amounts in 20% of plant species [2]. Alkaloids serve as crucial for plants' defense against diseases and herbivores and moreover for controlling growth [3]. They are considerably renowned for their extreme biological effects in medicine, functioning as anesthetics, cardioprotective, and anti-inflammatory substances. Morphine, strychnine, quinine, ephedrine, and nicotine are representatives of alkaloids that have medical relevance [4,5].

The occurrence of an isoquinoline or reduced isoquinoline ring system distinguishes the structurally heterogeneous family of chemical compounds known as isoquinoline alkaloids [5,6]. They are classified into several subclasses, notably benzylisoquinolines, protoberberines, tetrahydroprotoberberines, and benzophenanthridines, and originate primarily from phenethylamines or 1-benzylisoquinoline precursors. Plant groups such as the Berberidaceae, Papaveraceae, Fumariaceae, Apocynaceae, and Menispermaceae contain large amounts of these alkaloids [6,7]. Widespread pharmacological properties, such as antibacterial, analgesic, anti-inflammatory, anticholinergic, antiproliferative, and neuroprotective properties, are demonstrated by isoquinoline alkaloids. Notable examples include palmatine (anti-jaundice),

morphine and codeine (analgesic, antitussive), sanguinarine (NF-κB suppression), and berberine (hypoglycemic, antibacterial) [8,9]. Their therapeutic potential and drug delivery precision are impacted by their affinity to attach to a range of functional and serum proteins, nucleic acids, and plasma proteins [9,10].

Vincetene is a minor isoquinoline alkaloid with a benzopyrroloisoquinoline scaffold, typically found in trace amounts in plants belonging to the genera *Vincetoxicum* Wolf (Apocynaceae) and *Cynanchum* L. (Asclepiadaceae) [11,12]. Despite its structural instability and low abundance, vincetene holds significant pharmacological potential due to its unique chemical structure and its occurrence in ethnomedicinal plants traditionally used to treat a variety of ailments [11]. However, its role in modern pharmacological contexts remains largely unexplored.

Given the established neuropharmacological relevance of plant-derived isoquinoline alkaloids, this study aims to evaluate the anticipated medicinal benefit of vincetene against several neurological disorders. Specifically, the conditions selected — meningitis, encephalitis, and ataxia — represent a broad spectrum of neuroinflammatory and neurodegenerative disorders. Encephalitis and meningitis are characterized by acute inflammation of the brain and meningeal tissues, often involving immune dysregulation and oxidative stress pathways [13,14]. Alternatively, ataxia, marked by weakened motor coordination due to cerebellar disintegration, presents a contrasting neurological disorder that may be addressed through neuroprotective strategies [15]. By employing a combination of network pharmacology and molecular docking methods, this research seeks to clarify the multi-target neurotherapeutic potential of vincetene. This integrated approach permits a comprehensive analysis of the compound's efficacy across both inflammatory and degenerative neural pathologies.

2. Materials and Methods

2.1. ADME properties

The ADME (Absorption, Distribution, Metabolism, and Excretion) characteristics of vincetene were appraised using SwissADME (http://www.swissadme.ch/), a user-friendly web tool for predicting pharmacokinetic limitations and drug-likeness of small molecules. The 3D structure of vincetene was first illustrated using ChemDraw, and its SMILES (Simplified Molecular Input Line Entry System) notation was created with PubChem (https://pubchem.ncbi.nlm.nih.gov/). It was further submitted to SwissADME, which delivered thorough data on the compound's properties [16].

2.2. Toxicity prediction

The complete toxicity summary of vincetene was reviewed using the ProTox-II web server (https://tox-new.charite.de/protox_II/), a robust computational platform for calculating multiple toxicological endpoints based on molecular structure. The SMILES notation of vincetene was obtained using PubChem and submitted to ProTox-II. The tool provided predictions for oral toxicity, risks related to hepatotoxicity, cytotoxicity, carcinogenicity, immunotoxicity, mutagenicity, and so on [17].

2.3. Network pharmacology

The SMILES structure of vincetene was retrieved from the PubChem database and entered into SwissTargetPrediction (http://www.swisstargetprediction.ch/) to detect probable protein targets, with the organism filter set to *Homo sapiens*. Concurrently, disease-associated genes for ataxia, encephalitis, and meningitis were acquired from GeneCards (https://www.genecards.org/). Redundant entries were systematically removed. The intersecting targets between vincetene and each neurological disorder were visualized using the Jvenn (https://jvenn.toulouse.inrae.fr/app/index.html) diagram tool. These shared targets were used to build a protein-protein interaction (PPI) network using the STRING database (https://string-db.org/) with a confidence score threshold of >0.9, and the network was visualized in Cytoscape 3.9.1. To identify key regulatory genes, the CytoHubba plugin was used, ranking nodes based on closeness, degree, and radiality centrality metrics. The top-ranking genes common to all three metrics were characterized as hub genes and chosen for successive molecular docking studies to assess binding affinity and therapeutic relevance [18].

2.4. Gene ontology and KEGG pathway enrichment analysis

To investigate the biological relevance of vincetene's predicted targets, Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed using ShinyGO v0.82 (https://bioinformatics.sdstate.edu/go/) and SRPLOT (https://www.bioinformatics.com.cn/en). A total of 49 intersecting genes, identified as common targets between vincetene and the three neurological conditions, were submitted for enrichment analysis. GO terms were grouped into biological process (BP), cellular component (CC), and molecular function (MF), while KEGG analysis revealed the most significantly enriched signaling pathways. The cutoff for statistical significance was set at FDR<0.05, and results were visualized through dot plots and bar charts generated by the respective tools [18].

2.5. Molecular docking

Three-dimensional structures of target proteins (PDB IDs: 2Z83, 5KTR, and 1Q5K) were retrieved using the RCSB Protein Data Bank (https://www.rcsb.org/). Molegro Molecular Viewer was used for preparing the protein, which included eliminating water molecules, adding hydrogen atoms, and performing structural optimizations. Energy reduction was applied to ligand molecules, and the PyRx virtual screening tool was used for docking. The docking scores were used to assess binding affinities and interaction modalities. Using UCSF Chimera software and Biovia Discovery Studio, the best docked complexes were further visualized and examined for interaction patterns [19].

