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Comparative molecular docking study of selected phytochemicals from the genus *Hygrophila* for PCOD management

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Abstract
Polycystic Ovarian Disease (PCOD) is a complex endocrine disorder affecting millions of women worldwide, characterized by hormonal imbalances, metabolic dysfunction, and reproductive issues. Current therapeutic strategies often target symptoms, highlighting the need for novel, effective, and safer interventions. This study presents a comparative molecular docking analysis to evaluate the potential of selected phytochemicals from the *Hygrophila* genus as therapeutic agents for PCOD management. A comprehensive library of compounds previously isolated and identified from various *Hygrophila* species was screened against key protein targets implicated in PCOD pathogenesis, mainly on androgen receptors, insulin receptors, and enzymes involved in steroidogenesis. Molecular docking simulations were performed using a validated protocol to assess binding affinities, interaction profiles, and predicted inhibitory activities of the phytochemicals in comparison to known reference drug such as metformin. The results indicate that several *Hygrophila* phytochemicals exhibit promising binding interactions with high affinities for the targeted proteins, suggesting their potential to modulate hormonal pathways and inhibit the androgen action. This in silico investigation provides a foundation for further *in vitro* and *in vivo* studies to validate the therapeutic efficacy of these natural compounds in PCOD management.

Keywords: Polycystic ovarian disease, molecular docking, *hygrophila*, hyperandrogenism, phytochemicals

Introduction

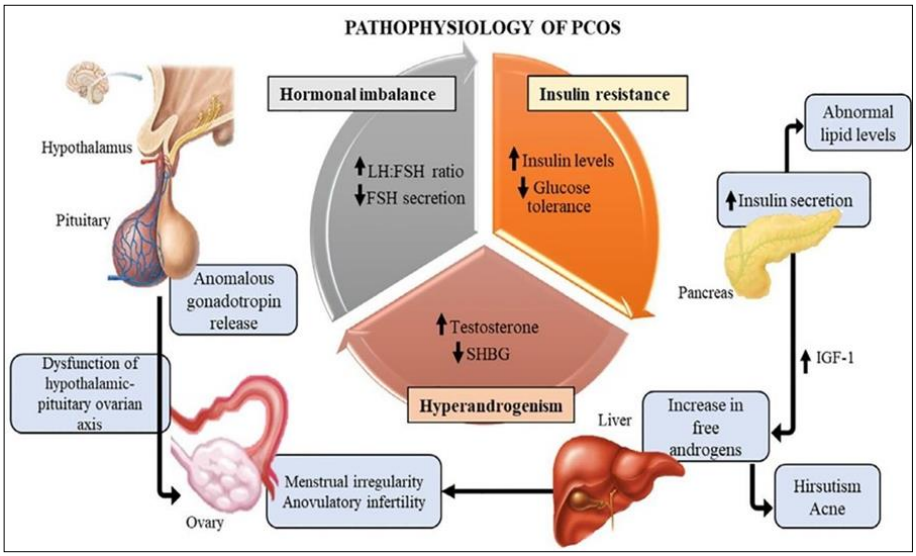
PCOD/PCOS is a pretty common endocrine disorder affecting 6-20% of women of reproductive age worldwide. It's got a range of symptoms like irregular periods, excess male hormones, and polycystic ovaries, plus metabolic issues like obesity, insulin resistance, and increased risk of diabetes and heart disease [1]. It also takes a toll on mental health, with anxiety, depression, and reduced quality of life being common. Basically, it's a complex condition that affects women's overall health and wellbeing [2].Polycystic ovarian syndrome (PCOS) is characterized by the presence of multiple small cysts along the ovarian perimeter. These polycystic ovaries exhibit an increased number of small cysts (<8 mm in size) and produce an abnormal number of follicles, with at least twice the normal quantity. However, the majority of these follicles fail to mature and release an egg, resulting in anovulation. The cysts are essentially follicles containing eggs that have not developed properly due to hormonal disturbances [3].

The global prevalence of PCOD/PCOS is significant, impacting approximately 10 million people worldwide. Current incidence rates are rising rapidly, attributed to factors like stress and lifestyle changes, with rates ranging from 3-10% globally, and varying by ethnicity and region. In India, prevalence rates differ across populations, with reported rates of: 18% in Tamil Nadu (Rotterdam criteria), 9-22% in Maharashtra and south India and 10.7% in south India. PCOD/PCOS is closely linked to metabolic syndrome, insulin resistance, and hyperinsulinism, highlighting its connection to lifestyle factors [4]. PCOD is classified as a syndrome rather than a disease due to its diverse symptomatology, influencing multiple disease processes concurrently. This condition has historically been subject to oversight and neglect [5].

Table 1: Causes and Symptoms of PCOD

Causes	Symptoms
1. Hormonal Dysregulation- Elevated levels of luteinizing hormone (LH) relative to follicle-stimulating hormone (FSH) and increase the androgen levels and Anti Müllerian hormone (AMH). 2. Genetic causes 3. long term metabolic complications such as type 2 diabetes, nonalcoholic fatty liver disease (NAFLD) 4. Environmental exposures such as bisphenol A (BPA), phthalates, and pesticides.[6-14]	▪ Acne, hirsutism, alopecia ▪ Insulin resistance ▪ Skin discoloration ▪ Insomnia ▪ Headache ▪ Weight gain ▪ Infertlity ▪ Menstrual Irregularities ▪ Diabetes

Pathophysiology of PCOD [14]



Molecular Docking

Computational tools, including molecular docking, dynamics simulations, and in silico ADME/Toxicity predictions, have become crucial in modern drug discovery. For two decades, they've streamlined identifying drug candidates by predicting protein-compound binding, understanding molecular interactions, and optimizing leads, thus reducing extensive lab testing. Molecular docking, in particular, rapidly identifies promising therapeutic agents from large libraries, predicting their stability and efficacy, which accelerates discovery, cuts costs, and enables exploring hard-to-synthesize compounds [15].

Combining traditional knowledge, phytochemical diversity, and computational tools like molecular docking offers a highly promising future for drug discovery. Many plant-derived compounds are already known for their significant medicinal properties. Some examples include apigenin, luteolin, ellagic acid, gallic acid, lupeol, phytol, lupenone, asterol, botulin and ellipticine.

