Content available at: https://www.ipinnovative.com/open-access-journals

IP International Journal of Comprehensive and Advanced Pharmacology

Journal homepage: www.ijcap.in

Original Research Article

# Study of hemp tribe HEMPOWHER granules on DHEA- induced PCOS in Sprague Dawley (SD) rat model

**Leela Priyanka G C[1], Balasekar Premkumar[1]*, Arumugam Meena[2], Arumugam Shanthy[3], Manepalli Nageswara Rao Gupta[4], Gopalakrishnan Saravanan[4], Sallabuthula Rajkumar[4]**

[1]Dept. of Pharmacology, K.K. College of Pharmacy affiliated to The Tamilnadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

[2]Dept. of Pharmaceutical Analysis, K.K. College of Pharmacy affiliated to The Tamilnadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

[3]Dept. of Pharmaceutics, K.K. College of Pharmacy affiliated to The Tamilnadu Dr. M.G.R Medical University, Chennai, Tamil Nadu, India

[4]Suraksha Pharma Group of Companies, Roorkee, Uttarakhand, India

## Abstract

**Background:** Polycystic ovary syndrome (PCOS) is the common hormonal condition that affects adult women of reproductive age. PCOS can cause hormonal imbalance, excess androgen levels, and cysts in the ovary; irregular periods with a lack of ovulation can make it difficult to become pregnant. Lifestyle changes can improve PCOS symptoms, but medications and fertility treatments are not effective. The goal of this study is to see how Hemp Tribe HempowHer effects PCOS caused by Dehydroepiandrosterone (DHEA) in rats, and to compare it with the standard drug metformin hydrochloride.

**Materials and Methods:** DHEA was injected into a group of female rats to induce PCOS. Twenty-one days after induction of PCOS, Hem Tribe HempowHer granules and Metformin Hydrochloride were administered to the PCOS-induced animals orally for 14 days. Their body weight, hormone levels, estrous cycles, and histopathological studies were conducted and compared with the normal, standard metformin hydrochloride-administered animals.

**Results**: The results indicated body weight reduction in both the metformin hydrochloride-treated group and the HempowHer-treated group. Vaginal smear after 21 days of PCOS induction and 14 days after treatment with HempowHer showed normalization of the estrous cycle when compared to PCOS-induced groups. Hormonal analysis 21 days after induction of PCOS followed by 14 days of treatment with HempowHer significantly regulated the hormonal levels of luteinizing hormone, testosterone, progesterone, prolactin, and insulin when compared to the PCOS-induced group. Significant reduction of atretic follicles and increase in corpus luteum shown in histopathological studies of HempowHer-treated animals when compared to the PCOS-induced group indicate that the HempowHer supplement increases the possibility of the regulation of the estrous cycle, reduces the formation of ovary cysts, and improves ovary health.

**Conclusion**: The HempowHer, as per the study, regulates the estrous cycle and hormonal levels pertaining to ovary health and reproduction, reduces cyst formation, and ameliorates symptoms of PCOS.

**Keywords:** Cannabinoids, Women's health, Fertility, Ovary, Preclinical, Androgen.

**Received:** 16-04-2025; **Accepted:** 17-05-2025; **Available Online**: 23-07-2025



## 1. Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrinal reproductive disorder in a coalition with metabolic abnormalities of women, especially at their reproductive stage. Irregularity in menstrual cycle and menstruation, hormonal imbalance, and unhealthy ovary formation are normally observed in PCOS women during their reproductive stage. PCOS is characterized by hyperandrogenism, hirsutism, irregular and painful menstrual cycles, amenorrhea, cystic ovaries, and anovulation. The metabolic features of PCOS are insulin resistance, hyperinsulinemia, a high incidence of impaired glucose tolerance, obesity, inflammation, endothelial dysfunction, hypertension, and dyslipidaemia, resulting in an increased risk of diabetes and cardiovascular diseases. Besides, compromised quality of

*Corresponding author: Balasekar Premkumar
Email: cologyprem@gmail.com

https://doi.org/10.18231/j.ijcaap.2025.014

life, anxiety, depression, and other mood disorders are also observed in PCOS.[1]

The global prevalence of PCOS is highly variable, from a minimum of 2.2% to a maximum of 26.0% of reproductive-age women; in India, it ranges from 3.7% to 22.5%.[2]

The key pathophysiological contributors to PCOS are hyperandrogenism, insulin resistance, and altered folliculogenesis. Hyperinsulinemia due to insulin resistance alters ovarian function, leading to excessive androgen production and the formation of unhealthy ovaries in women with PCOS. This Hyperandrogenism increases the amplitude of luteinizing hormone (LH) pulses, and androgen production in theca cells for its hyperactivity causes endocrine-based infertility.[3]

PCOS is the most common cause of anovulation, characterized by arrested growth of antral follicles. Even though the stopped growth of antral follicles likely shows the unusual hormone levels in PCOS (especially due to high insulin), more and more evidence suggests that there are problems with how follicles develop right from the very beginning, before they depend on gonadotropins. This leads primarily to excess small primary follicles and deformation of the consequent stages towards the selection of dominant follicles. The reduced follicle-stimulating hormone (FSH) responsiveness and the premature granulosa cell luteinization prevent the dominant follicle selection, leading to follicular cyst and follicular arrest.[5]

Cannabis sativa has been shown to possess significant anti-inflammatory effects by modulating immune responses. Previous research has confirmed both the effectiveness and safety of cannabinoids in the treatment of inflammatory conditions. There is a growing interest in the role of endocannabinoids as vital regulators of the female reproductive system. These compounds have been associated with various changes in this system, such as folliculogenesis, oocyte maturation, and the secretion of ovarian hormones. Additionally, endocannabinoids play a critical role in the pathophysiology of PCOS.[6] Despite this, the impact of cannabinoids has not been thoroughly assessed, and the modulation of endocrine regulation remains underexplored. Consequently, this study aims to examine the effects of a hemp seed formulation (HempowHer) in a rat model of PCOS, with a particular emphasis on estrous cyclicity and hormonal aspects.

## 2. Materials and Methods

Hemp Tribe HempowHer granules, formulated by MMC Healthcare Chennai, contain hemp seed powder, myo-inositol, D-chiro-inositol, zinc, and chromium per 15g. The active components of this formulation contain cannabinoids (**Figure 1**).