3. Results

3.1. Pharmacokinetic profile and drug-likeliness of vincetene

The physicochemical and pharmacokinetic properties of vincetene were reviewed via the SwissADME tool (Fig. 1, Table 1). The compound exemplified promising molecular descriptors, attaining all major drug-likeness guidelines,

Table 1. ADME properties of vincetene.

Physicochemical Properties						
Formula	**No. of heavy atoms**	**No. of arom. heavy atoms**	**No. of rotatable bonds**	**No. of H bond acceptors**	**No. of H bond donors**	**TPSA (Å^2)**
$C_{22}H_{27}NO_3$	26	10	4	4	1	41.93
Lipophilicity	**Water Solubility**			**Medicinal Chemistry**		
Consensus Log $P_{o/w}$	**Log *S* (ESOL)**	**Solubilty**	**Solubility class**	**PAINS**	**Lead likeliness**	**Synthetic accessbility**
3.54	-4.38	1.46e-02 mg/mL	Moderately soluble	0 alerts	No	3.94
Pharmacokinetics						
GI absorption	**BBB permeant**	**P-gp substrate**	**CYP1A2 inhibitor**	**CYP2C19 inhbitor**	**CYP2C9 inhbitor**	**CYP2D6 inhbitor**
Drug Likeliness						
Lipinski	**Ghose**	**Veber**	**Egan**	**Muegge**	**Bioavailability score**	
Yes	Yes	Yes	Yes	Yes	0.55	

including Lipinski, Ghose, Veber, Egan, and Muegge rules. Vincetene revealed high gastrointestinal absorption, BBB permeability, and was predicted not to be a P-glycoprotein substrate. No cytochrome P450 inhibition was apparent across CYP1A2, CYP2C19, CYP2C9, and CYP2D6 isoenzymes. The compound displayed adequate aqueous solubility and no PAINS alerts, with a bioavailability score of 0.55. The synthetic accessibility score was within a satisfying range, suggesting possible chemical synthesis for drug development.

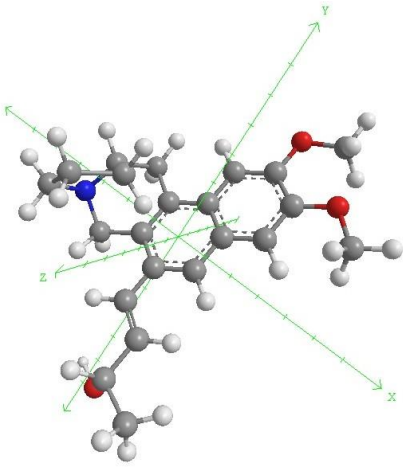

Fig. 1. Chemical structure of vincetene.

Table 2. Toxicity parameters of vincetene.

Organ Toxicity			Toxicity End Points		
Target	**Prediction**	**Probability**	**Target**	**Prediction**	**Probablity**
Hepatotoxicity	Active	0.67	Carcinogenicity	Inactive	0.62
Neurotoxicity	Active	0.87	Immunotoxicity	Active	0.96
Nephrotoxicity	Inactive	0.90	Mutagenicity	Inactive	0.97
Respiratory toxicity	Active	0.98	Cytotoxicity	Inactive	0.93
Cardiotoxicity	Inactive	0.77	Clincal toxicity	Inactive	0.56
Molecular Initiating Events			**Tox21-Stress Response Pathways**		
Target	**Prediction**	**Probablity**	**Target**	**Prediction**	**Probablity**
Thyroid hormone receptor α	Inactive	0.90	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element	Inactive	0.88
Transtyretin	Inactive	0.97	Heat shock factor response element	Inactive	0.88
Ryanodine receptor	Inactive	0.98	Mitochondrial Membrane Potential	Inactive	0.70
GABA receptor	Inactive	0.96	Phosphoprotein (Tumor Supressor) p53	Inactive	0.96
Acetylcholinesterase	Inactive	0.69	ATPase family AAA domain-containing protein 5	Inactive	0.99

3.2. Predicted toxicological profile of vincetene

Toxicological outlining of vincetene was performed using the ProTox-II platform (Table 2). The compound was predicted to be hepatotoxic (probability 0.67), neurotoxic (0.87), immunotoxic (0.96), and respiratory toxic (0.98), while it was predicted to be non-carcinogenic, non-mutagenic, non-nephrotoxic, and non-cytotoxic with high confidence scores (>0.90). In addition, vincetene showed no predicted activity for cardiotoxicity or clinical toxicity. Molecular initiating events and Tox21-stress pathway breakdown divulged no interactions with nuclear receptors, signaling proteins, or stress-responsive pathways. All targets including p53, GABA receptor, mitochondrial membrane potential, and antioxidant response elements were predicted to be inactive with high probabilities (>0.88).

3.3. Identification of core targets through network pharmacology

In the network pharmacology analysis, a total of 5022, 3389, and 6870 disease-correlated genes were recovered for encephalitis, meningitis, and ataxia, respectively. Vincetene-associated genes were recognized as 100. Venn diagram examination disclosed 49 intersecting genes common to vincetene and the three neurological conditions, representing the potential therapeutic targets (Fig. 2—3, Table 3). The inclusive PPI network conception determined broad interfaces among the 49 target genes, revealing its multi-target and interconnected therapeutic effect. In particular, the network analysis highlights the contribution of key signaling molecules such as PI3KCA, AKT isoforms, MTOR, SRC, and HSP90 proteins (Fig. 4).

