ISSN 2808-3229
Journal of Biodiversity and Biotechnology. 6(1), 1–9,
2026 URL: https://jurnal.uns.ac.id/jbb/article/view/115073
doi: http://dx.doi.org/10.20961/jbb.v6i1.115073

Natural Compounds in *Moringa oleifera* Leaves Targeting Estrogen Receptor Beta (ESR2) for PCOS Treatment: Insight from In Silico Docking

Aslikh Lana Dina[1*], Alin Robiah Al Adawiah[1], Ade Hilman Juhaeni[1]

[1]Department of Agrotechnology, Faculty of Agriculture, Universitas Siliwangi, Tasikmalaya, West Java, Indonesia

*Corresponding author: aslikhlanadina@unsil.ac.id

Abstract
Polycystic ovary syndrome (PCOS) is a health complication that often leads to infertility in women. PCOS, as a reproductive-metabolic disorder, is also related to breast cancer and other diseases. Nevertheless, there is no universal drug for PCOS treatment. Hence, exploring a new candidate's drugs is crucial. Estrogen receptor beta (ESR2) has become a significant marker for PCOS and has the potential to be used as a target for PCOS treatment. This study aims to explore the potential use of moringa as a nutraceutical. This study provides in silico data of selected compounds (naringenin, gallic acid, quinic acid, quercetin, apigenin, and kaempferol) in moringa leaves as a candidate drug for PCOS treatment targeting ESR2. Naringenin and apigenin showed a noteworthy calculated binding affinity score from docking into ESR2 (<- 7kcal/mol). Protein-protein analysis and gene analysis showed that ESR2 is expressed in varying tissues. It strengthens the potential use of moringa as a nutraceutical. This study showed that Moringa leaves have the potential to be used as a complement to PCOS treatment.

Keywords: Apigenin; Estrogen receptor beta; Kaempferol; Molecular docking; *Moringa oleifera*; Naringenin; Quercetin.

Cite this as: Dina, A.L., Adawiah, A.R.A., Juhaeni, A.H. (2026). Natural Compounds in *Moringa oleifera* Leaves Targeting Estrogen Receptor Beta (ESR2) for PCOS Treatment: Insight from In Silico Docking. 6(1), 1–9. doi: http://dx.doi.org/10.20961/jbb.v6i1.115073

Introduction

Polycystic ovary syndrome (PCOS) is a health complication associated with infertility, metabolic syndromes, and gynecological disorders. PCOS emerged as the most severe reproductive-metabolic disorder and became a global public health concern (1,2). Although there is an oral drug for treatment, there is no universal treatment available for PCOS (3). Clomiphene has been used for ovulation induction in women with PCOS and for improving fertility, but it is reported to have anti-estrogenic effects on the endometrium, cervical mucus, and an increased risk of multiple pregnancies. Hence, exploring new drug candidates and targets is crucial (1,3).

Nowadays, some investigations have focused on the potential association of PCOS with estrogen receptor alpha (ESR1) and estrogen receptor beta (ESR2) (4,5). Both ESR1 and ESR2 are expressed throughout the brain, but ESR2 is more widely distributed in the brain than ESR1. Some diseases, such as Ovarian dysgenesis 8 and Thyroid carcinoma Familial Medullary, are associated with ESR2 (6,7). Estrogen receptor beta (ESR2) is also known for inhibiting breast, endometrial, and ovarian cancer cell proliferation. Studying the potential of ESR2 as a target for treatment could provide the next candidate for symptom relief for women with PCOS, including for menopausal people (8–12).

Natural compounds from plants are attracting attention to phytomedicines and are becoming popular for various health issues due to their low toxicity and affordability (2,13). *Moringa oleifera* is a plant that is known as an herb for women's supplements and for other health purposes. Moringa leaves are consumed either fresh, cooked, or dried powder to treat insulin resistance, cardiovascular disease, and as a galactagogue (14–16). Although the data about the consumption of moringa for treating PCOS patients is limited, *Moringa oleifera*

leaves combined with hormone supplements could improve the rate of maturation of sheep oocytes (17).

Molecular docking has become an essential aspect of in silico drug development, which involves predicting the interaction between a small molecule and a protein target. Molecular docking is a useful tool for identifying the molecular targets of nutraceuticals in the management of disease. Further research on bioactive substances in Moringa oleifera for PCOS treatment can elaborate on its potential as a nutraceutical (food source) and be used in the management of diseases. Finding their molecular mechanism using molecular docking to predict the binding affinity of ligands to estrogen receptor beta can provide crucial information (18,19).

