IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

Network Pharmacology Analysis of Berberine in Polycystic Ovary Syndrome (PCOS)

Mohd Hasib Ahmed[1*], Kailash R. Biyani[2], Ramesh R. Pagore[3], Ravi H. Kale[4], Mohd Aves M Ayaz[5]
[1,3,5]Karmayogi Tatyasaheb Bondre Institute of Pharmacy, Chikhli, Dist. Buldhana
[2]Anuradha College of Pharmacy, Chikhli, Dist. Buldhana
[4]PRMSS Anuradha College of Pharmacy, Chikhli, Dist. Buldhana

Abstract: ***Background:*** *Polycystic Ovary Syndrome is a multifactorial endocrine disorder characterized by hyperandrogenism, insulin resistance, chronic inflammation, and ovarian dysfunction. Berberine, a bioactive alkaloid isolated from several medicinal plants, has shown promising pharmacological activities against metabolic and inflammatory diseases. The present study aimed to investigate the therapeutic mechanism of berberine against PCOS using a network pharmacology approach.* ***Methods:*** *The physicochemical properties, drug-likeness, and toxicity profile of berberine were analyzed using online computational tools including MolSoft, SwissADME, and Protox-III. Potential targets of berberine were identified through SwissTargetPrediction, while PCOS-related genes were collected from GeneCards, OMIM, and DisGeNET databases. Common targets between berberine and PCOS were identified and subjected to protein–protein interaction (PPI) analysis, Gene Ontology (GO), and KEGG pathway enrichment analysis. Hub targets and major signaling pathways associated with the therapeutic action of berberine were evaluated.* ***Results:*** *Berberine demonstrated acceptable drug-likeness properties with favorable molecular characteristics including molecular weight (336.4 g/mol), TPSA (40.8 Å²), and logP (3.12). Toxicity prediction indicated possible hepatotoxicity, neurotoxicity, respiratory toxicity, and immunotoxicity, while carcinogenicity and mutagenicity were predicted to be inactive. A total of several overlapping targets between berberine and PCOS were identified, including PTGS2, JAK2, PIK3CD, MAPK14, ROCK1, CDK4, SRC, PTPN1, CYP19A1, and HSD17B1. Network analysis revealed that berberine may regulate inflammatory responses, insulin resistance, steroidogenesis, and ovarian dysfunction through multiple pathways such as PI3K/Akt, JAK/STAT, MAPK, and inflammatory signaling pathways. Among the identified targets, PTGS2, JAK2, PIK3CD, MAPK14, and ROCK1 were recognized as major hub targets involved in the pathogenesis of PCOS.* ***Conclusion:*** *The present network pharmacology study demonstrated that berberine exerts therapeutic potential against PCOS through a multi-target and multi-pathway mechanism involving regulation of inflammation, oxidative stress, insulin signaling, and hormonal imbalance. The findings provide scientific evidence supporting the potential application of berberine as a promising phytotherapeutic candidate for the management of PCOS and may serve as a basis for future experimental and clinical investigations.*

Keywords: Polycystic Ovary Syndrome; Berberine; Network Pharmacology; Phytotherapy; Insulin Resistance; Hyperandrogenism; Molecular Targets; Protein–Protein Interaction (PPI); Gene Ontology (GO); KEGG Pathway Analysis; PI3K/Akt Signaling Pathway; JAK/STAT Signaling; MAPK Pathway; Inflammation; Oxidative Stress; Hormonal Regulation

I. INTRODUCTION

Polycystic Ovary Syndrome is one of the most common endocrine and metabolic disorders affecting women of reproductive age worldwide. The disorder is characterized by hyperandrogenism, menstrual irregularities, polycystic ovarian morphology, insulin resistance, obesity, chronic low-grade inflammation, and infertility. PCOS not only affects

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, May 2026 Impact Factor: 8.2

reproductive health but is also associated with long-term metabolic complications such as type 2 diabetes mellitus, cardiovascular disorders, dyslipidemia, and psychological disturbances. The complex and multifactorial nature of PCOS involves interactions among genetic, hormonal, inflammatory, and environmental factors, making its treatment challenging.[1-4]

Insulin resistance and hyperinsulinemia are considered central pathological features of PCOS and contribute significantly to androgen excess and ovarian dysfunction. In addition, chronic inflammation and oxidative stress further aggravate metabolic abnormalities and follicular dysregulation. Several signaling pathways including PI3K/Akt, MAPK, JAK/STAT, and inflammatory cytokine pathways have been implicated in the progression of PCOS. Current therapeutic approaches such as metformin, oral contraceptives, anti-androgens, and ovulation-inducing agents provide symptomatic relief; however, these therapies are often associated with adverse effects, limited efficacy, and recurrence of symptoms. Therefore, there is growing interest in identifying safer and more effective alternative therapeutic agents, particularly from natural sources.[5-8]

Berberine is a naturally occurring isoquinoline alkaloid widely distributed in medicinal plants such as Berberis vulgaris, Coptis chinensis, and Hydrastis canadensis. Berberine has attracted considerable scientific attention due to its broad spectrum of pharmacological activities including antidiabetic, anti-inflammatory, antioxidant, antihyperlipidemic, antimicrobial, and cardioprotective effects. Several experimental and clinical studies have suggested that berberine improves insulin sensitivity, regulates glucose metabolism, reduces androgen levels, and improves ovulatory function in women with PCOS. Despite these promising therapeutic effects, the precise molecular mechanisms underlying the action of berberine against PCOS remain incompletely understood.[9-11]

Recent advances in computational biology and systems pharmacology have enabled the development of network pharmacology as a powerful approach for understanding complex interactions between bioactive compounds, molecular targets, and disease pathways. Unlike the traditional “one drug–one target” concept, network pharmacology emphasizes multi-target and multi-pathway interactions, which are particularly relevant for phytochemicals and complex diseases such as PCOS. This approach integrates pharmacology, bioinformatics, systems biology, and molecular network analysis to identify therapeutic targets and elucidate mechanisms of action at a systemic level.[12,13]

Therefore, the present study aimed to investigate the therapeutic mechanisms of berberine against PCOS using a network pharmacology approach. The study involved the evaluation of physicochemical properties, drug-likeness, toxicity prediction, target identification, protein–protein interaction analysis, and pathway enrichment analysis. Furthermore, common targets between berberine and PCOS were identified to explore the potential molecular pathways involved in its therapeutic action. The findings of this study may provide a scientific basis for the development of berberine as a promising multi-target phytotherapeutic agent for the management of PCOS.

II. MATERIALS AND METHOD [14-17]

Collection of Compound Information

The phytochemical compound Berberine was selected for the present network pharmacology study based on its reported pharmacological activities against metabolic and endocrine disorders. The chemical information of berberine including molecular formula, molecular weight, canonical SMILES, InChIKey, and Compound CID was retrieved from PubChem. The 2D and 3D structures of the compound were downloaded in SDF format for further computational analysis.

