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Deciphering the Multi-Targeted Anti-Cancer Mechanisms of Lagenaria siceraria (Bottle Gourd) via Integrated Network Pharmacology and Molecular Docking: Inhibition of the PI3K-Akt Signalling Pathway

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ABSTRACT:

Background: Cancer remains a major cause of global mortality, driven by complex genetic alterations and environmental stimuli. Lagenaria siceraria (bottle gourd) has long been used in traditional medicine because of its diverse pharmacological properties In this work, we use an integrated network pharmacology and molecular docking strategy to clarify the bioactive constituents and molecular targets of L. siceraria in cancer treatment.

Methods: Bioactive phytoconstituents of L. siceraria were screened, and their possible protein targets were determined through comprehensive databases. A protein-protein interaction (PPI) network was generated using STRING v11.0 and analyzed in Cytoscape to determine hub genes. Functional enrichment analyses were carried out with Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis. ADME prediction was used to evaluate drug-likeness and pharmacokinetic characteristics. Finally, molecular docking simulations were performed against the high-degree hub target AKT1 (PDB ID: 3O96) to assess binding affinities relative to the reference drug doxorubicin.

Results: Network analysis identified three main bioactive compounds-quercetin, beta-sitosterol, and oleanolic acid—that interact with 73 protein targets. The PPI network (73 nodes, 513 edges) and KEGG analysis indicated that these compounds mainly affect the PI3K–Akt signaling pathway, together with pathways involved in cancer and EGFR tyrosine kinase inhibitor resistance. Molecular docking showed that beta-sitosterol has a higher binding affinity to AKT1 of -11 kcal/mol, supported by a strong network of hydrogen bonds and hydrophobic interactions (Trp80, Val270, Leu210), which is greater than the affinity of doxorubicin (-10.6 kcal/mol). ADME analysis further confirmed favorable drug-likeness, although the high lipophilicity indicates that optimized delivery systems will be required.

Conclusion: These findings indicate that Lagenaria siceraria produces strong anti-cancer effects via a multi-component, multi-target mechanism, particularly through inhibition of AKT1-mediated cell survival. The results also offer a mechanistic basis for developing L. siceraria-derived phytochemicals as new therapeutic agents for oncology.

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INTRODUCTION

Environmental factors are the main cause of cancer, a complex genetic disease. Carcinogens, or substances that cause cancer, can be found in food, water, the air, chemicals, and sunlight that individuals are exposed to. Over 90% of malignancies arise in epithelia, which is not surprising given that epithelial cells line the respiratory and digestive passages, cover the skin, and metabolise ingested toxins[1]. Cancer is a potentially fatal disease caused mainly by environmental factors that mutate genes encoding critical cell-regulatory proteins. The result ant aberrant cell behavior leads to expansive masses of abnormal cells that destroy surrounding normal tissue and can spread to vital organs resulting in disseminated disease, commonly a harbinger of imminent patient death [2]. Many herbal formulas used in Traditional Chinese Medicine (TCM) have been used for thousands of years to treat a wide range of illnesses, such as cancer, diabetes mellitus, and other conditions[3,4]. The emerging discipline of network pharmacology, founded on the integration of systems biology, bioinformatics, and high throughput histology, is gaining significant momentum within the scientific community[5,6,7].The practical framework of n etwork pharmacology typically entails constructing interaction networks from comprehensive databases, leveraging network analysis to prioritize key drugs and molecular targets, and performing experimental validation to verify computational predi ctions [8]. In order to prioritise disease-associated genes, identify drug-gene-disease correlations, and demonstrate the network regulation effects of TCM formulations, a novel method known as TCM network pharmacology was developed by combining TCM with network pharmacology analysis [9,10]. Additionally, as molecular docking may anticipate the binding manner and affinity strength, it is a theoretical approach for studying the interaction and recognition between protein receptors and small molecule ligands [11,12,13]. Collectively, network pharmacology and molecular docking can be complementarily inte grated for studying TCM, which can provide novel insights in active compounds screening and mechanism exploration, and may even trigger a revolution in the process of TCM modernization and internationalization. In the present study, a network pharmacology-based strategy, combined with molecular docking and in vitro validation, was performed to discover the active ingredients, potential targets, and molecular mechanism of HHS against cancer

Herbal medicines are a promising choice over modern synthetic drugs because of their low side effects and are thus considered to be safe and effective in treating human diseases. Several bioactive compounds have been isolated from *L. siceraria*, including triterpenoids, sterols, cucurbitacins, flavones, C-glycosides and saponin Flavonoid. These metabolites, which are promising candidates for anticancer, antianxiety, antidepressant, diuretic, antimicrobial, cytotoxic, antihyperlipidemic, cardio protective, analgesic, anti-inflammatory, anthelmintic, anti-hyperglycemic, antihepatotoxic, anti-urolithiatic, antistress, antiulcer, hepatoprotective, anthelmintic, immunomodulatory, and antioxidant [14].