Three topological metrics were implemented for defining hub genes with the aim of further studying the most significant contributors in the protein-protein interaction (PPI) network developed with the 49 intersecting genes: degree, radiality, and closeness centrality (Fig. 5). The closeness centrality analysis emphasized key nodes such as AKT2, AKT3, MTOR, PI3KCA, and RPS6KB1, indicating their strong proximity and influence within the network. Degree centrality disclosed that PI3KCA, AKT2, AKT3, and HSP90AA1 had the highest number of direct interactions, placing them as major hubs. Radiality similarly stressed the strategic network control roles of PI3KCA, AKT2, AKT3, and MTOR, suggesting their role in regulating communication across the network.

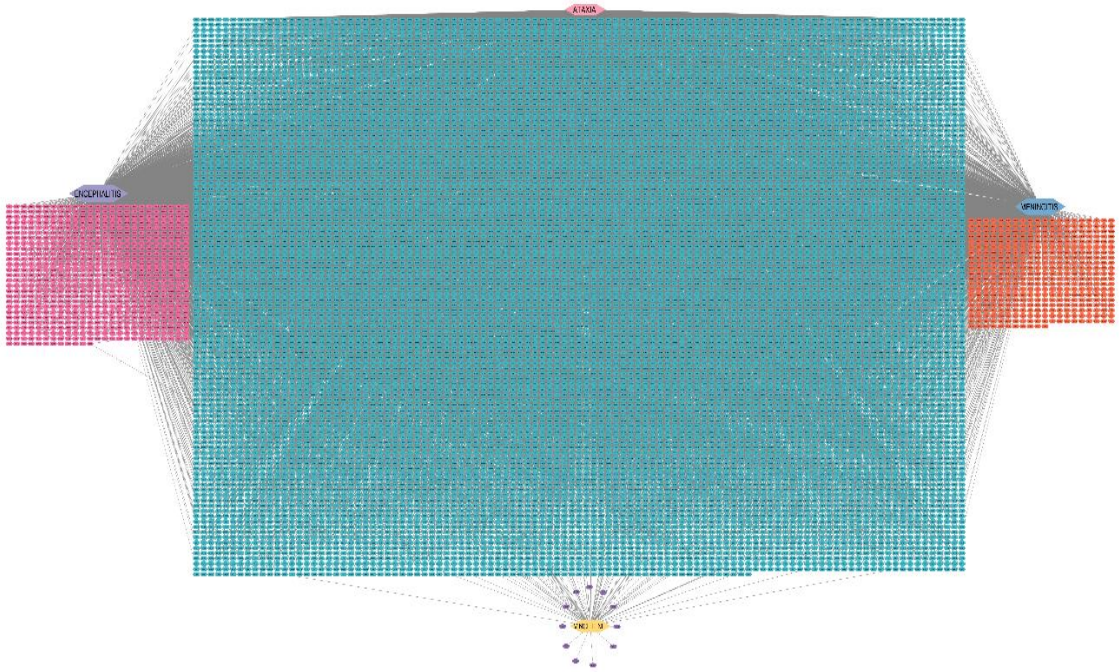

Fig. 2. Compound-disease target network highlighting interaction between vincetene and associated disease-targets.

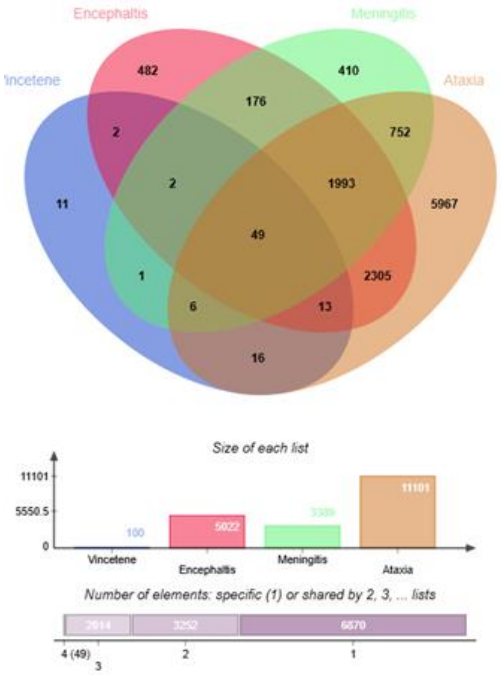

Fig. 3. Venn diagram illustrating intersecting genes between disease-related targets and vincetene-associated targets.

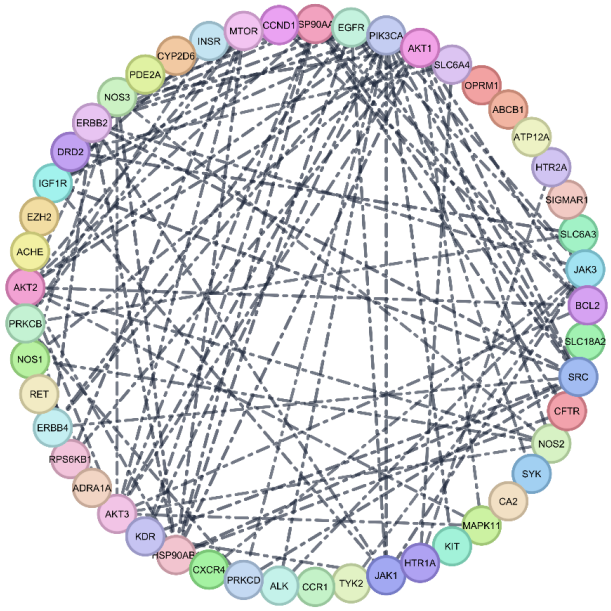

Fig. 4. Protein-protein interaction (PPI) network of intersecting genes.