Glyciphage Tablets (Metformin 500mg) were purchased from the drugstore. Dehydroepiandrosterone (DHEA) was used for induction of PCOS. Isoflurane was used for anaesthesia and excess was used for euthanasia. All other chemicals used were of pharmaceutical/analytical grade.[7]

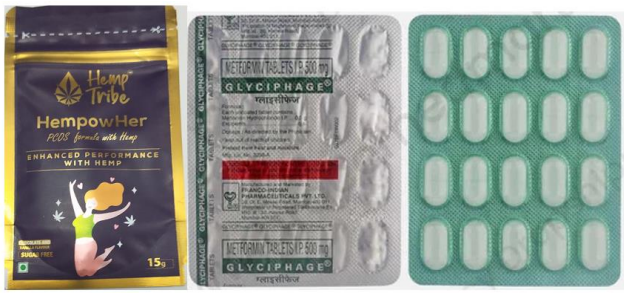



**Figure 1:** Hempowher and metformin formulations

### *2.1. Experimental animals*

We analysed the therapeutic efficacy of HempowHer in an in-vivo polycystic ovarian syndrome experimental model. The IAEC has approved the experimental animal protocol. We issued thirty female Sprague Dawley rats weighing 180-220 gm. Animals were caged in standard polypropylene cages and acclimatized for one week in the animal house at a controlled temperature of 25ºC ± 2°C and humidity of 60 ± 5% under a 12-hour light and dark cycle. All animal protocol experiments were carried out according to the guidance of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CCSEA) guidelines on the ethical use of animals. The animals were provided with food and water *ad libitum*.

### *2.2. Treatment protocol*

The rats were divided into groups as follows: a saline group (n =6) received 50 µL of sterile saline 0.9%; a DHEA group (n = 6) received 6 mg/kg of Dehydroepiandrosterone (DHEA) in sesame oil subcutaneously (s.c.); a standard group (n = 6) received Metformin; a low-dose treatment group (n = 6) received HempowHer; a high-dose treatment group (n = 6) received HempowHer. All dosages were diluted in 50 µL of normal saline (**Table 1**).

### *2.3. Induction of PCOS*

To induce PCOS, a dose of 6 mg/kg of body weight of DHEA was injected into the group of animals designated for the PCOS treatment over a period of 21 days. The DHEA was dissolved in sesame oil and was injected subcutaneously.

### *2.4. Study plan*

The plan was to track changes in body weight, check vaginal smears for estrous cycles, and collect blood samples for hormone tests and ovary examination.

### *2.5. Measurement of bodyweight*

Bodyweight of Sprague Dawley female rats was measured using a commercially available weighing balance. The body weight was measured at regular intervals throughout the experiment.[8]

**Table 1**: Treatment protocol

| Group | Treatment |
|---|---|
| Control | Normal saline throughout the study |
| PCOS Group (Negative group) | DHEA s.c for 21 days |
| Metformin Group | DHEA s.c for 21 days followed by 100mg/kg Metformin Hydrochloride p.o for 2 weeks |
| HempowHer low dose | DHEA s.c for 21 days followed by 200mg/kg HempowHer p.o for 2 weeks |
| HempowHer High Dose | DHEA s.c for 21 days followed by 400mg/kg HempowHerp.o for 2 weeks |

N=6 Female Sprague Dawley Rats in each group

*2.6. Vaginal smear collection*

Vaginal smear test was performed daily to determine the estrus stage. We took a vaginal smear 21 days after inducing PCOS with DHEA and a 4-day cycle. After this treatment with Metformin and Hemp Tribe HempowHer for 14 days and 4 days cycle again, the smear was taken.

A moistened (Normal Saline) cotton bud swab was inserted into the vagina. Gently the cells were removed from the vagina lumen and walls, transferred them to a glass slide, and allowed them to air-dry. The air-dried smears were fixed. The air-dried glass slide was stained with diluted phenolphthalein (1:20, v/v) for 20 minutes. We washed the stained smears by dipping the glass one or two times. The stained smears were allowed to air dry in a vertical position. Microscopic analysis using an optical microscope determined the stage of cyclicity.

Four phases of the estrous cycle comprised different predominant cells as

1. The proestrus consists of nucleated epithelial cells. 12 hours
2. Estrus consisting of flat, irregular, cornified epithelial cells without a nucleus. 12 hours
3. Metestrus consisting equal mixture of leukocytes, nucleated epithelial cells, and a few cornified epithelial cells. 21-24 hours
4. Diestrus consisting of many leukocytes. 57-60 hours

At the end of the treatment period, animals were anesthetized with a mixture of Isoflurane overdose.[8]

*2.7. Blood sampling and ovary harvesting*

The blood samples were taken by cardiac puncture. The serum was separated and used for estimation of PCOS related hormones. After sacrificing the animals, ovaries were harvested, removed the fat, weighed them, and fixed them in 10% formalin.

An enzyme-linked immunosorbent assay (ELISA) was used to measure the hormone levels of FSH, progesterone, LH, testosterone, prolactin, and insulin in the serum. We calculated the levels using biochemical kits.[9]

*2.8. Histopathology*

The harvested ovaries were cut into thin slices of 5 µm after being preserved in 10% formalin and placed in paraffin blocks, and then slides were made using hematoxylin and eosin stains. The slides were then examined for histopathological changes under a light microscope. Slides prepared from different parts of the ovary allowed counting the total number of follicles in each ovary.[10]

*2.9. Statistical analysis*

Statistical analysis of all data was expressed as mean ± SD (standard deviation). One-way ANOVA for repeated measures followed by Dunnet's test was used for multiple comparisons. Statistical analysis was done using Software Graph Prism version 10.03.

## 3. Results

*3.1. Body weight*

A significant increase in body weight was observed in the DHEA group, when compared to all the other groups. In all the other groups the body weight was found to be normal in comparison to the control group (**Table 2**).