Evaluation of Drug-Likeness and Physicochemical Properties

The drug-likeness score of berberine was predicted using the MolSoft online server. Physicochemical parameters including molecular weight, topological polar surface area (TPSA), hydrogen bond donors and acceptors, logP, logS, rotatable bonds, flexibility, density, pKa, and other molecular descriptors were analyzed using the SwissADME and related cheminformatics prediction tools. These properties were evaluated to determine the oral bioavailability and pharmacokinetic suitability of the compound according to Lipinski’s rule of five and related drug-likeness criteria.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

Toxicity Prediction Analysis

The toxicity profile of berberine was evaluated using the Protox-II Server. The toxicity assessment included organ toxicity, toxicity endpoints, nuclear receptor signaling pathways, stress response pathways, molecular initiating events, and cytochrome P450-mediated metabolism predictions. Parameters such as hepatotoxicity, neurotoxicity, cardiotoxicity, carcinogenicity, mutagenicity, immunotoxicity, and blood-brain barrier permeability were analyzed. The prediction probability values generated by the server were recorded for interpretation.

Prediction of Berberine Targets

Potential molecular targets of berberine were identified using the SwissTargetPrediction database. The canonical SMILES structure of berberine was uploaded to the platform and the species was selected as "Homo sapiens". Predicted targets with significant probability scores were collected and duplicate entries were removed. The obtained targets were standardized using the UniProt database to obtain official gene names and protein information.

Identification of PCOS-Associated Targets

Disease-related targets associated with Polycystic Ovary Syndrome were collected from publicly available databases including GeneCards, DisGeNET, and OMIM using the keyword "Polycystic Ovary Syndrome" or "PCOS". Retrieved targets from different databases were combined, standardized, and duplicate genes were eliminated to generate a final PCOS-associated target dataset.

Identification of Common Targets

The common targets between berberine-associated targets and PCOS-associated targets were identified using Venn diagram analysis. The overlapping targets were considered potential therapeutic targets of berberine against PCOS. These common targets were further used for network pharmacology analysis and pathway interpretation.

Protein–Protein Interaction (PPI) Network Construction

The common targets were imported into the STRING Database to construct a protein–protein interaction (PPI) network. The species was limited to "Homo sapiens" and the confidence score was set to medium confidence (0.4). Topological parameters including degree value, betweenness centrality, and closeness centrality were analyzed to identify hub targets.

Gene Ontology (GO) and KEGG Pathway Enrichment Analysis

Functional enrichment analysis of the common targets was performed using the DAVID Bioinformatics Resources and/or KEGG Pathway Database. Gene Ontology (GO) analysis was carried out under three categories: biological process (BP), molecular function (MF), and cellular component (CC). KEGG pathway enrichment analysis was conducted to identify major signaling pathways involved in the therapeutic action of berberine against PCOS. Pathways with p-values less than 0.05 were considered statistically significant.

Network Construction and Visualization

A compound–target–pathway network was constructed using Cytoscape software to visualize the interactions among berberine, common targets, and enriched pathways. The network topology parameters were analyzed to identify major hub targets and signaling pathways involved in the anti-PCOS activity of berberine.

III. RESULT AND DISCUSSION

Table 1: Parameter of Berberine

Parameter	Details
Compound Name	Berberine
Synonyms	berberine; 2086-83-1; Umbellatine; Berberin; Berbericine
Compound CID	2353
Molecular Formula (MF)	C20H18NO4+
Molecular Weight	336.4 g/mol

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

(MW)	
IUPAC Name	16,17-dimethoxy-5,7-dioxa-13-azoniapentacyclo[11.8.0.02,10.04,8.015,20]henicosa-1(13),2,4(8),9,14,16,18,20-octaene
SMILES	COC1=C(C2=C[N+]3=C(C=C2C=C1)C4=CC5=C(C=C4CC3)OCO5)OC
InChIKey	YBHILYKTIRIUTE-UHFFFAOYSA-N
InChI	InChI=1S/C20H18NO4/c1-22-17-4-3-12-7-16-14-9-19-18(24-11-25-19)8-13(14)5-6-21(16)10-15(12)20(17)23-2/h3-4,7-10H,5-6,11H2,1-2H3/q+1

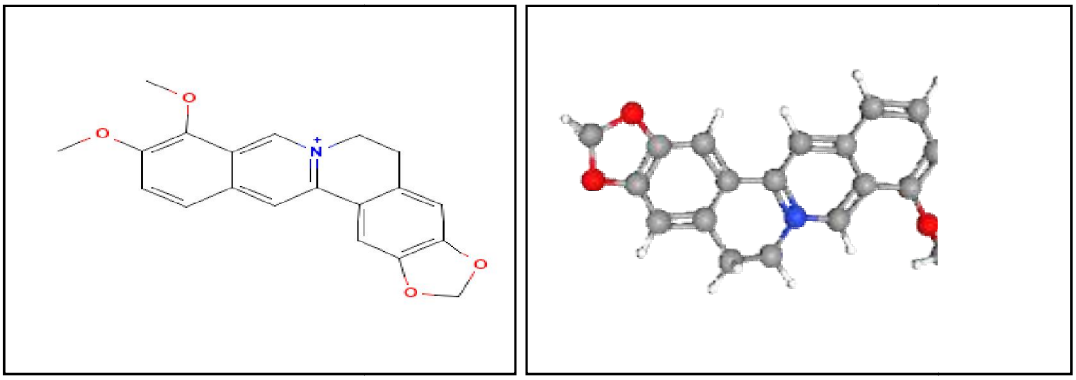

Fig 1: 2d and 3d structure of Berberine PubChem.

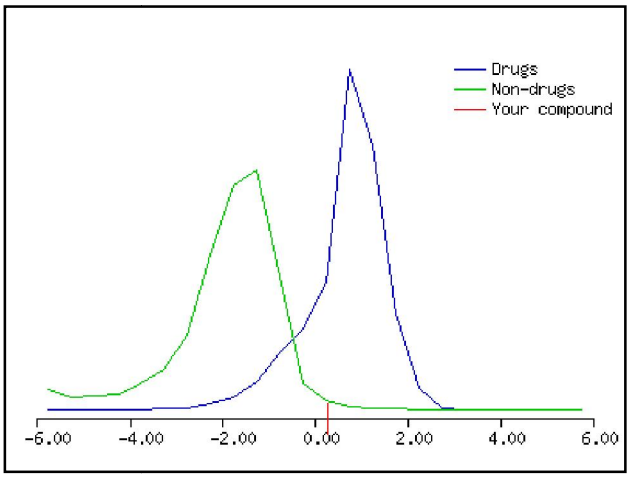

Fig 2: Drug-likeness model score: 0.29 (molsoft)

