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Evaluation of the Phytotherapeutic Potential of the Passiflora Species in the Management of PCOD Symptoms

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ABSTRACT

Polycystic Ovary Disease (PCOD) is a common endocrine and metabolic disorder in reproductive- aged women, often managed with pharmacological agents that carry adverse effects. This study evaluates the phytotherapeutic potential of *Passiflora foetida* and *Passiflora incarnata* ethanolic extracts in a letrozole-induced PCOD rat model. Aerial parts of both species were extracted using ethanol, and PCOD was induced in female Wistar rats (n = 30) through oral administration of letrozole (1 mg/kg/day for 21 days). Animals were assigned to five groups: normal control, disease control, metformin-treated (300 mg/kg), *P. foetida* (300 mg/kg), and *P. incarnata* (300 mg/kg), followed by a 28-day treatment period. Serum levels of LH, FSH, and testosterone were measured alongside body weight and histopathological assessments of the ovary, uterus, and liver. Molecular docking and ADMET analysis were also performed on key phytoconstituents. Treatment with both *Passiflora* species significantly restored hormonal balance ($p < 0.001$), reduced pathological weight gain, and improved histoarchitecture, with *P. foetida* demonstrating superior efficacy. Docking results revealed high binding affinities for vitexin (−9.83 kcal/mol) and luteolin (−9.53 kcal/mol), surpassing that of metformin (−5.43 kcal/mol), while ADMET predictions indicated favorable absorption and safety profiles. These findings support the therapeutic potential of *Passiflora* species—particularly *P. foetida*—as natural alternatives for PCOD management, warranting further clinical investigation.

Keywords: *Passiflora foetida, Passiflora incarnata, PCOD, phytotherapy, molecular docking*

1. INTRODUCTION

Polycystic Ovary Disease (PCOD), also referred to as Polycystic Ovary Syndrome (PCOS), is a widespread endocrine-metabolic disorder affecting women of reproductive age, with a global prevalence of approximately 8–13%.[2] In India, especially in urban regions, this prevalence is notably higher due to sedentary lifestyles, dietary habits, and increased stress levels. The condition is primarily characterized by hyperandrogenism, chronic anovulation, polycystic ovaries, insulin resistance, and obesity.[4] These clinical manifestations not only contribute to infertility and irregular menstrual cycles but also elevate the risk of long-term complications such as type 2 diabetes, cardiovascular disease, and endometrial carcinoma.

Current therapeutic strategies for PCOD include hormonal contraceptives, insulin sensitizers like metformin, anti-androgens, and ovulation-inducing agents such as clomiphene citrate. However, these treatments are often accompanied by adverse effects, poor patient compliance, and limited long-term effectiveness.[3] This has driven the exploration of alternative therapeutic options, particularly those derived from plant-based sources with traditional and ethnomedicinal relevance.[6]

Passiflora species, commonly known as passion flowers, have a long history of medicinal use for their anxiolytic, anti-inflammatory, sedative, and antioxidant properties. [1,5,13,15] Among them, *Passiflora foetida* and *Passiflora incarnata* are known to contain bioactive flavonoids, glycosides, alkaloids, and phenolic compounds that may exert beneficial effects on

hormonal balance, inflammation, and oxidative stress—all of which are implicated in the pathophysiology of PCOD.

[5,6,14]

The present study was designed to investigate and compare the phytotherapeutic potential of ethanolic extracts of *P. foetida* and *P. incarnata* in a letrozole-induced rat model of PCOD. The study includes a comprehensive evaluation of hormonal profiles, histopathological alterations, body weight regulation, and molecular docking and ADMET analysis of key phytoconstituents. This research aims to provide evidence-based validation of *Passiflora* species as natural, effective, and safer alternatives for the management of PCOD.

2. METHODOLOGY

Plant Material Collection and Authentication: The aerial parts of *Passiflora foetida* and

Passiflora incarnata were collected from various regions in and around Bengaluru, Karnataka, India. Botanical authentication was carried out at the Foundation for Revitalization of Local Health Traditions (FRLHT), Bengaluru. Voucher specimens were deposited in the departmental herbarium for future reference.[11]

Extraction Procedure: The collected plant materials were shade-dried for 10 days and coarsely powdered using a mechanical grinder. The powdered material (100 g) of each species was subjected to Soxhlet extraction using 70% ethanol for 6–8 hours. The extracts were filtered, concentrated under reduced pressure using a rotary evaporator, and dried at 40°C to obtain a semisolid mass. Extracts were stored in airtight containers under refrigeration until further use.[10] **Preliminary Phytochemical Screening:** Standard qualitative tests were conducted on the ethanolic extracts to identify major classes of phytoconstituents including alkaloids (Mayer's and Dragendorff's test), flavonoids (Shinoda test), tannins and phenolics (Ferric chloride test), glycosides (Keller–Killiani test), saponins (foam test), and steroids (Salkowski's test).[7,8,9] **Animals and Ethical Approval:** Thirty adult female Wistar albino rats (weighing 160–240 g) were procured and acclimatized under standard laboratory conditions: 12-hour light/dark cycle, temperature 22 ± 2°C, and free access to standard pellet diet and water. All experimental procedures were approved by the Institutional Animal Ethics Committee (Ref No: XXXI/MSRFPH/COG/UG-GP-21/27.02.2025) in accordance with CPCSEA guidelines.

Acute Oral Toxicity Study: An acute oral toxicity study was conducted as per OECD guideline

423. A separate set of female Wistar rats (n = 6) were administered the *Passiflora* extracts orally at a limit dose of 2000 mg/kg and observed continuously for 4 hours, then daily for 14 days for signs of toxicity, behavioral changes, and mortality. No signs of toxicity or mortality were recorded, confirming the safety of the extracts at the tested dose.

Induction of PCOD: Polycystic Ovary Disease was induced by administering letrozole orally at a dose of 1 mg/kg body weight once daily for 21 days. Induction was confirmed through estrous cycle monitoring and hormonal analysis.

Experimental Design: The rats were randomly divided into five groups (n = 6 per group):

- Group I: Normal control (no letrozole, no treatment)
- Group II: Disease control (letrozole only)
- Group III: Standard treatment (Metformin 300 mg/kg orally)
- Group IV: Test group (*P. foetida* extract 300 mg/kg orally)
- Group V: Test group (*P. incarnata* extract 300 mg/kg orally)

Treatments were administered orally once daily for 28 consecutive days.

Evaluation Parameters: At the end of the treatment period, body weight was recorded, and blood samples were collected via retro-orbital puncture under light anaesthesia. Serum was separated and stored at −20°C until hormonal analysis. The following ELISA kits were used:

- Rat Testosterone (T) ELISA Kit: Cusabio, Catalogue No. CSB-E05100r, Batch No. CUS- T-254154, Manufactured on January 20, 2025, Expiry Date: March 10, 2026.
- Rat FSH (Follicle Stimulating Hormone) ELISA Kit: Fine Test, Catalogue No. ER0960, Batch No. FT-FSH-254963, Manufactured on July 1, 2024, Expiry Date: August 25, 2025.
- Rat Luteinizing Hormone (LH) ELISA Kit: Cusabio, Catalogue No. CSB-E06870r, Batch No. CUS-LH-269874, Manufactured on May 1, 2025, Expiry Date: September 20, 2026.

Hormonal concentrations were quantified following the manufacturer's instructions. Rats were then sacrificed, and ovaries, uteri, and livers were dissected and preserved in 10% formalin for histopathological evaluation under a light microscope. At the end of the experimental trial, the three organs—liver, ovary, and uterus—were excised from each rat and flushed with

physiological saline. The collected tissues were fixed in 10% buffered formalin (pH 7.4) for 24–48 hours. Following fixation, samples were processed by sequential dehydration in ethanol, clearing in xylene, and infiltration with paraffin wax. Tissue blocks were sectioned at 4 µm thickness using a microtome (Leica RM 2125, Leica Microsystems GmbH, Wetzlar, Germany). The sections were mounted on clean glass slides, stained with haematoxylin and eosin, and then cover slipped using DPX mounting medium (S.D. Fine-Chem Ltd., Bengaluru, Karnataka, India). Prepared slides were examined and photographed under a light microscope (Labomed Lx-300) equipped with a camera (SJM-200C).