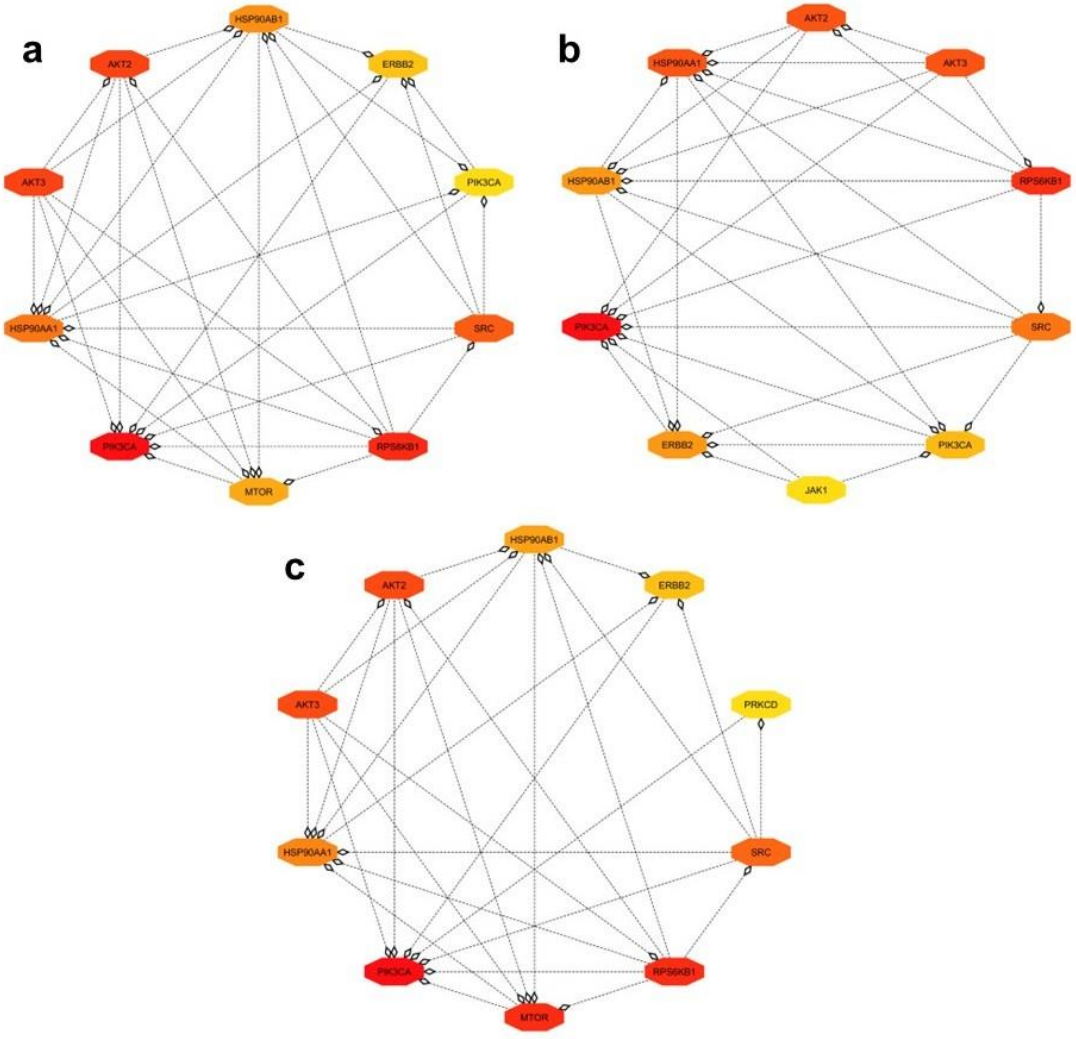

Fig. 5. Top 10 hub genes identified from PPI network based on (a) closeness centrality, (b) degree centrality and (c) radiality.

Table 3. Detailed description of compound-disease intersecting genes.

Gene symbol	Chromosome number	Position	Description
MTOR	1	11.1065	Mechanistic target of rapamycin kinase
JAK1	1	64.8332	Janus kinase 1
AKT3	1	243.4882	AT serine/threonine kinase 3
ALK	2	29.1928	ALK receptor tyrosine kinase
CXCR4	2	136.1143	C-X-C motif chemokine receptor 4
ERBB4	2	211.3757	Erb-b2 receptor tyrosine kinase 4
CCR1	3	46.2017	C-C motif chemokine receptor 1
PRKCD	3	53.1560	Protein kinase C delta
PIK3CA	3	179.1481	Phosphatidulinositol-4, 5-bisphosphate 3-kinase catalytic subunit alpha
KIT	4	54.6573	KIT proto-oncogene, receptor tyrosine kinase
KDR	4	55.0785	Kinase insert domain receptor
SLC6A3	5	1.3928	Solute carrier family 6-member 3
HTR1A	5	63.9527	5-hydroxytryptamine receptor 1A
HSP90AB1	6	44.2462	Heat shock protein 90 alpha family class B member 1
OPRM1	6	154.0105	Opioid receptor mu 1
EGFR	7	55.0190	Epidermal growth factor receptor
ABCB1	7	87.5030	ATP binding cassette subfamily B member 1
ACHE	7	100.8900	Acetylcholinesterase
CFTR	7	117.2871	CF transmembrane conductance regulator
EZH2	7	148.8073	Enhancer of zeste 2 polycomb repressive complex 2 subunit
NOS3	7	150.9910	Nitric oxide synthase 3
ADRA1A	8	26.7481	Adrenoceptor alpha 1A
CA2	8	85.4640	Carbonic anhydrase 2
SGMAR1	9	34.6347	Sigma non-opioid intercellular receptor 1
SYK	9	90.8018	Spleen associated tyrosine kinase
RET	10	43.0771	Ret proto-oncogene
SLC18A2	10	117.2411	Solute carrier family 18 member A2
CCND1	11	69.6412	Cyclin D1
PDE2A	11	72.5761	Phosphodiesterase 2A
DRD2	11	113.4096	Dopamine receptor D2
NOS1	12	117.2081	Nitric oxide synthase 1
ATP12A	13	24.6804	ATPase H+/K+ transporting non-gastric alpha2 subunit
HTR2A	13	46.8315	5-hydroxytryptamne receptor 2A
HSP90AA1	14	102.0807	Heat shock protein 90 alpha family class A member 1
AKT1	14	104.7693	AT serine/threonine kinase 1
IGF1R	15	98.6485	Insulin like growth factor 1 receptor
PRKCB	16	23.8360	Protein kinase C beta
NOS2	17	27.7568	Nitric oxide synthase 2
SLC6A4	17	30.1943	Solute carrier family 6-member 4
ERBB2	17	39.6879	Erb-b2 receptor tyrosine kinase 2
RPS6KB1	17	59.8930	Ribosomal protein S6 kinase B1
BCL2	18	63.1233	BCL2 apoptosis regulator
INSR	19	7.1123	Insulin receptor
TYK2	19	10.3505	Tyrosine kinase 2
JAK3	19	17.8248	Janus kinase 3
AKT2	19	40.2303	AKT serine/threonine kinase 2
SRC	20	37.3447	SRC proto-oncogene, non-receptor tyrosine kinase
CYP2D6	22	42.1265	Cytochrome P450 family 2 subfamily D member 6
MAPK11	22	50.2637	Mitogen-activated protein kinase 11

