INTEGRATIVE NETWORK PHARMACOLOGY AND MOLECULAR DOCKING REVEAL MULTI-TARGET THERAPEUTIC POTENTIAL OF ABELMOSCHUS ESCULENTUS PHYTOCONSTITUENTS AGAINST POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a multifactorial endocrine disorder characterized by hormonal imbalance, insulin resistance, and chronic inflammation. This study aimed to evaluate the therapeutic potential of phytoconstituents from Abelmoschus esculentus using an integrated network pharmacology and molecular docking approach. Compounds were screened based on pharmacokinetic properties, drug-likeness, and toxicity, followed by target prediction and intersection with PCOS-related genes. Protein–protein interaction (PPI) network analysis and pathway enrichment identified key targets, including EGFR, STAT3, TLR4, and MTOR, involved in PI3K–AKT, MAPK, JAK–STAT, and mTOR signaling pathways. Molecular docking demonstrated that Vitamin E exhibited the highest binding affinity, particularly with EGFR (−8.0 kcal/mol), followed by Vernolic acid and Linolenic acid. Additionally, selected compounds showed favorable pharmacokinetic and safety profiles. To the best of our knowledge, limited studies have explored the multi-target therapeutic potential of Abelmoschus esculentus phytoconstituents against PCOS using an integrated network pharmacology and molecular docking approach. These findings highlight their multi-target therapeutic potential; however, further experimental validation is required.

Key words: PCOS, Abelmoschus esculentus, Network Pharmacology, Molecular Docking, EGFR.

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Introduction

One of the most prevalent endocrine system conditions affecting women of reproductive age is polycystic ovary syndrome (PCOS), also known as hyperandrogenic anovulation (HA) or Stein–Leventhal syndrome [1 PCOS is a heterogeneous endocrine disorder with widely reported prevalence ranging between 4% and 20% depending on diagnostic criteria and population studied·.[2] The World Health Organization (WHO) estimates that in 2012 PCOS affected 116 million women (3.4%) globally [3]. This high frequency, as well as its link with ovulation and menstruation abnormalities, infertility, hair loss, and metabolic issues, underscores PCOS's significant financial burden [4,5] The primary symptoms of PCOS include hyperandrogenism, absent ovulation, and polycystic ovaries. Currently, there are no definitive diagnostic criteria for PCOS, as its pathology involves multiple factors such as endocrinology and gynaecology, making it difficult to categorize. [6-9]

The pathophysiology of PCOS is multifactorial and involves impaired gonadotropin-releasing hormone (GnRH) pulsatility, increased pituitary luteinizing hormone (LH) secretion [10], elevated androgen levels, insulin resistance, obesity [11], and chronic low-grade inflammation [12]. Hyperandrogenism is a key diagnostic feature characterized by elevated androgenic hormones, leading to clinical manifestations such as acne, hirsutism, and alopecia [13]. Additionally, insulin resistance, which reduces the cellular responsiveness to insulin and impairs glucose uptake and metabolism, is prevalent among PCOS patients. This can lead to obesity and is closely linked with the development of type 2 diabetes [14]. According to Barre et al., the high consumption of carbohydrates, hyperinsulinemia, hyperandrogenemia, and persistent low-grade inflammation are the four key contributors to pathophysiological alterations in PCOS[15].

PCOS can be well treated with conventional medicine, although long-term use may result in some negative effects. This may lead to encouraged a renewed interest in therapies derived from natural and plant sources. Evidence from scientific studies supports the safety and therapeutic efficacy of several complementary treatment approaches, including herbal remedies, in the management of certain diseases.[16]

Abelmoschus esculentus (L.) is a member of the Malvaceae family and it is commonly known as lady finger or okra.[17] Okra, recognized as a superfood (functional food), is increasingly gaining recognition for its high nutritional value and diverse therapeutic effects.[18] The profile of the bioactive components present in different parts of okra has been reported, which includes polyphenolic compounds, flavanol derivatives, carotene, protein (i.e., high lysine levels), folic acid, thiamine, riboflavin, niacin, vitamin C, oxalic acid, amino acids, oligomeric catechins, and newly identified bioactive component abscisic acid.[19] The study showed that antioxidant could prevent the prevalence of metabolic syndrome and most of the vegetables and fruit were rich with it. [20,21] Okra extract also had activity as an invitro non-enzymatic lipid inhibitor. [22] Computer-aided drug design (CADD) is an advanced technique that involves the utilization of virtual screening, molecular docking, and molecular dynamic simulation to screen a large set of molecules to yield fewer compounds that need to be validated further. Recent research has shown the implication of these techniques in saving time, money, and manpower for drug discovery protocol [23]

This study is designed under the "hypotheses" that A. esculentus have the potential to fight against PCOS . Accordingly, using plant phytochemicals having antioxidant properties can be helpful for scavenging various reactive oxygen species, which contribute to the prevention of PCOS. Therefore, the present study aims to systematically investigate the therapeutic potential of phytoconstituents derived from *Abelmoschus esculentus* against PCOS using an integrated network pharmacology and molecular docking approach. To the best of our knowledge, this study provides a comprehensive systems-level investigation of Abelmoschus esculentus phytoconstituents in PCOS, which has been insufficiently explored. The findings of this study are expected to provide a scientific basis for the development of novel multi-target therapeutic agents derived from natural sources.