Materials and Methods

Molecular Docking

Molecular docking is a computational method used to predict how two molecules, typically a ligand and a protein, will bind together to form a stable complex. It determines their preferred orientation, which then helps estimate the strength (binding affinity) of their association. As a key Structure-Based Drug Design (SBDD) technique, protein-ligand docking specifically mimics the binding of a ligand to a protein's active site. This process predicts the ligand's "pose" (orientation) within the binding site and assigns a score representing the binding strength. The insights gained from molecular docking, including binding energy, free energy, and complex stability, are invaluable for computer-assisted drug design and predicting ligand-receptor interactions [16].

Software used

- Chem sketch
- Argus 4.0.1
- Discovery studio
- Auto dock tools

Procedure [17, 18]

Protein Preparation

The proteins were obtained from Protein Data Bank (prefer more than 1.7A ^{0}) and downloaded. Import the protein file in discovery studio and the steps as to be followed,

- Delete Hetero atoms
- Remove ligand
- Finally, the protein saves as PDB file format.

Ligand Preparation

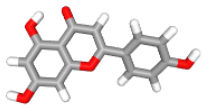
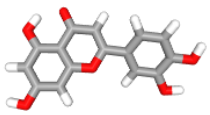
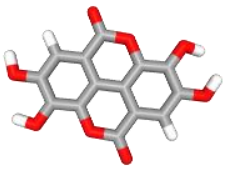
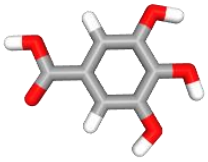
- The ligand was obtained from Pubchem software and downloaded 3D Confirmer SDF format.
- Then the ligand was opened in discovery studio and save as PDB file format.

Auto dock Procedure

1. Open Auto Dock, go to file, read molecule and open the protein
2. Go to edit option, click hydrogen and add polar only and ok.
3. Go to edit option, click charges, add kollmann charges and ok.
4. Go to Grid option, click macromolecule, choose and select the protein molecule and save the format for protein name-fix.pdbqt.
5. Go to ligand option, click input and open and turn to change pdb format, choose ligand and open.
6. Go to ligand option, click input, choose and select ligand, click selected molecule for autodock.
7. Go to edit option, click hydrogen and add polar only and ok.
8. Go to edit option, click charges, add computegasteiger and ok.
9. Go to ligand option, click torsion tree and click detect root (small ball formed in ligand)
10. Go to ligand option, click torsion tree and click set number of torsions and dismiss.
11. Go to ligand option, click torsion tree and click choose torsion and done.
12. Go to ligand option, click output and the file saves as ligand.pdbqt format.

13. Go to grid option, click macromolecule, choose protein, select molecule and ok, saves as protein name-fix.pdbqt.
14. Go to grid option, click set map types, choose ligand and select ligand.
15. Go to grid option, click grid box and adjust (protein and ligand covered by grid box), and go to file and click close saving current.
16. Go to grid option and click output, save gpf in the format of protein name-fix-ligand.gpf.
17. Go to grid option, select grid box and click file, select output grid dimension file and save as grid.txt format, and click close saving current
18. Go to docking option, select macromolecule and click rigid file and choose protein-fix.pdbqt format and open it.
19. Go to docking option, click ligand choose and select ligand and accept.
20. Go to docking option, select search parameter and click genetic algorithm and accept.
21. Go to docking option, select output and click Lamarckian GA and save in the format of protein name-fix-ligand.dpf.
22. Go to run option, select run autogrid, click second browse, select Autocrid 4 and open, click third browse and select already saved gpf file, open and launch.
23. Go to run option select run autogrid, click second browse, select Autodock 4 and open, click third browse and select already saved dpf file, open and launch.
24. After the completion, then close the autodock and open the DLG file in word format.
25. Click the current DLG file and check the docking score of the compounds, select the highest docking score and its run number.
26. Open Auto dock, go to analysis and click docking, open the DLG file.
27. Go to analysis and click macromolecule, open it.
28. Go to analysis and click confirmation and play, select the highest score number, select the symbol like this (&) and click write complex, saves in the format of protein name-fix-ligand.ring.pdbqt, close the auto dock.
29. Open discovery studio, select file and click new molecule window and minimize the discovery studio.
30. Select and drag the ring format for discovery studio.
31. Go to structure, click label and add amino acid.
32. In left side of discovery studio, click receptor ligand interaction and 2D diagram and save as the file.

Table 1: Phytoconstituents of Hygrophila species

S. No	Phytoconstituent [19-21]	Structure
1.	Apigenin	
2.	Luteolin	
3.	Ellagic acid	
4.	Gallic acid	

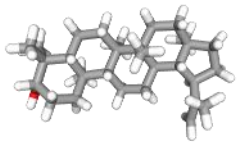
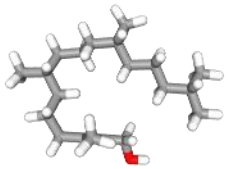
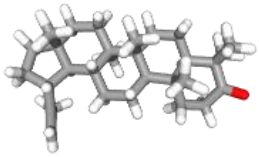
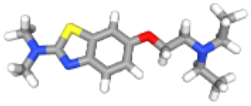
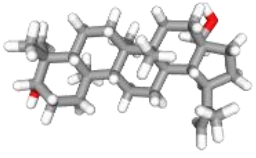
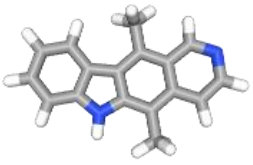
5.	Lupeol	
6.	Phytol	
7.	Lupenone	
8.	Asterol	
9.	Betulin	
10.	Ellipticine	

Table 2: Molecular formula, Molecular weight and Category of Phytoconstituents

S. No	Phytoconstituent	Molecular Formula	Molecular Weight	Category
1.	Apigenin	$C_{15}H_{10}O_5$	270.24 g/mol	Flavonoids
2.	Luteolin	$C_{15}H_{10}O_6$	286.24 g/mol	Flavonoids
3.	Ellagic acid	$C_{14}H_6O_8$	302.19 g/mol	Hetero tetracyclic compound
4.	Gallic acid	$C_7H_6O_5$	170.12 g/mol	Tri-hydroxybenzoic acid
5.	Lupeol	$C_{30}H_{50}O$	426.7 g/mol	Pentacyclic triterpenoid
6.	Phytol	$C_{20}H_{40}O$	296.5 g/mol	Diterpenoid
7.	Lupenone	$C_{30}H_{48}O$	424.7 g/mol	Triterpenoid
8.	Asterol	$C_{15}H_{23}N_3OS$	293.4 g/mol	Benzothiazoles
9.	Betulin	$C_{30}H_{50}O_2$	442.7 g/mol	Triterpenoid
10.	Ellipticine	$C_{17}H_{14}N_2$	246.31 g/mol	Alkaloid