3.4. GO and KEGG enrichment analysis of vincetene-associated targets

GO enrichment analysis was performed on the intersecting genes between vincetene-associated targets and genes linked to ataxia, encephalitis, and meningitis. KEGG pathway analysis revealed remarkable enrichment in numerous cancer-related and signaling pathways. The top pathways included EGFR tyrosine kinase inhibitor resistance, non-small cell lung cancer, endocrine resistance, and so on, with the highest fold enrichment observed for EGFR tyrosine kinase inhibitor resistance. Gene structure scrutiny quantified that the coding sequence lengths (P=2.8E-07), transcript lengths (P=9.4E-08), and genome spans (P=9.7E-05) of the intersecting genes were expressively atypical from the genome background, indicating a tendency toward shorter lengths.

Significant differences were also witnessed in the 5′ UTR and 3′ UTR lengths, while GC content did not differ. Exon number study divulged anomalies, with the intersecting gene set showing a discrete exon allocation parallel to the plausible genome-wide allocation (Fig. 6—7). The target genes have a chief role in phosphorylation, kinase activity modulation, and synaptic membrane components, according to the GO enrichment analysis. These mechanisms have significance for neural signaling, synaptic plasticity, and neuroprotection. Cancer-related pathways such as PI3K-Akt, ErbB, and HIF-1 signaling were found by KEGG, nonetheless they are not exclusive to oncogenesis (Fig. 8—9). In the neurological system, they play an equally important role in mediating stress responses, synaptic repair, neuron development, and survival. Hence, the functional enrichment justifies the importance of the chosen genes in the wider context of neurological diseases and strongly supports their neurological relevance despite their overlap with cancer pathways.

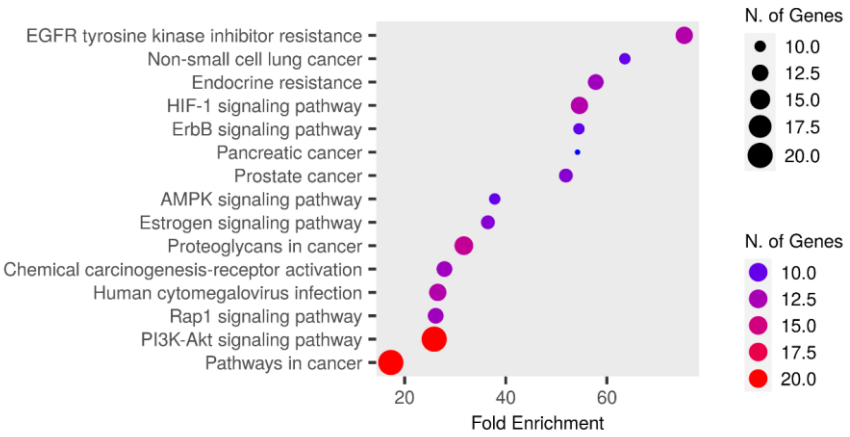

Fig. 6. GO analysis of target genes associated with vincetene.