This study aims to explore the potential use of moringa for PCOS treatment using in silico analysis and to contribute to the new demands for functional food and the exploration of regional biodiversity for the global market. Exploring novel medicinal plants and discovering the molecular mechanisms of target proteins accelerated pharmacological research (20). Biological processes give ideas about the molecular activities working inside the cellular environment (12). Recently, scientific databases have made it possible for us to share information about genes, proteins, and medicinal plant data for research work. The increasing data on protein structure-function relationships makes it possible to screen virtually all new drug candidates (21–23).

Material and Methods

Identifying of bioactive compound

Identify the chemical content of moringa leaves by the literature review method. The 3D structure of molecules was retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov/), the screening of drug research status of the compounds was retrieved from ChEMBL (https://www.ebi.ac.uk/chembl/).

Protein data and bioactive molecules structures retrieval

The amino acid sequence of ESR2 (Q62986) was retrieved from Uniprot (https://www.uniprot.org/). This study uses the ESR2 sequence from *Rattus norvegicus* as a consideration for future research. *Rattus norvegicus* has been used as a model for physiology, behavior, and complex human disease (24). The 3D structure was retrieved from the Protein Data Bank (RSCB PDB) (https://www.rcsb.org/) (PDB ID: 1HJ1) (25). The protein structures were visualized using Chimera 1.19 (26). Screening ESR2 mRNA expression location summary in normal human tissues from GTEx using the Genecards database (https://genecards.org/) (27).

Molecular docking analysis

The target proteins and small molecule compounds were processed using Chimera 1.19 (26). The processed PDB-format and the molecular compound were imported into Swissdock (https://www.swissdock.ch/) for molecular docking with AutoDock Vina (28,29). The protein is being designed as a target. Biovia Discovery Studio 2025 was employed for visualizing the docking results.

Protein-protein association network and functional analysis

Analyze protein-protein interaction using STRING (https://string-db.org/) (30). The protein for PCOS target was imported into the Metascape database (https://metascape.org/gp/index.html#/) for enrichment analysis.

Pharmacokinetics toxicity prediction analysis

The selected compounds underwent physicochemical properties and drug-likeness analysis using SwissADME (https://www.swissadme.ch/) (31–33). The biological activity prediction of ligands employed the PASS (Prediction of Activity Spectra for Substances) Server (http://www.way2drug.com/passonline) (34).

Results and Discussion

Polycystic ovary syndrome, as a reproductive-metabolic disorder, is also associated with the estrogen receptor beta gene (*ESR2*). Virtually screening the substances in moringa into ESR2 can optimize the early stages of discovery of nutraceuticals. The mRNA of *ESR2* can be expressed throughout the varied organs in the body (Table 1), thus consumption of moringa leaves not only affects the reproductive system but also nutritional needs and affects other systems in the body.

Table 1. The mRNA expression of *ESR2* in human normal tissue.

Tissue	System affected
Whole blood	Immune
White blood cells	Immune
Lymph node	Immune
Brain	Nervous
Cortex	Nervous
Cerebellum	Nervous
Spinal cord	Nervous
Tibial nerve	Nervous
Heart	Muscle
Artery	Muscle
Skeletal muscle	Muscle
Small intestine	Internal
Colon	Internal
Adipocyte	Internal
Kidney	Internal
Liver	Internal
lung	Internal
Spleen	Internal
Stomach	Internal
Esophagus	Internal
Bladder	Internal
Pankreas	Secretory
Thyroid	Secretory
Salivary gland	Secretory
Adrenal gland	Secretory
Pituitary	Secretory
Breast	Secretory
Skin	Secretory
Ovary	Reproductive
Uterus	Reproductive
Placenta	Reproductive
Testis	Reproductive
Prostate	Reproductive

Based on a previous study, *Moringa oleifera* leaves notably contain apigenin, quercetin, naringenin, gallic acid, quinic acid, and kaempferol (35–37). The drug research of those compounds from ChEMBL shows that those compounds are increasingly being researched until 2024. Exploring the potential of moringa leaves that contain those compounds will reveal another benefit of moringa leaves.

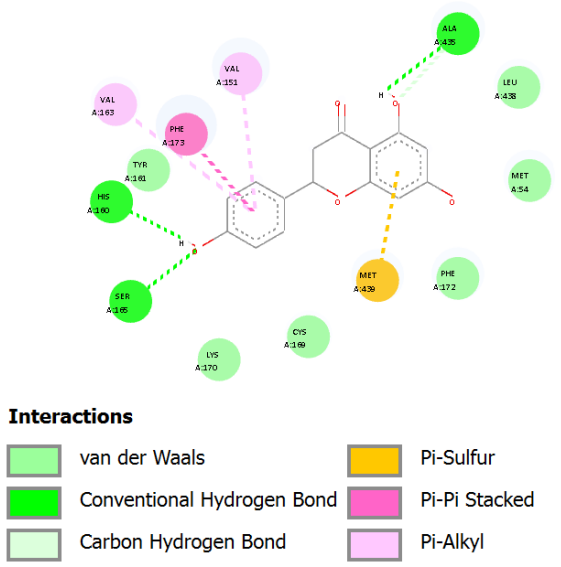

Figure 1. Docking result of ESR2 and naringenin (binding interaction residues: Ala435, Met439, Phe173, Tyr161, His190, and Ser165).

