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Study of the Effect of Fresh Green *Asparagus officinalis* L. Stems Extract and Metformin Drug on Induced Polycystic Ovary Syndrome (PCOS) in Female Albino Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

During this research, Polycystic Ovary Syndrome (PCOS) was studied and the effect of Metformin Drug and an extract of fresh *Asparagus officinalis L.* stems on it was studied. The study involved 20 adult female albino rats divided into four groups, each containing five female rats. The first group received a physiological saline solution, while the second group was induced with Polycystic Ovary

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Syndrome (PCOS) by being dosed with Letrozole. The third group, after the induction of PCOS, was treated with Metformin, and the fourth group was dosed with Fresh *Asparagus officinalis L.* stems extract. The study focused on hormonal and Histological changes. The results showed that the group of rats with PCOS induced by Letrozole had a significant decrease in the levels of Progesterone (Prog.) and Oestradiol (E2) hormones, and a significant increase in Testosterone (Testo.) compared to the control group. Dosing rats with Fresh *Asparagus officinalis L.* stems extract led to a significant decrease in (E2) hormone level and a significant increase in Progesterone (Prog.) hormone level compared with the control group. Dosing rats with Metformin led to a significant decrease in (E2) hormone level and a significant increase in Progesterone (Prog.) and Testosterone (Testo.) hormone levels compared to the control group. The results also indicated significant changes in hormone levels between Treatment groups and PCOS induction group. The histological study revealed changes in the shape of the ovary, the appearance of cystic structures, congestion of blood vessels, and increased ovarian cellularity. Metformin showed fewer Histological changes, while *Asparagus officinalis L.* stems extract had a therapeutic effect with moderate severity, leading to the disappearance of cystic vesicles and the appearance of corpus luteum and primary vesicles. In conclusion, we conclude that both the therapeutic agents Metformin and the extract of Fresh *Asparagus officinalis L.* stems showed a therapeutic effect on Polycystic Ovary Syndrome, as Metformin drug showed a treatment for this Syndrome, but it requires a long period to show this result, meaning we need more than 28 days, which is the duration of the study, but *Asparagus officinalis L.* stems extract had Faster healing effect within just 28 days. Fresh Green, tender *Asparagus officinalis L.* stems is one of the significant medicinal plants that is used to treat or prevent polycystic ovarian syndrome. Research has shown that it is an effective treatment for the condition. Future researchers studying polycystic ovarian syndrome will find this article useful.

Keywords: Polycystic Ovary Syndrome (PCOS); Asparagus officinalis L.; metformin drug.

1. INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a common hormonal disorder affecting women of childbearing age. It is characterized by menstrual irregularities, insulin resistance, and excess androgen levels. Symptoms worsen over time and can lead to fertility issues, High Cholesterol, metabolic irregularities, high blood pressure, type 2 diabetes, and atherosclerosis. PCOS can also impact daily activities and result in weight gain [1].

Depending on the criteria applied in previous studies, 5-15% of women worldwide suffer from Polycystic Ovary Syndrome (PCOS), which is one of the most prevalent metabolic reproductive disorders in women in the world, Hyperandrogenism (HA), Ovulatory Dysgenesis (OD), Polycystic Ovary Dysfunction (PCOM), Gonadal Abnormalities, Insulin Resistance (IR), and compensatory hyperinsulinemia are among the somewhat variable symptoms of PCOS [2,3]. An amalgamation of environmental and genetic factors contribute to PCOS development. There are three main risk factors for the condition: obesity, inactivity, and a family history. A diagnosis is derived from two of the following three findings: Cysts on the ovaries, absent ovulation, and high testosterone levels. Cysts might be detected by ultrasound. Similar symptoms are produced by hypothyroidism, adrenal hyperplasia, and elevated blood prolactin levels [4].

To manage Polycystic Ovary Syndrome (PCOS), it is important to focus on controlling weight gain and reducing insulin levels through a healthy diet and regular exercise. These factors are believed to be fundamental causes of PCOS. Women with PCOS often have elevated levels of Gonadal-Releasing Hormone (GnRH), leading to increased production of Follicle Growth-Stimulating Hormone (FSH) and Luteinizing hormone (LH) [5]. In addition, the ovaries of women with PCOS typically have an oval shape and contain cysts in the outer layer (Cortex), which are visible as protrusions, These small cysts are regular in shape and resemble pearl beads. They contain immature eggs filled with fluids, causing an enlargement of the ovary due to a significant increase in the size of the follicles (Priyadarshani et al., 2022). Histologically, they contain many cystic follicles due to an excess of Androgen, which destroys the granulosa cell layers and causes an increase in Theca Layer. This condition also leads to a lack of ovulation, resulting in immature ovarian vesicles and a

decrease in the number of corpus luteum (Teede et al., 2018).