Material and methods

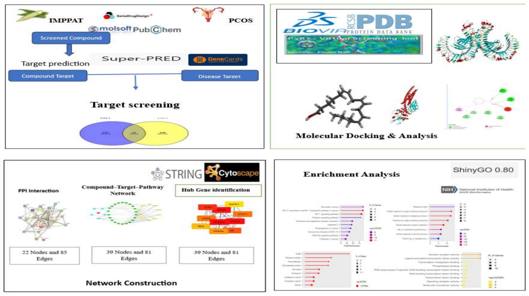


Fig. No 1 Overview of In-Silico methods

Network pharmacology

1.1 Abelmoschus esculentus (L.) phytochemical compound collection and screening

The phytoconstituents of *Abelmoschus esculentus* were collected from the IMPPAT database. The information about every compound present in okra is obtain from this database. IMPPAT is a manually curated digital repository that provides information on more than 4000 Indian medicinal plants, their phytochemicals, and the therapeutic relevance of these compounds, either experimentally or computationally derived.[24]

1.1 Pharmacokinetic predication of compound of *Abelmoschus esculentus* (L.)

The SMILES was obtain for each compound of okra by using PubChem website. Using SwissAdme, we predicted the pharmacological properties of the *Abelmoschus esculentus* (L.). The BOILED-Egg model provides accurate prediction of pharmacokinetics and behaviour of the small molecules via computing the lipophilicity and polarity of molecules. As we know ADME is essential for finding how drugs behave.[25] And to check the drug-likeness (DL) of compounds we used the MolSoft database.[26] The Lipinski's rule violation led to the selection of oral bioavailability score and drug likeness as pharmacokinetic parameter. To evaluate their multiple target, phytocompound with an oral bioavailability score of >_ 0.30 and drug likeness score of > 0 with zero violation for Lipinski's rule were chosen. Additionally the parameter like molecular weight, lipophilicity, donor and acceptor of hydrogen bonds and polar surface area were assessed. compound that follow all the criteria of Lipinski's rule were filter out for further analysis.

1.2 Evaluation of the toxicity of compounds

Toxicity (T) prediction was performed using the ProTox 3.0 server (https://tox.charite.de/protox3/) [39]. ProTox 3.0 is a comprehensive tool that integrates various elements such as molecular resemblance, fragment tendencies, commonly occurring features, and machine learning based on fragment similarity and cluster cross-validation. It utilizes a total of 61 models to predict various toxicity endpoints. These include acute toxicity, organ toxicity, toxicological endpoints, molecular initiating events, metabolism, adverse outcomes (Tox21) pathways, and toxicity targets. The lethal dose (LD50) values were also evaluated to assess compound toxicity. [27]

1.3 Target identification of compounds in *Abelmoschus esculentus* (L.)

The target predication is done by using SuperSpeed. The protein targets of the biologically active substances were obtained utilizing the Super-PRED which can be consequently mined details for several phytocompounds. To create a possible target database pertaining to *Abelmoschus esculentus* bioactives, filtered targets based on the median probability. Protein targets preferred names were mapped by importing their UniProt IDs into a string database.[28]

PCOD disease related target identification

PCOS related targets were obtain by using Gene Card database. Gene Card is an integrated and continuously updated database of human genes. The database integrates gene related data from genomic, transcriptomic, and proteomic sources until functional information is obtained from selected web sources. [29]

Discovery of common targets

The intersecting genes between the target *Abelmoschus esculentus* dataset and the PCOS gene panel were identified using VENNY 2.1.0. Lists from both sources were uploaded, and overlapping genes were extracted as potentially relevant for mechanistic exploration.[30]

Protein–protein interaction (PPI) network

To elucidate interactions between cross-targets, the Drug and disease cross-target data were imported into the STRING database, "Homo sapiens" was used as the species, "highest confidence (>0.4)" was used as the minimum interaction threshold, and the remaining parameters remained at their original default settings.[31] Then, saved the protein-protein interaction (PPI) network of the obtained intersecting target in "TSV" format. In the network illustration, nodes symbolized active constituents and target genes, while edges illustrated interactions between them.[32]

KEGG and GO Pathway Enrichment

The GO database, including BP, molecular function, and cellular component (CCs), was used to explore the potential biological molecular mechanisms [33]. The KEGG database has also been used to identify biological functions and candidate targets[34]