Protein selected for docking studies

Androgen receptors

- 1E3G
- 1I37
- 1T5Z

Protein Information

1E3G

- **DOI:** https://doi.org/10.2210/pdb1E3G/pdb
- **Classification:** Androgen Receptor
- **Organism:** Homo sapiens
- **Expression System:** Escherichia coli BL21(DE3)
- **Mutation:** No
- **Deposited:** 2000-06-14
- **Released:** 2001-06-14
- **Depositing authors:** Matias, P.M., Donner, P., Coelho, R.,

Experimental Data Snapshot

- **Method:** X-Ray Diffraction
- **Resolution:** 2.40 Å
- **R- Value free:** 0.297
- **R- Value work:** 0.210
- **R- Vale observed:** 0.210

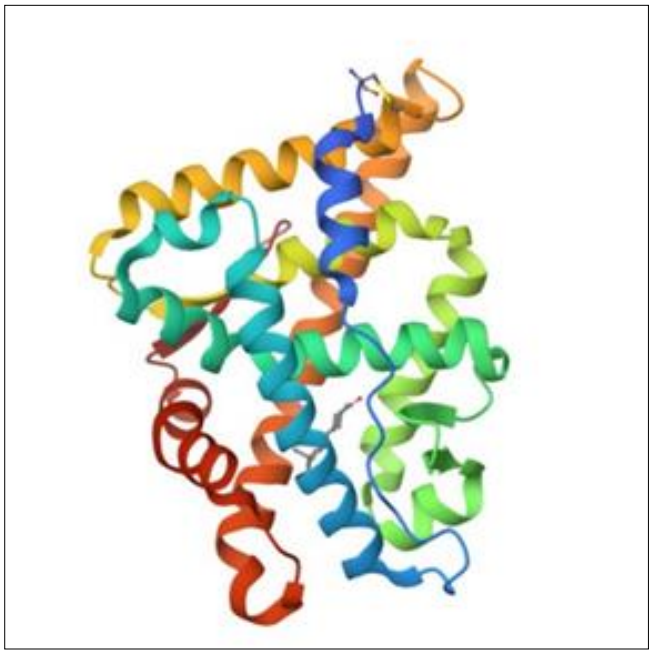


Fig 1: Structure of 1E3G protein

1I37

- **DOI:** https://doi.org/10.2210/pdb1I37/pdb
- **Classification:** Hormone/ Growth factor
- **Organism:** Rattus norvegicus
- **Expression System:** Escherichia coli BL21(DE3)
- **Mutation:** No
- **Deposited:** 2001-02-13
- **Released:** 2001-03-21
- **Depositing authors:** Sack, J.S.

Experimental Data Snapshot

- **Method:** X-Ray Diffraction
- **Resolution:** 2.00 Å
- **R- Value free:** 0.312
- **R- Value work:** 0.242

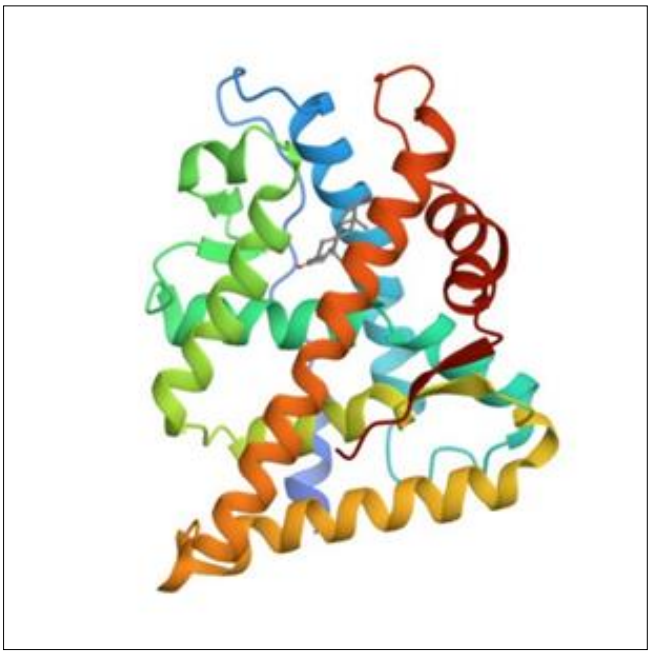


Fig 2: Structure of 1I37 Protein

1T5Z

- **DOI:** https://doi.org/10.2210/pdb1T5Z/pdb
- **Classification:** Hormone/ Growth factor
- **Organism:** Homo sapiens
- **Expression System:** Escherichia coli
- **Mutation:** No
- **Deposited:** 2004-05-05
- **Released:** 2005-01-25
- **Depositing authors:** Estebanez-Perpina, E., Moore, J.M.R., Mar, E.,

Experimental Data Snapshot

- **Method:** X-Ray Diffraction
- **Resolution:** 2.30 Å
- **R- Value free:** 0.260
- **R- Value work:** 0.228