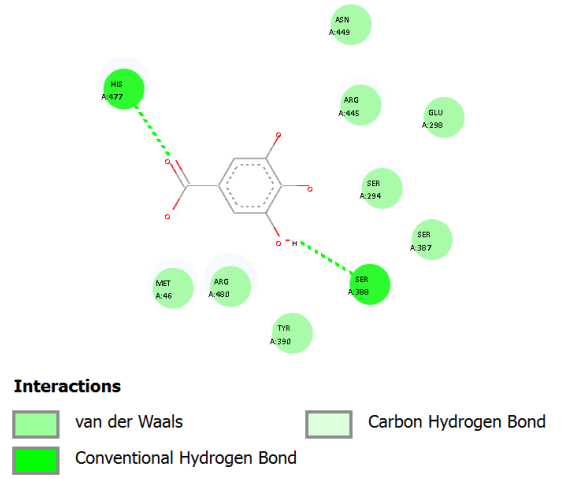

Figure 2. Docking result of ESR2 and gallic acid (binding interaction residues: His477 and Ser388).

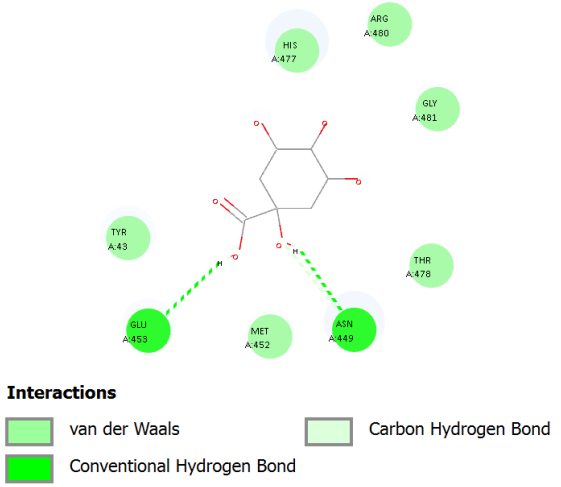

Figure 3. Docking result of ESR2 and quinic acid (binding interaction residues: Glu453, Met452, and ASN449).

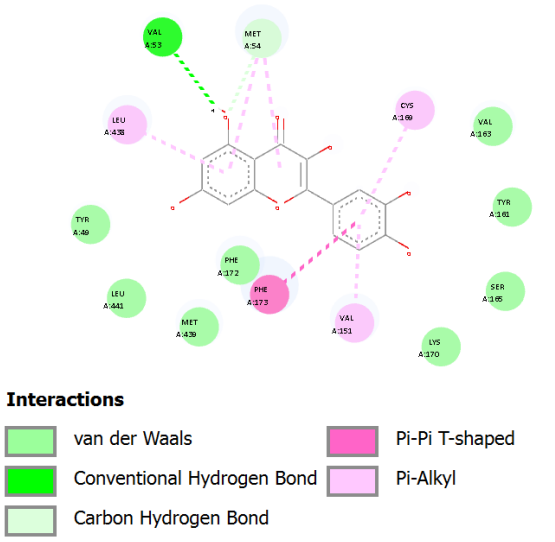

Figure 4. Docking result of ESR2 and quercetin (binding interaction residues: Val53, Met54, Cys169, Val151, Phe, 173, and Leu438).

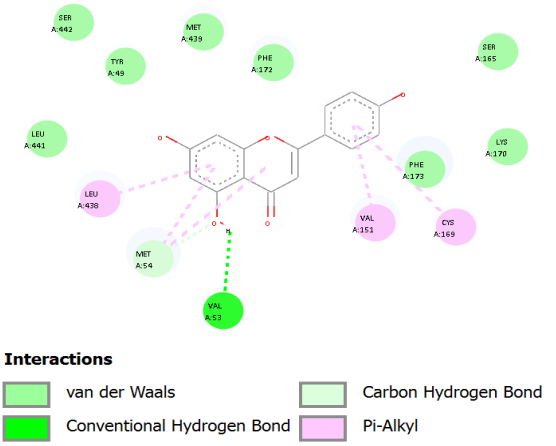

Figure 5. Docking result of ESR2 and apigenin (binding interaction residues: Met54, Val53, Leu438, Val151, and Cys169).