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

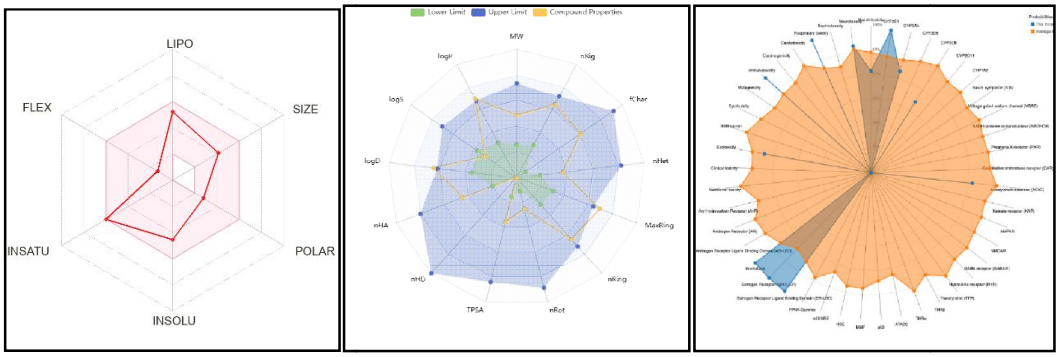

Fig 3: Radar plot of Swiss ADME , ADMTE and toxicity PROTOX plot of berberin

Table 2: Physicochemical Properties of the Compound

Property	Value	Comment
Molecular Weight	336.12	Contains hydrogen atoms; Optimal range: 100–600
Volume	338.078	Van der Waals volume
Density	0.994	Density = MW / Volume
nHA	5.0	Number of hydrogen bond acceptors; Optimal: 0–12
nHD	0.0	Number of hydrogen bond donors; Optimal: 0–7
nRot	2.0	Number of rotatable bonds; Optimal: 0–11
nRing	5.0	Number of rings; Optimal: 0–6
MaxRing	21.0	Number of atoms in the biggest ring; Optimal: 0–18
nHet	5.0	Number of heteroatoms; Optimal: 1–15
fChar	1.0	Formal charge; Optimal: −4 to +4
nRig	25.0	Number of rigid bonds; Optimal: 0–30
Flexibility	0.08	Flexibility = nRot / nRig
Stereo Centers	0.0	Stereo centers; Optimal: ≤ 2
TPSA	40.8	Topological Polar Surface Area; Optimal: 0–140
logS	−5.059	Logarithm of aqueous solubility value
logP	3.12	Logarithm of n-octanol/water distribution coefficient at pH 7.4
logD	3.21	Logarithm of n-octanol/water distribution coefficient
pKa (Acid)	9.224	Indicates acidity/basicity strength
pKa (Base)	3.986	Indicates acidity/basicity strength
Melting Point	162.709 °C	Above 25°C, therefore classified as a solid
Boiling Point	349.547 °C	Below 25°C would be classified as a gas

Table 3: Toxicity Model Report

Classification	Target	Prediction	Probability
Organ toxicity	Hepatotoxicity	Active	0.69
	Neurotoxicity	Active	0.87
	Nephrotoxicity	Inactive	0.90
	Respiratory toxicity	Active	0.98
	Cardiotoxicity	Inactive	0.77
Toxicity end	Carcinogenicity	Inactive	0.62

DOI: 10.48175/568

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

points	Immunotoxicity	Active	0.96
	Mutagenicity	Inactive	0.97
	Cytotoxicity	Inactive	0.93
	BBB-barrier	Inactive	1
	Ecotoxicity	Active	0.73
	Clinical toxicity	Inactive	0.56
	Nutritional toxicity	Inactive	0.74
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	Inactive	0.97
	Androgen Receptor (AR)	Inactive	0.99
	Androgen Receptor Ligand Binding Domain (AR-LBD)	Inactive	0.99
	Aromatase	Active	1
	Estrogen Receptor Alpha (ER)	Active	0.99
	Estrogen Receptor Ligand Binding Domain (ER-LBD)	Active	1
	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	Inactive	0.99
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/antioxidant responsive element (nrf2/ARE)	Inactive	0.88
	Heat shock factor response element (HSE)	Inactive	0.88
	Mitochondrial Membrane Potential (MMP)	Inactive	0.70
	Phosphoprotein (Tumor Supressor) p53	Inactive	0.96
	ATPase family AAA domain-containing protein 5 (ATAD5)	Inactive	0.99
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	Inactive	0.90
	Thyroid hormone receptor beta (THRβ)	Inactive	0.78
	Transtyretrin (TTR)	Inactive	0.97
	Ryanodine receptor (RYR)	Inactive	0.98
	GABA receptor (GABAR)	Inactive	0.96
	Glutamate N-methyl-D-aspartate receptor (NMDAR)	Inactive	0.92
	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	Inactive	0.97
	Kainate receptor (KAR)	Inactive	0.99
	Achetylcholinesterase (AChE)	Active	0.69
	Constitutive androstane receptor (CAR)	Inactive	0.98
	Pregnane X receptor (PXR)	Inactive	0.92
	NADH-quinone oxidoreductase (NADHOX)	Inactive	0.97
	Voltage gated sodium channel (VGSC)	Inactive	0.95
	Na+/I- symporter (NIS)	Inactive	0.98
Metabolism	Cytochrome CYP1A2	Inactive	0.76
	Cytochrome CYP2C19	Inactive	0.87
	Cytochrome CYP2C9	Active	0.56
	Cytochrome CYP2D6	Inactive	0.63
	Cytochrome CYP3A4	Active	0.71
	Cytochrome CYP2E1	Inactive	0.98

DOI: 10.48175/568

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

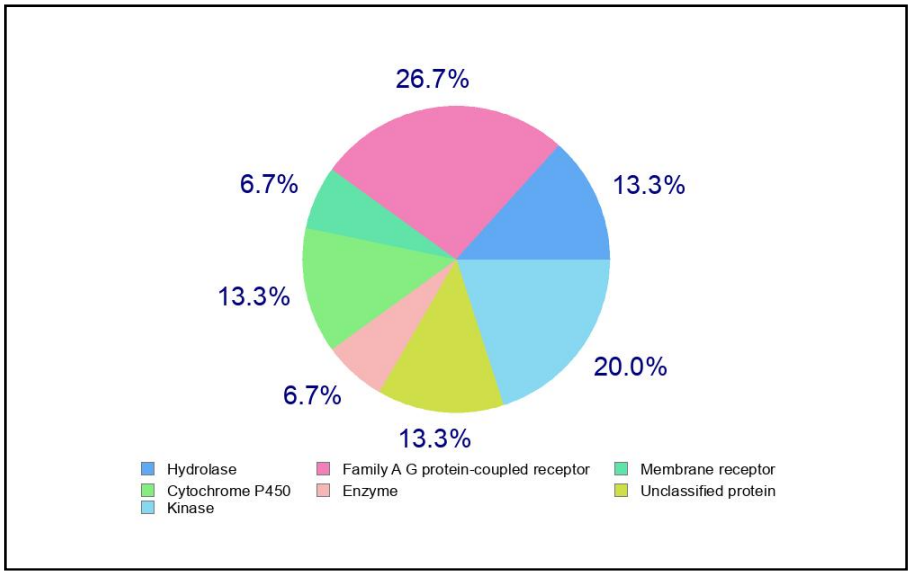

Fig 4: Target of berberine

Table 4: Target of berberine

Target	Common name	Uniprot ID	ChEMBL ID	Target Class	Probability*
Acetylcholinesterase	ACHE	P22303	CHEMBL220	Hydrolase	0.775101
Serotonin 2b (5-HT2b) receptor	HTR2B	P41595	CHEMBL1833	Family A G protein-coupled receptor	0.758299
Butyrylcholinesterase	BCHE	P06276	CHEMBL1914	Hydrolase	0.758299
Adrenergic receptor alpha-2	ADRA2C	P18825	CHEMBL1916	Family A G protein-coupled receptor	0.758299
Alpha-2b adrenergic receptor	ADRA2B	P18089	CHEMBL1942	Family A G protein-coupled receptor	0.758299
Muscarinic acetylcholine receptor M1	CHRM1	P11229	CHEMBL216	Family A G protein-coupled receptor	0.758299
Sigma opioid receptor	SIGMAR1	Q99720	CHEMBL287	Membrane receptor	0.758299
Cytochrome P450 2D6	CYP2D6	P10635	CHEMBL289	Cytochrome P450	0.758299
SUMO-activating enzyme	SAE1 UBA2	Q9UBE0 Q9UBT2	CHEMBL2095174	Enzyme	0.71657
Ras-related C3 botulinum toxin substrate 1	RAC1	P63000	CHEMBL6094	Unclassified protein	0.105608
Cell division control protein 42 homolog	CDC42	P60953	CHEMBL6088	Unclassified protein	0.09724