**Table 2:** Initial and final body weights for all the treatment groups

| Groups | Body weight | |
|---|---|---|
| | Initial | Final |
| Control | 253.33 ± 6.80 | 249 ± 4.50(after 21 days) *** |
| PCOS Group (Negative group) | 234.38 ± 0.57 | 386.66 ± 7.76(after 21 days) |
| Metformin Group | 226.40 ± 8.65 | 255.33 ±5.50(after treatment) *** |
| HempowHer low dose | 225.12 ± 5.29 | 263 ± 5.25(after treatment) *** |
| HempowHer High Dose | 237.35 ± 2.08 | 256.33 ± 2.51(after treatment) *** |

***p<0.001, in comparison with the disease control.

*3.2 Estrous cycle analysis*

*3.2.1. Before induction*

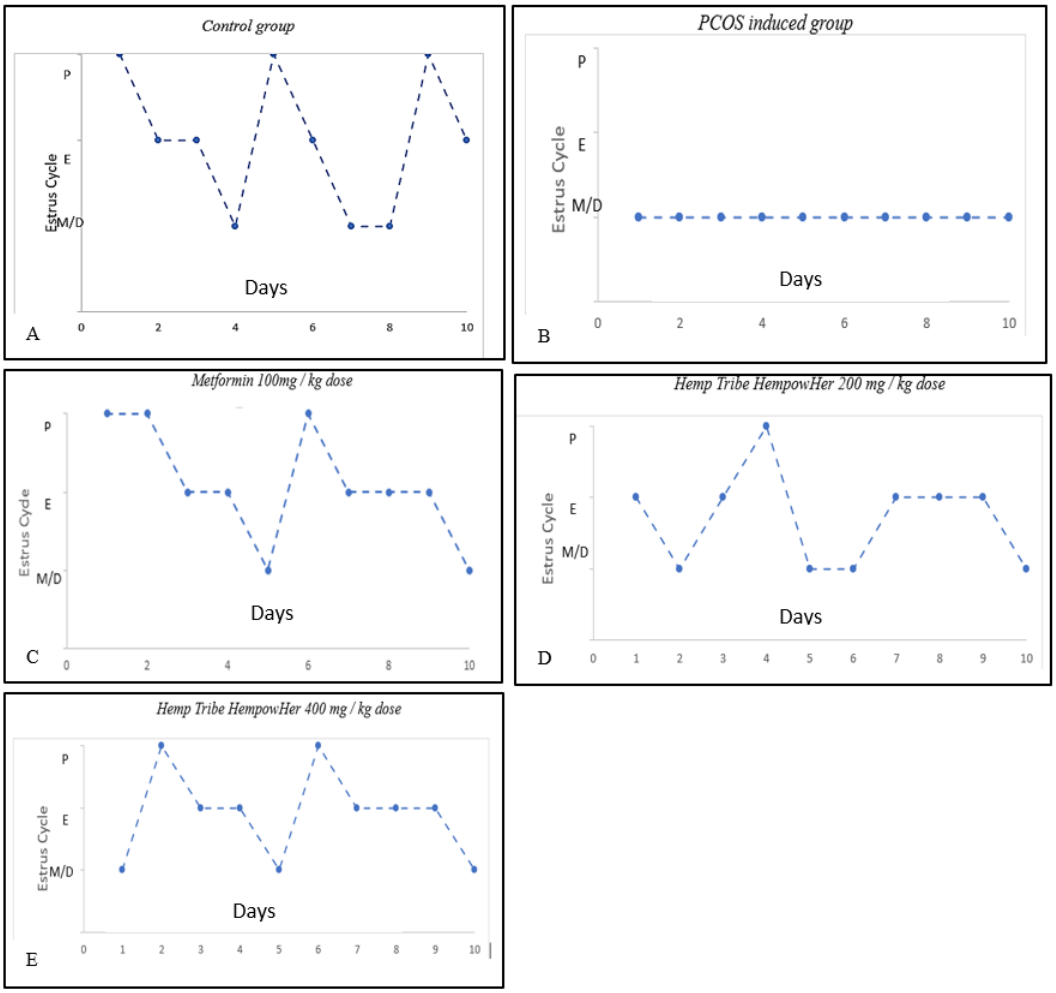
All the groups showed proestrus (epithelial cell with nucleus, few leukocytes), estrus (cornified with few epithelial cells and leukocytes), metestrus (predominant cornified cells), and diestrus (mostly leukocytes) phases observed in a 4-day cycle

*3.2.2. After induction of PCOS*

All the groups showed a prolonged diestrus phase except the normal control group.

*3.2.3. After treatment*

The estrous cycle regularized to regular phases in the HempowHer-treated and metformin-treated groups, but the negative control group showed only a prolonged diestrus phase. (**Figure 2**).




**P = Prosterous phase E = Estrous phase M/D = Metestrus and Diestrus phases**

**Figure 2**: **A):** Normal control; **B):** PCOS disease control; **C):** Metformin; **D**): Hemp Tribe HempowHer (low dose); **E):** Hemp Tribe HempowHer (High Dose)

*3.2.4. Hormones*

Following the induction of PCOS, the levels of FSH and LH hormones markedly decreased, followed by a substantial increase post-treatment. A significant rise was observed in the negative control group. We noted a substantial increase in the high dose of HempowHer, which was comparable to metformin therapy (**Figure 3**, **Figure 4**).

Testosterone levels rose markedly in all groups, except for the normal control group. Post-treatment, testosterone levels dramatically decreased in both the metformin and HempowHer groups. Progesterone levels also showed a similar trend (**Figure 5**).

The levels of insulin, estradiol, and prolactin did not demonstrate any treatment differences when compared to the negative control group (**Figure 6**, **Figure 7**). A significant difference was noted between the induction groups and the normal control group; however, no substantial inference was established post-treatment.

*3.10. Ovary weight and cysts in ovaries*

The ovarian weights from the DHEA group were significantly increased at 14 and 21 days after DHEA injection compared with the normal group. Consistent with these results, the ovarian size was also increased. In the treatment groups, the ovarian weights were less than in the PCOS group.

*3.11. Ovarian histopathology*

According to the histopathology the mean volume of atretic follicles has significantly increased in negative control, compared to control group. On the other hand, the results show a marked decrease after treatment with metformin and the HempowHer treatment groups. In contrast to the atretic cystic follicles, no corpus luteum was seen in the ovaries of negative control groups; more corpus luteum and Graafian follicles were observed in the ovaries of rats treated with low-dose and high-dose Hemp Tribe HempowHer (**Figure 8**).