Building network of Active Component-Target-Pathway

The network between phytoconstituents, targets, and pathways was built using Cytoscape 3.7.2.[35] Cytoscape is an open-source software platform for visualizing molecular interaction networks, to construct and integrate the networks manually based on annotations, gene expression profiles and other data. The core distribution provides a basic set of features for data integration, analysis, and visualization. The network's edges represented the interactions between pathways, targets, and components that could be utilized in *Abelmoschus esculentus*'s treatment of PCOS, while the network's nodes represented compounds, targets and pathways

Hub gene identification

The CytoHubba plugin that uses maximal clique centrality approach, was employed to detect hub genes and nodes with significant levels within the network. The presence of the highest degree emphasizes the substantial correlations between the genes under consideration.[36] Key targets associated with *Abelmoschus esculentus* in the PCOS process were identified using topological centrality metrics, specifically by comparing the median Degree and Closeness centrality values. The Degree value represents the number of direct connections associated with a node, and an increased number of connections correlates with enhanced node influence. Betweenness centrality (BC) refers to the shortest paths between all pairs of nodes within the network, where a lower value suggests the node is less central. Closeness centrality (CC) is defined as the inverse of the average shortest path length between a particular node and all other nodes in the network, with lower values indicating reduced efficiency in signal propagation among the nodes.[37]

MOLECULAR DOCKING

Molecular docking can help to validate key targets in network pharmacology.[38] It is a widely used in drug discovery that aims to predict the binding conformation of small molecule ligands to appropriate target binding sites. Docking can identify new compounds with therapeutic potential, predict ligand-target interactions at the molecular level, or depict structure-activity relationships without prior knowledge of the chemical structures of other target modulators.[39]

The 3D structures of selected phytoconstituents (ligands) were retrieved from the PubChem small molecule database (https://pubchem.ncbi.nlm.nih.gov/) in the '.sdf' format and converted into'.pdb' format using Discovery Studio, while potential genes' structures were obtained from RCSB PDB in PDB format. The proteins were prepared by removing impurities, including water molecules, using Discovery Studio software to avoid interference and converted into a proper readable PDBQT file format.

PyRx, a virtual screening software, was employed for molecular docking, while BIOVIA Discovery Studio was utilized for visualizing the 2D conformations of ligand and receptor protein affinities. The selection of the best drug candidates was made on the basis of good docking scores and RMSD values. PyRx provided information on the occupancy of the ligand within the active sites of the target molecules through docking scores.

Result

Screening of active phytoconstituent in *Abelmoschus esculentus*

Using IMPPAT software the chemical component of *Abelmoschus esculentus* Only compounds reported in the seeds of *A. esculentus* were considered for further analysis., resulting in total 61 phytoconstituents were obtain. The SMILES of each phytocompound were retrieved from the PubChem database.

Pharmacokinetic predication of compound of *Abelmoschus esculentus* (L.)

Pharmacokinetic properties and drug-likeness of the identified phytoconstituents were evaluated using SwissADME and the MolSoft server. Drug-likeness was assessed based on positive drug-likeness scores obtained from MolSoft. The physicochemical properties, including lipophilicity, molecular size, polarity, solubility, saturation, and flexibility, were analyzed and visualized using the bioavailability radar provided by SwissADME. Compounds that did not meet the established drug-likeness and pharmacokinetic criteria were excluded from further analysis. After applying these screening parameters, a total of five compounds were identified as potential candidates with favourable pharmacokinetic profiles and were selected for subsequent studies (Table 1).

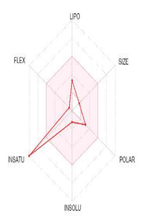
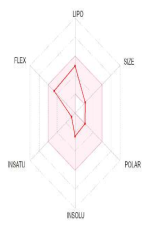
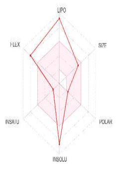
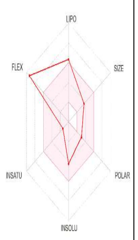
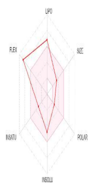
name of metabolites	Lipinski Violation	Bioavailability radar	Bioavailability score	Drug-Likeness	GI absorption
Nicotinic acid	0		0.85	0.29	high
Pentyl 3-methyl butanoate	0		0.55	0.56	high
Vitamin E	1		0.55	0.29	Low
Vernolic acid	0		0.85	0.30	High
Linolenic acid	1		0.85	0.29	High

Table. No.1Pharmacokinetic and Drug-Likeness Evaluation of Selected Phytoconstituents Based on ADME Parameters

Evaluation of the toxicity of compounds

Toxicity assessment of compounds is a critical step in drug discovery, ensuring the safety and efficacy of potential therapeutic agents. In silico tools for molecular docking offer a cost-effective and efficient means to predict drug toxicity, allowing researchers to evaluate potential drug candidates for their safety profiles before advancing to costly In-vitro and In-vivo experiments. Compound toxicity was assessed through a comprehensive analysis of six distinct toxicity factors, encompassing hepatotoxicity, carcinogenicity, mutagenicity and nuclear receptor signalling pathways which includes Aryl hydrocarbon Receptor (AhR), Androgen Receptor (AR),Androgen Receptor Ligand Binding Domain (AR-LBD), Aromatase, Estrogen Receptor Alpha (ER), Estrogen Receptor Ligand Binding Domain (ER-LBD), Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma). These parameters provide insight into the potential safety and biological risks associated with the selected compounds. The predicted toxicity profiles of the selected compounds are summarized in Table 2.