DOI: 10.48175/568

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, May 2026 Impact Factor: 8.2

Ribosomal protein S6 kinase 1	RPS6KB1	P23443	CHEMBL4501	Kinase	0.09724
Serine/threonine-protein kinase Aurora-A	AURKA	O14965	CHEMBL4722	Kinase	0.09724
Serine/threonine-protein kinase Aurora-B	AURKB	Q96GD4	CHEMBL2185	Kinase	0.09724
Cytochrome P450 11B2	CYP11B2	P19099	CHEMBL2722	Cytochrome P450	0.09724
Perforin-1	PRF1	P14222	CHEMBL5480	Other ion channel	0.09724
Glutamate receptor ionotropic, AMPA 1	GRIA1	P42261	CHEMBL2009	Ligand-gated ion channel	0.09724
Thromboxane-A synthase	TBXAS1	P24557	CHEMBL1835	Cytochrome P450	0.09724
15-hydroxyprostaglandin dehydrogenase [NAD+]	HPGD	P15428	CHEMBL1293255	Enzyme	0.09724
Excitatory amino acid transporter 1	SLC1A3	P43003	CHEMBL3085	Electrochemical transporter	0.09724
GABA-A receptor; alpha-3/beta-3/gamma-2	GABRB3 GABRA3 GABRG2	P28472 P34903 P18507	CHEMBL2094120	Ligand-gated ion channel	0.09724
GABA-A receptor; alpha-1/beta-3/gamma-2	GABRB3 GABRG2 GABRA1	P28472 P18507 P14867	CHEMBL2094121	Ligand-gated ion channel	0.09724
GABA-A receptor; alpha-5/beta-3/gamma-2	GABRB3 GABRG2 GABRA5	P28472 P18507 P31644	CHEMBL2094122	Ligand-gated ion channel	0.09724
Serine/threonine-protein kinase PIM1	PIM1	P11309	CHEMBL2147	Kinase	0.09724
Serine/threonine-protein kinase PIM2	PIM2	Q9P1W9	CHEMBL4523	Kinase	0.09724
Hepatocyte growth factor receptor	MET	P08581	CHEMBL3717	Kinase	0.09724
Serotonin 3a (5-HT3a) receptor (by homology)	HTR3A	P46098	CHEMBL1899	Ligand-gated ion channel	0.09724
G protein-coupled receptor kinase 5	GRK5	P34947	CHEMBL5678	Kinase	0.09724
Cytochrome P450 11B1	CYP11B1	P15538	CHEMBL1908	Cytochrome P450	0.09724
Inosine-5'-monophosphate dehydrogenase 2	IMPDH2	P12268	CHEMBL2002	Oxidoreductase	0.09724
PI3-kinase p110-alpha/p85-alpha	PIK3CA PIK3R1	P42336 P27986	CHEMBL2111367	Enzyme	0.09724
Coagulation factor VII/tissue factor	F3	P13726	CHEMBL4081	Surface antigen	0.09724
Cytochrome P450 19A1	CYP19A1	P11511	CHEMBL1978	Cytochrome P450	0.09724
Branched-chain-amino-acid aminotransferase, mitochondrial	BCAT2	O15382	CHEMBL3616354	Transferase	0.09724

DOI: 10.48175/568

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, May 2026 Impact Factor: 8.2

Transient receptor potential cation channel subfamily M member 8 (by homology)	TRPM8	Q7Z2W7	CHEMBL1075319	Voltage-gated ion channel	0.09724
Intercellular adhesion molecule-1	ICAM1	P05362	CHEMBL3070	Adhesion	0.09724
Selectin E	SELE	P16581	CHEMBL3890	Adhesion	0.09724
Monoamine oxidase B	MAOB	P27338	CHEMBL2039	Oxidoreductase	0.09724
PI3-kinase p110-delta subunit	PIK3CD	O00329	CHEMBL3130	Enzyme	0.09724
PI3-kinase p110-beta subunit	PIK3CB	P42338	CHEMBL3145	Enzyme	0.09724
PI3-kinase p110-gamma subunit	PIK3CG	P48736	CHEMBL3267	Enzyme	0.09724
MAP kinase-activated protein kinase 2	MAPKAPK2	P49137	CHEMBL2208	Kinase	0.09724
Poly [ADP-ribose] polymerase 10	PARP10	Q53GL7	CHEMBL2429708	Enzyme	0.09724
Serine/threonine-protein kinase Chk2	CHEK2	O96017	CHEMBL2527	Kinase	0.09724
CDK8/Cyclin C	CCNC CDK8	P24863 P49336	CHEMBL3038474	Kinase	0.09724
Cell division protein kinase 8	CDK8	P49336	CHEMBL5719	Kinase	0.09724
c-Jun N-terminal kinase 3	MAPK10	P53779	CHEMBL2637	Kinase	0.09724
1-acylglycerol-3-phosphate O-acyltransferase beta	AGPAT2	O15120	CHEMBL4772	Enzyme	0.09724
Protein-glutamine gamma-glutamyltransferase	TGM2	P21980	CHEMBL2730	Enzyme	0.09724
Acyl-CoA desaturase (by homology)	SCD	O00767	CHEMBL5555	Enzyme	0.09724
X-box-binding protein 1	XBP1	P17861	CHEMBL1741176	Unclassified protein	0.09724
Thymidylate synthase	TYMS	P04818	CHEMBL1952	Transferase	0.09724
Dihydrofolate reductase	DHFR	P00374	CHEMBL202	Oxidoreductase	0.09724
GABA-A receptor; alpha-2/beta-3/gamma-2	GABRA2 GABRB3 GABRG2	P47869 P28472 P18507	CHEMBL2094130	Ligand-gated ion channel	0.09724
Rho-associated protein kinase 1	ROCK1	Q13464	CHEMBL3231	Kinase	0.09724
cAMP-dependent protein kinase alpha-catalytic subunit	PRKACA	P17612	CHEMBL4101	Kinase	0.09724
Muscarinic acetylcholine receptor M4	CHRM4	P08173	CHEMBL1821	Family A G protein-coupled receptor	0.09724
Tyrosine-protein kinase JAK2	JAK2	O60674	CHEMBL2971	Kinase	0.09724
Tyrosine-protein kinase LCK (by homology)	LCK	P06239	CHEMBL258	Kinase	0.09724
Cyclin-dependent kinase 9	CDK9	P50750	CHEMBL3116	Kinase	0.09724
Protein-tyrosine phosphatase 1B	PTPN1	P18031	CHEMBL335	Phosphatase	0.09724
5-lipoxygenase activating protein	ALOX5AP	P20292	CHEMBL4550	Other cytosolic protein	0.09724
Serine/threonine-protein kinase Chk1	CHEK1	O14757	CHEMBL4630	Kinase	0.09724
Stem cell growth factor receptor	KIT	P10721	CHEMBL1936	Kinase	0.09724

DOI: 10.48175/568

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, May 2026 Impact Factor: 8.2