MATERIALS AND METHODS

Protein–protein interaction (PPI) network

Analysis of protein–protein interactions (PPIs) is a crucial tool for understanding the complex participation of proteins in a variety of biological processes. This method helps to gain a thorough grasp of biological processes, functional modalities, and cellular architecture. The complex network of linked proteins was investigated using the sophisticated virtual screening tool STRING 11.0 (https:// string- db. org/). Carefully submitted to the STRING database, the pertinent genetic components offer crucial information on complex PPIs. The parameters for determining the degree of confidence in interactions between target proteins were carefully calibrated for the highest reliability, surpassing the data confidence threshold set at 0.9, and the PPI network's development was carefully adapted to the setting of "Homo sapiens." Different proteins are represented by unique nodes in this complex network visualisation, and interactions between various protein entities are carefully depicted by the connecting edges[15].

Compound and disease-target genes

The bioactive substances found in bottle gourds, or Lagenaria siceraria, were methodically gathered from published phytochemical literature. Cucurbitacins, flavonoids, and phytosterols like apigenin and quercetin were among the main phytoconstituents taken into account for the network pharmacology analysis. Previous research has identified sterols, flavonoids, and cucurbitacins as significant bioactive components of *L. siceraria*. Furthermore, *L. siceraria* fruit has been used to isolate and characterise cucurbitacin I.

The potential protein targets of the selected *L. siceraria* compounds were identified using Swiss Target Prediction databases. The retrieved protein targets were standardized according to their corresponding official gene symbols before further analysis.

Cancer-associated target genes were independently collected from GeneCards and databases using the selected cancer indication as the search term. Duplicate genes were removed, and the resulting compound-related targets were compared with cancer-associated genes. The overlapping genes were considered potential therapeutic targets of *L. siceraria* against cancer[16,17].

Construction of a compound-target network

After conducting the protein–protein interaction analysis, the next step was to clarify the complex molecular mechanisms involved. This was achieved by building a detailed compound–target network using Cytoscape, visualization software version 3.10.4. This network structure is essential for understanding and analyzing the interactions between bioactive components and their specific targets. This approach helps to reveal the pathways involved in this complex biological network [18].

GO and KEGG pathway annotation

The ShinyGo platform was used to annotate the Kyoto Encyclopedia of Genes and Genomes (KEGG) and Gene Ontology (GO) pathways. In order to improve the accuracy of the data prediction, the GO analysis sought to investigate the gene cluster within the network. GO offers a methodically arranged list of standardised words pertaining to cellular components, molecular functions, and biological processes. It includes carefully chosen and anticipated gene annotations from these terms in a variety of species. The identification of crucial biological processes in relation to the goals of the study is made easier by the annotation of biological processes using GO as a resource for pathway enrichment analysis. The roles and metabolic pathways of the genes and compounds in the network under study were also investigated using KEGG. By mapping the pathways related to disease traits, this study sheds light on the complicated interactions between molecules and disease mechanisms [19,20].

Ligand preparation

The ligands and the approved drug structure (doxorubicin) were retrieved from the official U.S. National Library of Medicine PubChem website (https://pubchem.ncbi.nlm.nih.gov/). Afterward, the structures were imported into PyRx 0.8 using the Open Babel tool, and an energy minimization (optimization) step was carried out while considering key parameters such as elements, hybridization, and connectivity. This workflow employed the universal force field [21]. The ligands were then converted into the AutoDock Ligand format (PDBQT).

Target preparation

This study investigated the three-dimensional (3D) structures of ATK1 (PDB: 3096). PyMOL software (The PyMOL Molecular Graphics System, Version 2.4.1 Schrödinger, LLC) was used to visualize the downloaded structures. The target structures were optimized, purified, and prepared for docking with Discovery Studio Visualizer 2020. This procedure included removing unwanted water molecules and bound ligands from the protein structures, followed by saving the processed files in PDB format in the same folder. For docking studies of the selected ligands and the approved drug (doxorubicin), AutoDock Vina 1.1.2 in PyRx 0.8 was used [22].Preparation of Ligands The molecular structures of the active compounds in pomegranate molasses, specifically Quercetin, beta-Sitosterol, Oleanolic acid, were retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov/).

ADME Prediction Test

The ADME prediction test analyzed in the Swiss ADME application provides insights into the physicochemical properties and pharmacokinetic activities of several compounds, particularly metabolites from Lagenaria siceraria (bottle gourd), such as Quercetin, beta-Sitosterol, Oleanolic acid with standard chemotherapy drugs doxorubicin.