Molecular Docking Studies: Key phytoconstituents identified in literature (*e.g.*, vitexin, luteolin) were subjected to molecular docking using Schrödinger Maestro software. Protein targets relevant to PCOD pathophysiology (e.g., aromatase, androgen receptor) were selected from the Protein Data Bank (PDB). Ligand structures were drawn using ChemDraw and optimized using LigPrep. Binding affinities (kcal/mol) were recorded, and ligand interactions visualized. [14,16]

ADMET Prediction: In silico ADMET profiling was performed using SwissADME and pkCSM tools. Parameters assessed included gastrointestinal absorption, hepatotoxicity, blood–brain barrier permeability, and clearance.[5]

Statistical Analysis: All results were expressed as mean ± standard deviation (SD). Statistical

significance was evaluated using one-way ANOVA followed by Tukey's post hoc test. A p-value

<0.05 was considered statistically significant. GraphPad Prism version 9.0 was used for data analysis.

3. RESULT

Phytochemical screening: Phytochemical screening revealed the presence of major classes of bioactive compounds such as flavonoids, glycosides, phenolics, alkaloids, and saponins in both *P. foetida* and *P. incarnata* extracts. These compounds are known for their endocrine modulating, antioxidant, and anti-inflammatory properties and may contribute to therapeutic benefits in PCOD.

[1,5,6,13]

Acute Oral Toxicity: No signs of toxicity or adverse behavioral changes were observed in the acute oral toxicity study conducted prior to the main experiment, indicating that both *Passiflora* extracts are safe at the tested doses. [3,6]

Body weight: Body weight, which increased notably in PCOD-induced rats, was significantly reduced following treatment with both extracts and metformin. The *P. foetida* group showed the greatest reduction in pathological weight gain, suggesting better metabolic regulation.[3] **Hormones:** Significant improvements in hormonal parameters were observed in the treatment groups. Compared to the disease control group, both extract-treated groups and the metformin group showed a marked decrease in testosterone levels and restoration of LH and FSH levels toward normal ranges ($p < 0.0001$).[4] Among the plant extracts, *P. foetida* demonstrated the most pronounced effect on hormonal normalization, closely matching metformin efficacy.

Table No 1: Serum Hormone Levels in Rats (Mean ± SD)

Sample / Treatment	LH (mIU/mL)	FSH (mIU/mL)	Testosterone (ng/mL)
Normal Control	2.41 ± 0.25	3.76 ± 0.29	3.90 ± 0.31
PCOD Control (Induced)	1.08 ± 0.12	1.64 ± 0.18	1.27 ± 0.12
Metformin (Standard)	2.25 ± 0.19	3.45 ± 0.30	2.94 ± 0.22
1 – *P. foetida*	1.85 ± 0.22	2.91 ± 0.28	2.48 ± 0.31
2 – *P. incarnata*	2.13 ± 0.25	3.12 ± 0.34	2.76 ± 0.27

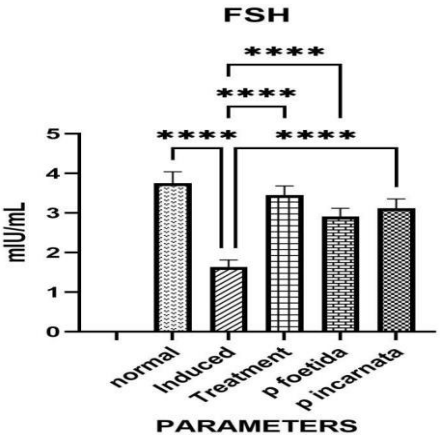


Fig No 1: Effect of treatments on serum follicle-stimulating hormone (FSH) levels.

Letrozole induction resulted in reduced FSH levels, which were significantly improved following treatment with metformin, *P. foetida*, and *P. incarnata* (**p < 0.0001), with *P. foetida* showing the most notable effect.**

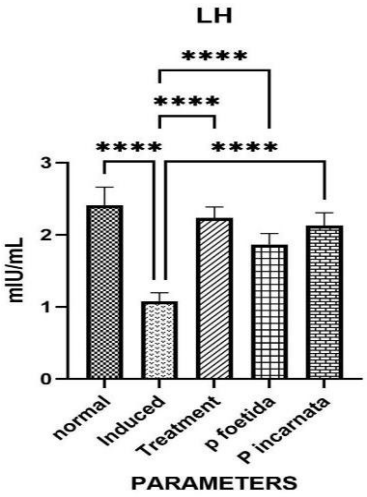


Fig No 2: Serum luteinizing hormone (LH) concentrations in experimental rats. LH levels were significantly increased in PCOD-induced animals and were restored toward normal in groups treated with metformin and both *Passiflora* extracts (**p < 0.0001).**

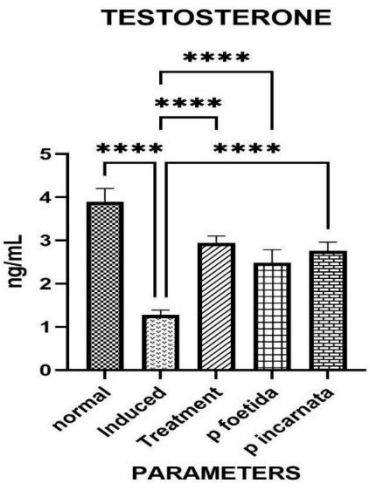


Fig No 3 Effect of *Passiflora foetida* and *Passiflora incarnata* extracts on serum testosterone levels in letrozole-induced PCOD rats. Treatment with both extracts significantly reduced elevated testosterone levels compared to the PCOD control group (**p < 0.0001). *P. foetida* exhibited a more pronounced reduction, comparable to metformin.**

Histopathology: Histopathological analysis supported these biochemical findings. In the disease control group, ovarian sections displayed multiple immature follicles, cystic formations, and disrupted stroma. Uterine tissues appeared atrophic with a thin endometrium, and the liver showed signs of fatty degeneration. In contrast, the extract-treated groups showed substantial tissue recovery. The *P. foetida* group demonstrated nearly normal ovarian folliculogenesis, improved endometrial thickness, and restored hepatic architecture, while the *P. incarnata* group showed moderate improvement. [6,15]

Rat Liver:

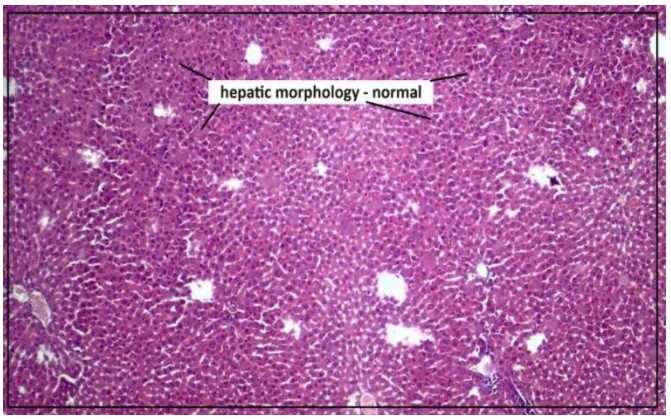


Fig No 4: Normal Control – Rat Liver: showing: hepatic morphology- normal, central vein (CV) & Portal vein (PV) – NAD+ (X50)

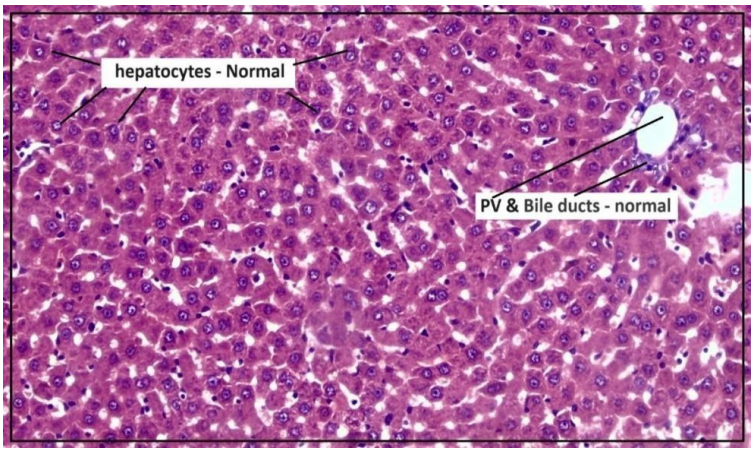


Fig No 5: Normal Control – Rat Liver: showing: hepatocytes - Normal, around Portal vein (PV)– normal Bile ducts - normal - NAD+ (X100)