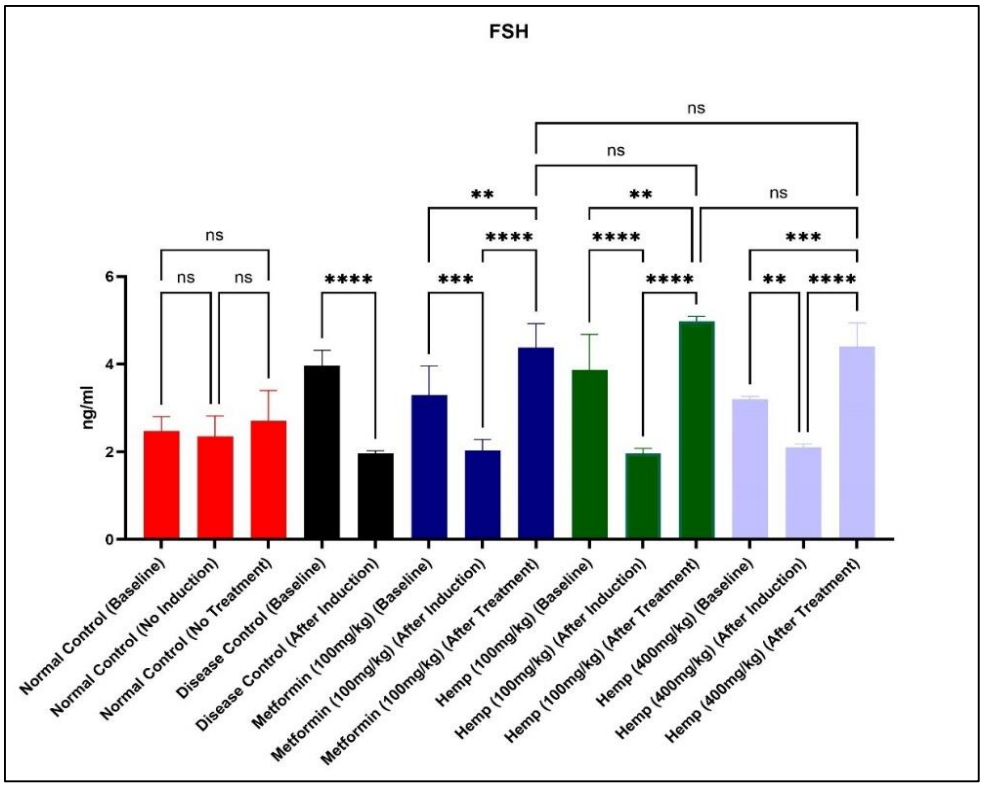



**Figure 3:** FSH levels in the different treatment groups

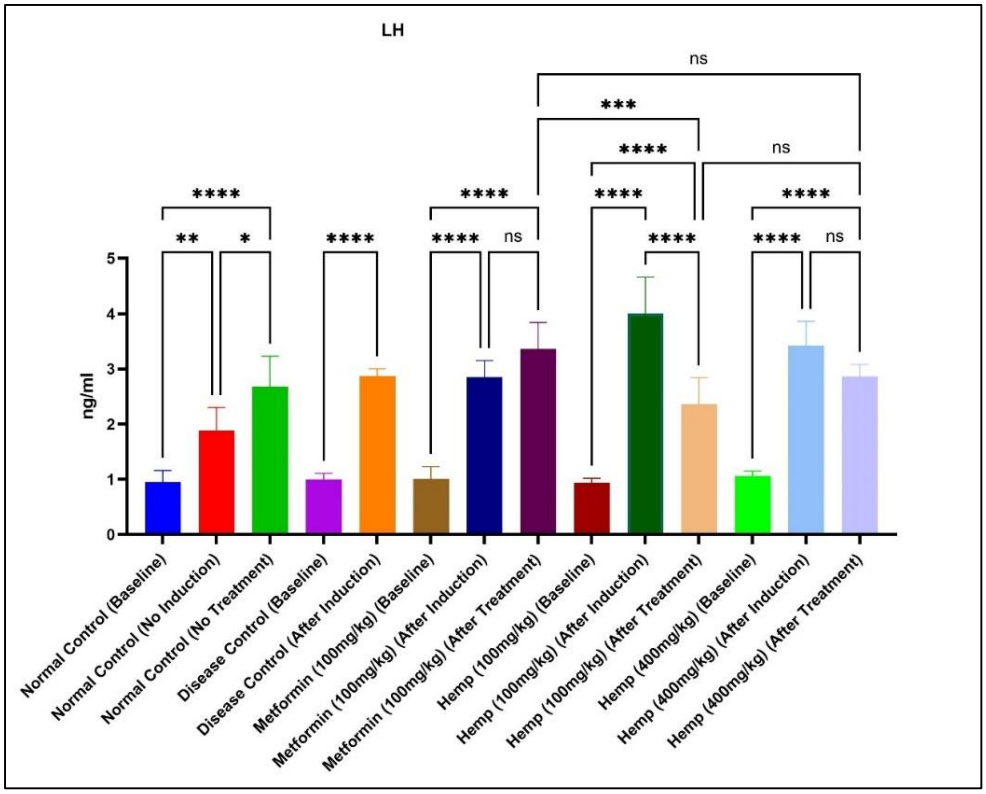



**Figure 4:** LH levels in the different treatment groups

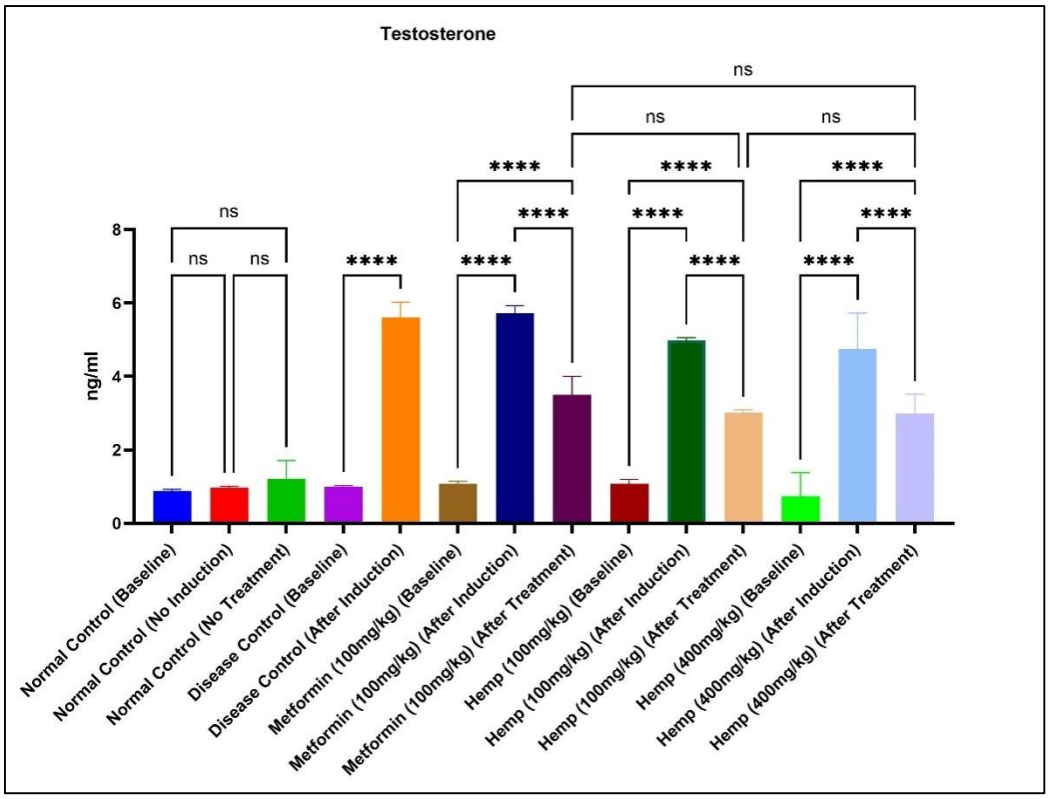



**Figure 5**: Testosterone levels in the different treatment groups

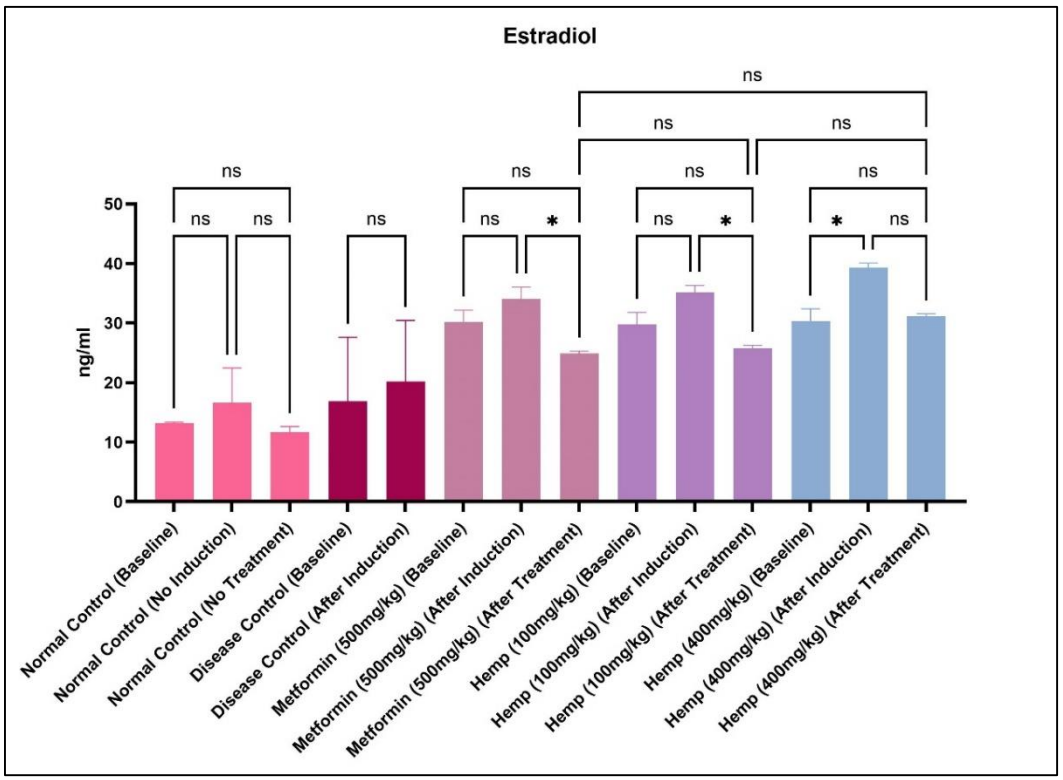



**Figure 6**: Estradiol levels in the different treatment groups

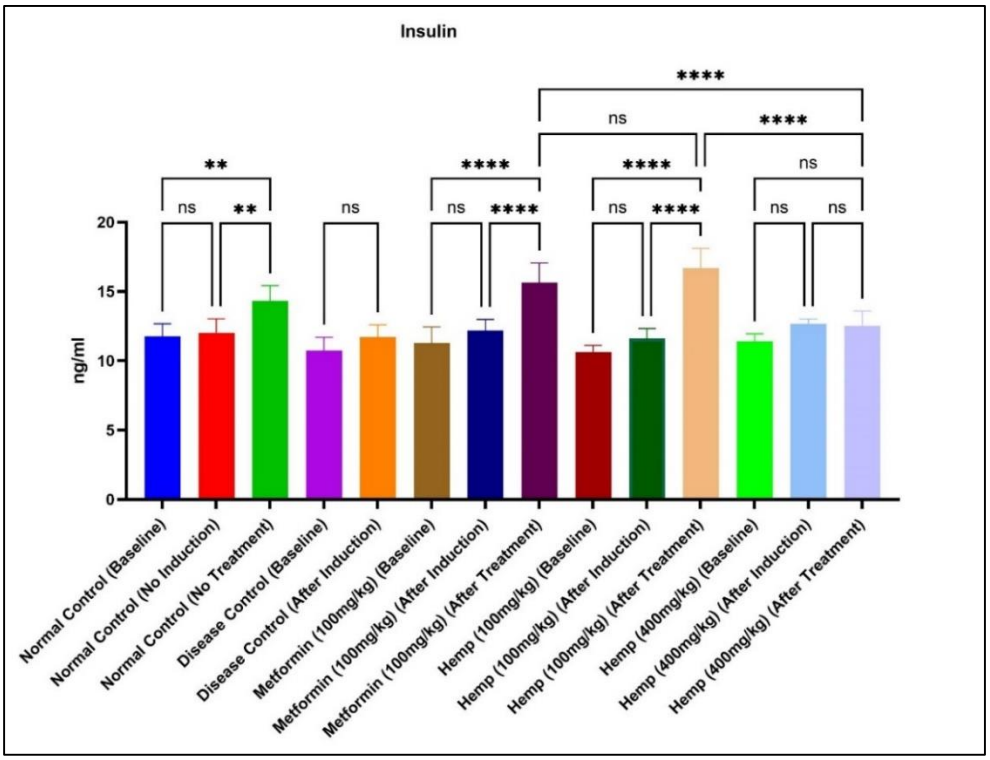



**Figure 7:** Insulin levels in the different treatment groups

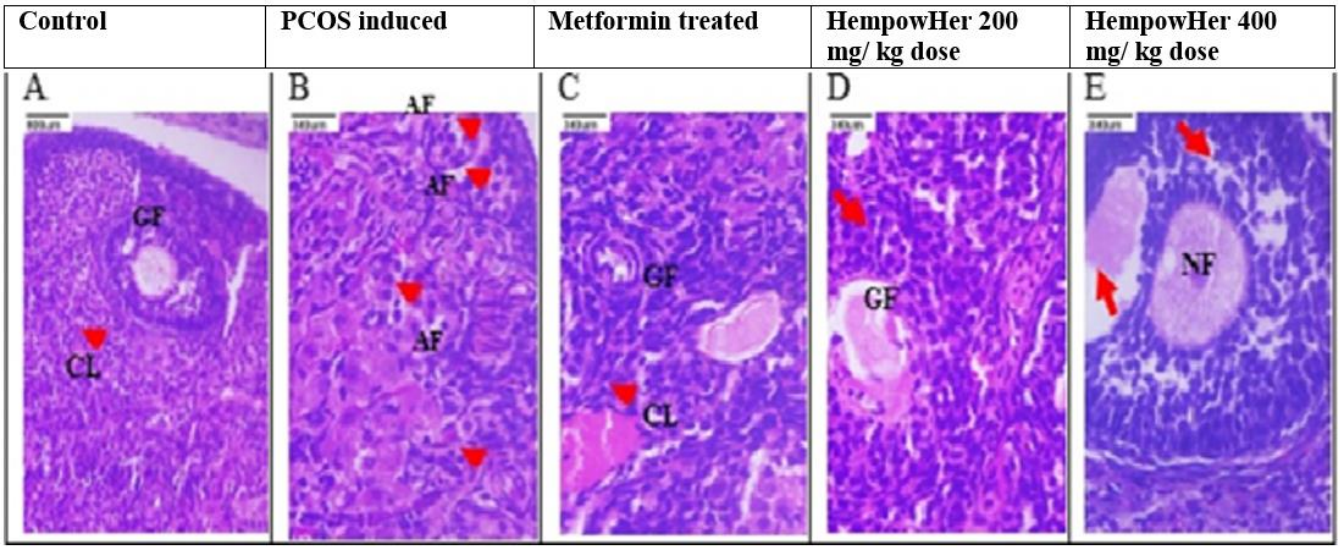



**Figure 8:** Histopathology of rat ovaries with **A**): Control group showing normal corpus luteum and Graafian follicle, **B):** PCOS induced -there were many atretic follicles observed; no corpus luteum was observed. **C):** Metformin & **D)**: Low-dose (HempowHer) treatment & **E):** High-dose (HempowHer) treatment—more growing follicles were observed, and corpora lutea were also observed. CL – Corpus luteum, GF – Growing follicle, AF – Atretic follicle, NF – Normal follicle

## 4. Discussion

Polycystic ovarian syndrome, abbreviated as PCOS, is a disorder found among reproductive women. The symptoms of PCOS are infertility and anovulation, menstrual disorders, and metabolic disturbances.