Tyrosine-protein kinase SRC	SRC	P12931	CHEMBL267	Kinase	0.09724
MAP kinase-interacting serine/threonine-protein kinase MNK1	MKNK1	Q9BUB5	CHEMBL4718	Kinase	0.09724
Inhibitor of nuclear factor kappa B kinase beta subunit	IKBKB	O14920	CHEMBL1991	Kinase	0.09724
MAP kinase p38 alpha	MAPK14	Q16539	CHEMBL260	Kinase	0.09724
Leucine-rich repeat serine/threonine-protein kinase 2	LRRK2	Q5S007	CHEMBL1075104	Kinase	0.09724
Rho-associated protein kinase 2	ROCK2	O75116	CHEMBL2973	Kinase	0.09724
Serine-protein kinase ATR	ATR	Q13535	CHEMBL5024	Kinase	0.09724
Amine oxidase, copper containing	AOC3	Q16853	CHEMBL3437	Enzyme	0.09724
Beta-adrenergic receptor kinase 2	GRK3	P35626	CHEMBL1075166	Kinase	0.09724
Serine/threonine-protein kinase PLK1	PLK1	P53350	CHEMBL3024	Kinase	0.09724
G-protein coupled receptor kinase 2	GRK2	P25098	CHEMBL4079	Kinase	0.09724
Neuropeptide Y receptor type 5	NPY5R	Q15761	CHEMBL4561	Family A G protein-coupled receptor	0.09724
Mitogen-activated protein kinase kinase kinase kinase 4	MAP4K4	O95819	CHEMBL6166	Kinase	0.09724
Nerve growth factor receptor Trk-A	NTRK1	P04629	CHEMBL2815	Kinase	0.09724
Tyrosine-protein kinase ABL	ABL1	P00519	CHEMBL1862	Kinase	0.09724
Cyclin-dependent kinase 1/cyclin B1	CDK1 CCNB1	P06493 P14635	CHEMBL1907602	Other cytosolic protein	0.09724
Mineralocorticoid receptor	NR3C2	P08235	CHEMBL1994	Nuclear receptor	0.09724
Progesterone receptor	PGR	P06401	CHEMBL208	Nuclear receptor	0.09724
Dopamine D4 receptor	DRD4	P21917	CHEMBL219	Family A G protein-coupled receptor	0.09724
Cyclooxygenase-2	PTGS2	P35354	CHEMBL230	Oxidoreductase	0.09724
Dopamine D3 receptor	DRD3	P35462	CHEMBL234	Family A G protein-coupled receptor	0.09724
Cyclin-dependent kinase 2	CDK2	P24941	CHEMBL301	Kinase	0.09724
Cyclin-dependent kinase 4	CDK4	P11802	CHEMBL331	Kinase	0.09724
NAD-dependent deacetylase sirtuin 2	SIRT2	Q8IXJ6	CHEMBL4462	Eraser	0.09724
Adenosine A2a receptor	ADORA2A	P29274	CHEMBL251	Family A G protein-coupled receptor	0.09724
Adenosine A3 receptor	ADORA3	P0DMS8	CHEMBL256	Family A G protein-coupled	0.09724

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

				receptor	
Metabotropic glutamate receptor 5	GRM5	P41594	CHEMBL3227	Family C G protein-coupled receptor	0.09724
Glutaminyl-peptide cyclotransferase	QPCT	Q16769	CHEMBL4508	Enzyme	0.09724
Macrophage colony stimulating factor receptor	CSF1R	P07333	CHEMBL1844	Kinase	0.09724
Cannabinoid receptor 2	CNR2	P34972	CHEMBL253	Family A G protein-coupled receptor	0.09724
Runt-related transcription factor 1/Core-binding factor subunit beta	CBFB	Q13951	CHEMBL1615386	Unclassified protein	0.09724
Estradiol 17-beta-dehydrogenase 1	HSD17B1	P14061	CHEMBL3181	Enzyme	0.09724
Phenylethanolamine N-methyltransferase	PNMT	P11086	CHEMBL4617	Enzyme	0.09724
Poly [ADP-ribose] polymerase 2	PARP2	Q9UGN5	CHEMBL5366	Enzyme	0.09724
Prostaglandin E synthase	PTGES	O14684	CHEMBL5658	Enzyme	0.09724
40S ribosomal protein S27	RPS27	P42677	CHEMBL1932893	Unclassified protein	0.09724

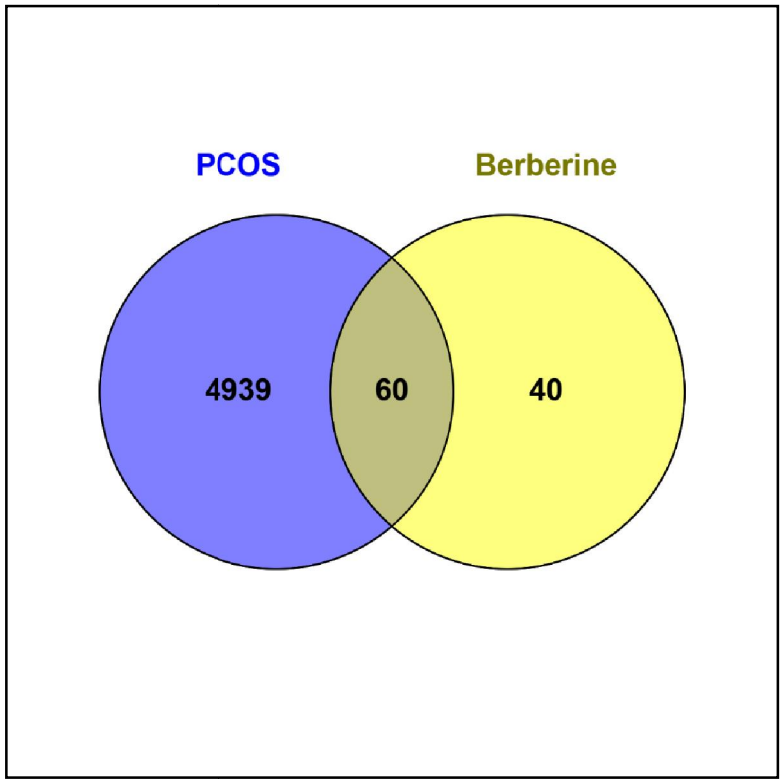

Table 5: Common Targets of PCOS and Berberine

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

Disease	Compound	Common Targets
PCOS	Berberine	CHEK2, MET, KIT, CYP19A1, ATR, PIK3CD, CDK4, JAK2, SRC, DHFR, NTRK1, CHEK1, CDC42, PRF1, PRKACA, PIK3CG, ABL1, AGPAT2, PIK3CB, CYP11B1, PGR, CSF1R, PTGS2, NR3C2, F3, ICAM1, CYP11B2, SELE, CDK2, PTPN1, HSD17B1, MAPK14, CYP2D6, DRD3, RPS6KB1, IKBKB, AURKA, XBP1, LCK, GRM5, ACHE, MAPK10, BCHE, PLK1, ADRA2B, ROCK1, TRPM8, PARP2, GRK2, ADORA2A, HPGD, CDK9, MAOB, CHRM1, HTR2B, SCD, GRK3, NPY5R, ROCK2, SIRT2