Docking procedure

The purified target structures were loaded into the docking software PyRx 0.8 using the "Load molecule" option from the File toolbar. Afterward, the receptor structure was converted into an AutoDock macromolecule in PDBQT format via the right-click option. Binding affinity was also assessed using the Vina Wizard Tool in PyRx 0.8. Both ligands and targets, prepared as PDBQT files, were selected for the docking procedure. In the molecular docking simulation, three-dimensional grid boxes were defined for AKT1 (PDB: 3096), with size_X = 57.4255 Å, size_Y = 61.2803 Å, and size_Z = 59.2219 Å. Once the molecules were selected, active amino acid residues were identified to define the cavity by using the "Toggle

Selection Spheres" option in PyRx. The grid box was then positioned to include all active binding sites and key residues. Subsequently, docking was performed on the ligands and targets to evaluate their binding affinity.

Identification of cavity and active amino acid residues: The protein's active amino acid residues were identified using BIOVIA Discovery Studio Visualizer (version 24.1.023298). The analysis of docking poses, along with ligand–protein interactions, was carried out by importing the output files into PyRx software. This workflow enabled the recognition of different interaction types.

Physiochemical Activity

This table presents the structural characteristics of each compound, including the number of heavy atoms, aromatic heavy atoms, the proportion of sp3 carbons, and molar refractivity. These properties can indicate a compound's stability and its potential reactivity in biological systems. For example, oleanolic acid shows the highest molar refractivity (136.65), which suggests it may have a larger molecular size and greater polarity than quercetin (78.03). Quercetin is comparatively smaller and more hydrophilic.

Lipophilicity

Lipophilicity is expressed as the logarithm of the octanol–water partition coefficient (Log P), which is an important factor governing a compound's ability to cross biological membranes, such as the blood-brain barrier. Compounds with high lipophilicity tend to accumulate in adipose tissues, while hydrophilic compounds exhibit higher solubility in water. β-Sitosterol demonstrates substantial lipophilicity (Log P ~ 6.73), whereas oleanolic acid has a moderate Log P value of 4.88, suggesting it may be absorbed more effectively but may also be cleared from the body more quickly.

Water Solubility

The predicted water solubility of the selected compounds varied markedly. Quercetin showed relatively higher aqueous solubility, with Log S values of −3.19 (ESOL) and −3.96 (Ali), while doxorubicin had a Log S value of −3.91. By contrast, β-sitosterol and oleanolic acid exhibited very low solubility, with Log S values ranging from −7.32 to −9.67, indicating poor aqueous solubility. Overall, quercetin and doxorubicin were more water-soluble than β-sitosterol and oleanolic acid.

RESULTS

Construction and analysis of the target PPI network

Construction and analysis of the target PPI network

The target genes corresponding to each component were rigorously evaluated for building and visualizing a protein–protein interaction (PPI) network using STRING v_11. High-confidence interaction data for the target proteins were retained by applying a stringent cutoff, with a score greater than 0.9. As shown in Fig. 1, the resulting PPI network comprised 73 nodes and 513 edges, and each edge denoted a distinct protein–protein interaction (PPI). In addition, the average node degree—i e., the number of connected targets within the network—was found to be 14.1. The local clustering coefficient of 0.532 indicates the number of targets connected to the network. The PPI network analysis emphasized the involvement of key targets.

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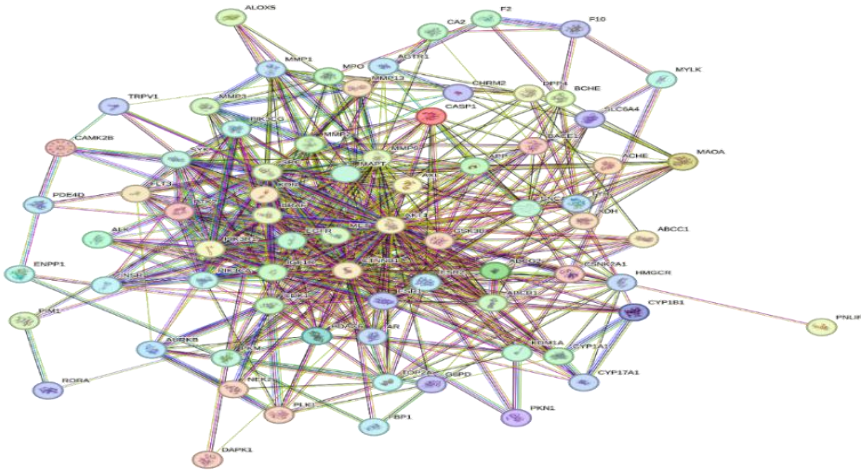

Fig. 1. Protein–protein interaction network obtained from STRING v_11.0 database.