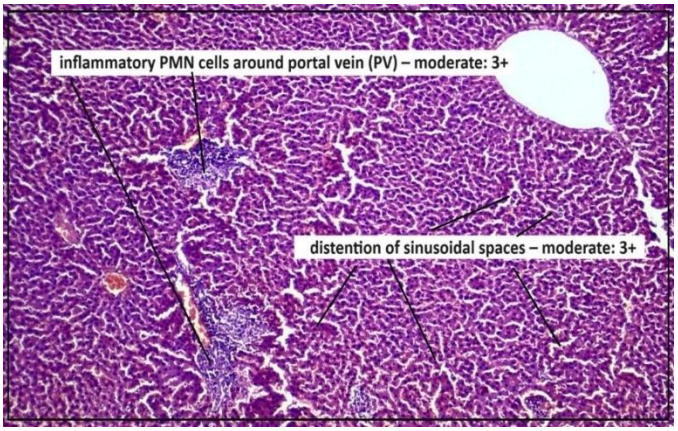


Fig No 6: Disease Control – Rat Liver: distention of sinusoidal spaces & inflammatory PMN cells around portal vein (PV) – moderate: 3+ (X50)

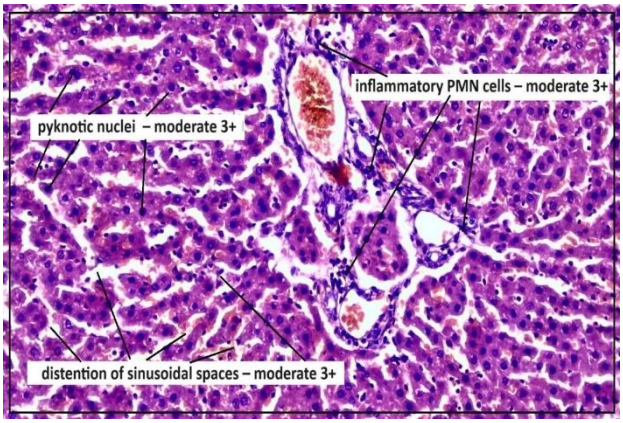


Fig No 7: Disease Control – Rat Liver: distention of sinusoidal spaces & pyknotic nuclei with inflammatory PMN cells around portal vein (PV) – moderate 3+ (X100)

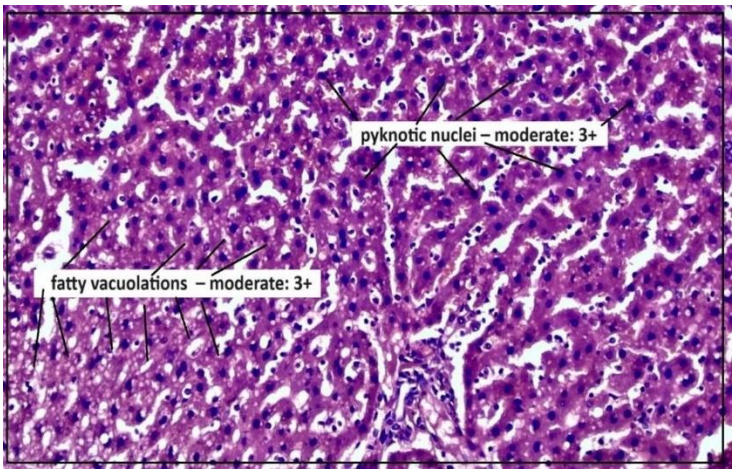


Fig No 8: Disease Control – Rat Liver: showing: fatty vacuolations & pyknotic nuclei – moderate: 3+ (X100)

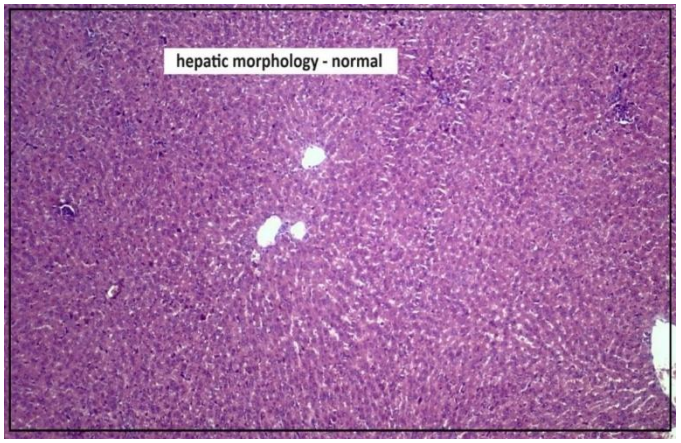


Fig No 9: Standard (Metformin) – Rat Liver: showing: hepatic morphology- normal, central vein (CV) & Portal vein (PV) – NAD+ (X50)

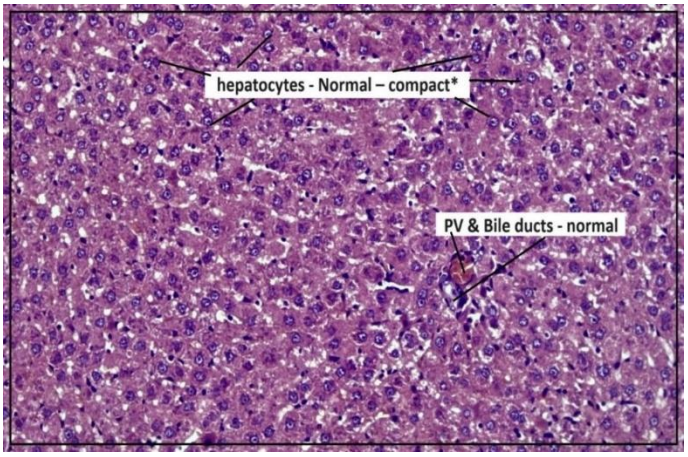


Fig No 10: Standard (Metformin) – Rat Liver: hepatocytes - Normal – compact*, around Portal vein (PV) – normal Bile ducts - normal - NAD+, fatty vacuolations – mild 2+ (X100)

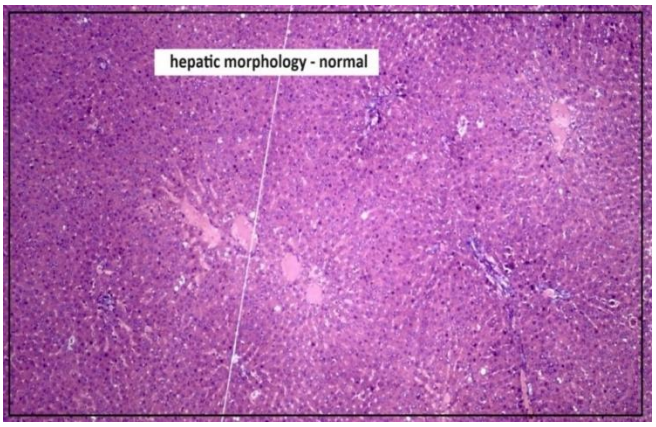


Fig No 11: Test Drug *Incarnata* treated – Rat Liver: showing: hepatic morphology- normal – NAD+, central vein (CV) & Portal vein (PV) – NAD+ (X50)

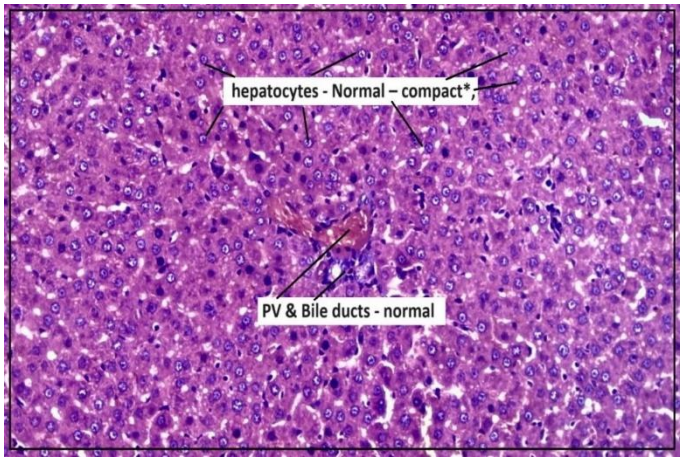


Fig No 12: Test Drug *Incarnata* treated – Rat Liver: showing: hepatocytes -Normal- normal– compact*, - NAD+, Portal vein (PV) Bile ducts - normal - NAD+ (X100)