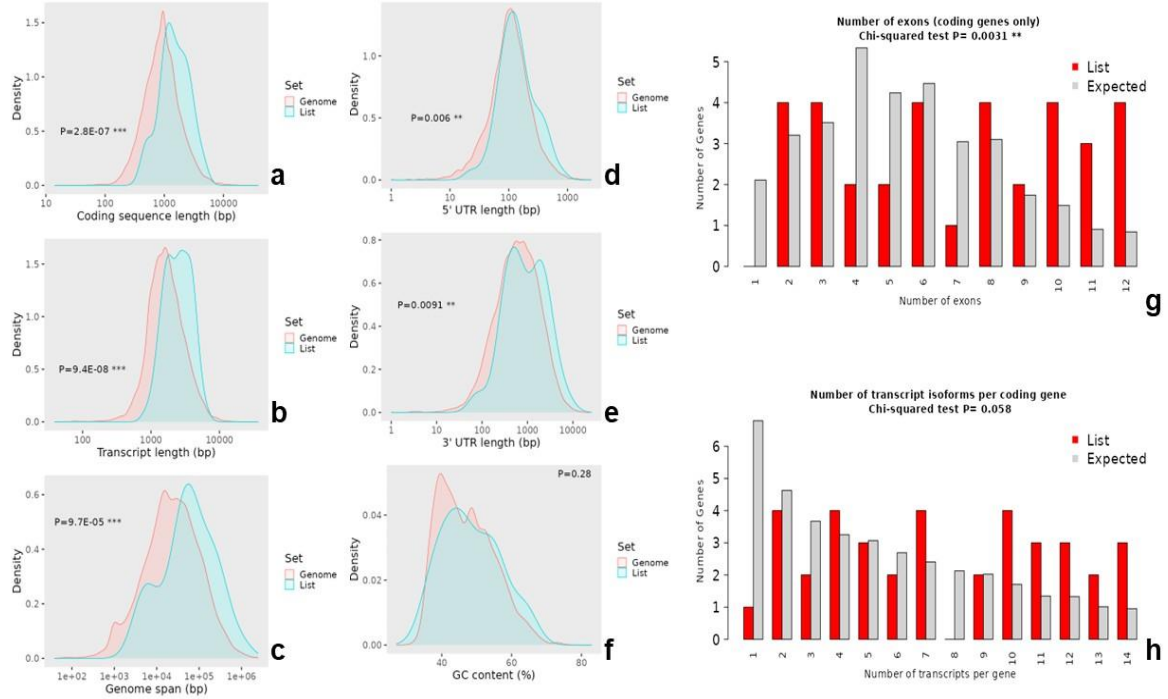

Fig. 7. Gene structural characteristics and transcript features of intersecting genes where (a) coding sequence length (CDS); (b) transcript length; (c) genomic span; (d) 5′ untranslated region (UTR) length; (e) 3′ UTR length; (f) GC content; (g) distribution of no. of exons per coding gene (observed-red; expected-grey); (h) distribution of transcript isoforms per gene (observed-red; expected-grey).

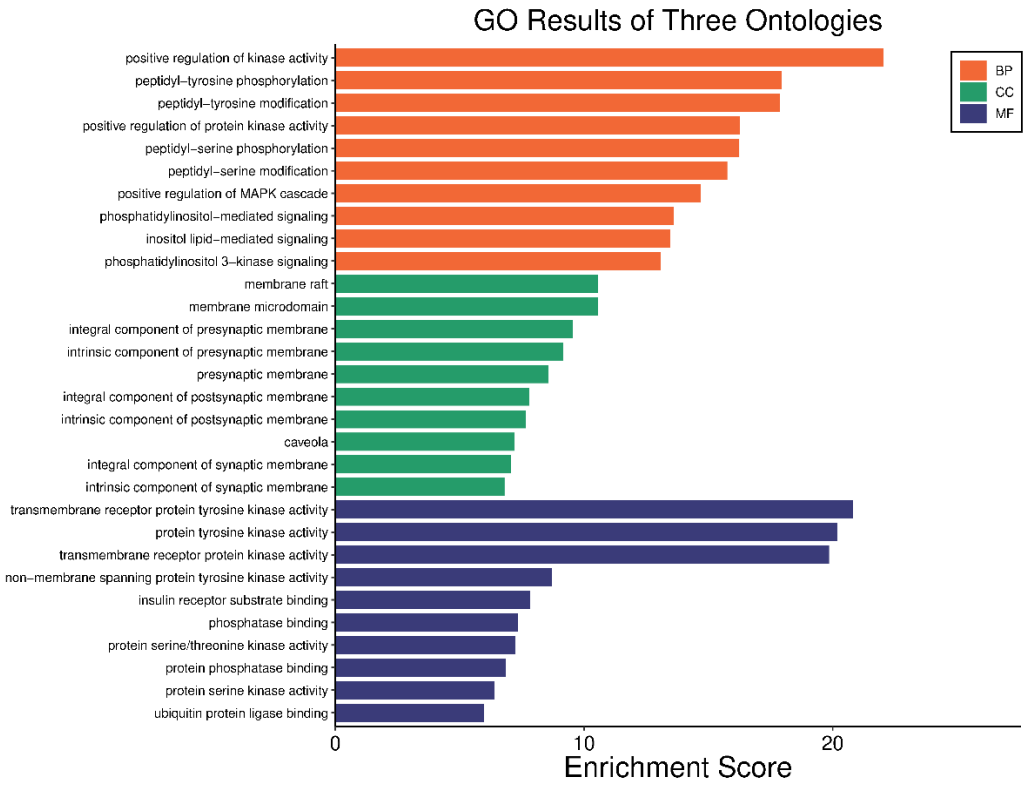

Fig. 8. GO enrichment analysis of intersecting genes between vincetene targets and disease-associated genes.