Arrangement and construction of disease-target network

To investigate the signaling pathways and functional consequences of the selected target genes, Cytoscape was used to import and analyze the data. This workflow enabled the generation of a comprehensive compound–target network. As depicted in Fig. 2, the network illustrates the complex mechanisms underlying the pharmacological effects of the compounds in cancer therapy. The database contained three distinct ingredients and reported interactions with 73 target proteins. Notably, network analysis highlighted that multiple components converge on diverse targets, implying potential synergistic regulation by the active biochemical constituents. This multifaceted interaction may support not only the therapeutic effectiveness of these agents in anxiety management, but also the treatment of other related diseases and disorders. Detailed information on the network's topological parameters is provided in Table S3 of the Supplementary material, underscoring the essential contribution of each target to the overall network architecture. In network pharmacology, understanding topological parameters is critical because it offers quantitative descriptors for characterizing the structure, function, and dynamics of complex biological networks. Such information is also helpful for discovering candidate drug targets, clarifying disease mechanisms, and informing therapeutic decision-making.

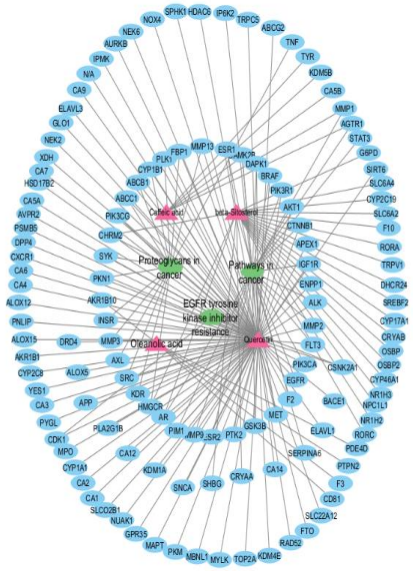

Fig 2. Compound-target-cancer network constructed by Cytoscape v_3.10.4

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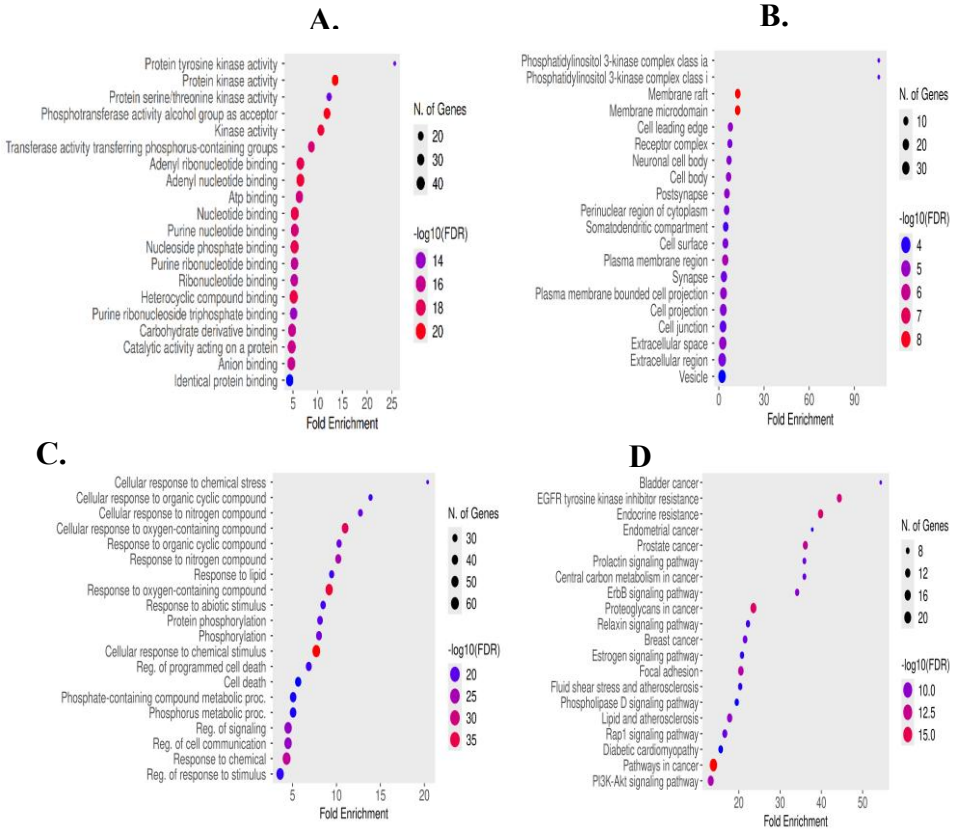

Fig. 3. A. GO Molecular function, B. GO Cellular Component, C. GO Biological Process, D. KEGG pathway.

Table 1. ADME predictions and physiochemical activities of the phytoconstituents.

Compound	Physiochemical Activity							
	Num. Heavy Atoms	Num. Arom. Heavy Atoms	Fraction Csp3	Num. Rotatable Bonds	Num. H-bond Acceptors	Num. H Bond Donors	Molar Refractivity	TPSA
Quercetin	22	16	0	1	7	5	78.03	131.36 Å²
beta-Sitosterol	30	0	0.93	6	1	1	133.23	20.23 Å²
Oleanolic acid	33	0	0.9	1	3	2	136.65	57.53 Å²
Doxorubicin	39	12	0.44	5	12	6	132.66	206.07 Å²

Table 2. Lipophilicity of the phytoconstituents.