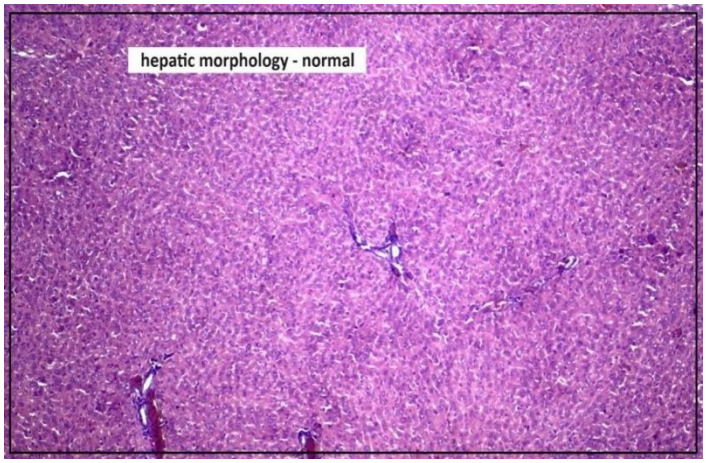


Fig No 13: Test Drug *Passiflora Foetida* treated – Rat Liver: showing: hepatic morphology- normal, central vein (CV) & Portal vein (PV) – NAD+ (X50)

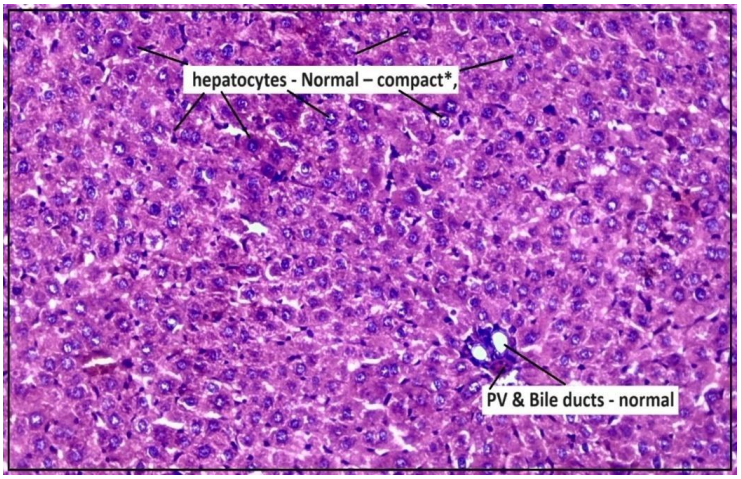


Fig No 14: Test Drug *Passiflora Foetida* treated – Rat Liver: showing: hepatocytes Normal – compact*, around Portal vein (PV) – normal Bile ducts - normal - NAD+ (X100)

Table No. 2: Liver/Drug response on PCOD Induced Liver

Group	**Histopathological findings Rat Liver**	**Scorings / gradation**
Normal Control	hepatic morphology- normal, hepatocytes, portal vein & bile duct – normal - NAD^+	NAD^+
Disease control Letrozole	distention of sinusoidal spaces & fatty vacuolations– moderate: 3+ pyknotic nuclei with inflammatory PMN cells around portal vein (PV) – moderate 3+	moderate 3+
Std - Metformin	Normal hepatocytes -– compact*, central vein (CV) - NAD^+ (Test Drug induced beneficial response*)	NAD^+ compact*
Test Drug – treated *Pasiflora incarnata*	hepatic morphology- normal, hepatocytes - compact*, portal vein & Bile ducts - normal - NAD^+ (Test Drug induced beneficial response*)	NAD^+ compact*

Test Drug – treated *Passiflora Foetida* Species	hepatic morphology- normal, hepatocytes – compact*, portal vein & bile duct – normal - NAD^+ (Test Drug induced beneficial response*)	NAD^+ compact*

Rat Ovary:

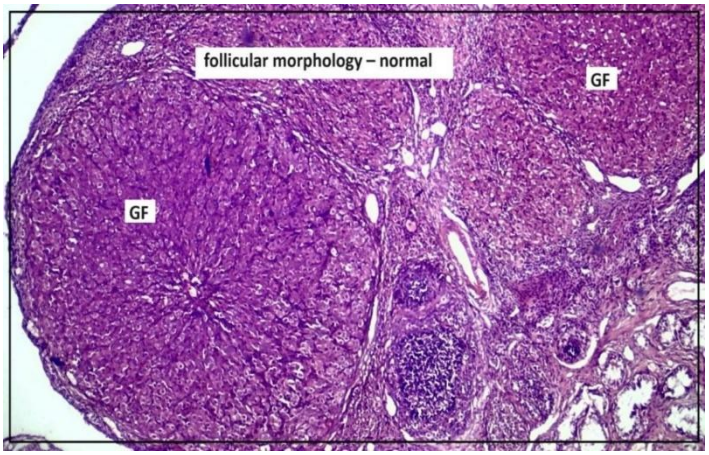


Fig No. 15: Normal Control - Rat Ovary: showing follicular morphology – normal - NAD* with Corpus Leuteum (CL) evident (X50)

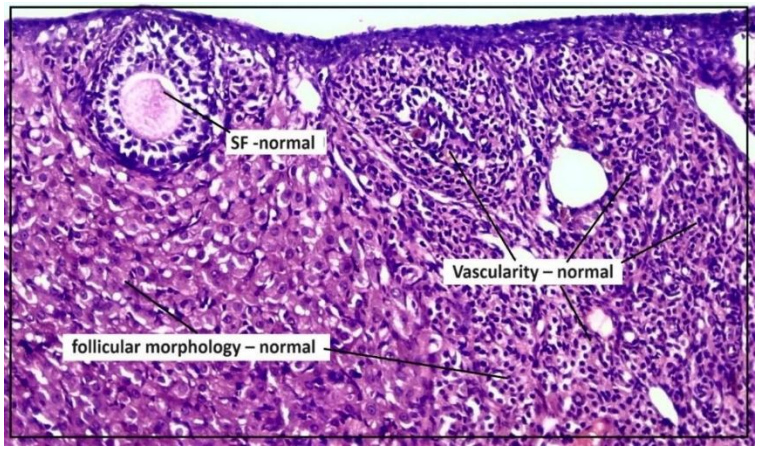


Fig No 16: Normal Control - Rat Ovary: showing follicular morphology – normal - NAD* with Vascularity – normal, Graafian Follicle (GF), secondary follicle (SF) (X100)

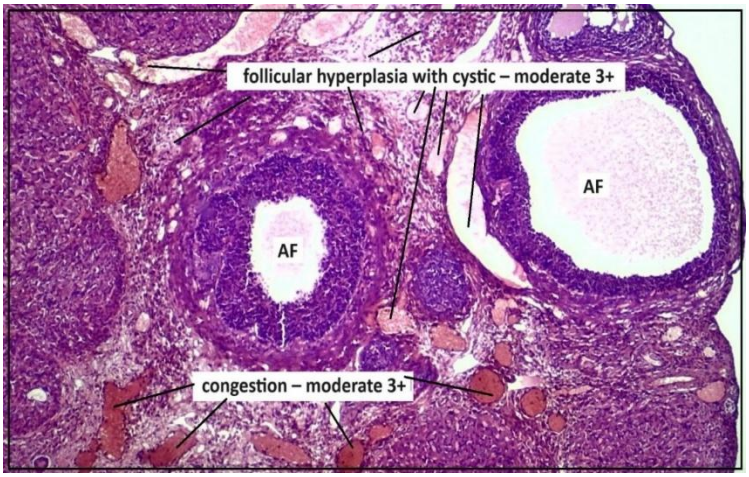


Fig No 17: Disease Control (Let – induced) Rat Ovary: showing the follicular hyperplasia with cystic & congestion – moderate 3+ Antral follicle (AF) (X50)