[11] The recommended treatments for women with PCOS, especially for PCOS patients with obesity, are lifestyle and nutrition interventions and weight loss. The current study shows that metabolic disorders in patients with PCOS may be improved by the intervention of dietary factors such as anti-inflammatory foods. Among dietary factors, omega-3 fatty acids play an important role in immune regulation, insulin sensitivity, and cellular differentiation.[12]

The HempowHer could be used as a dietary supplement for improving excessive oxidative stress-mediated folliculogenesis disorder and hyperinsulinemia in women with PCOS.[13] Consumption of omega-3 fatty acids could improve some cardiometabolic health issues in women with

PCOS by lowering the production of certain free radicals and could boost the activity of antioxidant enzymes. The nutrients in the hemp seeds and the content like myo-inositol, D-chiro-inositol, zinc, and chromium in the HempowHer could be responsible for their effective mechanism of action, especially in PCOS treatment.

Among the various models available for inducing PCOS in rats, the DHEA- induced PCOS model was chosen for this study. DHEA is a male hormone, androgen, which was found to be high in PCOS, which justifies this model.[15]

DHEA-induced PCOS rats gained more weight, but the treatment with Metformin or HempowHer did not show a significant increase in weight. Obesity is a common finding in PCOS and aggravates many of its reproductive and metabolic features. The relationship between PCOS and obesity is complex, not well understood, and most likely involves a combination of genetic and environmental factors.[16,17]

Women with PCOS exhibit irregular menstrual cycles and chronic anovulation, which are the primary clinical manifestations of PCOS.[17] Hence, estrus cyclicity in PCOS rats was monitored, wherein PCOS rats exhibited arrested estrus cyclicity in the late diestrus phase of the cycle as compared to control groups. The cyclicity was normalized in the treatment groups, exhibiting reversion to normal cycles in PCOS rats.

Follicle-stimulating hormone levels lead to follicular development and ovulation through an increase in the glutamine levels.[18] In the current study, the PCOS-induced control group had significantly lower when compared to the HempowHer- and Metformin-treated groups, and vaginal smears also revealed reversal of estrous cyclicity to normal levels. This showed that regularization of the menstrual cycle in the treated groups when compared to the PCOS groups. Histopathological studies also showed more growing follicles with corpus luteum without atretic follicles for the regularization of ovary function and menstrual cycle for fertility in the treated groups.