Phytoconstituents	Class	Predicted LD50	Hepatotoxicity	Carcinogenicity	Mutagenicity	Nuclear receptor or signalling pathways
Nicotinic acid	5	3720mg/kg	Active	Inactive	Inactive	Inactive
Vitamin E	5	5000mg/kg	Inactive	Inactive	Inactive	Inactive
Vernolic acid	5	5000mg/kg	Inactive	Inactive	Inactive	Inactive
Linolenic acid	6	10000mg/kg	Inactive	Inactive	Inactive	Inactive
Pentyl 3-methylbutanoate	6	12210mg/kg	Inactive	Inactive	Inactive	Inactive

Table 2. The predicted toxicity profiles of the selected compounds

Target identification of compounds in *Abelmoschus esculentus* (L.) & PCOS related Target Identification

The core target genes of the compounds which pass the pharmacokinetics criteria were retrieved from superpred database. Total 551 potential target were found from five active phytoconstituents. Among these, vitamin E exhibited the highest number of predicted targets(138), followed by Pentyl 3-methylbutanoate(123), vernolic acid (111), nicotinic acid (88) and linolenic acid (89) as illustrated in the compound–target interaction network (Figure 2).

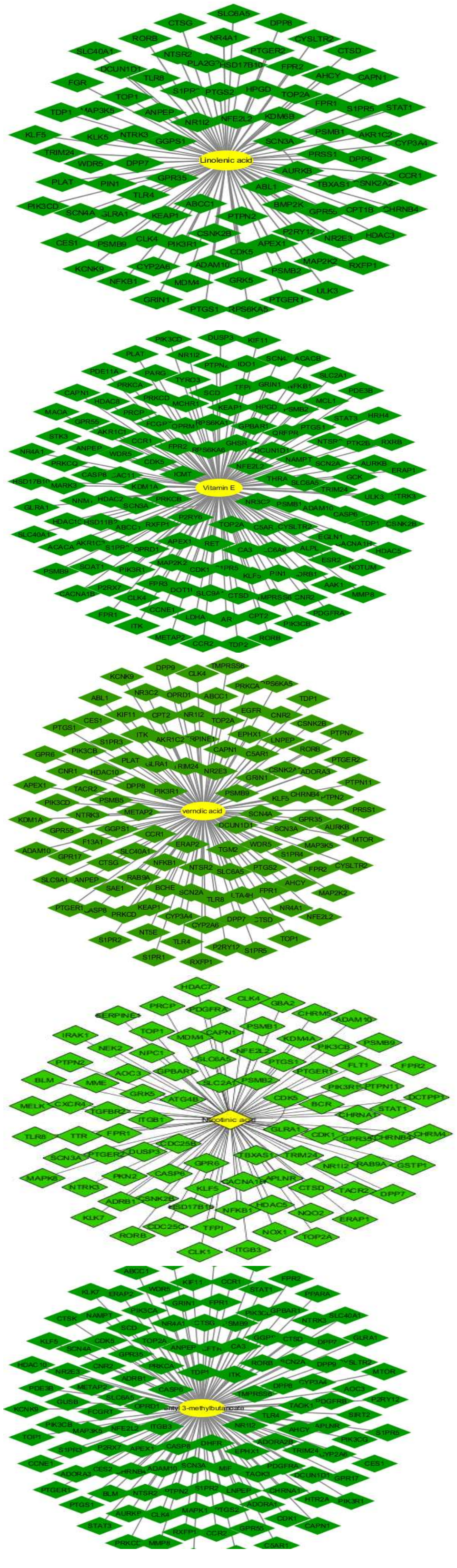


Fig No. 2 Compound–Target Interaction Network of Selected Phytoconstituents Against PCOS-Associated Targets.