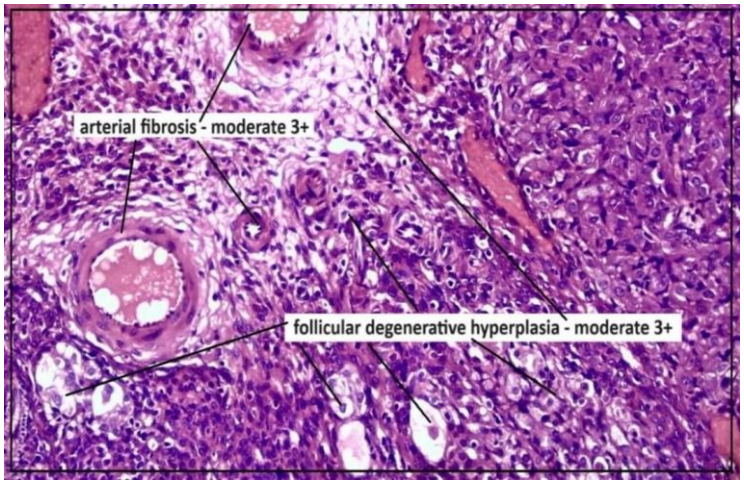


Fig No 18: Disease Control (Let – induced) Rat Ovary: showing follicular degenerative hyperplasia & arterial fibrosis - moderate 3+ (X100)

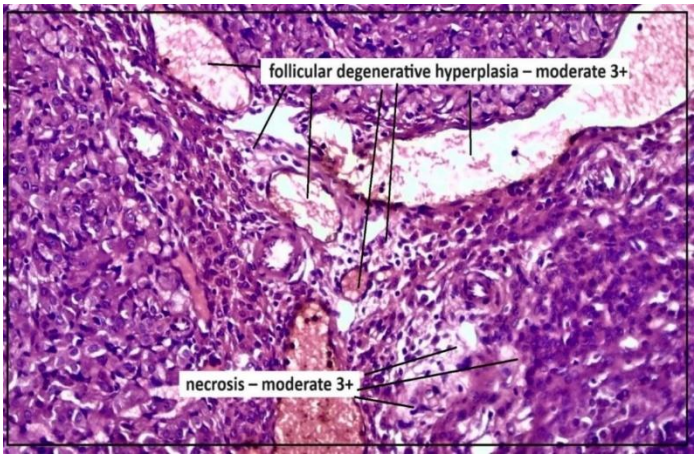


Fig No 19: Disease Control (Let – induced) Rat Ovary: showing follicular degenerative hyperplasia with necrosis – moderate 3+ (Degenerative changes*) (X100)

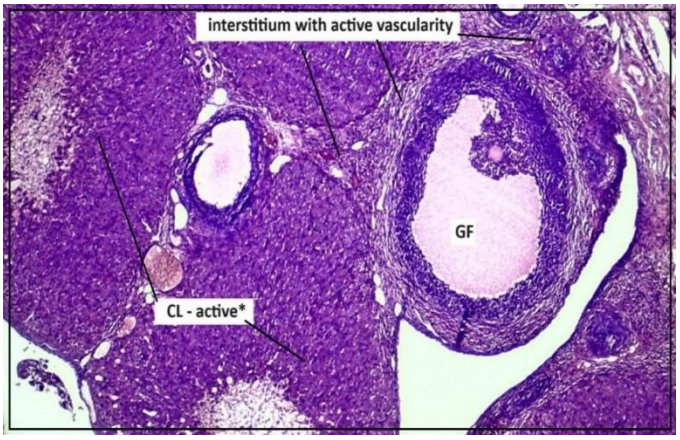


Fig No 20: Std – Metformin Rat Ovary: showing the presence of interstitium with active vascularity (X50) – corpus luteum (CL), & Graafian Follicle (GF) – Active*

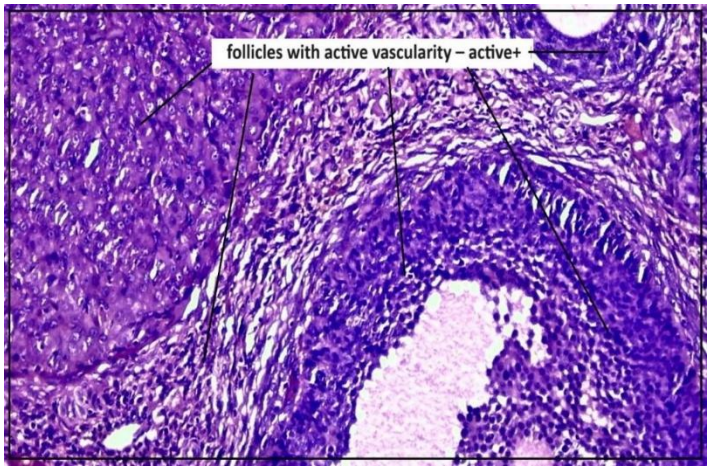


Fig No 21: Std – Metformin Rat Ovary: showing follicles with active vascularity – active+ (X100), Graafian Follicle (GF) secondary follicle (SF) – Active* (Drug induced beneficial response*)

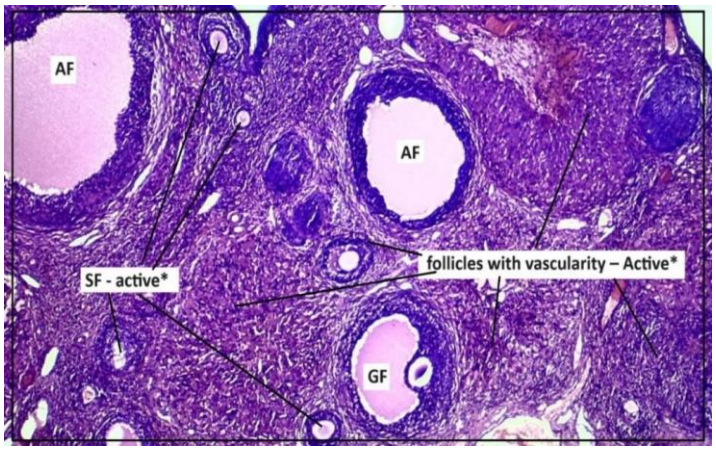


Fig No 22: Test dose - *Incarnata* treated Rat Ovary: showing follicles with vascularity – Active* Graafian Follicle (GF) secondary follicle (SF) Antral follicles (AF), (X50) corpus luteum (CL), evident

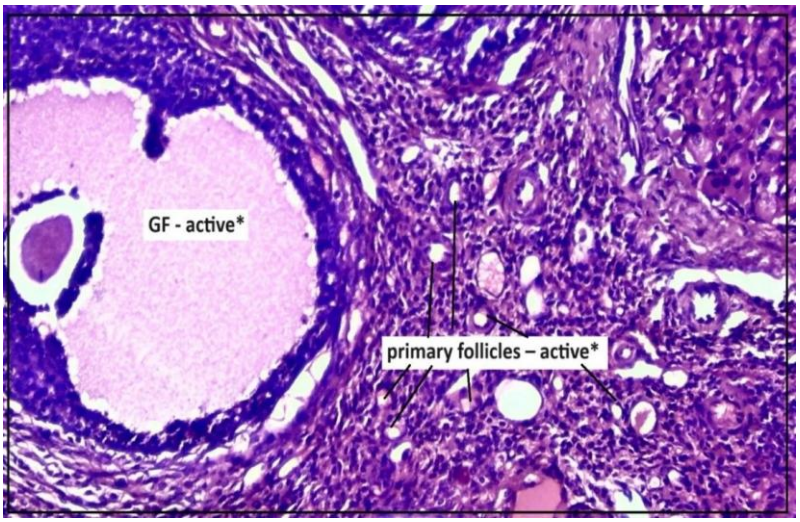


Fig No 23: Test dose - *Incarnata* treated Ovary: showing the presence of primary & secondary follicles – active* with interstitium active vascularity – moderate* (X100)