Ovaries, or female gonads, appear anatomically as paired endocrine intraperitoneal organs located in the right and left lower quadrants of the female abdominal cavity. It is important to note that the ovaries are the female pelvic reproductive organs that house the eggs and participate in reproduction and generation of sex hormones [6]. The size of the ovary is 5 * 3 * 4 cm or 3 mm in a mature female rat and weighs about 60 mg during reproductive age. The ovary consists of three main parts: the outer cortex, the central medulla, and the ovarian network [7].

Traditional medicine methods and returning to nature to treat many diseases. This is because medicines are currently produced from chemical substances, but previously our ancestors used plants as a natural and basic source for treating diseases because they do not contain side effects on the human body if used correctly (Saadawi et al., 2021), and medicines produced from plants have proven to be the main treatment in the complementary medicine system, and have been widely used since ancient times, and this was an impetus for the use of medicinal plants and their vital benefits in the production of drugs and medicines (de Sousa Araújo et al., 2016).

Treatments for Polycystic Ovary Syndrome range from medication to surgery. Complementary and alternative therapies are now a viable option due to the limited efficacy of long-term treatments and their potential side effects Recent estimates indicate that complementary therapies are becoming more and more popular ، Treatments for Polycystic Ovarian Syndrome have included the use of a variety of plants, including *Saraca asoka*, *Moringa olifera*, *Asparagus racemosus*, and *Cimicifuga racemose* [4].

In the treatment of Polycystic Ovary Syndrome, many Medicinal Plants were used, and one of these plants is *Asparagus officinalis L.* plant, which was used to treat Polycystic Ovary Syndrome, according to a study [8] when it used the roots of this plant because of the effective substances it contains in treating this syndrome, and during This study also points out the importance of the fresh, tender stem, which contains many chemicals such as biologically active sugars, steroid saponins, flavonoids, dietary fiber, and many minerals such as (K, Ca, and Mg), and is also rich in vitamins such as (A, B1, B2, C, and E). And Essential Amino Acids, and Folic Acid (Lee et al., [9], Motoki et al., [10], and one of the most unique compounds found in *Asparagus officinalis L.* stems is Asparagine Acid (1,2-dithiolane-4-carboxylic acid), which is a compound that contains On sulfur [11], which appears to have a significant influence on both Flavor and Biological properties of asparagus, asparagus acid is considered a distinctive feature of this plant as this acid is a 1,2-dithioleane ring system (Mitchell and Waring, [11], Hildebrandt et al., [12]. Since then other sulfur-containing compounds have been discovered, including Asparaptin and white and Green *Asparagus officinalis L.* stems spears [13]. The main phenolic compound in fresh tender asparagus extract was caffeic acid accompanied by Rutin, Quercetin, Various Saponins, and Four Lignans [14].

Glucophage (Metformin) treatment is one of the types of treatments used to treat Polycystic Ovary Syndrome, and it is the most widely used treatment due to the lack of side effects of this treatment. Some of the previous studies indicate that the effectiveness of this treatment is minimal, but subsequent research has proven its effectiveness. The main advantage of treatment is that it requires a long period of time to complete the healing process, and this period varies for women with Polycystic Ovary Syndrome [15]. This medication is usually prescribed to treat type 2 Diabetes, but it can also be used to treat Polycystic Ovary Syndrome. In order to increase Insulin Sensitivity, it may be especially beneficial for those who want to increase their fertility and those who have Insulin Resistance [4].

Research Objective: This study Aims to know the effect of Fresh Green *Asparagus officinalis L.* stems and the drug metformin on polycystic ovary syndrome, and which treatment gives a greater and faster effect. Also, our goal in conducting this study is to shed light on Fresh Green *Asparagus officinalis L.*stems, which contains effective compounds in treating many diseases. Of diseases, including Polycystic Ovary Syndrome, it has very few or no side effects. Also reduce the use of chemical medications that have side effects on the body.

2. MATERIALS AND METHODS

2.1 Experimental Animals

In this experiment, white rats (20) sexually mature female rats were used. They were brought from the College of Pharmacy - University of Karbala. They were more than (9) weeks old and weighed (160) grams or more. The females were placed in separate cages and monitored for two weeks. Before starting the experiment to adapt and ensure her health is good and that she is not pregnant. The floor of the cages was furnished with sawdust, and the animals were placed under appropriate conditions in terms of temperature, ventilation, and lighting. They were divided into four groups (Negative Control group, PCOS-induction group, a group in which PCOS was induced and treated with the drug Metformin, and a group in which PCOS was induced and treated with Fresh *Asparagus officinalis L.* stems extract).