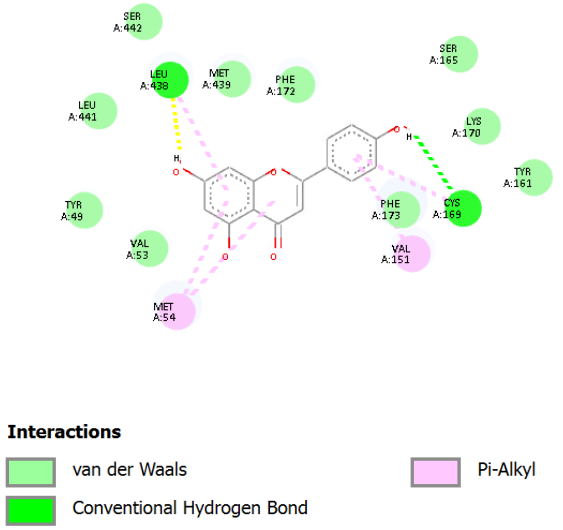

Figure 6. Docking result of ESR2 and kaempferol (binding interaction residues: Met54, Leu438, Phe173, Val151, and Cys169).

Table 2. Calculate the affinity of ligands.

Ligand	Calculated Affinity (kcal/mol)
Naringenin	-7.764
Gallic acid	-5.009
Quinic acid	-4.770
Quercetin	-7.520
Apigenin	-7.754
Kaempferol	-7.611

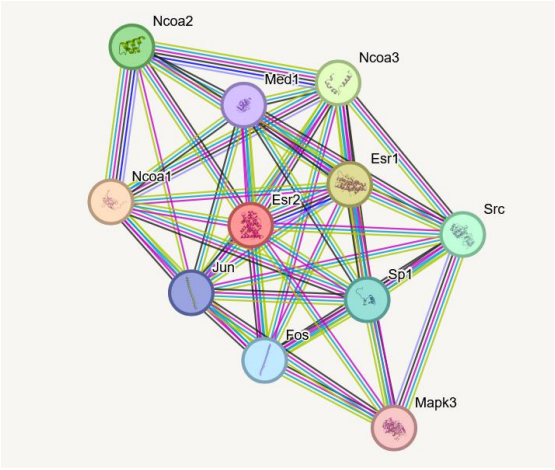

Figure 7. Protein-protein interaction analysis.

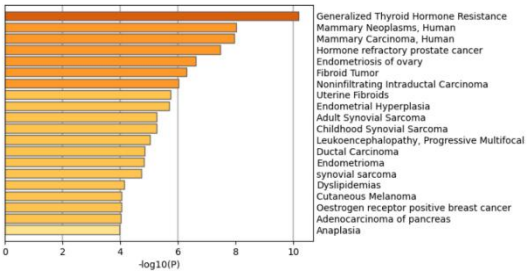

Figure 8. Summary of enrichment analysis in DisGeNET.

Table 4. The predicted ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties of ligands.

Ligand	Solubility	GI Absorption	CYP2C19 Inhibitor
Naringenin	Soluble	High	No
Gallic acid	Very soluble	High	No
Quinic acid	Highly soluble	Low	No
Quercetin	Soluble	High	No
Apigenin	Soluble	High	No
Kaempferol	Soluble	High	No