The diseased related target were retrieved from the GeneCards database by using keyword "PCOS". After removing duplicate entries and consolidating the data, we identified a total of 450 unique PCOS related targets were searched. Subsequently, the predicted targets of *Abelmoschus esculentus* phytoconstituents were intersected with PCOS-related targets, resulting in 22 overlapping genes, which were considered potential therapeutic targets. These common targets were visualized using a Venn diagram (figure 3)

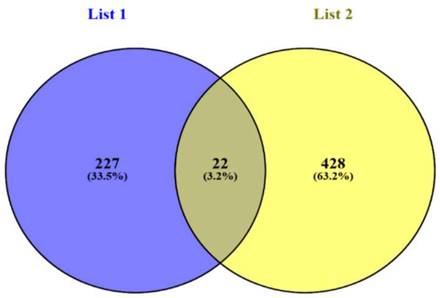


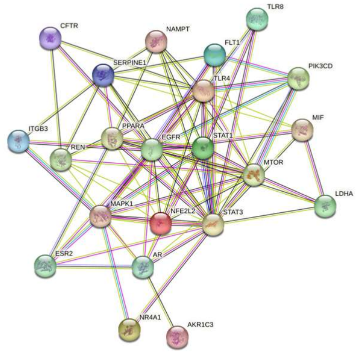
Fig. No.3 Venn diagram showing the shared target of *Abelmoschus esculentus* (L.) and genes associated with PCOS.

Protein–protein interaction (PPI) network

Interactions among the identified overlapping targets were analyzed to understand their functional relationships and involvement in PCOS-related biological mechanisms. We first established the PPI networks to explore the interactions between potential targets. 22 overlapping targets were further imported into the STRING database to construct a PPI network, and the final PPI network consisted of 22 nodes and 85 edges, with a significant PPI enrichment p-value of 2.22×10^{-16}, indicating strong functional connectivity among the targets. A confidence score threshold of 0.400 (medium confidence) was applied for network construction (figure 4)

Fig. No.4 PPI network of the common targets of *Abelmoschus esculentus* and PCOS. Each node represents a common target, with larger nodes indicating higher degree values; edges denote protein–protein interactions, and thicker edges indicate stronger interactions.

To investigate the mechanism of *Abelmoschus esculentus*'s PCOS impact, a network map of gene targets was created using the Cytoscape software to reveal relationship between A. *esculentus* and multiple PCOS gene targets. The hub genes were identified by filtering out the gene network obtained through Cytoscape based on maximal cliques' centrality (MCC) topology by using the Cytohubba plug-in of Cytoscape.



Topological analysis using the Network Analyzer plugin revealed that the average degree, betweenness centrality, and closeness centrality values were 7.73, 0.03463, and 0.60856, respectively. Among them, there are 18 nodes whose degree value, Betweenness Centrality, and Closeness Centrality are all greater than the average. They may be the main targets for A. *esculentus* to play a role.

KEGG and GO Pathway Enrichment

To find out which metabolic pathways and biological processes *Abelmoschus esculentus* (L.) may be able to influence therapeutically in the treatment of PCOS, KEGG enrichment and GO functional annotation analyses were performed by using DAVID database. Gene ontology (GO) analysis of 22 intersecting targets was carried out to understand the core targets involved in cellular component (CC), molecular function (MF), and biological process (BP). There were 22 CC, 38 MF and 119 BP that were identified. The top 10 terms of BP, CC, and MF were obtained at a threshold cutoff of $p < 0.05$ and FDR <0.05, respectively. Figure

KEGG pathways associated with the common targets were identified using the ShinyGO program v. 0.8. The standardized gene symbols of each target were uploaded to ShinyGO, specifying the species as *Homo sapiens* and setting the FDR cut-off value at 0.05.Pathways were selected by FDR ($p < 0.05$) and sorted by fold enrichment, on the basis of these top 20 pathways were selected.