2.2 Induction of Polycystic Ovary Syndrome

To induce Polycystic Ovary Syndrome in females Albino rats, we used Letrozole. We dissolved 1 mg of Letrozole in 1% Carboxymethylcellulose powder (CMC) and administered the dose orally using the Gavage dosing tool once a day for 28 days. The dosage for each group was calculated based on the average weights of the animals according to the equation: Peng et al., [16], Wang et al., [17].

Dose weight mg/kg = Animal weight x Prescribed dose weight * 1000

2.3 Prepare *Asparagus officinalis L.* Stems Extract

To prepare Fresh Green *Asparagus officinalis L.* stems extract, each bundle of asparagus stems was weighed separately and then cut into medium, equal pieces. These pieces were then placed in an electric blender with 10 ml of distilled water. After blendihg, the juice was extracted and filtered using medical gauze and Whatman no. filter papers. The resulting filtrate was stored in a sterile glass bottle and then transferred to heat-resistant glass containers. The filtrate was dried in an electric oven at 45 C^0 to obtain a dry extract in powder form. The dry extract was collected, stored in a sealed tube, and kept in the refrigerator until used in the experiment. This process was repeated multiple times to obtain a sufficient amount of dry extract [18].

2.4 Preparation of Glucophage (Metformin)

The drug Metformin Glucophage, produced by Merck Sante s.a.s, 2 rue du Pressoir Vert-45400 SEMOY-France, was used. Each box contains 5 strips, each strip contains 20 tablets, and each tablet contains 500mg of Metformin. This dosage is commonly used for humans. The therapeutic dose required for the study was calculated based on the equation for converting the therapeutic dose from humans to animals, as outlined in AL-Safi, [19].

2.5 Measurement of Hormone Concentration

The rats were anesthetized with Chloroform, then 3 ml of blood was drawn by a heart stab method, then they were placed in Gel Tube Bottles and then taken to Laboratory to measure the concentration of Hormones (Luteinizing Hormone (LH), Follicle-Stimulating Hormone (FSH), Estradiol (E2), Progesterone (Prog). .), and Testosterone (Testo.) following the instructions provided with the test kit for each. hormone according to the method described [20].

2.6 Histological Preparations

The ovarian sample was preserved in a 10% Formaldehyde Solution (38% formaldehyde, 100 ml in 900 ml tap water) after it was removed from the animal. After 48 hours, it was taken out of the formalin in order to make histological preparations following the method described by Suvarna et al., [21].

3. RESULTS AND DISCUSSION

3.1 Hormonal Study

The results presented in Table (1) indicated that rats with induced Polycystic Ovary Syndrome (G2) and orally administered letrozole for 28 days experienced a significant decrease ($P<0.05$) in the levels of both Progesterone hormone (Prog.) and Estradiol hormone (E2). There was also a decrease, though not statistically significant, in the level of Follicle-Stimulating Hormone (FSH), a significant increase ($P<0.05$) in Testosterone(Testo.) level, and a non-significant increase in Luteinizing Hormone (LH) compared to the control group (G1). On the other hand, dosing the rats with Fresh *Asparagus officinalis L.* stems extract (G4)

resulted in a significant decrease (P<0.05) in the level of (E2) hormone, a non-significant decrease in Testosterone (Testo.) level, a significant increase (P<0.05) in Progesterone (Prog.) hormone level, and a non-significant increase in (LH) level compared to the control group (G1). Dosing rats with Metformin (G3) led to a significant decrease (P<0.05) in (E2) hormone level and a significant increase in Progesterone (Prog.) hormone level, with a non-significant increase in LH level compared to the control group (G1). The results showed a significant increase (P<0.05) in the level of the hormone Prog, a significant decrease in the level of the hormone (E2), and a non-significant decrease in the levels of hormones (Testo. and LH) in the treatment group (G3) compared to the induction group (G2). In the case of PCOS, the results in Table No. (1) indicate a significant increase (P<0.05) in the level of Testosterone (Testo.), a non-significant increase in Luteinizing hormone (LH), and a significant decrease in the levels of hormones (E2 and Prog.) in Fresh *Asparagus officinalis L.* stems extract group (G4) compared with the PCOS induction group.

The results presented in Table (1) indicate that female rats with induced Polycystic Ovary Syndrome exhibited a significant increase in blood serum Testosterone (Testo.) concentration. Meanwhile, there was no significant change in Luteinizing Hormone (LH) concentration and a non-significant decrease in Follicle-Stimulating Hormone (FSH) concentration. Additionally, there was a significant decrease in the concentrations of the hormones Oestradiol (E2) and Progesterone (Prog.) compared to the control group. These findings align with a previous study by (Fritz and Speroff, [22], which also reported significantly higher serum (LH and Testo.) concentrations in PCOS patients. Furthermore, these results are consistent with the findings of (Kandasamy et al., [23], who observed significant increases in (LH and Testo.) concentrations and significant decreases in (E2 and Prog.) concentrations in PCOS patients compared to the control group ‹The results also revealed a non-significant decrease in (FSH) concentration, which parallels the findings of (Kafali et al. [24]. Their study demonstrated that oral administration of Letrozole led to a significant increase in (LH and Testo.) concentrations in Adult Female rats, along with a significant decrease in (E2) concentration within the PCOS group. Moreover, a significant decrease in (Prog.) levels was also noted in the PCOS group.