Testosterone level was significantly higher in the PCOS-induced group compared to the normal control group. Testosterone levels in HempowHer treatment groups were decreased compared to the PCOS induced group. The ovaries are stimulated to produce excessive amounts of androgens, particularly testosterone, through the release of excessive LH by the anterior pituitary gland or through high levels of insulin in the blood. Hyperandrogenism is a key factor in the pathogenesis of most PCOS cases, as it leads to cystogenesis by impairing the maturation of developing follicles in the ovaries. Hyperandrogenism is the key feature of PCOS, resulting primarily from excess androgen production in the ovaries and, to a lesser extent, in the adrenals.[19,20]

Steroid hormones synthesized by the ovaries function as autocrine agents and are crucial in regulating ovarian cell apoptosis. Estrogen serves as a crucial determinant for the viability of both granulosa cells and the corpus luteum. Estrogen can increase the levels of genes that prevent cell death while also boosting the levels of genes that promote cell death, which can lead to cell death in ovarian cysts and help reduce the symptoms of PCOS.[21,22] The current study found that the treatment groups had improved estrogen levels compared to the disease control group.

The hormone progesterone is essential for both pregnancy and the regulation of the reproductive cycle. The PCOS-induced group had a strikingly high level of progesterone, while the groups treated with HempowHer and metformin maintained lower progesterone levels when compared to the PCOS-induced group. This slight reduction in the progesterone level helps to enhance the estrogen level during ovulation and normalize the menstrual cycle. During the fall in progesterone, the menstrual cycle takes place. Higher progesterone levels lead to menstrual irregularities.[23,24]

Insulin resistance can lead to infertility and elevated androgen levels, which intensify the characteristics of PCOS. Furthermore, the insulin-sensitizing medication metformin can ameliorate irregularities, enhance ovulation, and increase birth rates in individuals with PCOS, particularly in the presence of insulin resistance.[25-27] Consequently, a robust correlation is expected between PCOS and insulin resistance.[28] In this study, insulin was normal in the PCOS-induced group compared to the normal control group. The study showed no significant difference between the groups.

Hypersecretion of prolactin leads to amenorrhea, galactorrhoea, and infertility. Prolactin decreases the levels of FSH, where FSH was responsible for the development of follicles in the ovaries.[29-33] Prolactin levels in the PCOS-induced control group were significantly higher when compared to the control. Prolactin level was significantly decreased in the metformin treatment group. Administration of HempowHer showed a significant decrease in prolactin level.

The current study showed that the HempowHer had the potential to ameliorate polycystic ovarian syndrome, which is statistically comparable with metformin. PCOS patients also suffer from weight gain, whereas the HempowHer-treated group showed no significant increase in weight when compared to the PCOS-induced group. HempowHer has ameliorated the hormone levels, which are the major causes of PCOS, by showing a reduction in the levels of LH, testosterone, and prolactin and upregulating the levels of FSH and progesterone. Insulin levels were not affected significantly compared to PCOS-induced and treatment groups, except HempowHer high-dose group showed a slight reduction in the insulin level, which indicates there is the possibility of a reduction in insulin resistance. It was found

that the HempowHer group had fewer immature atretic follicles than the PCOS-induced group. Improvement in the amelioration of hormones and enzymes reduction in atretic follicles in the ovaries by the HempowHer-treated group suggests that it could be an ideal supplement for PCOS to reduce its symptoms, especially for the normalization of the menstrual cycle and fertility.

## 5. Conclusion

HempowHer has the property to regulate the estrous cycle, inhibit the gain in body weight during PCOS, and reduce the immature follicles by regulating the hormonal levels. Further studies are warranted to confirm the therapeutic validity of HempowHer in clinical studies and combination with existing allopathic medicines could also be explored.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

## 8. Ethical Approval

Ethical No.: 10562/KKCP/2023.