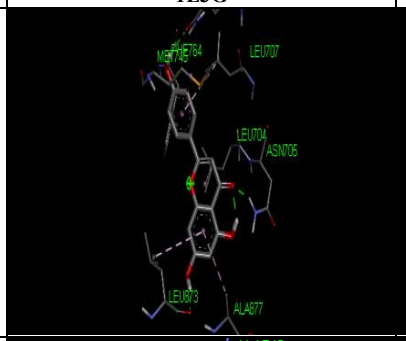
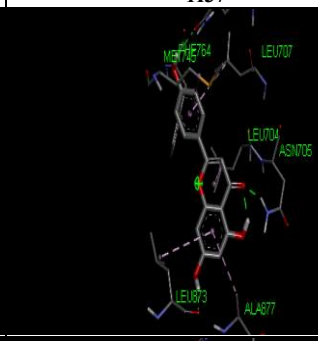
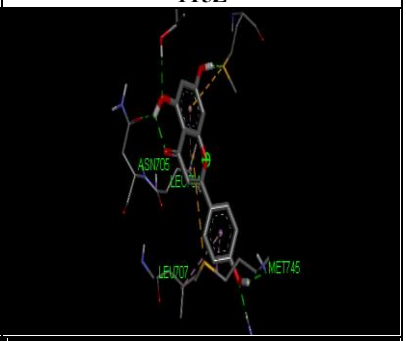
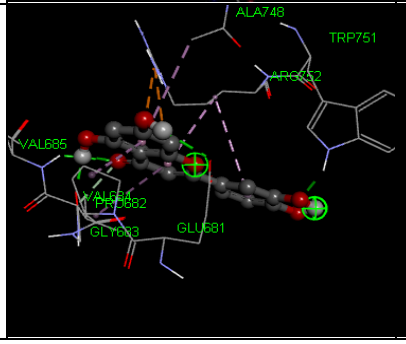
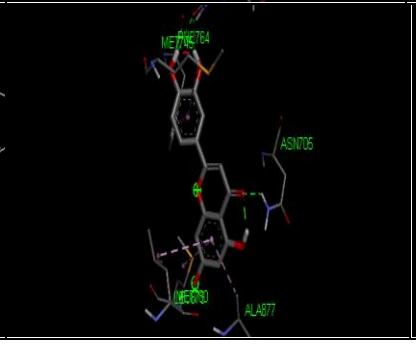
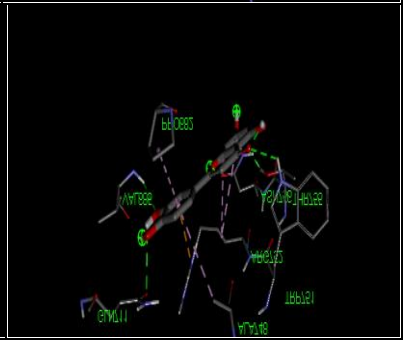
Fig 3: Structure of 1T5Z Protein

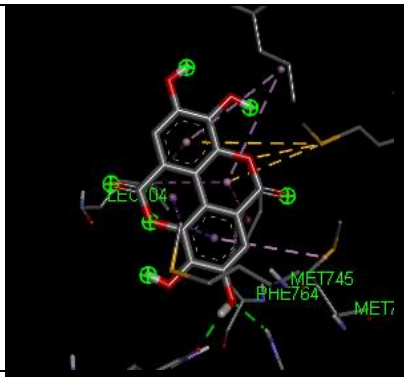
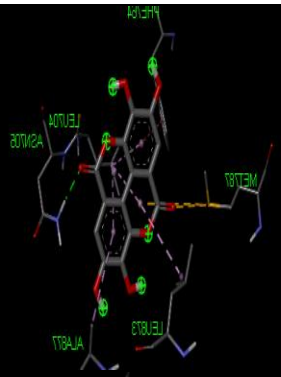
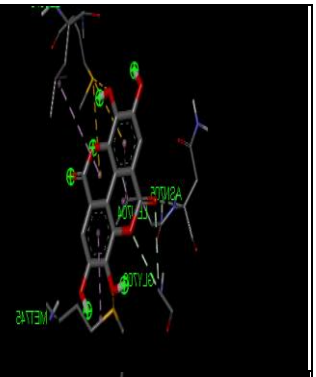
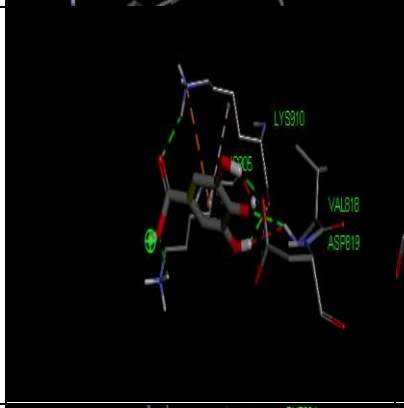
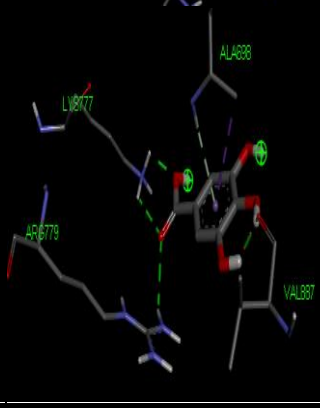
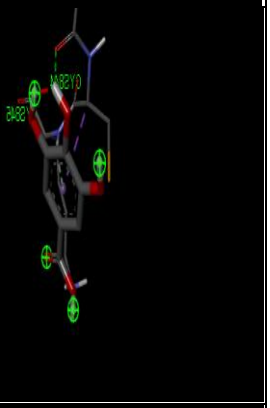
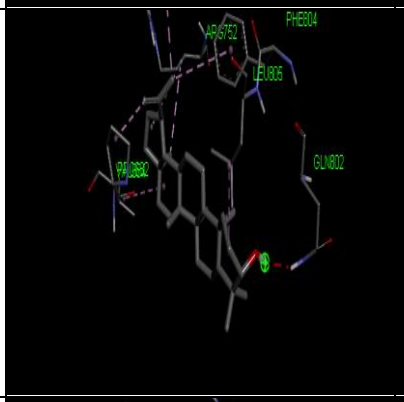
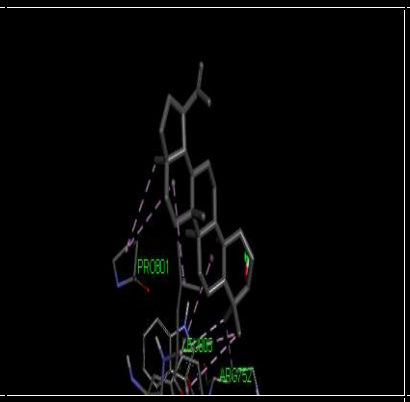
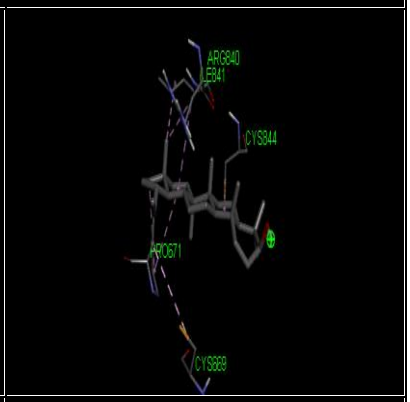
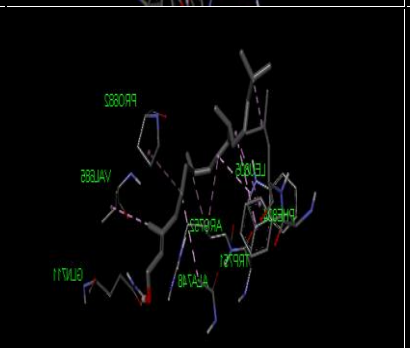
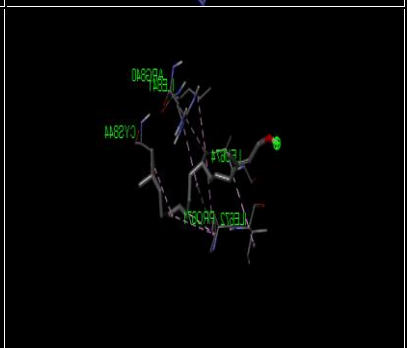
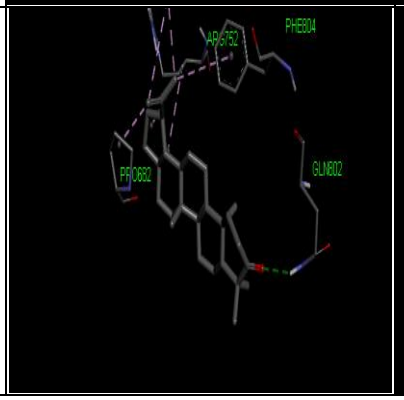
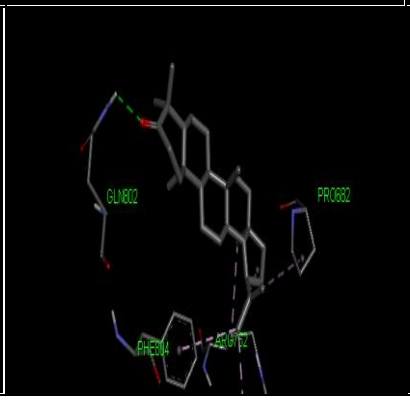
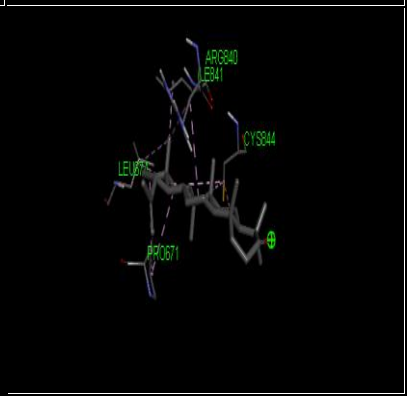
Results