Compound	Lipophilicity					
	Log Po/w (iLOGP)	Log Po/w (XLOGP3)	Log Po/w (WLOGP)	Log Po/w (MLOGP)	Log Po/w (SILICOS-IT)	Consensus Log Po/w
Quercetin	1.63	1.59	1.99	-0.56	0.14	0.79

beta-Sitosterol	6.73	9.34	8.02	6.73	7.04	7.78
Oleanolic acid	4.88	7.49	7.23	5.82	5.85	6.6
Doxorubicin	2.58	1.27	-0.32	-2.1	1.17	0.52

Table 3 Water solubility of the phytoconstituents.

Compound	**Water Solubility**		
	Log S (ESOL)	Log S (Ali)	Log S (ESOL)
Quercetin	-3.19 1.96e-01mg/ml; 6.49e-04mol/l Soluble	Quercetin	-3.96 3.32e-02mg/ml; 1.10e-04 mol/l Soluble
beta-Sitosterol	-7.9 5.23e-06 mg/ml; 1.26e-08 mol/l Poorly soluble	beta-Sitosterol	-9.67 8.90e-08 mg/ml;2.15e-10 mol/l Poorly soluble
Oleanolic acid	-7.32 2.16e-05mg/ml;4.74e-08 mol/l Poorly soluble	Oleanolic acid	-8.53 1.34e-06 mg/ml; 2.94e-09mol/l Poorly soluble
Doxorubicin	-3.91 6.72e-02 mg/ml; 1.24e-04 mol/l Soluble	Doxorubicin	-3.91 6.72e-02 mg/ml; 1.24e-04 mol/l Soluble

Table 4 Go Biological process.

Description	**Count in gene set**	**False discovery rate**
Regulation of apoptotic process	35	1.24×10^{-17}
Response to endogenous stimulus	34	1.48×10^{-17}
Positive regulation of molecular function	36	1.48×10^{-17}
Response to organic cyclic compound	28	1.25×10^{-16}
Regulation of phosphorylation	32	1.38×10^{-16}
Regulation of localization	39	1.55×10^{-16}

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Table 5 Go Molecular Function

Description	Count in gene set	False discovery rate
Protein tyrosin kinase activity	13	4.78×10^{-12}
Protein kinase activity	27	4.49×10^{-19}
ATP binding	33	1.81×10^{-15}
Protein serine/threonine kinase activity	18	7.72×10^{-12}
Adenyl ribonucleotide binding	36	2.04×10^{-17}

Table 6 Go cellular components

Description	Count in gene set	False discovery rate
Membrane raft	13	1.65×10^{-7}
Cell leading edge	12	2.01×10^{-5}
Plasma membrane region	20	6.89×10^{-6}
Membrane	57	5.65×10^{-5}
Plasma membrane	48	3.13×10^{-8}

Table 6 KEGG pathways.

Description	Count in gene set	False discovery rate
Pathways in cancer	23	3.38e-16
Proteoglycans in cancer	15	1.97e-13
Endocrine resistance	12	4.66e-13
EGFR tyrosine kinase inhibitor resistance	11	1.7e-12
Prostate cancer	11	1.38e-11
Focal adhesion	13	3.68e-11
PI3K-Akt signaling pathway	15	1.88e-10

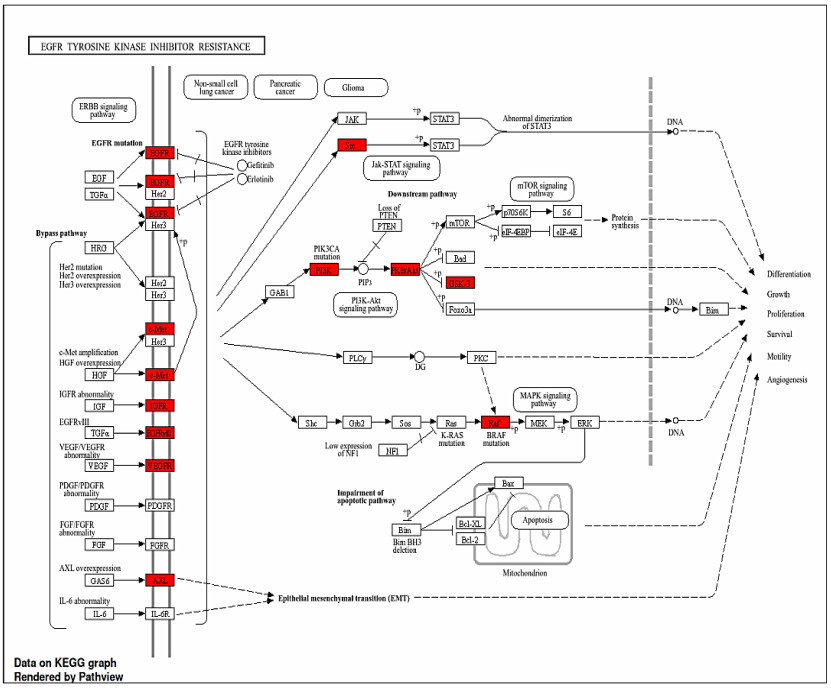

Fig.8 EGFR tyrosine kinase inhibitor resistance

Table 7 Estimated Free Energy of Binding, H-Bond Interactions and Hydrophobic Interactions between compounds and receptors.