Table 5. Biological activity prediction

Ligand	Pa	Pi	Biological Activity
Naringenin	0.964	0.003	Membrane integrity agonist
	0.956	0.002	HMOX1 expression enhancer
	0.949	0.003	CYP1A1 substrate
	0.944	0.004	CYP1A substrate
	0.934	0.002	CYP1B substrate
	0.928	0.002	UGT1A10 substrate
	0.918	0.004	CYP1A2 substrate
	0.918	0.004	Chlordecone reductase inhibitor
	0.911	0.005	HIF1A expression inhibitor
	0.892	0.002	Histidine kinase inhibitor
Gallic acid	0.955	0.002	Arylacetonitrilase inhibitor
	0.954	0.002	Chlordecone reductase inhibitor
	0.950	0.002	Dehydro-L-gulonate decarboxylase inhibitor
	0.950	0.003	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
	0.944	0.002	Glutathione thiolesterase inhibitor
	0.943	0.002	Alkane 1-monooxygenase inhibitor
	0.941	0.003	Sugar-phosphatase inhibitor
	0.938	0.002	NADPH-cytochrome-c2 reductase inhibitor
	0.934	0.001	Threonine aldolase inhibitor
Quinic acid	0.936	0.003	Sugar-phosphatase inhibitor
	0.929	0.004	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
	0.916	0.003	Glucan endo-1,6-beta-glucosidase inhibitor
	0.915	0.004	Alkenylglycerophosphocholine hydrolase inhibitor
	0.907	0.003	Ribulose-phosphate 3-epimerase inhibitor
	0.904	0.000	Quinate 5-dehydrogenase inhibitor
	0.895	0.003	Pullulanase inhibitor
	0.882	0.003	Exoribonuclease II inhibitor
	0.876	0.003	UDP-N-acetylglucosamine 4-epimerase inhibitor
	0.855	0.002	Phosphatase inhibitor
Quercetin	0.973	0.002	Membrane integrity agonist
	0.969	0.002	HIF1A expression inhibitor
	0.962	0.001	Peroxidase inhibitor
	0.957	0.002	HMOX1 expression enhancer
	0.951	0.001	CYP1A inducer
	0.944	0.002	UGT1A6 substrate
	0.945	0.004	CYP1A substrate
	0.940	0.001	Antimutagenic
	0.940	0.003	CYP1A1 substrate
	0.939	0.002	UGT1A10 substrate
Apigenin	0.973	0.001	Chlordecone reductase inhibitor
	0.967	0.002	Membrane integrity agonist
	0.946	0.002	Membrane permeability inhibitor
	0.946	0.004	CYP2C12 substrate
	0.942	0.002	2-Dehydropantoate 2-reductase inhibitor
	0.941	0.002	Kinase inhibitor
	0.936	0.001	Aryl-alcohol dehydrogenase (NADP+) inhibitor
	0.937	0.003	Aldehyde oxidase inhibitor
	0.931	0.001	P-benzoquinone reductase (NADPH) inhibitor
	0.931	0.003	Anaphylatoxin receptor antagonist
Kaempferol	0.983	0.001	Chlordecone reductase inhibitor
	0.974	0.002	Membrane integrity agonist
	0.969	0.002	HIF1A expression inhibitor
	0.965	0.001	2-Dehydropantoate 2-reductase inhibitor
	0.961	0.001	Aryl-alcohol dehydrogenase (NADP+) inhibitor
	0.959	0.001	Kinase inhibitor
	0.959	0.001	P-benzoquinone reductase (NADPH) inhibitor
	0.957	0.002	Membrane permeability inhibitor
	0.956	0.001	Peroxidase inhibitor
	0.951	0.001	Quercetin 2,3-dioxygenase inhibitor

Molecular docking results provide insight into the potential binding interaction between selected moringa compounds and ESR2. Naringenin and apigenin demonstrated a strong affinity for ESR2, indicating potentially more effective interaction. Quinic acid exhibits the lowest affinity (-4.770 kcal/mol) for ESR2 rather than other compounds (Table 2). The strong affinity of quercetin, apigenin, and kaempferol is noteworthy. Molecular docking visualization demonstrated ligand interaction with ESR2, exhibiting van der Waals, conventional hydrogen bond, carbon hydrogen bond, Py-Alkil, and Pi-Pi T-shaped. The binding interaction involves residues Leu-A:405, Leu-A:385, Ser-A:402, Ser-A:388, Glu-A:453, Asn-A:449, Val-A:53, Met-A:54, Leu-A:436, Cys-A:169, Phe-A:173, Val-A:151, Leu-A:438, and Phe-A:172. Hydrogen bonding acts as a protein stability factor and depends on the polarity of its environment. Naringenin showed a Pi-sulfur bond that contributed to enzyme activity and stability, which often affects drug design (38). The docking result also shows Pi-alkyl interaction and Pi-Pi T-shaped between the aromatic ring of the ligand and the residues such as Leu-A:405, Val-A:151, Met-A:54, Leu-A:438, and Cys-A:169 (Figure 2a, 2d, 2e, and 2f). This non-covalent interaction stabilizes the binding of the compound within the ESR2 active site. Protein interaction is one of the aspects of predicting the protein function of target proteins and the drug ability of molecules. The ESR2 is related to Ncoa3 (Figure 7). This gene was known as a breast cancer target for chemotherapy (39).

The ESR2 is related to thyroid hormone resistance, endometrioma, mammary neoplasms, and mammary carcinoma (Figure 8). These results provide insight into the idea that treatment targeting ESR2 can also be used to treat other diseases. All the ligands are soluble and showed no CYP2C19 inhibitor activity, which is a lower risk of DDIs to ensure drug safety and efficacy (40). Computational drug development involves predicting biological activity to evaluate the therapeutic effect. The results showed that Pa (Probability active) and Pi (Probability inactive). All ligands showed a high Pa score. Naringenin, quercetin, and kaempferol showed HIF1A expression inhibitor activity (Table 5). Hypoxia-inducible factor-1α (HIF-1A) is widely distributed in human cells and is expected to have potential clinical applications for tumors and diabetes disease (41). Naringenin, quercetin, apigenin, and kaempferol are related to membrane integrity agonists. Membrane integrity is crucial for cell survival and signaling pathways and is involved in metabolic disease (42). Naringenin and quercetin can act as a CYP1A substrate. The CYP1A substrate (Human Cytochrome P450 1A1) is involved in the metabolism of drugs, activation of certain toxins, and environmental pollutants (43). This study's results strengthen the previous studies' information: quercetin, naringenin, apigenin, and gallic acid affect LH, FSH, estrogen, and androgen (44–48). The docking results also highlight the potential use of moringa for PCOS treatment and the necessity for further research.