Table 3:

S. No	Phytoconstituents			
		1E3G	1I37	1T5Z
1.	Apigenin	-10.403	-9.973	-8.753
2.	Luteolin	-8.160	-10.136	-7.775
3.	Ellagic acid	-10.258	-9.496	-9.144
4.	Gallic acid	-7.537	-7.614	-6.527
5.	Lupeol	-7.948	-8.109	-7.802
6.	Phytol	-9.203	-9.139	-7.681
7.	Lupenone	-8.621	-8.568	-7.813
8.	Asterol	-7.463	-6.995	-7.314
9.	Betulin	-8.246	-8.227	-7.291
10.	Ellipticine	-8.944	-8.074	-8.175
11.	Metformin (Standard)	-5.645	-4.958	-4.086

Table 4: Protein Ligand Interaction

Phytoconstituent	1E3G	1I37	1T5Z
Apigenin			
Luteolin			

Ellagic acid			
Gallic acid			
Lupeol			
Phytol			
Lupenone			

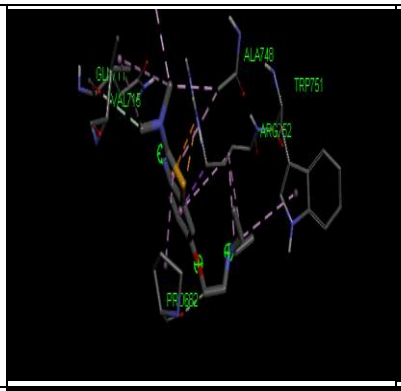
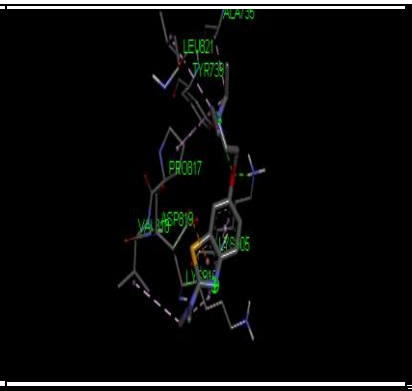
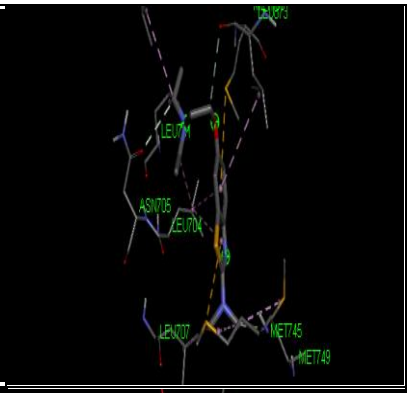
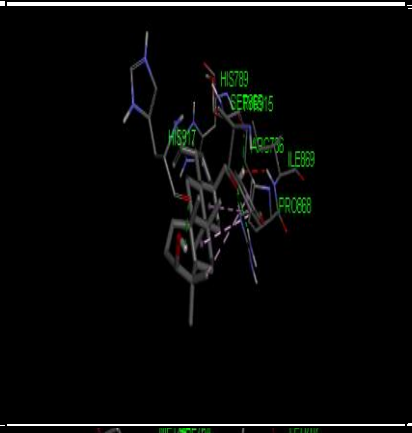
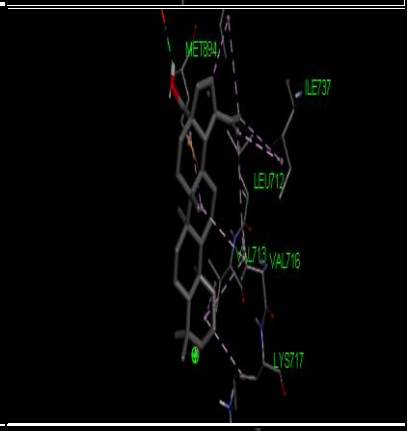
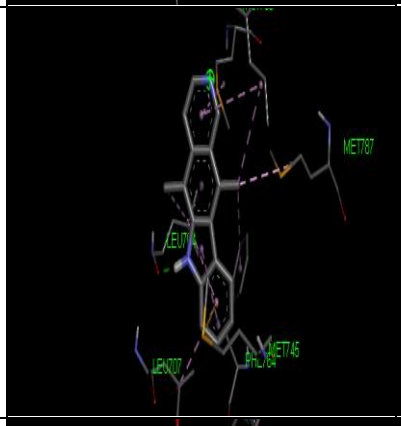
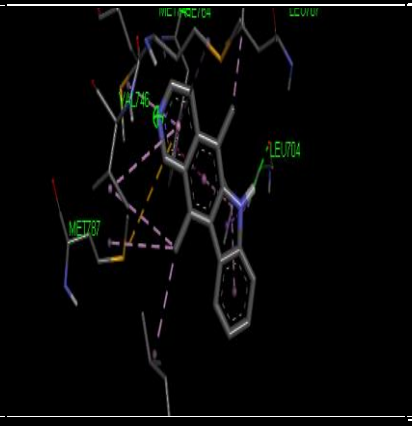
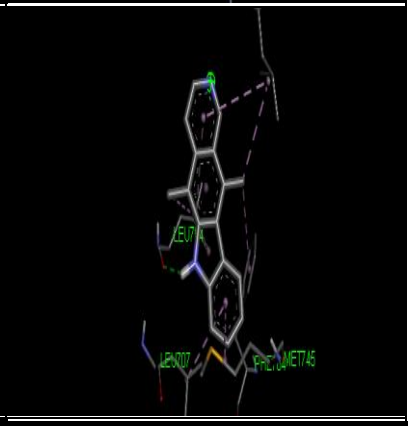
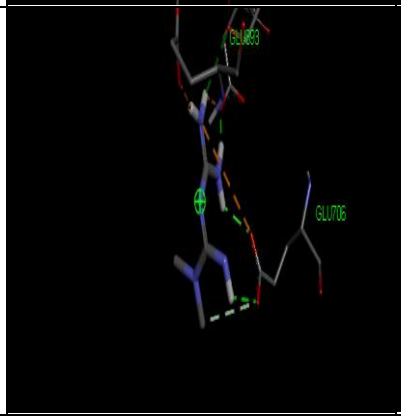
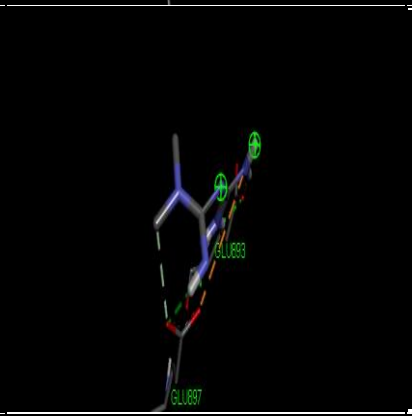
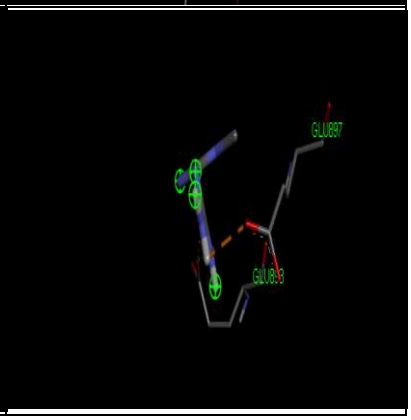
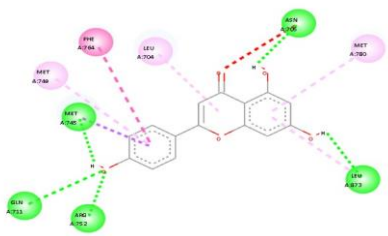
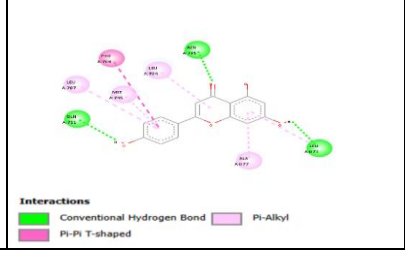
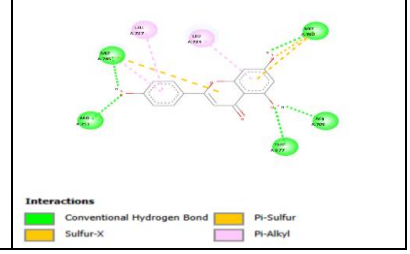