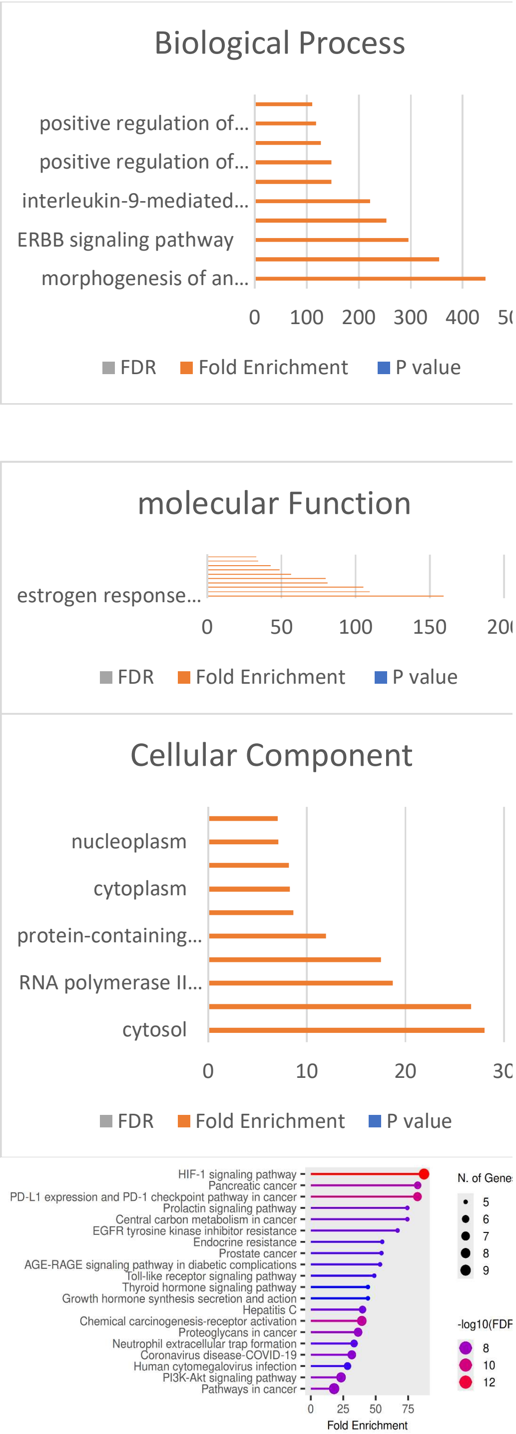


Fig No.5 Representation of enriched pathways and functional annotation in the form of lollipop & clustered bar chart (A) represent the GO biological process. (B) Shows GO molecular function. Whereas, (C) represent GO cellular process and (D) represent enriched KEGG pathways.

Building network of A ponent-Target-Pathway

To further elucidate the therapeutic mechanism of *Abelmoschus esculentus* in the treatment of PCOS, a compound–target–pathway network was constructed using Cytoscape. The network comprised a total of 39 nodes and 81 edges, representing complex interactions among phytoconstituents, target genes, and enriched pathways. In the network, nodes correspond to active compounds, protein targets, and signaling pathways, while edges represent their interactions. The cyan node represents *Abelmoschus esculentus*, yellow circular nodes denote enriched pathways, and green square nodes indicate overlapping genes associated with both the plant and PCOS. This integrative network highlights the multi-component, multi-target, and multi-pathway characteristics of *A. esculentus* in PCOS management (Fig. 5).

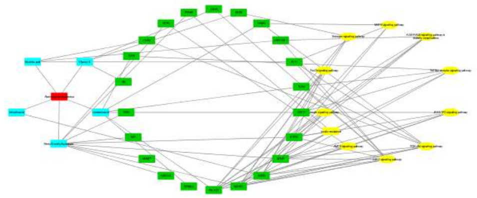


Fig No.6 Component- Target-Pathway of *Abelmoschus esculentus* (L.) and PCOS

Cytohubba identification

To identify key regulatory targets with in–protein interaction (PPI) network, topological analysis was performed using the CytoHubba plugin in Cytoscape. Nodes were ranked based on Degree, Betweenness Centrality, and Closeness Centrality, which reflect the importance of nodes in network connectivity, information flow, and communication efficiency, respectively. Among t AT3 exhibited the highest degree (18), its strong interaction with other nodes, followed by EGFR (16) ,TLR4 (14) and mTOR(13). The high centrality of these targets suggests their critical roles in regulating inflammatory responses, insulin signaling, and hormonal imbalance, which are key pathological features of PCOS.

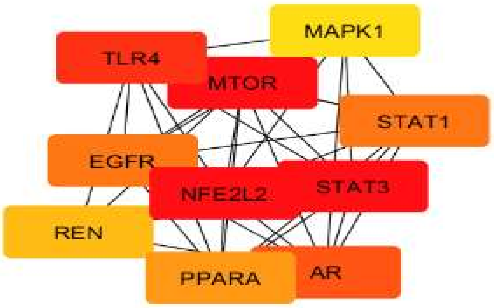


Figure 7. Hub gene network of top 10 targets identified from the PPI network.

Gene Symbol	**Degree**	**Betweenness Centrality**	**Closeness Centrality**
ST AT 3 EG FR TL R4 MT OR MA PK 1 ST AT 1 PP AR A NF E2L 2 AR RE N	18 16 14 13 11 10 10 9 9 8	0.20 059 0.14 8963 0.08 0964 0.05 2251 0.06 148 0.02 4989 0.01 6276 0.10 2024 0.00 5743 0.03 369 0.02 1179	0.875 0.807692 0.724138 0.724138 0.677419 0.65625 0.636364 0.636364 0.636364 0.617647 0.617647

Table No.3 Topological Properties of Hub Genes in the Protein–Protein Interaction Network

MOLECULAR DOCKING

The present study employed molecular docking to evaluate the binding affinity of selected okra-derived phytoconstituents against key protein targets implicated in the pathophysiology of polycystic ovary syndrome (PCOS), including STAT3, EGFR, TLR4, and mTOR. The docking results were compared with the standard drug **Metformin**, which is widely used in PCOS management for improving insulin sensitivity and modulating metabolic pathways.

Among the investigated compounds, **Vitamin E** demonstrated the highest binding affinity across all selected targets, particularly against EGFR (-8.0 kcal/mol), indicating a strong potential for inhibitory activity. This superior interaction suggests that Vitamin E may play a significant role in modulating epidermal growth factor receptor signaling, which is associated with abnormal follicular development and ovarian dysfunction in PCOS. Additionally, its strong binding with STAT3, TLR4, and mTOR highlights its potential multi-target therapeutic effect, especially in regulating inflammation and oxidative stress, both of which are central to PCOS pathology.