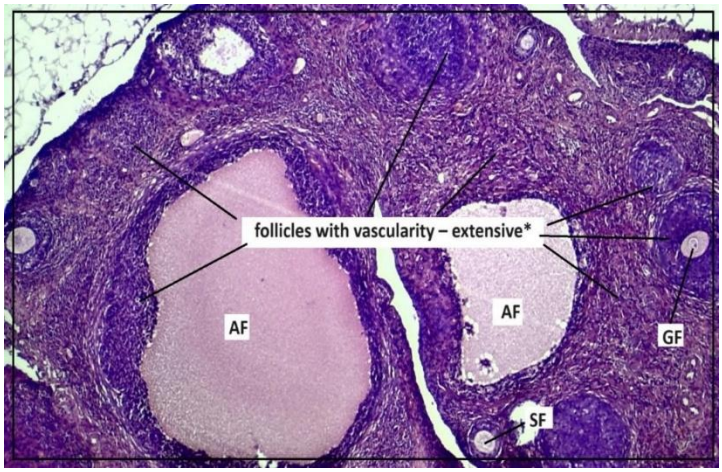
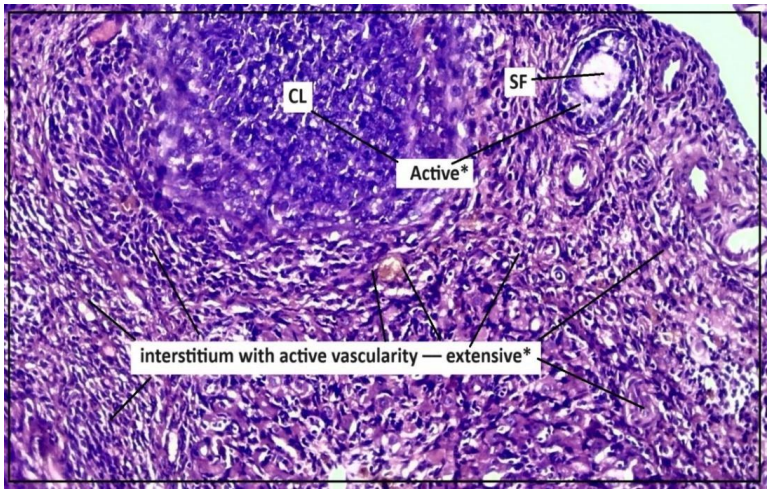


Fig No 24: Test- *Foetida* treated - Rat Ovary: showing the presence of follicles with active vascularity – extensive* (X50) corpus luteum (CL) secondary follicle (SF)



Group	**Histopathological findings Rat Ovary**	**Scorings / gradation**
Normal Control	follicular morphology – normal - NAD* with Corpus Leuteum (CL), secondary follicle (SF)	NAD+
Disease control Letrozole	follicular hyperplasia with cystic – moderate 3+ follicular degenerative hyperplasia & arterial fibrosis with congestion & necrosis – moderate 3+ (Degenerative changes)	moderate 3+
Std - Metformin	follicles & interstitium with active vascularity – moderate + secondary follicle (SF) Graafian Follicle (GF) – Active* (Drug induced beneficial response*)	Active*
Test Drug – treated *Passiflora Incarnata*	presence of primary & Secondary follicles – Active* with interstitium active vascularity – moderate*	Active* moderate*
Test Drug – treated *Passiflora Foetida*	the presence of follicles with active vascularity— extensive* Primary (PF) & Secondary follicle (SF) – active* interstitium with active vascularity — extensive* (Drug induced beneficial response*)	extensive* – active*

Rat Uterus:

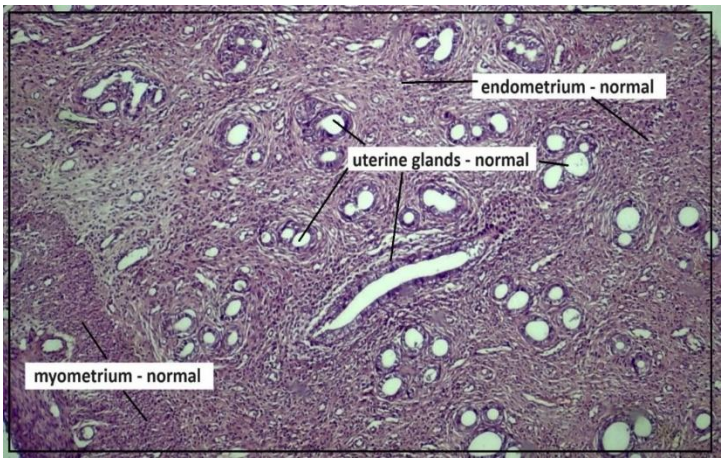


Fig No 26: Normal Control – Rat Uterus: showing uterine glands with endometrium & myometrium - normal- NAD+ evident (X50)

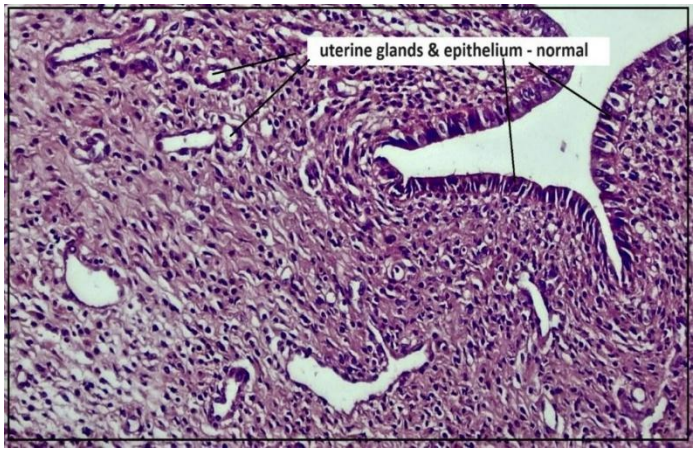


Fig No 27: Normal Control – Rat Uterus: showing uterine glands & epithelium - normal- Active* NAD+ (X100)

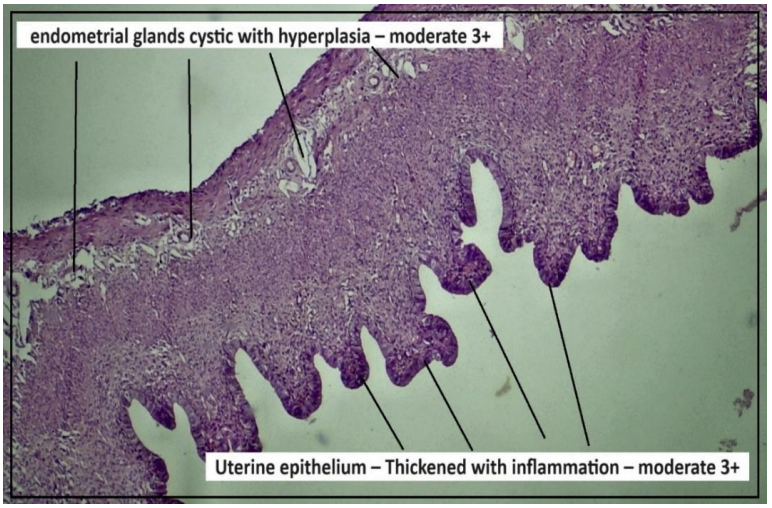


Fig No 28: Disease control - Rat Uterus: showing endometrial glands cystic with hyperplasia Uterine epithelium – Thickened with inflammation – moderate 3+ (Degenerative changes) (X50)

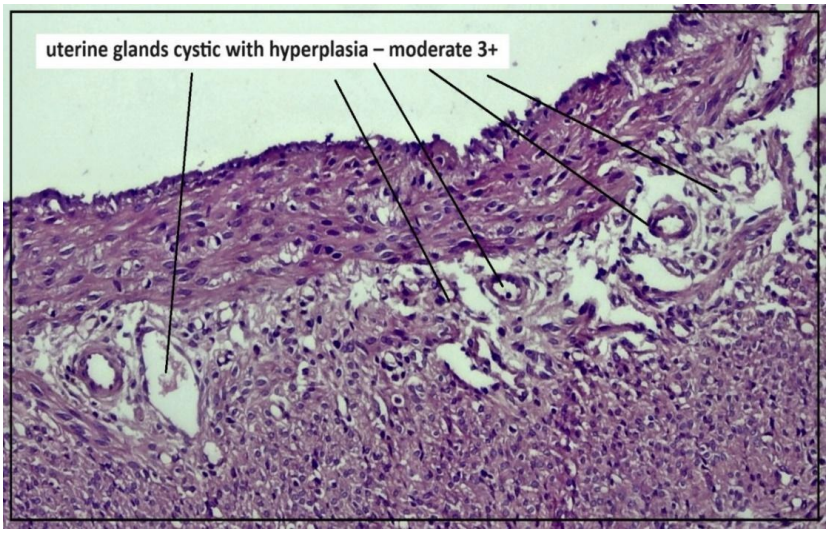


Fig No 29: Disease control - Rat Uterus: showing uterine glands cystic with hyperplasia – moderate 3+ (X100)