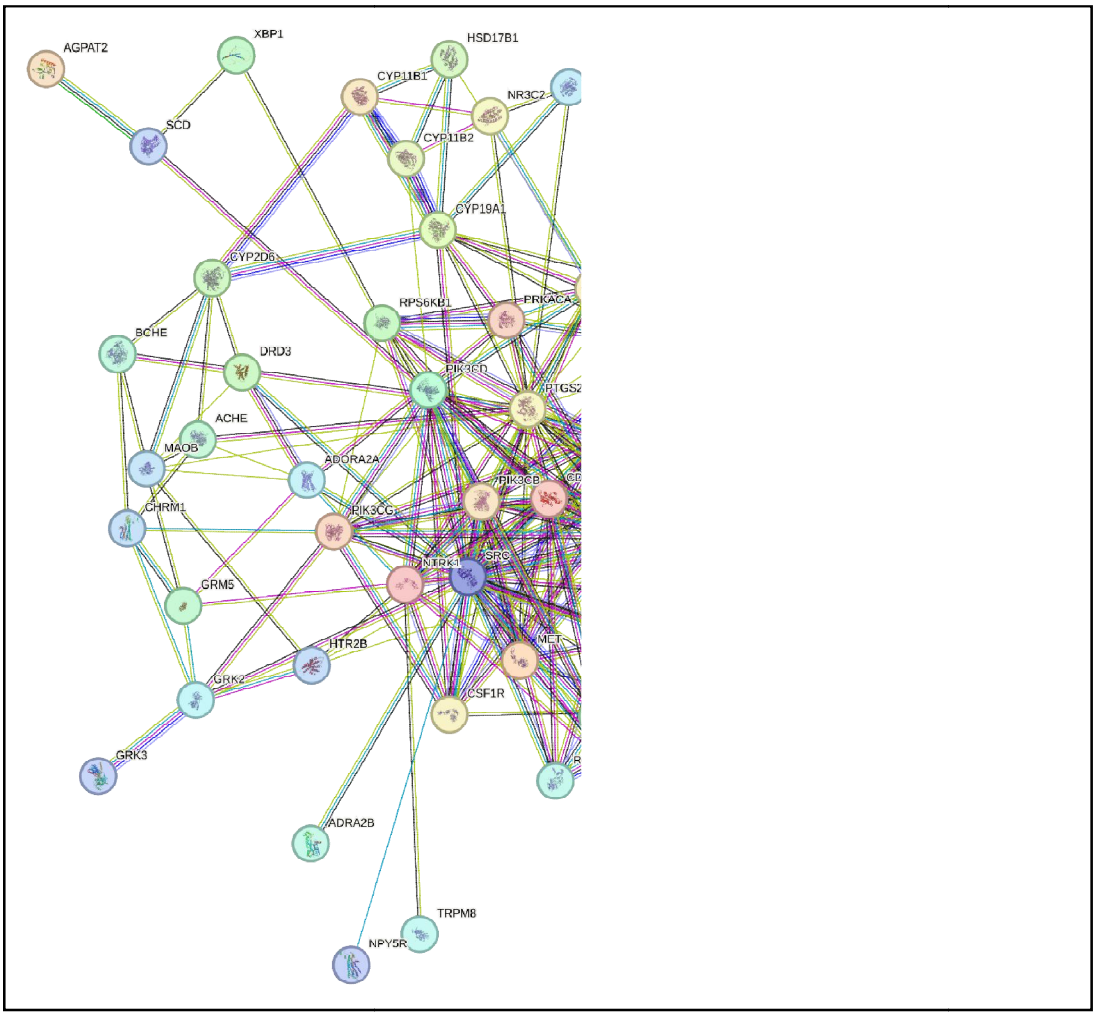

Fig 6: PPI of Target of berberine

Table 6: Top 5 Potential Targets of PCOS and Berberine

Sr. No.	Target	Role in PCOS and Therapeutic Significance of Berberine
1	PTGS2	Involved in inflammation and ovarian dysfunction; berberine may reduce inflammatory

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

		responses.
2	JAK2	Regulates JAK/STAT signaling associated with insulin resistance and inflammation in PCOS.
3	PIK3CD	Part of the PI3K signaling pathway involved in glucose metabolism and insulin signaling.
4	MAPK14	Mediates stress and inflammatory signaling pathways contributing to PCOS pathology.
5	ROCK1	Associated with insulin resistance, oxidative stress, and metabolic dysfunction in PCOS.

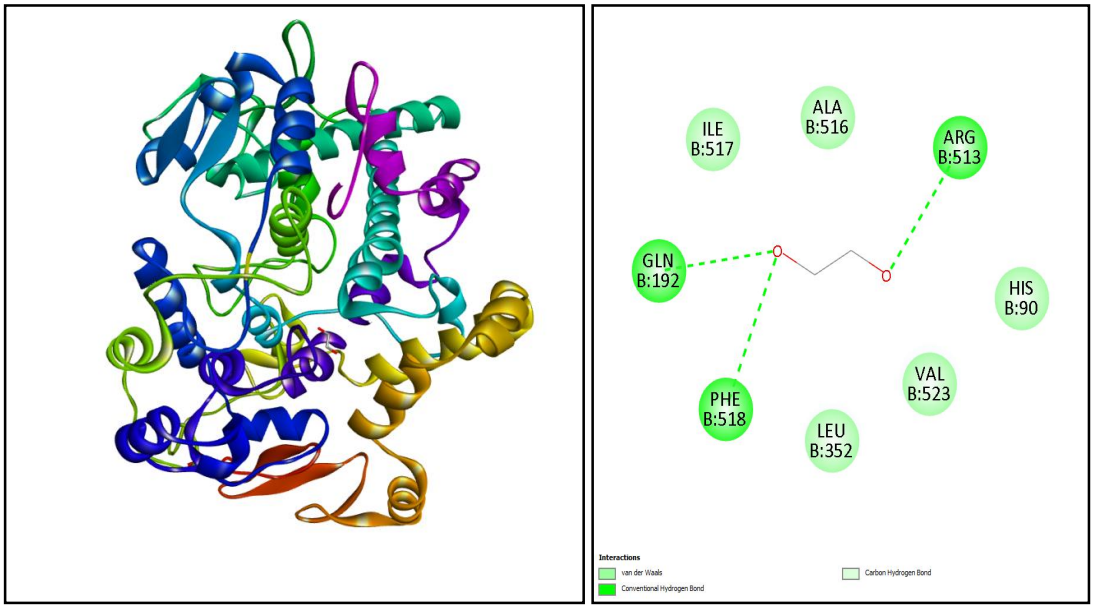

Fig 7: 2 D AND 3 D of berberine with PTGS2 docking with Swiss Dock and visualized in Discovery studio

IV. DISCUSSION OF RESULTS

Network Pharmacology Analysis of Berberine in Polycystic Ovary Syndrome (PCOS)

The present network pharmacology investigation explored the therapeutic potential of Berberine against Polycystic Ovary Syndrome by integrating compound profiling, drug-likeness prediction, toxicity assessment, target identification, and common target analysis. The findings suggest that berberine exerts multi-target pharmacological actions against PCOS-associated metabolic, inflammatory, endocrine, and ovarian dysfunction pathways.

Berberine demonstrated favorable physicochemical characteristics with a molecular weight of 336.4 g/mol, TPSA of 40.8 Å², logP of 3.12, and limited rotatable bonds, indicating good membrane permeability and acceptable oral bioavailability. The MolSoft drug-likeness score of 0.29 suggests moderate drug-like behavior and supports its suitability as a bioactive phytochemical candidate. The compound also showed balanced hydrophilic-lipophilic properties that may facilitate cellular uptake and biological interaction with intracellular signaling proteins.