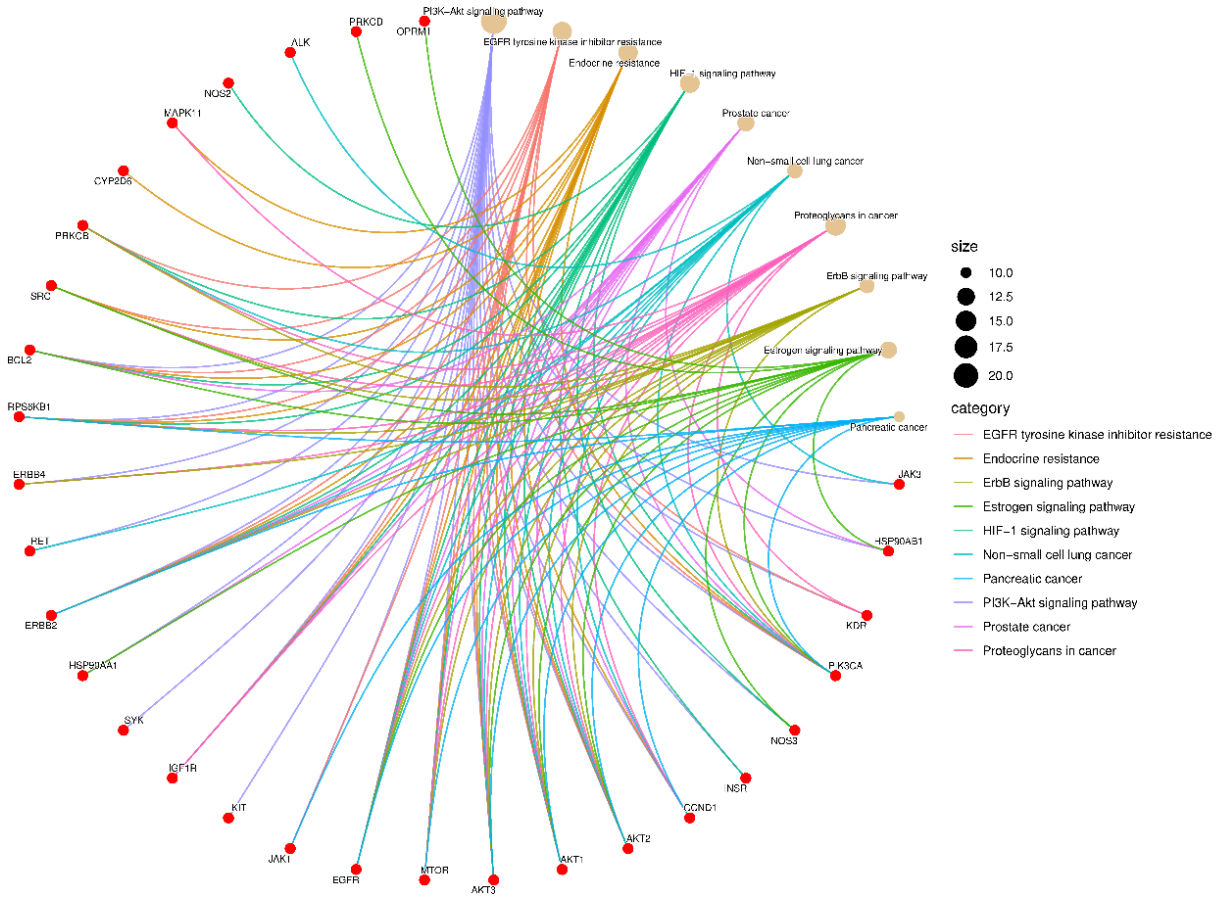

Fig. 9. KEGG pathway-gene interaction network of intersecting targets between vincetene and disease-associated genes.

3.5. Binding efficiency of vincetene against three proteins

Molecular docking analysis revealed that vincetene presented prominent binding affinities with proteins associated with encephalitis, meningitis, and ataxia. Against encephalitis-related protein 2Z83, vincetene demonstrated a binding energy of -7.6 kcal/mol, forming one hydrogen bond and interacting sterically with key residues including HIS 488, VAL 545, and PRO 544. In meningitis-associated protein 5KTR, vincetene indicated a binding energy of -6.1 kcal/mol with one hydrogen bond and interactions involving ARG 239, GLU 252, and TYR 236. The strongest binding was observed with the ataxia-related protein 1Q5K, where vincetene achieved a binding energy of -8.8 kcal/mol, forming one hydrogen bond and engaging with residues such as TYR 134, LEU 188, and CYS 199 (Fig. 10, Table 4).

Table 4. Molecular docking results.

Compound-Disease	Protein	Binding efficiency (kcal/mol)	No. of H bonds	Steric interactions
Vincetene-Encephalitis	2Z83	-7.6	1	HIS 488, VAL 545, PRO 292, PRO 544, PRO 432, LEU 444, ALA 603, ARG 600, ALA 607, VAL 601, PHE 611, TRP 610, ASP 542, LEU 543
Vincetene-Meningitis	5KTR	-6.1	1	ARG 239, GLU 252, PRO 249, VAL 235, PRO 26, TYR 236, LEU 25, GLU 27, ARG 232
Vincetene-Ataxia	1Q5K	-8.8	1	TYR 134, LEU 188, CYS 199, THR 138 GLN 185, ILE 62, VAL 135 ALA 83, ASP 133, VAL 110, LEU 132, VAL 70, GLY 65, GLY 68, PHE 67, LYS 85, ASP 200

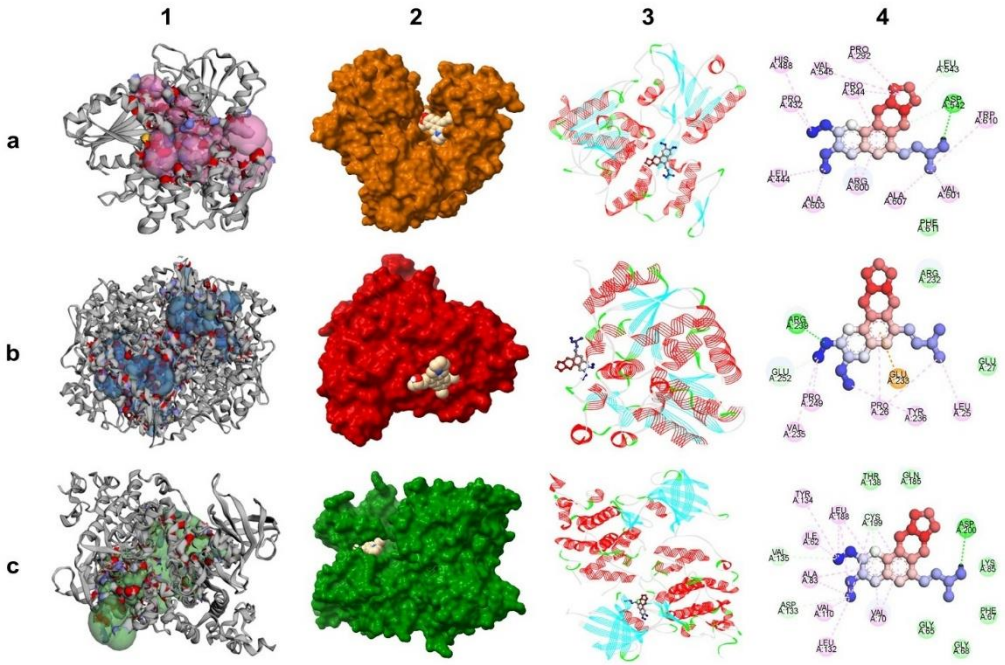

Fig. 10. Molecular docking visualization of vincetne with three target proteins (**a) 2Z83; (B) 5KTR; (C)** 1Q5K. Column 1 illustrates the predicted binding pockets within the protein structure (semi-transparent mesh highlighting cavity regions); column 2 presents the surface representation of each protein colored distinctly to show the ligand (white stick model) bound within the active site; column 3 displays the cartoon ribbon models of the proteins in complex with the ligand; column 4 shows 2D interaction maps detailing hydrogen bonding, hydrophobic interactions, and other non-covalent forces between vincetene and active site residues.