Conclusion

Polycystic ovary syndrome (PCOS) emerged as the most severe reproductive-metabolic disorder and became a global public health concern. Estrogen receptor beta (ESR2) is considered the most significant marker of PCOS. The *Moringa leaves* are already known as a herb for women's supplements and for other health purposes. Discovering the potential of bioactive substances in *Moringa oleifera* leaves needs strong proof of their molecular mechanism. Molecular docking is a useful tool to predict the ligand-receptor interaction through computer-based methods. Molecular docking enables researchers to study the nutraceuticals within moringa bioactive substances in a target protein. This study provides insight into selected compounds (naringenin, gallic acid, quinic acid, quercetin, apigenin, and kaempferol) in *Moringa oleifera* leaves for PCOS treatment. Docking results showed naringenin and apigenin have the highest calculated affinity among other compounds. All ligands have drug-like characteristics and low toxicity. This study's results can be a foundation for further research on moringa's potential as a nutrient that supports women's health.

Acknowledgments

The authors would like to express our gratitude to the LPPM Universitas Siliwangi for their support for this research.

Conflict of Interest

The authors have declared that no competing interests exist.

References

[1] Koohnavard F, Ahmadi K, Eftekhar E, Edalatmanesh MA. Computational Screening of FDA-approved Drugs to Identify Potential Aromatase Receptor Inhibitors for Polycystic Ovary Syndrome. J Biomol Struct Dyn. 2023;41(24):5507–15519.

[2] Choudhury AA, Rajeswari VD. Polycystic ovary syndrome (PCOS) increases the risk of subsequent gestational diabetes mellitus (GDM): A novel therapeutic perspective. Life Sci. 2022;310:121069.

[3] Choudhury AA, Bhattarai A, Sahoo S, Roy SD, Laskar NA, Firoz A. In Silico drug discovery of Solanum torvum as a phytotherapeutic aromatase inhibitor for PCOS-induced infertility: A comparative study with FDA-approved drugs. Silico Res Biomed. 2025;1(100003):3050–7871.

[4] Liaqat I, Jahan N, Krikun G, Taylor HS. Genetic Polymorphism in Pakistani Women with Polycystic Ovary Syndrome. Reprod Sci. 2015;22(3):347–57.

[5] Zhou S, Wen S, Sheng Y, Yang M, Shen X, Chen Y, et al. Association of Estrogen Receptor Genes Polymorphisms with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis based on Observational Studies. Front Endocrinol. 2021;12(726184):1–13.

[6] Lang-Muritano M, Sproll P, Wyss S, Kolly A, Hürlimann R, Konrad D, et al. Early-Onset Complete Ovarian Failure and Lack of Puberty in a Woman With Mutated Estrogen Receptor β (ESR2). J Clin Endocrinol Metab. 2018;103(10):3748–56.

[7] Smith J, Read ML, Hoffman J, Brown R, Bradshaw B, Campbell C, et al. Germline ESR2 mutation predisposes to medullary thyroid carcinoma and causes up-regulation of RET expression. Hum Mol Genet. 2016;25(9):1836–45.

[8] Hartman J, Ström A, Gustafsson JÅ. Estrogen receptor beta in breast cancer—Diagnostic and therapeutic implications. Steroids. 2009;74(8):635–41.

[9] Jia M, Dahlman-Wright K, Gustafsson JÅ. Estrogen receptor alpha and beta in health and disease. Best Pr Res Clin Endocrinol Metab. 2015;29(4):557–68.

[10] Lazennec G, Bresson D, Lucas A, Chauveau C, Vignon F. ERβ Inhibits Proliferation and Invasion of Breast Cancer Cells. Endocrinology. 2001;142(9):4120–4130.

[11] Yu K, Huang ZY, Xu XL, Li J, Fu XW, Deng SL. Estrogen Receptor Function: Impact on the Human Endometrium. Front Endocrinol. 2022;13(827724):1–16.

[12] Frick KM, Fleischer AW, Schwabe MR, Abdelazim FA, Sem DS, Donaldson WA. Not your mother's hormone therapy: Highly selective estrogen receptor beta agonists as next-generation therapies for menopausal symptom relief. Horm Behav. 2025;173(105773):1–41.