Targets	Compounds	PubChem ID	Binding Affinity	Hydrophobic Interactions	Hydrogen bonding
AKT1	Quercetin	5280343	-9	LEU264, TRP80, LEU210, VAL270	A:VAL271, A:TYR272, A:SER205, A:ILE290
	beta-Sitosterol	222284	-11	UNK1, LYS268, VAL270	SER205, LYS268, UNK1
	Oleanolic acid	10494	-10.1	-	ARG328, ALA329
	Doxorubicin	31703	-10.6	LEU264, LYS268, VAL270, LYS268	ASN53, SER205, LYS268, VAL271, YR272, TRP80

The fig. 4 displays the two-dimensional (2D) molecular interaction map of the ligand-flavonoid quercetin Overall, binding affinity is primarily determined by a broad network of conventional hydrogen bonds in conjunction with hydrophobic interactions. Specifically, the hydroxyl groups located on the chromone and phenyl rings promote conventional hydrogen bonding with the side chains of Ser205, Ile290, Val271, and Tyr272 (shown in green), which helps maintain the ligand within the catalytic site. Hydrophobic stabilization is further strengthened by ππ–ππ stacking involving the aromatic indole ring of Trp8, and by ππ–alkyl interactions with Val270 and Leu210. In addition, the electronic environment is stabilized via a ππ–anion interaction with Asp292 (orange) and a ππ–sigma interaction involving Leu264, collectively indicating a strong complementarity between the ligand and the amino acid residues lining the Hsp90 binding cavity.

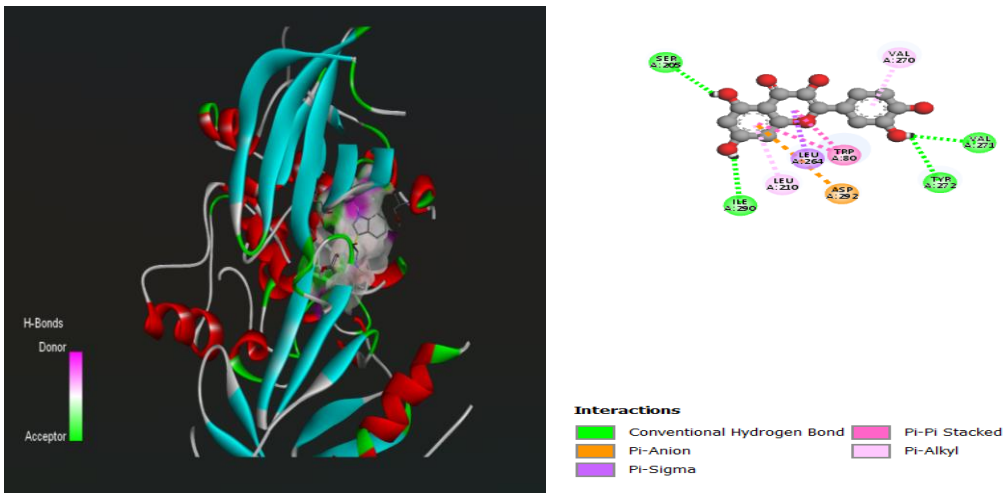

Fig.4 2D interaction & Qurecetin 3D binding modes in AKT serine/threonine kinase 1 complexed active site (PDB ID:3096).

The fig. 5 illustrates the two-dimensional (2D) molecular interaction map of the ligand flavonoid quercetin, specified by its structural scaffold, within the binding pocket of the Hsp90-alpha N-terminal domain (corresponding to PDB ID 3O96). Overall, binding affinity is primarily determined by a broad network of conventional hydrogen bonds in combination with hydrophobic interactions. Notably, the hydroxyl groups on the chromone and phenyl rings facilitate conventional hydrogen

bonding with the side chains of Ser205, Ile290, Val271, and Tyr272), thereby helping to position the ligand within the catalytic site. Hydrophobic stabilization is further strengthened by ππ-ππ stacking involving the aromatic indole ring of Trp80 and by ππ-alkyl contacts with Val270 and Leu210 (light pink). In addition, the electronic environment is stabilized through a ππ-anion interaction with Asp292 and a ππ-sigma interaction involving Leu264, collectively indicating a strong complementarity between the ligand and the amino acid residues lining the Hsp90 binding cavity.