The toxicity prediction model revealed both beneficial pharmacological potential and certain safety concerns. Berberine was predicted to exhibit hepatotoxicity, neurotoxicity, respiratory toxicity, and immunotoxicity with varying probabilities, indicating that prolonged or high-dose exposure may require careful therapeutic monitoring. However, the compound showed inactive predictions for carcinogenicity, mutagenicity, cardiotoxicity, and nephrotoxicity, suggesting a comparatively acceptable toxicological profile. The inactive prediction for blood-brain barrier penetration further indicates limited central nervous system exposure. Importantly, the Tox21 analysis predicted activity toward estrogen receptor alpha (ERα), estrogen receptor ligand binding domain, and aromatase (CYP19A1), which is highly relevant because hormonal imbalance and hyperandrogenism are major pathological features of PCOS.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, May 2026 Impact Factor: 8.2

Target prediction analysis identified several biologically relevant proteins associated with endocrine regulation, inflammation, insulin resistance, ovarian dysfunction, and metabolic disturbances. The identified targets included kinases, cytochrome P450 enzymes, inflammatory mediators, GPCRs, and transcription regulators. These targets indicate that berberine may influence multiple signaling cascades simultaneously, which is a major advantage in the treatment of multifactorial disorders such as PCOS.

The overlap analysis between PCOS-associated genes and berberine targets identified several common targets including PTGS2, JAK2, PIK3CD, MAPK14, ROCK1, CDK4, SRC, PTPN1, CYP19A1, and HSD17B1. These targets are strongly associated with insulin resistance, chronic inflammation, ovarian follicular dysfunction, steroidogenesis, and metabolic syndrome, all of which contribute to PCOS progression.

Among the identified targets, PTGS2 emerged as one of the most significant. PTGS2 encodes cyclooxygenase-2 (COX-2), a key inflammatory enzyme involved in prostaglandin biosynthesis and ovarian inflammatory responses. Overexpression of PTGS2 has been linked to abnormal follicular development and ovulatory dysfunction in PCOS patients. Berberine may suppress PTGS2-mediated inflammatory signaling, thereby reducing ovarian inflammation and improving reproductive function.

The JAK2 target plays an essential role in the JAK/STAT signaling pathway, which contributes to inflammatory cytokine signaling and insulin resistance in PCOS. Inhibition of JAK2 by berberine may reduce chronic low-grade inflammation and improve insulin sensitivity. Similarly, PIK3CD and other PI3K-related targets suggest modulation of the PI3K/Akt signaling pathway, a critical pathway regulating glucose metabolism, insulin signaling, and ovarian steroidogenesis. Dysregulation of this pathway is commonly observed in PCOS, and berberine-mediated modulation may help restore metabolic homeostasis.

MAPK14 (p38 MAPK) is another important inflammatory signaling mediator associated with oxidative stress and cellular apoptosis. Activation of MAPK14 contributes to ovarian tissue inflammation and metabolic dysfunction. Berberine may attenuate MAPK14 signaling, thereby reducing oxidative stress and inflammatory damage. ROCK1, another key target identified, is associated with insulin resistance, endothelial dysfunction, and oxidative stress. Suppression of ROCK1 activity may contribute to improved insulin sensitivity and metabolic regulation in PCOS patients.

The identification of CYP19A1 (aromatase) and HSD17B1 further supports the endocrine-regulating potential of berberine. Aromatase is involved in estrogen biosynthesis, while HSD17B1 regulates steroid hormone metabolism. Modulation of these enzymes may help correct hormonal imbalance and hyperandrogenism, which are hallmark features of PCOS.

In addition to endocrine and inflammatory pathways, berberine also targeted proteins associated with cell cycle regulation such as CDK2, CDK4, CHEK1, CHEK2, PLK1, and AURKA. These proteins are involved in granulosa cell proliferation and ovarian follicular development. Their regulation suggests that berberine may influence abnormal ovarian cell growth and follicular maturation in PCOS.

Overall, the network pharmacology findings indicate that berberine exerts therapeutic effects against PCOS through a multi-target and multi-pathway mechanism involving inflammatory suppression, insulin sensitization, hormonal regulation, oxidative stress reduction, and ovarian function improvement. The major pathways implicated include PI3K/Akt signaling, JAK/STAT signaling, MAPK signaling, inflammatory prostaglandin pathways, and steroid hormone biosynthesis pathways. These results scientifically support the traditional and emerging therapeutic use of berberine in the management of PCOS and provide a strong basis for future experimental and clinical validation studies.

V. CONCLUSION

The present study systematically investigated the therapeutic potential of Berberine against Polycystic Ovary Syndrome using a network pharmacology approach. The findings demonstrated that berberine possesses favorable physicochemical and drug-likeness properties along with significant biological activity against multiple molecular

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429 Volume 6, Issue 4, May 2026 Impact Factor: 8.2

targets associated with PCOS pathology. The integrated analysis identified several important common targets including PTGS2, JAK2, PIK3CD, MAPK14, ROCK1, CDK4, SRC, CYP19A1, and PTPN1, which are closely involved in inflammation, insulin resistance, steroid hormone biosynthesis, oxidative stress, and ovarian dysfunction. Enrichment analysis suggested that berberine regulates several important signaling pathways such as PI3K/Akt, MAPK, JAK/STAT, and inflammatory pathways that contribute to the progression of PCOS. Among the identified targets, PTGS2, JAK2, PIK3CD, MAPK14, and ROCK1 emerged as major therapeutic targets due to their critical role in inflammatory responses, metabolic dysregulation, and endocrine abnormalities. The multi-target nature of berberine indicates its ability to simultaneously modulate several pathological mechanisms involved in PCOS. Overall, the study provides a scientific basis for the therapeutic application of berberine in PCOS management and highlights the usefulness of network pharmacology in elucidating complex phytochemical–disease interactions. Further in vitro, in vivo, and clinical studies are required to validate these findings and explore the clinical efficacy and safety of berberine in the treatment of PCOS.