## References

1. Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis, and diagnosis. *Nat Rev Endocrinol*. 2011;7(4):219–31.
2. Zangeneh FZ, Jafarabadi M, Naghizadeh MM, Abedinia N, Haghollahi F. Psychological distress in women with polycystic ovary syndrome from Imam Khomeini Hospital, Tehran. *J Reprod Infertil.* 2012;13(2):111–5.
3. Ahmad I, Shagufta. Recent developments in steroidal and nonsteroidal aromatase inhibitors for the chemoprevention of estrogen-dependent breast cancer. *Eur J Med Chem*. 2015;102:375–86.
4. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. *Endocr Rev*. 2012;33(6):981–1030.
5. Wang D, Wang W, Liang Q, He X, Xia Y, Shen S, et al. DHEA-induced ovarian hyperfibrosis is mediated by TGF-β signaling pathway. *J Ovarian Res*. 2018;11(1):6.
6. Kaushik S, Satapathy T, Roy A, Gupta PP, Purabiya P. Endocannabinoid activation and polycystic ovary syndrome: A systematic review. *Res J Pharm Tech*. 2020;13(1):448–52.
7. Ab Hamid N, Abu Bakar AB, Mat Zain AA, Nik Hussain NH, Othman ZA, Zakaria Z, et al. Composition of Royal Jelly (RJ) and its anti-androgenic effect on reproductive parameters in a polycystic ovarian syndrome (PCOS) animal model. *Antioxidants*. 2020;9(6):499.
8. Osuka S, Nakanishi N, Murase T, Nakamura T, Goto M, Iwase A, et al. Animal models of polycystic ovary syndrome: A review of hormone-induced rodent models focused on the hypothalamus-pituitary-ovary axis and neuropeptides. *Reprod Med Biol*. 2018;18(2):151–60.
9. Iwasa T, Matsuzaki T, Tungalagsuvd A, Munkhzaya M, Yiliyasi M, Kato T, et al. Effects of chronic DHEA treatment on central and peripheral reproductive parameters, the onset of vaginal opening and the estrous cycle in female rats. *Gynecol Endocrinol*. 2016;32(9):752–5.
10. Imani B, Eijkemans MJ, de Jong FH, Payne NN, Bouchard P, Giudice LC, et al. Free androgen index and leptin are the most prominent endocrine predictors of ovarian response during clomiphene citrate induction of ovulation in infertility. *J Clin Endocrinol Metab*. 2000;85(2):676–82.
11. Raja MA, Maldonado M, Chen J, Zhong Y, Gu J. Development and evaluation of curcumin-encapsulated self-assembled nanoparticles as potential remedial treatment for pCOS in a female rat model. *Int J Nanomedicine.* 2021;16:6231–47.
12. Gu Y, Zhou G, Zhou F, Li Y, Wu Q, He H, et al. Gut and Vaginal Microbiomes in PCOS: Implications for Women's Health. *Front Endocrinol (Lausanne).* 2022;13:808508
13. Joshi A. PCOS stratification for precision diagnostics and treatment. *Front Cell Dev Biol.* 2024;12:1358755.
14. Szczuko M, Kikut J, Szczuko U, Szydłowska I, Nawrocka-Rutkowska J, Ziętek M, et al. Nutrition strategy and lifestyle in polycystic ovary syndrome—narrative review. *Nutrients*. 2021;13(7):2452.
15. Han Y, Wu H, Sun S, Zhao R, Deng Y, Zeng S, Chen J. Effect of high-fat diet on disease development of polycystic ovary syndrome and lifestyle intervention strategies. *Nutrients.* 2023;15(9):2230.
16. Coşar A, Özcan P, Tanoglu FB, Tok OE, Özkara G, Timur HT, et al. Comparative effects of the antioxidant glutathione with metformin and Diane-35 on hormonal, metabolic, and inflammatory indicators in a DHEA-induced PCOS rat model. *Gynecol Endocrinol.* 2024;40(1):2302086.
17. Han Q, Wang J, Li W, Chen ZJ, Du Y. Androgen-induced gut dysbiosis disrupts glucolipid metabolism and endocrinal functions in polycystic ovary syndrome. *Microbiome.* 2021;9(1):101.
18. Armanini D, Boscaro M, Bordin L, Sabbadin C. Controversies in the pathogenesis, diagnosis, and treatment of PCOS: Focus on insulin resistance, inflammation, and hyperandrogenism. *Int J Mol Sci*. 2022;23(8):4110.
19. Zhang KH, Zhang FF, Zhang ZL, Fang KF, Sun WX, Kong N, et al. Follicle-stimulating hormone controls granulosa cell glutamine synthesis to regulate ovulation. *Protein Cell.* 2024;15(7):512–29
20. Greff D, Juhász AE, Váncsa S, Váradi A, Sipos Z, Szinte J, et al. Inositol is an effective and safe treatment in polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials. *Reprod Biol Endocrinol*. 2023;21(1):10.
21. Malini NA, Roy GK. Influence of Insulin on LH, Testosterone, and SHBG in Various PCOS Categories Based on the Mode of Secretion of LH in Relation to FSH Levels. *Acta Endocrinol (Buchar).* 2021;17(3):313–18.
22. MacLean JA 2nd, Hayashi K. Progesterone Actions and Resistance in Gynecological Disorders. *Cells*. 2022;11(4):647
23. Naseri L, Khazaei MR, Khazaei M. Potential Therapeutic effect of bee pollen and metformin combination on testosterone and estradiol levels, apoptotic markers, and total antioxidant capacity in a rat model of polycystic ovary syndrome. *Int J Fertil Steril*. 2021;15(2):101–7.
24. He Y, Li X, Li Y, Kuai D, Zhang H, Wang Y, et al. Dehydroepiandrosterone with a high-fat diet treatment at inducing polycystic ovary syndrome in a rat model. *Steroids*. 2024;206:109424.
25. Zhao F, Cui W, Fang C, Luo Y, Zhang C. Chiglitazar ameliorates dehydroepiandrosterone-induced polycystic ovary syndrome in rats. *J Ovarian Res.* 2024;17(1):229.
26. Wang Z, Nie K, Su H, Tang Y, Wang H, Xu X, et al. Berberine improves ovulation and endometrial receptivity in polycystic ovary syndrome. *Phytomedicine.* 2021;91:153654.
27. Yong Z, Mimi C, Yingjie L, Yichen G, Yansu Y, Zhi Z, et al. Mangiferin ameliorates polycystic ovary syndrome in rats by modulating insulin resistance, gut microbiota, and ovarian cell apoptosis. *Front Pharmacol.* 2024;15:1457467.
28. Zia T, Liaqat I, Shahzad KA, Lashari MH, Fouad D, Ataya FS, et al. Ameliorative effect of Fagonia indica-coated chitosan nanoparticles on the ovulatory pattern in a PCOS rat model. *J Ovarian Res*. 2025;18(1):44.

29. Vakili S, Koohpeyma F, Samare-Najaf M, Jahromi BN, Jafarinia M, Samareh A, et al. The effects of l-tartaric acid on ovarian histostereological and serum hormonal analysis in an animal model of polycystic ovary syndrome. *Reprod Sci.* 2024; 31(11):3583–94.
30. Sharafieh G, Salmanifarzaneh F, Gharbi N, Sarvestani FM, Rahmanzad F, Razlighi MR, et al. Histological and molecular evaluation of Mentha arvensis extract on a polycystic ovary syndrome rat model. *JBRA Assist Reprod*. 2023; 27(2):247–53.
31. Fang YQ, Ding H, Li T, Zhao XJ, Luo D, Liu Y, Li Y. N-acetylcysteine supplementation improves endocrine-metabolism profiles and ovulation induction efficacy in polycystic ovary syndrome. *J Ovarian Res.* 2024;17(1):205.
32. Noroozzadeh M, Behboudi-Gandevani S, Zadeh-Vakili A, Ramezani Tehrani F. Hormone-induced rat model of polycystic ovary syndrome: A systematic review. *Life Sci*. 2017;191:259–72.
33. Kumar GS, Tirgar P, Dalal M. Development and evaluation of novel rodent model of PCOS mimicking clinical phenotype in human disease. *Middle East Fertil Soc J*. 2022;27(1):25.

**Cite this article:** Priyanka LGC, Premkumar B, Meena A, Shanthy A, Gupta MNR, Saravanan G, Rajkumar S. Study of hemp tribe HEMPOWHER granules on DHEA- induced PCOS in Sprague Dawley (SD) rat model. *IP Int J Compr Adv Pharmacol*. 2025;10(2):94–103.