Linolenic acid also exhibited notable binding affinity, particularly against mTOR (-6.6 kcal/mol), suggesting its possible involvement in metabolic regulation and insulin signaling pathways. Since mTOR plays a critical role in cellular growth and energy homeostasis, the inhibition of this pathway may contribute to improved metabolic outcomes in PCOS. Similarly, Vernolic acid showed strong interaction with EGFR (-6.8 kcal/mol), indicating its relevance in targeting proliferative signaling pathways.

In contrast, Nicotinic acid and Pentyl 3-methylbutanoate displayed comparatively weaker binding affinities, indicating limited inhibitory potential against the selected targets. However, their moderate interactions may still contribute to a synergistic effect when present in combination with other bioactive compounds.

Importantly, several phytoconstituents demonstrated better binding affinity than Metformin, suggesting their potential as alternative or complementary therapeutic agents. While Metformin primarily acts through indirect modulation of metabolic pathways, the phytoconstituents identified in this study appear to exert more direct interactions with multiple protein targets, indicating a possible advantage in multi-target drug design.

Overall, the findings suggest that Vitamin E, followed by Linolenic acid and Vernolic acid, may serve as promising lead compounds for further investigation in PCOS treatment. However, these results are based on in silico analysis, and further validation through in vitro and in vivo studies is necessary to confirm their therapeutic efficacy and safety.

Phytoconstituents	STAT3	EGFR	TLR4	MTOR
Nicotinic acid	-4.5	-5.8	-4.8	-5.9
Vitamin E	-5.9	-8	-6.2	-6.1
Vernolic acid	-4.9	-6.8	-5.3	-5.1
Linolenic acid	-4.9	-6.5	-5.1	-6.6
Pentyl 3-methylbutanoate	-4.4	-5.4	-4.8	-5.3
Metformin (Standard)	-4.4	-4.9	-5.2	-5.2

Table No.4 Binding affinities of phytoconstituents and standard drug against selected PCOS targets

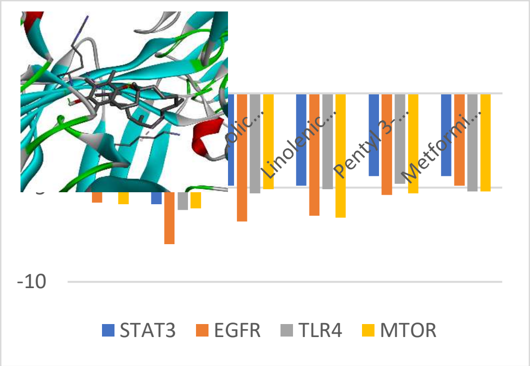
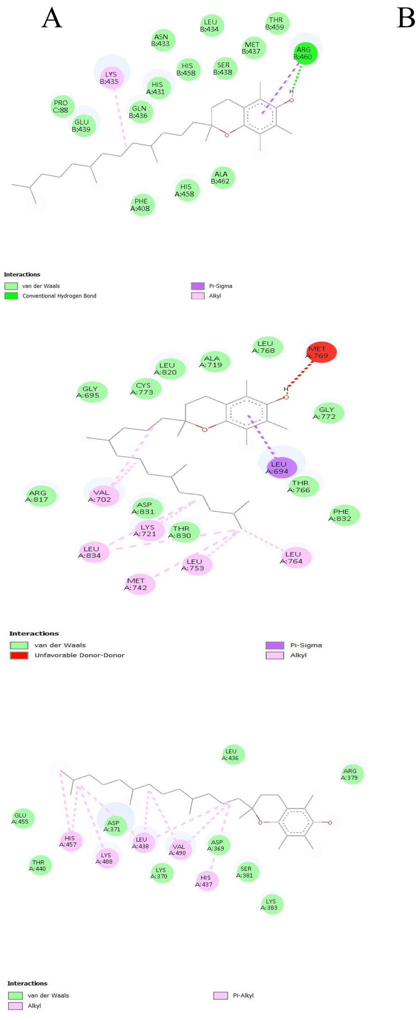


Fig. No.8 Comparative binding energies of phytoconstituents and Metformin against STAT3, EGFR, TLR4, and mTOR targets.

The top-performing ligand–target complexes were selected based on binding affinity and interaction profile for detailed visualization. They are represent in figure



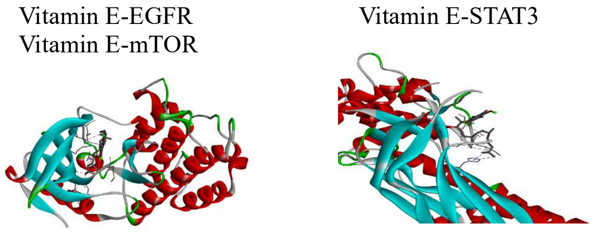


Fig No.9 Molecular docking interaction analysis of selected phytoconstituents with PCOS-related targets. (A–C) 2D interaction diagrams of Vitamin E with EGFR, TLR4, and STAT3 showing key hydrogen bonding and hydrophobic interactions.