4. Discussion

The possible benefits of vincetene as a multi-targeted therapeutic substitute for three neurological illnesses, specifically encephalitis, meningitis, and ataxia, are showcased by the current *in silico* assessment. In drug discovery and development, monitoring ADMET aspects is a necessity since this data impacts significant assumptions at every stage of the drug development workflow by supporting the determination of the safety and effectiveness of chemical compounds [20]. Earlier studies on three new alkaloids revealed strong drug-likeness with positive pharmacokinetic characteristics, such as high gastrointestinal absorption, no Lipinski violations, and adequate bioavailability scores [21]. Caffeic, ferulic, p-coumaric, and sinapic acids demonstrated somewhat greater lipophilicity and equivalent or superior ADME features, such as blood-brain barrier permeability and non-inhibition of the main CYP450 enzymes [22]. Furthermore, unlike the reference compound, remdesivir, oxysophorodine, berbamine, neferine, and 10'-hydroxyusambernsine demonstrated nominal toxicity profiles and

no CYP3A4/CYP2D6 inhibition, reinforcing safer metabolic behavior [23]. Vincetene is unique among the examined compounds since it satisfies all the main drug-likeness filters, has a positive solubility and synthetic accessibility profile, and indicates both BBB permeability and non-inhibition of vital CYP450 enzymes. In accordance with toxicity research, some alkaloids had suitable toxicity profiles, with medium risks for all organ systems and less harmful scores than reference medications like galantamine and donepezil [21]. On the other hand, p-coumaric acid was inert across all toxicity endpoints, whereas ferulic acid and caffeic acid showed substantial immunotoxicity but minimal hepatotoxicity [22]. Compared to alkaloids like berberine and 10′-hydroxyusambarensine, which displayed AMES toxicity and hepatotoxicity, the compounds stand out for their lower mutagenic and organ-specific hazards [23]. Relative to the analogs discussed above, vincetene can be comprehended as safe.

Network pharmacology integrates systems biology and pharmacology to explore the relationships among multiple compounds, their target molecules, and associated pathways, providing a deeper understanding of drug mechanisms [24]. A vital aspect of this strategy is target prediction, which focuses on ligand- and receptor-based techniques such as molecular docking, pharmacophore modeling, QSAR, and 2D/3D similarity, which provide higher accuracy when integrated [25,26]. By focusing on disease networks in lieu of individual molecules, network pharmacology supplies a thorough method for comprehending the intricate relationships between numerous bioactive substances and molecular targets, which makes it an invaluable tool for creating therapies that effectively treat neurological disorders [27]. With functional predominance in neurotransmitter activation and circulatory pathways, *Uncaria* alkaloids were linked to 254 potential targets, 23 of which overlapped with genes linked to both hypertension and Alzheimer's disease [28]. The mTOR, STAT3, and AKT1 hub genes were considerably enriched in autophagy, amyloid clearance, oxidative stress regulation, and mTOR signaling pathways, whereas 17 polyphenols showed convergence on 203 Alzheimer's-related targets [29]. Likewise, ingredients from *Tinospora cordifolia* showed associations with 591 human proteins, demonstrating a wide neuroregulatory function through enrichment spanning cAMP, MAPK, PI3K-Akt, and numerous neurotransmitter synaptic pathways [30]. Collectively, these results, along with outcomes of vincetene, provide credence to the diverse pharmacological potential of phytochemicals in regulating intricate disease networks.

An essential computational method for simulating the atomic-level interactions between small molecules and target proteins is molecular docking. This allows for the prediction of ligand binding affinities and poses, providing information about molecular processes underpinning ligand-receptor interactions and supporting structure-based drug design [31]. Numerous bioactive substances were subjected to molecular docking investigations, which showed encouraging medicinal potential. With a LibDock score of 120.153 and a binding energy of -3.65569 kcal/mol, doronine demonstrated a strong binding to human COX-2, suggesting its anti-inflammatory properties [32]. Compounds produced from marine brown algae had a strong affinity for the RNA-dependent RNA polymerase of the Japanese encephalitis virus, indicating antiviral action [33]. The potential of (−)-dendroparishiol to prevent meningitis was demonstrated by its strong binding to bacterial meningitis-related targets such as TNF, IL-1ß, and p38 MAPK [34]. Flavan-3-ol from Calophyllum macrophyllum also demonstrated significant affinity to the CviR receptor, suggesting its eligibility against bacterial and parasitic meningitis [35]. Additionally, novel heterocyclic compounds showed neurotropic potential, where some compounds bound strongly to GABA_A receptors (ΔG ≈ -10.0 kcal/mol) and others to the 5HT_{1A} receptor (ΔG = -9.3 ± 0.46 kcal/mol), indicating potential anxiolytic and antidepressant effects [36]. As opposed to these findings, vincetene showed encouraging promise in molecular docking experiments, demonstrating a strong binding affinity to important targets implicated in neurological diseases, indicating that it might be used as a treatment for these challenges.

5. Conclusions

Vincetene has strong molecular docking patterns with important proteins, notable network pharmacological interactions with neurological illness targets, and generally good pharmacokinetic and physicochemical characteristics. These promising outcomes encourage more research into vincetene as a potential treatment for neurological disorders such as ataxia, meningitis, and encephalitis.

Author Contributions: Conceptualization, A.P.; methodology, A.P.; validation, A.P. and A.R.; investigation, A.P.; resources, A.P.; data curation, A.P.; writing—original draft preparation, A.P.; writing—review and editing, A.P., A.R., and K.T.; visualization, A.P.; supervision, K.T.; project administration, A.P.; funding acquisition, A.P. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Acknowledgments: The authors express their sincere gratitude towards the faculties and research scholars of PG and Research Department of Botany, Kongunadu Arts and Science College, Coimbatore, Tamil Nadu, India.

Conflicts of Interest: The authors declare no conflict of interest.

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