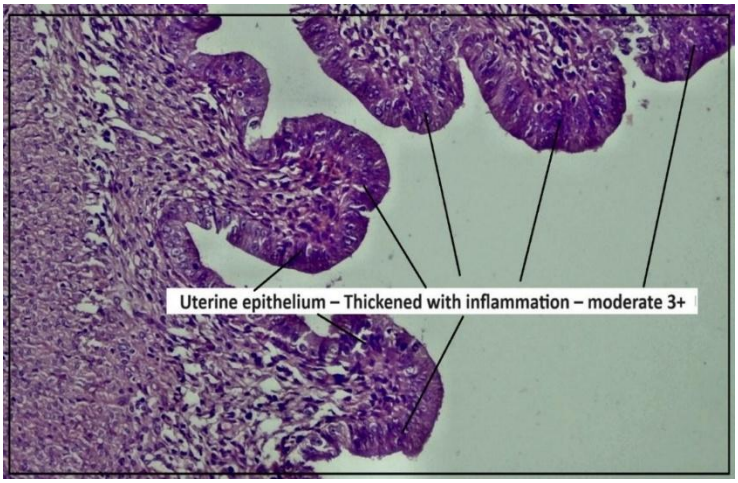


Fig No 30: Disease control - Rat Uterus: showing Uterine epithelium – Thickened with inflammation – moderate + (X100)

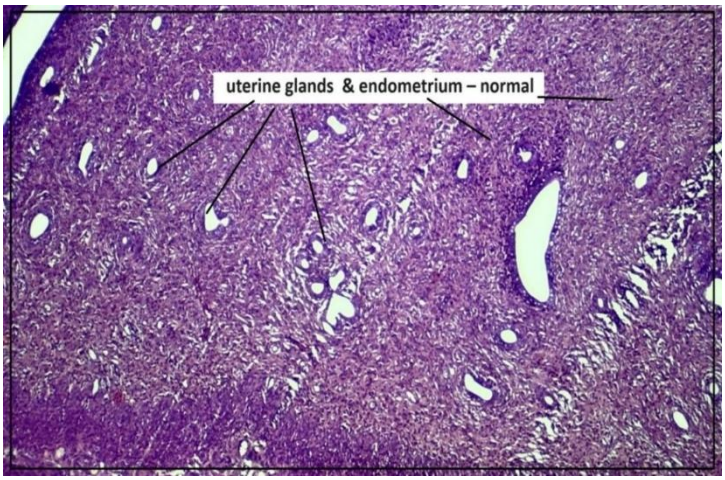


Fig No 31: Std – Metformin Rat Uterus: showing uterine glands & endometrium – normal- NAD+ (X50)

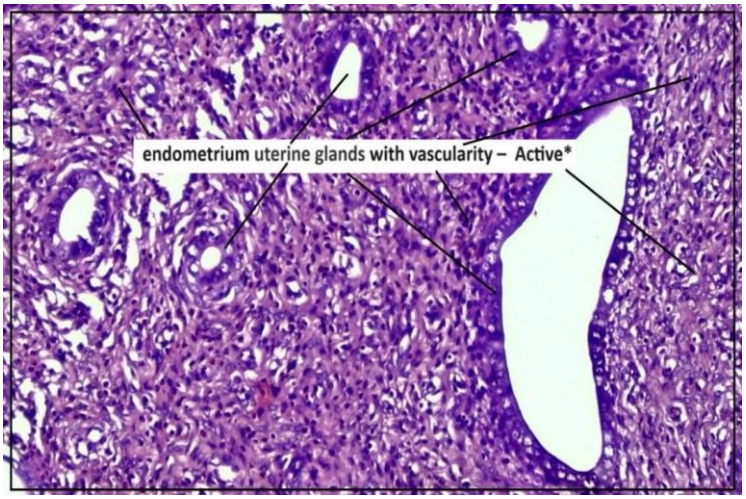


Fig No 32: Std – Metformin Rat Uterus: showing the endometrium uterine glands with vascularity – Active* (X100) (Drug induced beneficial response*)

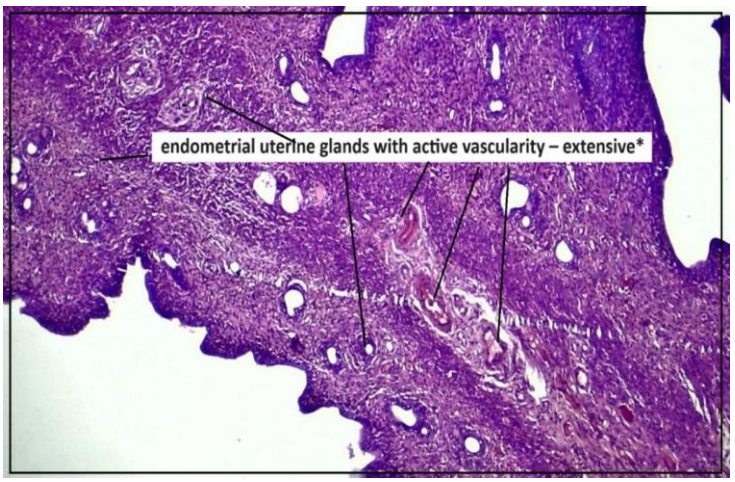


Fig No 33: Test dose - *Incarnata* treated Rat Uterus: showing the endometrial uterine glands with active vascularity – extensive* (X50)

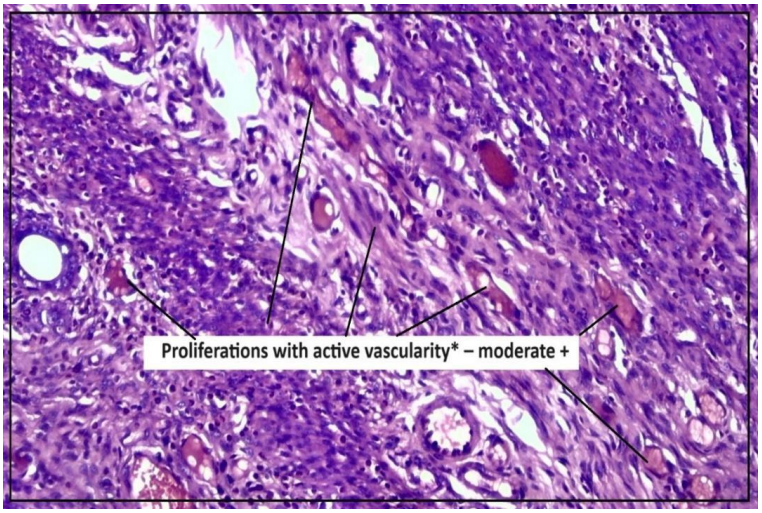


Fig No 34: Test dose - *Incarnata* treated Rat Uterus showing the endometrial uterine glands epithelium - active* Proliferations with active vascularity* – moderate + (X100)

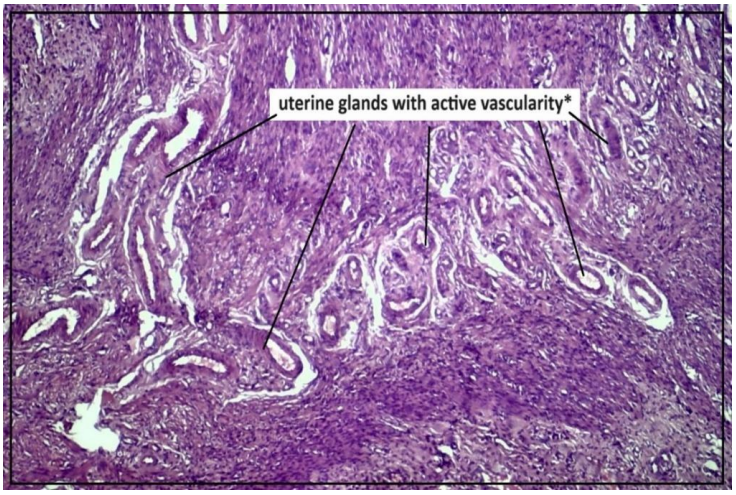


Fig No 35: Test- *Foetida* treated Rat Uterus: showing the uterine glands with active vascularity – extensive*(X50)