Vitamin E exhibited strong binding with EGFR through a conventional hydrogen bond with **ARG460**, along with hydrophobic interactions involving **LYS435, HIS431, SER438, and MET437**, contributing to the stability of the complex. The interaction of Vitamin E with STAT3 was primarily stabilized by hydrophobic interactions involving **ASP371, VAL490, LEU438, and LYS488**, with no significant hydrogen bonding observed. Vitamin E binding with mTOR showed predominant hydrophobic interactions with **LEU694, VAL702, and LEU753**, along with an unfavourable donor–donor interaction observed at **MET769**.

Discussion

The present study employed an integrated network pharmacology and molecular docking approach to elucidate the therapeutic potential of phytoconstituents derived from Abelmoschus esculentus in the management of polycystic ovary syndrome (PCOS). PCOS is a complex endocrine disorder involving multiple pathological mechanisms, including insulin resistance, chronic inflammation, and hormonal imbalance. Therefore, a multi-target therapeutic strategy is considered more effective for its management.

Network pharmacology analysis identified 22 overlapping targets between okra-derived phytoconstituents and PCOS-associated genes, suggesting a potential mechanistic link. Protein–protein interaction (PPI) network analysis revealed significant interactions among these targets, with key nodes demonstrating high degree and centrality values, indicating their importance in disease regulation. Further, GO and KEGG enrichment analyses indicated that these targets are involved in critical biological processes such as cellular response to hormone stimulus, intracellular receptor signaling pathways, and metabolic regulation. Notably, pathways such as PI3K–AKT, MAPK, JAK–STAT, and mTOR were significantly enriched, all of which are known to play crucial roles in PCOS pathophysiology.

To validate these findings at the molecular level, docking analysis was performed against key protein targets, including EGFR, STAT3, TLR4, and mTOR. Among the selected phytoconstituents, Vitamin E demonstrated the strongest binding affinity, particularly with EGFR (−8.0 kcal/mol), suggesting a stable ligand–protein interaction. The presence of a hydrogen bond with ARG460, along with multiple hydrophobic interactions, indicates strong binding stability within the active site. This interaction may influence EGFR-mediated signaling pathways, which are implicated in abnormal follicular development and ovarian dysfunction in PCOS.

In contrast, the interaction of Vitamin E with STAT3 was primarily mediated by hydrophobic interactions, with no significant hydrogen bonding observed. Despite this, the interaction may still contribute to modulation of the JAK–STAT signaling pathway, which is associated with inflammation and insulin resistance in PCOS. Similarly, the interaction with mTOR was characterized by hydrophobic interactions along with an unfavorable donor–donor interaction, indicating moderate binding stability. Given the role of mTOR in metabolic regulation and insulin signaling, such interactions may still hold therapeutic significance.

Additionally, Vernolic acid and Linolenic acid exhibited notable binding affinities, particularly with EGFR and mTOR, respectively, suggesting their potential contribution to the overall therapeutic effect. Although Nicotinic acid and Pentyl 3-methylbutanoate demonstrated comparatively weaker binding affinities, their presence may contribute to synergistic interactions in a multi-component system.

Importantly, several phytoconstituents exhibited binding affinities comparable to or higher than the standard drug metformin for specific targets, indicating their potential as alternative or complementary therapeutic agents. Unlike metformin, which primarily acts through indirect metabolic regulation, these phytoconstituents appear to directly interact with multiple protein targets, supporting a multi-target therapeutic mechanism.

Overall, the integration of network pharmacology and molecular docking provides a comprehensive understanding of the potential mechanisms by which okra-derived phytoconstituents may exert therapeutic effects in PCOS. This approach highlights the advantage of natural compounds in targeting multiple pathways simultaneously in complex diseases.

Conclusion

The present study demonstrates that phytoconstituents derived from Abelmoschus esculentus exhibit significant therapeutic potential against polycystic ovary syndrome through a multi-target mechanism. Network pharmacology analysis identified key targets and pathways involved in PCOS, including EGFR, STAT3, TLR4, and mTOR, which are associated with inflammation, insulin resistance, and ovarian dysfunction.

Molecular docking results further validated these findings, with Vitamin E emerging as the most promising compound due to its strong and consistent binding affinity, particularly with EGFR. The interaction analysis highlighted the importance of hydrogen bonding and hydrophobic interactions in stabilizing ligand–protein complexes.

The combined network pharmacology and docking approach underscores the potential of okra-derived phytoconstituents as multi-target therapeutic agents for PCOS management. However, as this study is based on in silico analysis, further experimental validation through in vitro and in vivo studies is required to confirm these findings.

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