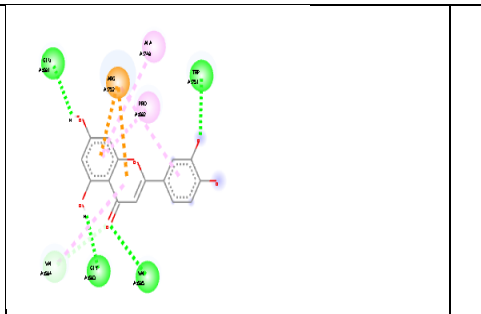
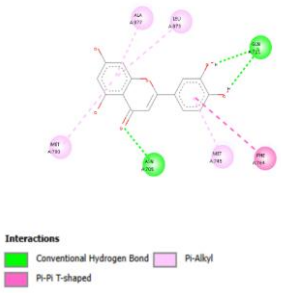
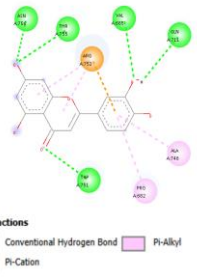
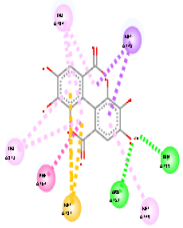
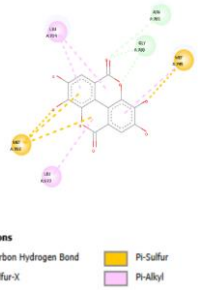
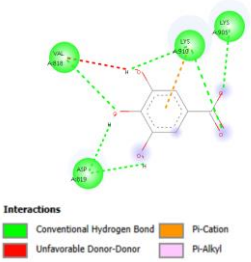
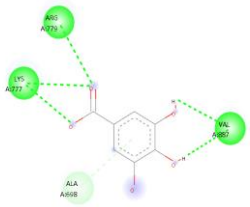
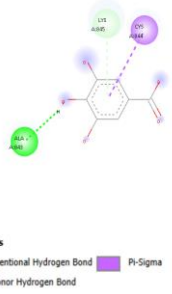
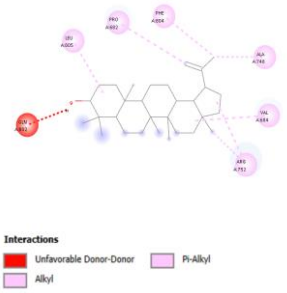
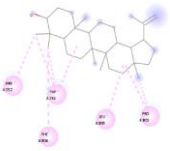
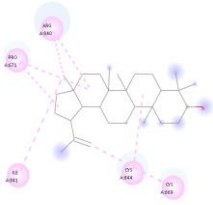
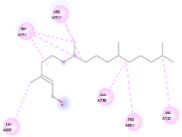
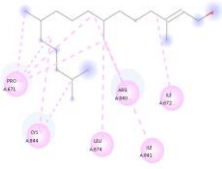
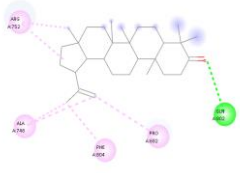
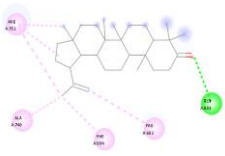
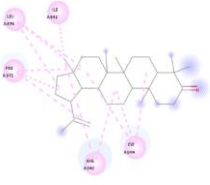
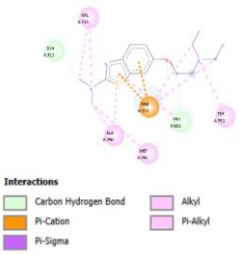
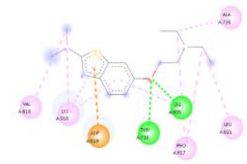
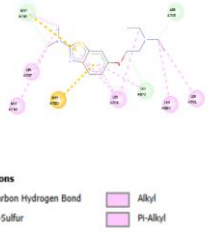
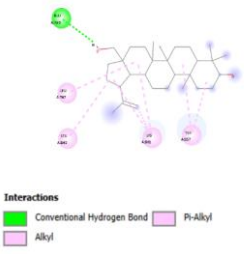
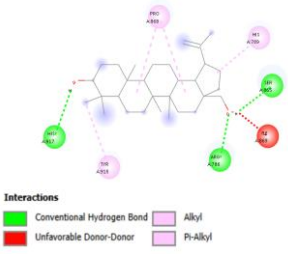
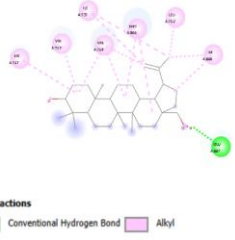
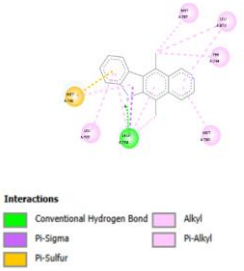
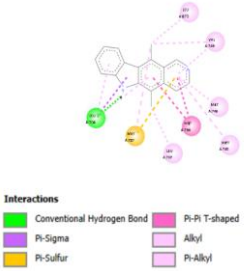
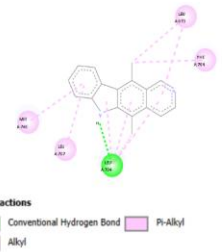
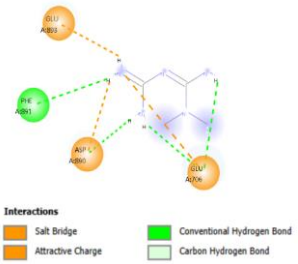
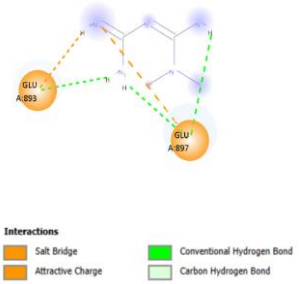
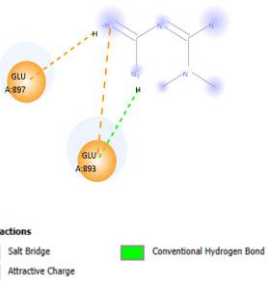
Asterol			
Betulin			
Ellipticine			
Metformin (Standard)			