[13] Abbas G, Al Harrasi A, Hussain H, Hamaed A, Supuran CT. The management of diabetes mellitus: Imperative role of natural products against dipeptidyl peptidase-4, α-glucosidase, and sodium-dependent glucose co-transporter 2 (SGLT2). Bioorg Chem. 2019;5(86):305–15.

[14] Verma AR, Vijayakumar M, Mathela CS, Rao C V. In vitro and in vivo antioxidant properties of different fractions of Moringa oleifera leaves. Food Chem Toxicol. 2009;47(9):2196–201.

[15] Fungtammasan S, Phupong V. The effect of Moringa oleifera capsule in increasing breast milk volume in early postpartum patients: A double-blind, randomized controlled trial. Eur J Obstet Gynecol Reprod Biol. 2022;16(100171):1–5.

[16] Vergara-Jimenez M, Almatrafi MM, Fernandez ML. Bioactive Components in Moringa Oleifera Leaves Protect against Chronic Disease. Antioxidants (Basel). 2017;6(4):1–1.

[17] Barakat IAH, Khalil WKB, Al-Himaidi AR. Moringa oleifera extract modulates the expression of fertility related genes and elevation of calcium ions in sheep oocytes. Small Rumin Res. 2015;130:67–75.

[18] Agu PC, Afiukwa CA, Orji OU, Ezeh EM, Ofoke IH, Ogbu CO, et al. Molecular docking as a tool for the discovery of molecular targets of nutraceuticals in diseases management. Scie Rep. 2023;13:13398.

[19] Sahoo RN, Pattanaik S, Pattnaik G, Mallick S, Mohapatra R. Review on The Use of Molecular Docking as The First Line Tool in Drug Discovery and Development. Indian J Pharm Sci. 2022;84(5):1334–7.

[20] Yabuuchi H, Hayashi K, Shigemoto A, Fujiwara M, Nomura Y, Nakashima M, et al. Virtual screening of antimicrobial plant extracts by machine learning classification of chemical compounds in semantic space. PLoS One. 2023;18(5):1–12.

[21] Naaz S, Balramnavar VM, Kaur A. Medicinal Plant Databases: Analyzing Strengths, Weaknesses and Innovations for Future Improvements. Life Sci Res Commun. 2024;1(1):31–41.

[22] Mumtaz A, Masud A, Ayub N, Fatima Y, Shah M. The Significance of Anti-Mullerian Hormone in the Identification of Polycystic Ovarian Syndrome among Pakistani Women. J Soc Obs Gynaecol Pak [Internet]. 2023;13(3):293–7. Available from: https://jsogp.net/index.php/jsogp/article/view/652

[23] Narayana S, Ananad C, Kumari NS, Sonkusere S, Babu SVS. Impact of Aromatase Enzyme and its Altered Regulation on Polycystic Ovary Syndrome (PCOS): A Key Factor in Pathogenesis of PCOS. Indian J Med Spec. 2023;14(4):206–11.

[24] Smith JR, Bolton ER, Dwinell MR. The Rat: A Model Used in Biomedical Research. Methods Mol Biol. 2019;2018:1–41.

[25] Pike ACW, Brzozowski AM, Walton J, Hubbard RE, Thorsell AG, Li YL, et al. Structural Insights into the Mode of Action of a Pure Antiestrogen. Structure. 2001;9(2):p145-153.

[26] Pettersen EF, Goddard TD, Huang CC, Couch GS, Greenblatt DM, Meng EC, et al. UCSF Chimera--a visualization system for exploratory research and analysis. J Comput Chem. 2004;25(13):1605–12.

[27] Wang X, Lai J, Xu F, Liu M. Network Pharmacology and Molecular Docking: Exploring the Mechanism of Peppermint in Mastitis Prevention and Treatment in Dairy Cows. Vet Sci. 2025;12(2):1–19.

[28] Bugnon M, Röhrig UF, Goullieux M, Perez MAS, Daina A, Michielin O, et al. SwissDock 2024: major enhancements for small-molecule docking with Attracting Cavities and AutoDock Vina. Nucleic Acid Res. 2024;52(W1):W324–W332.

[29] Eberhardt J, Santos-Martins D, Tillack AF, Forli S. AutoDock Vina 1.2.0: New Docking Methods, Expanded Force Field, and Python Bindings. J Chem Inf Model. 2021;61(8):3891–3898.

[30] Szklarczyk D, Nastou K, Koutrouli M, Kirsch R, Mehryary F, Hachilif R, et al. The STRING database in 2025: protein networks with directionality of regulation. Nucleic Acid Res. 2025;53(D1):D730–D737.

[31] Daina A, Michielin O, Zoete V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017;7(42717):1–13.