Future Perspectives / Way Forward

The present network pharmacology study demonstrated the promising therapeutic potential of Berberine against Polycystic Ovary Syndrome through modulation of multiple molecular targets and signaling pathways. Although the computational findings provide strong mechanistic insights, further experimental and clinical investigations are necessary to validate these observations and translate them into therapeutic applications. Future studies should focus on **in vitro validation** of the identified hub targets such as PTGS2, JAK2, PIK3CD, MAPK14, and ROCK1 using ovarian granulosa cell lines, adipocytes, and insulin-resistant cellular models. Gene and protein expression studies using RT-PCR, western blotting, and ELISA may help confirm the regulatory effects of berberine on inflammatory cytokines, insulin signaling molecules, and steroidogenic enzymes. Further **in vivo studies** using appropriate animal models of PCOS are required to evaluate the pharmacological efficacy of berberine on ovarian morphology, hormonal imbalance, insulin resistance, oxidative stress, and reproductive function. Histopathological analysis and biochemical assessments may provide deeper understanding of its therapeutic mechanisms. Molecular docking and molecular dynamics simulation studies should be extended to investigate the binding stability and interaction patterns of berberine with major therapeutic targets. Such studies may aid in understanding structure–activity relationships and optimization of berberine-based derivatives with improved potency and reduced toxicity. Since berberine exhibited predicted hepatotoxicity and neurotoxicity in toxicity analysis, future research should also emphasize **toxicological evaluation and dose optimization** to ensure long-term safety. Pharmacokinetic and bioavailability studies are necessary because berberine is known to have limited oral bioavailability. Advanced drug delivery systems such as nanoparticles, nanoemulsions, liposomes, and phytosomes may be explored to enhance the solubility, absorption, stability, and therapeutic effectiveness of berberine. These novel formulations may improve targeted delivery and reduce systemic toxicity. In addition, future clinical studies involving PCOS patients should be conducted to validate the efficacy of berberine in improving insulin sensitivity, ovulation, menstrual regularity, lipid profile, and hormonal balance. Comparative clinical studies with standard drugs such as metformin may further establish its therapeutic relevance. The integration of network pharmacology with transcriptomics, proteomics, metabolomics, and artificial intelligence-based prediction models may provide more comprehensive insights into the molecular mechanisms of berberine in PCOS management. Such multidisciplinary approaches may facilitate the development of personalized phytomedicine-based therapeutic strategies. Overall, the present findings provide a strong scientific foundation for future translational research and support the potential development of berberine as a multi-target phytotherapeutic agent for the effective management of PCOS.

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

REFERENCES

1. Stańczak, N. A., Grywalska, E., & Dudzińska, E. (2024). The latest reports and treatment methods on polycystic ovary syndrome. *Annals of medicine*, *56*(1), 2357737. https://doi.org/10.1080/07853890.2024.2357737
2. Di Lorenzo, M., Cacciapuoti, N., Lonardo, M. S., Nasti, G., Gautiero, C., Belfiore, A., Guida, B., & Chiurazzi, M. (2023). Pathophysiology and Nutritional Approaches in Polycystic Ovary Syndrome (PCOS): A Comprehensive Review. *Current nutrition reports*, *12*(3), 527–544. https://doi.org/10.1007/s13668-023-00479-8
3. Su, P., Chen, C., & Sun, Y. (2025). Physiopathology of polycystic ovary syndrome in endocrinology, metabolism and inflammation. *Journal of ovarian research*, *18*(1), 34. https://doi.org/10.1186/s13048-025-01621-6
4. Helvaci, N., & Yildiz, B. O. (2025). Polycystic ovary syndrome as a metabolic disease. *Nature reviews. Endocrinology*, *21*(4), 230–244. https://doi.org/10.1038/s41574-024-01057-w
5. Wang, K., & Li, Y. (2023). Signaling pathways and targeted therapeutic strategies for polycystic ovary syndrome. *Frontiers in endocrinology*, *14*, 1191759. https://doi.org/10.3389/fendo.2023.1191759
6. Zhang, Y., Chen, Z. J., & Zhao, H. (2025). Polycystic ovary syndrome: A metabolic disorder with therapeutic opportunities. *Cell metabolism*, *37*(10), 1932–1949. https://doi.org/10.1016/j.cmet.2025.08.002
7. Dokras A. (2025). Polycystic ovary syndrome in 2025-insights and innovations. *Fertility and sterility*, *124*(5 Pt 2), 907–909. https://doi.org/10.1016/j.fertnstert.2025.09.025
8. Lete, I., Martínez, A., Lasaga, I., Centurión, E., & Vesga, A. (2024). Update on the combination of myo-inositol/d-chiro-inositol for the treatment of polycystic ovary syndrome. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*, *40*(1), 2301554. https://doi.org/10.1080/09513590.2023.2301554
9. Li, Z., Wang, Y., Xu, Q., Ma, J., Li, X., Yan, J., Tian, Y., Wen, Y., & Chen, T. (2023). Berberine and health outcomes: An umbrella review. *Phytotherapy research : PTR*, *37*(5), 2051–2066. https://doi.org/10.1002/ptr.7806
10. Gasmi, A., Asghar, F., Zafar, S., Oliinyk, P., Khavrona, O., Lysiuk, R., Peana, M., Piscopo, S., Antonyak, H., Pen, J. J., Lozynska, I., Noor, S., Lenchyk, L., Muhammad, A., Vladimirova, I., Dub, N., Antoniv, O., Tsal, O., Upyr, T., & Bjørklund, G. (2024). Berberine: Pharmacological Features in Health, Disease and Aging. *Current medicinal chemistry*, *31*(10), 1214–1234. https://doi.org/10.2174/0929867330666230207112539
11. Wang, K., Yin, J., Chen, J., Ma, J., Si, H., & Xia, D. (2024). Inhibition of inflammation by berberine: Molecular mechanism and network pharmacology analysis. *Phytomedicine : international journal of phytotherapy and phytopharmacology*, *128*, 155258. https://doi.org/10.1016/j.phymed.2023.155258
12. Li, M., Cui, Y., Wu, X., Yang, X., Huang, C., Yu, L., Yi, P., & Chen, C. (2025). Integrating network pharmacology to investigate the mechanism of quercetin's action through AKT inhibition in co-expressed genes associated with polycystic ovary syndrome and endometrial cancer. *International journal of biological macromolecules*, *297*, 139468. https://doi.org/10.1016/j.ijbiomac.2025.139468
13. Zheng, R., Shen, H., Li, J., Zhao, J., Lu, L., Hu, M., Lin, Z., Ma, H., Tan, H., Hu, M., & Li, J. (2023). Qi Gong Wan ameliorates adipocyte hypertrophy and inflammation in adipose tissue in a PCOS mouse model through the Nrf2/HO-1/Cyp1b1 pathway: Integrating network pharmacology and experimental validation in vivo. *Journal of ethnopharmacology*, *301*, 115824. https://doi.org/10.1016/j.jep.2022.115824
14. Guan, H. R., Li, B., Zhang, Z. H., Wu, H. S., He, X. L., Dong, Y. J., Su, J., Lv, G. Y., & Chen, S. H. (2023). Integrated bioinformatics and network pharmacology to explore the therapeutic target and molecular mechanisms of Bailing capsule on polycystic ovary syndrome. *BMC complementary medicine and therapies*, *23*(1), 458. https://doi.org/10.1186/s12906-023-04280-6

IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, May 2026
Impact Factor: 8.2

15. Hai, B., Zhang, Y., Huang, J., Mprah, R., & Wang, M. (2025). Exploring the key ingredients and mechanisms of Banxia Xiexin decoction for the treatment of polycystic ovary syndrome based on network pharmacology and experimental validation. *Annals of medicine*, *57*(1), 2503921. https://doi.org/10.1080/07853890.2025.2503921
16. Cheng, K., Lin, J., Wu, M., Wang, J., Liu, X., Yang, K., Ni, C., Liu, Q., Wu, J., & Wu, W. (2025). Berberine promotes hair growth by targeting Axin2 and activating Wnt/β-catenin pathway. *Phytomedicine : international journal of phytotherapy and phytopharmacology*, *141*, 156669. https://doi.org/10.1016/j.phymed.2025.156669
17. Hu, W., Xie, N., Pan, M., Zhang, Q., Zhang, H., Wang, F., & Qu, F. (2024). Chinese herbal medicine alleviates autophagy and apoptosis in ovarian granulosa cells induced by testosterone through PI3K/AKT1/FOXO1 pathway. *Journal of ethnopharmacology*, *318*(Pt B), 117025. https://doi.org/10.1016/j.jep.2023.117025