Table 5: Amino acids binding site of the ligand

Ligand	1E3G	1I37	1T5Z
Apigenin			

Luteolin			
Ellagic acid			
Gallic acid			
Lupeol			
Phytol			
Lupenone			

Asterol			
Betulin			
Ellipticine			
Metformin (Standard)			

Discussion

The present study employed a comprehensive molecular docking approach to investigate the therapeutic potential of selected phytochemicals from the *Hygrophila* genus against key protein targets such as 1E3G, 1I37 and 1T5Z involved in Polycystic Ovarian Disease (PCOD) pathogenesis. Our findings reveal that several identified *Hygrophila* compound s exhibit significant binding affinities and favorable interaction profiles with critical PCOD-related proteins, suggesting their mechanistic potential in managing this complex disorder.

Specifically, the high binding affinities observed for certain *Hygrophila* phytochemicals against androgen receptors are particularly noteworthy. PCOD is often characterized by hyperandrogenism, which contributes to symptoms like hirsutism and anovulation. The identification of compounds that can effectively bind to and potentially antagonize androgen receptors suggests a direct mechanism by which these natural products could mitigate androgen excess, similar to anti-androgenic drugs currently in use but potentially with fewer side effects. The detailed analysis of specific amino acid interactions further supports the stability and specificity of these binding events, offering insights into structure-activity relationships for future drug design.