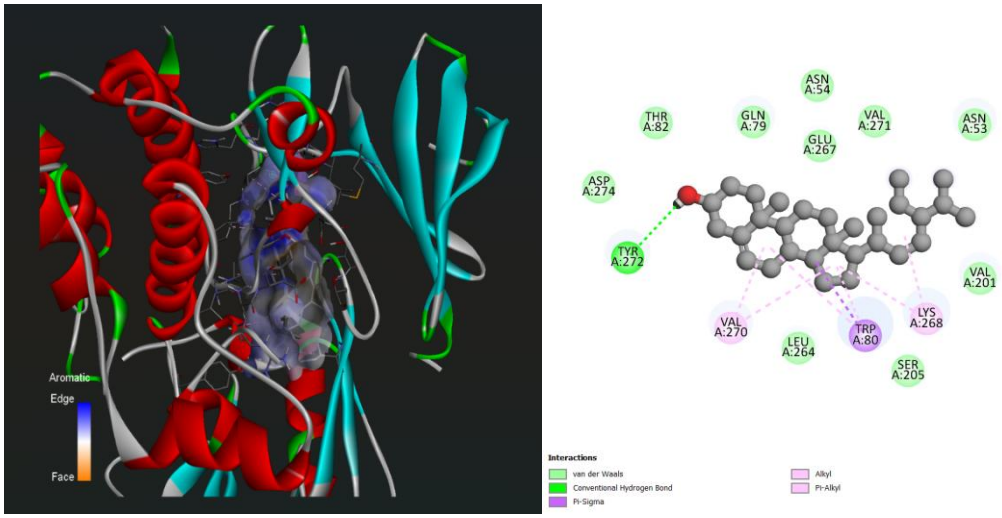

Fig 5 2D interaction & Beta-sitasterol 3D binding modes in AKT serine/threonine kinase 1 complexed active site (PDB ID:3096).

The fig.6 illustrates the two-dimensional molecular interaction landscape of a ligand, identified structurally as the flavonoid quercetin, within the binding pocket of the Hsp90-alpha N-terminal domain. Binding affinity is primarily determined by a robust network of conventional hydrogen bonds alongside hydrophobic interactions. Specifically, the hydroxyl groups on the chromone and phenyl rings support conventional hydrogen bonding with the side chains of Ser205, Ile290, Val271, and Tyr272, thereby anchoring the ligand in the catalytic site. Hydrophobic stabilization is further strengthened by ππ–ππ stacking involving the aromatic indole ring of Trp80 and by ππ–alkyl interactions with Val270 and Leu210 (shown in light pink). In addition, the local electronic environment is stabilized via a ππ–anion interaction with Asp292 and a ππ–sigma interaction involving Leu264, reflecting a high degree of compatibility between the ligand and the amino acid residues lining the Hsp90 binding cavity.

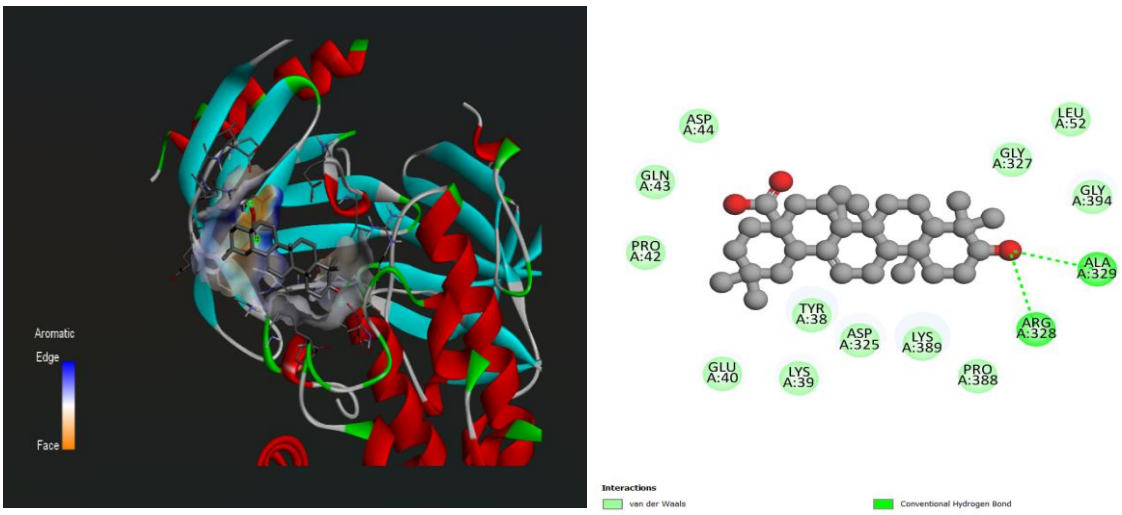

Fig 6 2D interaction & Olenolic acid 3D binding modes in AKT serine/threonine kinase 1 complexed active site (PDB ID:3096).