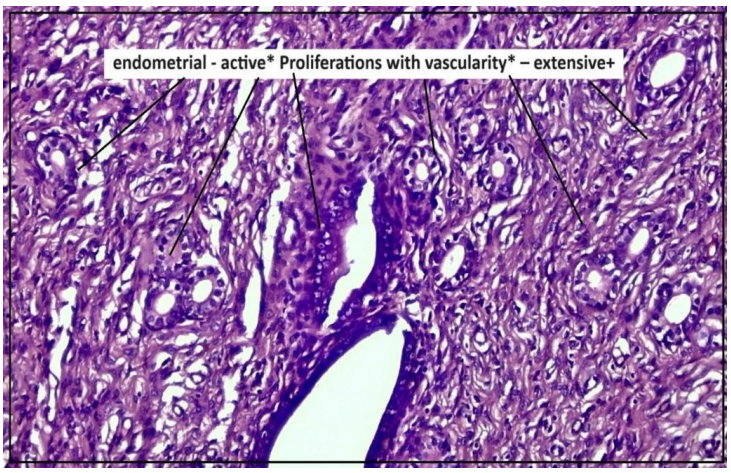


Fig No 36: Test- *Foetida* treated Rat Uterus: showing the endometrial - active* Proliferations with vascularity* – extensive+ (X100) (Drug induced beneficial response*)

Table No 4: Uterus/ Drug Response in PCOD Induced Uterus

Group	Histopathological findings Rat Uterus	Scorings / gradation
Normal Control	uterine epithelium & glands - normal- NAD+ evident	Normal NAD^+
Disease control Letrozole	endometrial glands cystic with Hyperplasia moderate 3+ Uterine epithelium – Thickened with inflammation – moderate + (Degenerative changes) *	moderate 3+
Std - Metformin	endometrial epithelium & uterine glands with active vascularity – Active* (Drug induced beneficial response*)	NAD^+ extensive*
Test Drug – treated *Incarnata*	endometrial uterine glands - active* Proliferations with active vascularity* – moderate + (Drug induced beneficial response*)	active* moderate +

Test Drug – treated *Passiflora Foetida* Species	The endometrium - active* Proliferations with uterine glands - active vascularity* – extensive+ (Drug induced beneficial response*)	active* extensive+

Molecular Docking: Molecular docking analysis revealed that vitexin and luteolin—key flavonoids in *Passiflora* species—exhibited high binding affinities for aromatase and androgen receptor targets, with docking scores of −9.83 kcal/mol and −9.53 kcal/mol, respectively, surpassing metformin (−5.43 kcal/mol). [5,14] These interactions suggest potential modulation of hormonal pathways relevant to PCOD.

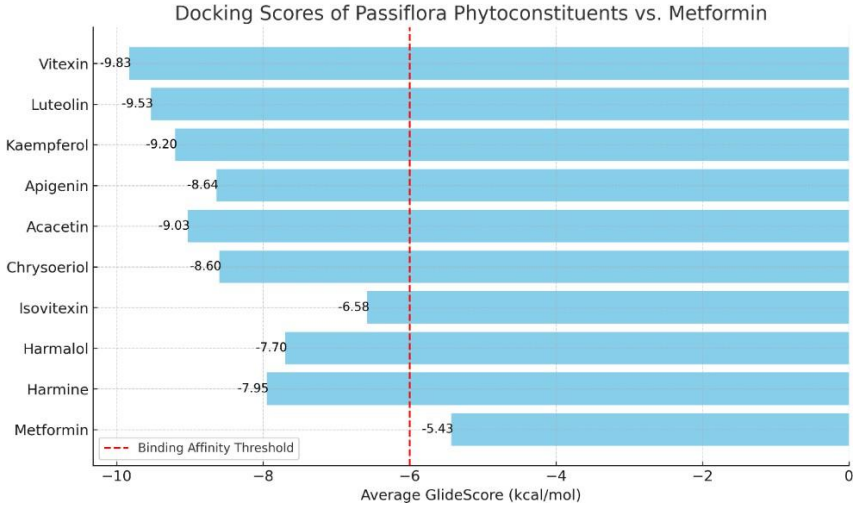


Fig No 37: Docking scores of selected phytoconstituents from *Passiflora foetida* and *Passiflora incarnata* in comparison with metformin. Vitexin and luteolin showed the strongest binding affinities across multiple PCOD-related targets.

ADMET: ADMET profiling predicted favourable drug-like properties for both compounds, including good gastrointestinal absorption, low hepatotoxicity, and minimal blood–brain barrier permeability. These pharmacokinetic features further support the potential of *Passiflora* compounds as safe oral therapeutics.[5]

Table No 5: In Silico ADMET Properties of Selected Phytoconstituents

Compound	GI Absorption	BBB Permeability	CYP450 Inhibition	AMES Toxicity	Hepatotoxicity	Total Clearance
Vitexin	High (81.13%)	No (−0.907)	CYP1A2, CYP2C9	No	No	0.495 mL/min/kg
Luteolin	Moderate (74.29%)	No (−0.939)	CYP1A2, CYP2C9	No	No	0.477 mL/min/kg
Kaempferol	High (93.25%)	No (−0.734)	CYP1A2, CYP2C9	No	No	0.566 mL/min/kg

Acacetin	High (94.32%)	Yes (0.196)	CYP1A2, CYP2C9	No	No	0.663 mL/min/k g
Harmine	High (93.50%)	Yes (0.417)	CYP1A2	No	No	0.650 mL/min/k g

4. DISCUSSION

The findings of this study highlight the significant therapeutic potential of *Passiflora foetida* and *Passiflora incarnata* extracts in ameliorating the biochemical and histopathological abnormalities associated with PCOD. [1,5,6] The presence of phytoconstituents such as flavonoids, glycosides, alkaloids, and saponins in both species likely contributes to their multi-faceted effects, including hormonal regulation, antioxidative activity, and anti-inflammatory properties. [5,6,13] These phytochemicals may interact with key enzymes and receptors involved in steroidogenesis and insulin signalling pathways, thereby mitigating the endocrine and metabolic dysfunction characteristic of PCOD. [4,14]

The marked improvement in hormonal profiles, particularly the reduction in testosterone levels and normalization of LH and FSH levels, suggests effective modulation of the hypothalamic-pituitary-ovarian (HPO) axis. This restoration is crucial in reversing anovulation and associated symptoms in PCOD. The superior performance of *P. foetida* in comparison to *P. incarnata* can be attributed to its higher flavonoid content and better binding affinity observed in molecular docking studies. [14,16]

Histological improvements in ovarian, uterine, and hepatic tissues further validate the systemic benefits of these extracts. In PCOD-induced rats, the overall restoration of ovarian follicles, regeneration of endometrial lining, and resolution of hepatic steatosis indicate reversal of pathological changes. These effects were more prominent in the *P. foetida*-treated group, supporting its enhanced bioactivity. [6,15]

The molecular docking results confirmed that vitexin and luteolin, major flavonoids in *Passiflora* species, possess strong binding affinities to aromatase and androgen receptors—key targets implicated in PCOD. These interactions may contribute to the observed hormonal corrections. Moreover, in silico ADMET analysis revealed favorable pharmacokinetic and safety profiles, strengthening the translational potential of these compounds. [5,14]

Comparatively, the efficacy of *P. foetida* was on par with metformin, a standard pharmacological treatment for PCOD, but without its associated side effects.[3] Therefore, *Passiflora* extracts, especially *P. foetida*, offer promising natural alternatives for long-term PCOD management. However, further preclinical toxicological assessments and clinical trials are necessary to validate these findings and ensure safety in human subjects.[6]

5. CONCLUSION

Both *Passiflora* species hold promise in PCOD management, with *P. foetida* demonstrating superior therapeutic potential. Their multi-target action—including hormonal regulation, tissue recovery, and molecular interaction with key targets—along with favourable safety and pharmacokinetic profiles, supports their viability as plant-based alternatives to conventional pharmacological therapies. The findings of this study underscore the need for further toxicological studies and well-designed clinical trials to validate the efficacy and safety of *Passiflora* extracts in human populations, potentially offering a safer and more holistic approach to long-term PCOD management. [1,6,13]

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