The comparative analysis with known reference drugs further strengthens the plausibility of our findings. In several instances, the binding affinities of the *Hygrophila* phytochemicals such as apigenin, luteolin, ellagic acid, gallic acid, lupeol, phytol, lupenone, asterol, botulin and ellipticine were comparable to, or even surpassed, those of established PCOD therapeutics when docked against the same targets. This suggests that these natural compounds could offer novel scaffolds or lead molecules with potentially improved efficacy or reduced toxicity profiles. The in-silico nature of this study, however, necessitates caution in extrapolation. While docking provides valuable insights into potential interactions, it does not account for pharmacokinetic properties such as absorption, distribution, metabolism, and excretion (ADME), nor does it fully predict bioavailability or *in vivo* toxicity.

The identified lead compounds warrant further experimental validation through *in vitro* assays to confirm their binding, antagonistic, or agonistic activities against the targeted proteins. Subsequent cellular and animal model studies would be crucial to assess their pharmacokinetic profiles,

efficacy in modulating PCOD symptoms, and safety. Ultimately, this research contributes to the growing body of evidence supporting the exploration of traditional medicinal plants as rich sources for modern drug discovery, particularly for multifactorial diseases like PCOD where current treatments often fall short.

Conclusion

This comparative molecular docking study provides compelling evidence for the potential therapeutic role of selected phytochemicals from the *Hygrophila* genus in the management of Polycystic Ovarian Disease (PCOD). Our in-silico analysis demonstrated that several compounds derived from *Hygrophila* species exhibit significant binding affinities and favorable interaction profiles with three key molecular targets implicated in PCOD pathogenesis, specifically the androgen receptor.

The observed strong interactions suggest that these phytochemicals could effectively modulate hormonal imbalances. These findings are particularly encouraging given the ongoing need for novel, multi-target therapeutic options with potentially fewer side effects than current treatments. While further experimental validation is essential to confirm these predictions, this study successfully identifies promising lead compounds from the *Hygrophila* genus, paving the way for future *in vitro* and *in vivo* investigations into their efficacy and safety for PCOD management. This research underscores the valuable contribution of traditional medicinal plants to modern drug discovery efforts, offering a fresh perspective on natural product-based therapies for complex endocrine disorders.

Acknowledgments

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References

1. Azziz R, Woods KS, Reyna R, *et al*. The prevalence and features of the polycystic ovary syndrome in an unselected population. Journal of Clinical Endocrinology and Metabolism,2004:89(6):2745-2749.
2. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Human Reproduction Journal,2004:19(1):41-47.
3. Palvi M. Review of Polycystic Ovary Syndrome Along with Data Mining. IJSRD, 2018, 6.
4. Epidemology pathogenesis, genetic and management of polycystic ovarian syndrome in India. The Indian journal of medical research, Wolters Kluwer-Medknow publications, PMCID: PMC6902362,2019:150(4):333-344.
5. Papaioannou S, Tzafettas J. Anovulation with or without PCOD hyper-androgenaemia and hyper-insulinaemia as promoters of endometrial and breast cancer. Best Practice and Research: Clinical Obstetrics and Gynaecology, 2024, 19-27.
6. Sir-Petermann T, Hitchsfeld C, Maliqueo M, *et al*. Birth weight in offspring of mothers with polycystic ovarian syndrome. Human Reproduction,2005:20(8):2122-2126.
7. Teede HJ, Misso ML, Deeks AA, *et al*. Assessment and management of polycystic ovary syndrome: summary of an evidence-based guide line. The Medical Journal of Australia,2011:195(6):65-112.
8. Welt CK, Carmina E. Lifecycle of polycystic ovary syndrome (PCOS): from in utero to menopause. The Journal of Clinical Investigation,2013:98(12):4629-4638.
9. Palomba S, de Wilde MA, Falbo A, *et al*. Pregnancy complications in women with polycystic ovary syndrome. Human Reproduction Update,2015:21(5):575-592.
10. Macut D, Simic T, Lissounov A, *et al*. Insulin resistance in non-obese women with polycystic ovary syndrome: relationship with adipocytokines. European Journal of Endocrinology,2011:164(6):873-878.
11. Rutkowska AZ, Diamanti-Kandarakis E. Poly cystic ovary syndrome and environmental toxins. Fertility and Sterility Journal,2016:106(4):948-958.
12. Kandaraki E, Chatzigeorgiou A, Livadas S, *et al*. Endocrine disruptors and polycystic ovary syndrome (PCOS): elevated serum levels of bisphenol A in women with PCOS. Journal of Clinical Endocrinology and Metabolisn,2011:96(3):E480-484.
13. Sharvi, Gupta S, Umang. Etiology of Polycystic Ovarian Disease (PCOD): Systematic Review. International Journal of Toxicological and Pharmacological Research,2025:15(1):82-87.
14. Suokhrie K, Julitta K, Pachuau L, Ramdinpuii CL. Polycystic Ovarian Disease (PCOD): A Review Article. International Journal of Research and Analytical Reviews,2023:10(4):695-701.
15. Kaushik A, Kaushik JJ, Lal N. Phytochemicals and Molecular Docking: A Futuristic Approach for Drug Discovery. Trends in Pharmacology and Toxicology,2025:1(1):49-55.
16. Nagavalli D, Nishvanth F, Jaikrishna T. In-silico studies of *Abutilon indicum* phytoconstituents in anti-viral activity. World Journal of Pharmacy and Pharmaceutical Sciences,2024:13(3):713-734.
17. Rizvi SMD, Shakil S, Haneef M. A simple click by click protocol to perform docking: AutoDock 4.2 made easy for non-bioinformaticians. EXCLI Journal Experimental and Clinical Sciences,2013:23(12):831-857.
18. Pal S, Chaudhary M, Kala K. Autodock & Autodock Vina: Development, Capabilities, & Applications in Molecular Docking. International Journal of Pharmaceutical Sciences,2025:3(5):3005-3019.
19. Sethiya NK, Ahmed NM, Shekh RM, Kumar V, Singh PK, Kumar V. Ethnomedicinal, phytochemical and Pharmacological updates on *Hygrophila auriculata* (Schum.) Hiene: an overview. Journal of Integrative Medicine,2018:18:1-30.
20. Ravisankar M, Ester VCJ. Determination of bioactive compounds in *Hygrophila auriculata* leaf extract using GC-MS technique. International Journal of Chemical Studies,2017:5(3):729-733.
21. Srisat A, Kokate P. Fluorescence, Phytoconstituent screening, TLC and LC-MS analysis of *Hygrophila auriculata* from Akola region (MS), India. Vyomhansjournals.
DOI: https://doi.org/10.34256/adbor.25.23.183.