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The fig.7 illustrates two-dimensional interaction of the ligand within the binding pocket of AKT1 (PDB ID: 3O96) to provide a detailed scientific description of its hydrogen bonding and hydrophobic interaction. The binding stability is significantly bolstered by conventional hydrogen bonds formed between the ligand's hydroxyl and carboxyl groups and the amino acid residues ASN53, SER56, and GLN79, complemented by a carbon hydrogen bond with SER205. These polar interactions are augmented by a robust hydrophobic framework, characterized by ππ-ππ stacked interactions with the aromatic ring of TRP80 and a π π-sigma interaction with VAL270. Furthermore, the ligand's hydrophobic moiety is anchored via alkyl and ππ-alkyl interactions involving LEU210 and LEU264, which collectively enhance the lipophilic complementarity within the pocket. Although an unfavorable donor-donor interaction is noted with ASN199, the overall binding architecture suggests a high affinity driven by the synergy of multiple hydrogen bonds and extensive hydrophobic contacts, typical of potent kinase inhibitors.

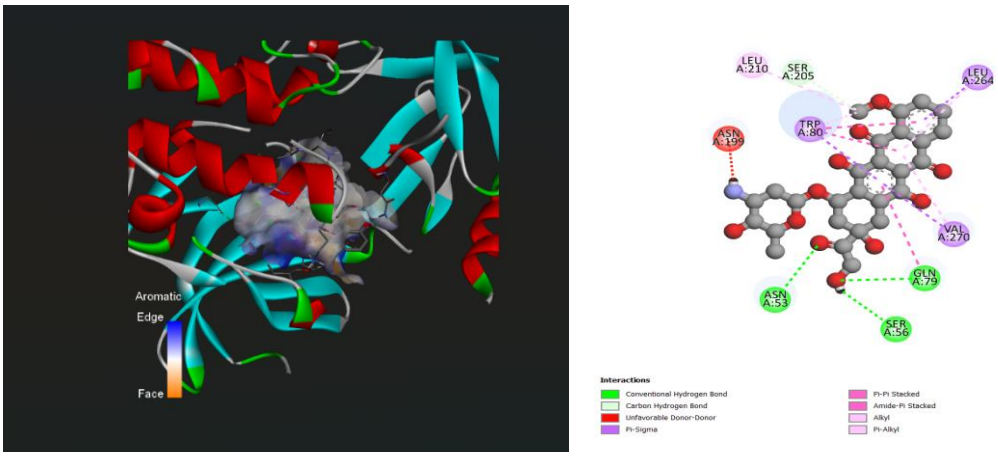

Fig.7 2D interaction & 3D Doxorubicin binding modes in AKT serine/threonine kinase 1 complexed active site (PDB ID:3096).

DISCUSSION

This study provides a comprehensive framework for understanding the pharmacological potential of Lagenaria siceraria (bottle gourd) in cancer treatment using an integrated approach of network pharmacology, molecular docking, and ADMET analysis. The results confirm a "multi-component, multi-target, and multi-pathway" mechanism, primarily driven by bioactive constituents such as quercetin, beta-sitosterol, and oleanolic acid. These compounds interfere with cancer hallmarks by inhibiting proliferation and inducing apoptosis, specifically targeting the PI3K-Akt signaling pathway. PPI network analysis highlights high connectivity among hub targets, suggesting that *L. siceraria* effectively regulates cell survival and metabolism. Molecular docking identified AKT1 as a critical hub, with beta-sitosterol demonstrating a superior binding affinity of -11 kcal/mol, surpassing the reference drug doxorubicin. This high affinity is supported by a robust framework of hydrogen bonds and hydrophobic interactions within the AKT1 kinase domain, providing a mechanistic basis for the plant's known cytotoxic effects against lung and breast cancer cell lines. While ADMET analysis reveals that the high lipophilicity of beta-sitosterol and oleanolic acid may present challenges for systemic bioavailability, their potent binding efficacy underscores their therapeutic promise. The findings suggest that optimizing delivery systems, such as nano-emulsions, could maximize the clinical index of these phytochemicals.

CONCLUSION

In conclusion, the computational evidence presented here identifies Lagenaria siceraria as a promising candidate for anti-cancer drug development, primarily through the modulation of the PI3K-Akt-mediated apoptotic pathway. The major scientific implication is the potential of beta-sitosterol as a high-affinity allosteric inhibitor of AKT1. Nevertheless, it is crucial to recognize that these findings are based on in silico predictions. The limitations of the present study include the lack of dynamic simulation to assess complex stability over time and the need for in vivo toxicity assessments. Future research must prioritize experimental validation using cell-based assays and animal models to confirm the inhibitory concentration (IC50) and therapeutic safety of these phytochemicals.

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