[32] Daina A, Michielin O, Zoete V. iLOGP: A Simple, Robust, and Efficient Description of n-Octanol/Water Partition Coefficient for Drug Design Using the GB/SA Approach. J Chem Inf Model. 2014;54(12):3284–301.

[33] Daina A, Zoete V. A BOILED-Egg To Predict Gastrointestinal Absorption and Brain Penetration of Small Molecules. ChemMedChem. 2016;11(11):1117–21.

[34] Filimonov DA, Lagunin AA, Gloriozova TA, Rudik A V., Druzhilovskii DS, Pogodin P V., et al. Prediction of the Biological Activity Spectra of Organic Compounds Using the Pass Online Web Resource. Chem Heterocycl Comp. 2014;50:444–57.

[35] El-Shehawi AM, Alkafafy M, El-Shazly S, Sayed S, Farouk S, Alotaibi S, et al. Moringa oleifera leaves ethanolic extract ameliorates high fat diet-induced obesity in rats. J King Saud Univ. 2021;33:101552–61.

[36] Kashyap P, Kumar S, Riar CS, Jindal N, Baniwal P, Guiné RPF, et al. Recent Advances in Drumstick (Moringa oleifera) Leaves Bioactive Compounds: Composition, Health Benefits, Bioaccessibility, and Dietary Applications. Antioxidants. 2022;11(402):1–37.

[37] Hamadou M, Bassogog CBB, Obadias FV, Assaly AD, Mune MAM. Moringa oleifera potential for the treatment and prevention of COVID-19 involving molecular interaction, antioxidant properties and kinetic mechanism. PLoS One [Internet]. 2025;20(12):e0337904. Available from: https://doi.org/10.1371/journal.pone.0337904

[38] Daeffler KNM, Lester HA, Dougherty DA. Functionally Important Aromatic-Aromatic and Sulfur-π Interactions in the D2 Dopamine Receptor. J Am Chem Soc. 2012;134(36):14890–14896.

[39] Gupta A, Hossain MM, Miller N, Kerin M, Callagy G, Gupta S. NCOA3 coactivator is a transcriptional target of XBP1 and regulates PERK–eIF2α–ATF4 signalling in breast cancer. Oncogene. 2016;35(45):5860–5871.

[40] Lebreton L, Boyer JC, Lafay-Chebassier C, Hennart B, Baklouti S, Cunat S, et al. French- Speaking Network of Pharmacogenetics (RNPGx) Recommendations for Clinical Use of Mavacamten. Clin Pharmacol Ther. 2024;117(2):387–98.

[41] Xu R, Wang F, Yang H, Wang Z. Action Sites and Clinical Application of HIF-1α Inhibitors. Molecules. 2022;27(11):3426–40.

[42] Choi MK, Son S, Hong M, Choi MS, Kwon JY, Lee J. Maintenance of Membrane Integrity and Permeability Depends on a Patched-Related Protein in Caenorhabditis elegans. Genetics. 2016;202(4):1411–1420.

[43] Walsh AA, Szklarz GD, Scott EE. Human Cytochrome P450 1A1 Structure and Utility in Understanding Drug and Xenobiotic Metabolism. J Biol Chem. 2013;288(18):12932–12943.

[44] Yuan J, Li Z, Yu Y, Wang X, Zhao Y. Natural Compounds in The Management of Polycystic Ovary Syndrome: a Comprehensive Review of Hormonal Regulation and Therapeutic Potential. Front Nutr. 2025;12:1520695.

[45] Shah MZ ul haq, Shrivastva V kumar, Mir MA, Sheikh WM, Ganie MA, Rather GA, et al. Effect of Quercetin on Steroidogenesis and Folliculogenesis in Ovary of Mice with Experimentally-Induced Polycystic Ovarian Syndrome. Front Endocrinol. 2023;14:1153289.

[46] Shah MZUH, Soni M, Shrivastava VK, Mir MA, Muzamil S. Gallic Acid Reverses Ovarian Disturbances in Mice with Letrozole-induced PCOS via Modulating Adipo R1 Expression. Toxicol Rep. 2022;20(9):1938–49.

[47] Peng F, Hu Y, Peng S, Zeng N, Shi L. Apigenin Exerts Protective Effect and Restores Ovarian Function in Dehydroepiandrosterone Induced Polycystic Ovary Syndrome Rats: a biochemical and Histological Analysis. Ann Med. 2022;54(1):578–87.

[48] Wu YX, Yang XY, Han BS, Hu YY, An T, Lv BH, et al. Naringenin Regulates Gut Microbiota and SIRT/PGC-1α signaling pathway in rats with letrozole-induced polycystic ovary syndrome. Biomed Pharmacother. 2022;153:113286.