Hyperandrogenism is the primary feature of PCOS, mainly stemming from increased androgen production in the ovaries and, to a lesser extent, in the adrenals. The underlying mechanisms include increased Androgen production, Hyperinsulinemia due to insulin resistance, and increased theca cell volume in the enlarged ovarian stroma. This study observed a decrease in Progesterone (Prog.) and Estrogen (E2) levels in the PCOS group, consistent with a previous study [25]. Elevated Testosterone (Testo.) levels indicate the accumulation of androgens because Letrozole, acting as a nonsteroidal aromatase inhibitor, prevents the conversion of androgen substrates to Estrogen (E2). The low Estrogen (E2) levels weaken negative feedback on (LH) production in the pituitary gland, leading to increased (LH) levels [24], which further stimulates the theca cells to secrete Testosterone (Testo.). High (LH) levels are negatively associated with Progesterone (Prog.) levels during the luteal phase in women with Polycystic Ovary Syndrome, suggesting that low levels of Progesterone (Prog.) may be linked to excessive (LH) secretion in this Syndrome. It has been suggested that high (LH) concentrations may stimulate the observed high androgen synthesis in this syndrome using (Prog.) as a precursor and that (LH) induced hyperandrogenism suppresses (Prog.) synthesis, although these possibilities require further confirmation, according to a study [26].

The results of the current study revealed that administering Metformin drug (Meto.) (500 mg/kg body weight daily) led to a non-significant decrease in (LH) and (Testo.) levels. This aligns with the findings of (AL-Mozie [27], who observed that treating rats induced with Polycystic Ovary Syndrome (PCOS) using (Meto.) resulted in a non-significant decrease in (Testo.) levels linked to an increase in Sex Hormone Binding Globulin (SHBG). Elevated (Testo.) levels in PCOS likely indicate the accumulation of Androgens due to the conversion of androgen substrates to Estrogens. This process can be inhibited by an aromatase inhibitor. The decrease in Testosterone concentration in Metformin group reflects a reduction in androgen biosynthesis by the ovaries, and decreased Estrogen production due to inhibiting aromatase can result in an increase in (LH) secretion in Hypothalamus and Pituitary Gland, possibly through negative reactions to Estrogen [28].

Table 1. Effect of Polycystic Ovary Syndrome (PCOS), treatment with Metformin (Meto.), and asparagus stem extract(Asp.) on levels of Luteinizing Hormone (LH), Follicle Growth Stimulating Hormone (FSH), Oestradiol (E2), Testosterone (Testo.), and Progesterone (Prog.) in Blood Serum of Albino Female rats

Standards	LH IU/ml	FSH IU/ml	E2 ng/ml	Testo ng/ml	Prog ng/ml
Control group G1	0.49 ± 0.130	0.064 ± 0.006	21.87 ± 0.83 **(*)**	0.42 ± 0.083 (**)	**34.25 ± 1.881 (***)**
Induction PCOS G2	0.53 ± 0.024	0.04 ± 0.012	17.26 ±0.79 (**)	3.53 ± 0.585 (*)	**28.41 ± 1.700 (****)**
Metformin drug group G3	0.42 ± 0.055	0.06 ±0.017	7.95 ± 0.53 (*****)	2.78 ± 0.377 (*)	**50.28 ± 1.491 (*)**
Asparagus stems extract G4	0.54 ± 0.051	0.064 ±0.012	15.01 ± 0.72 (***)	0.36 ± 0.076 (**)	**48.82 ± 1.209 (*)(**)**
L.S.D	0.248	0.121	1.99	0.778	**4.140**

Mean ± standard error

Different symbols (,**,***,****,*****) indicate significant differences vertically at the probability level (P < 0.05)*

Several studies, including Marcondes et al.,[29], have observed a positive effect of Metformin on Hyperandrogenism in women with Polycystic Ovary Syndrome ، Lowering Circulating Insulin levels with metformin may improve Hyperandrogenaemia as reported by (Baillargeon et al., [30], Ortega Gonzalez et al.,[31]. It was noted that free Testosterone and Estradiol decreased significantly in Metformin-treated group compared to the PCOS induction group due to improvement in Hyperandrogenism or due to the effect of feedback on increased ovarian production of (E2) hormone, which leads to the resumption of healthy and natural follicle formation ,The positive effect of Metformin on Hyperandrogenism in PCOS may be attributed to the decreased Pituitary secretion of (LH) and decreased ovarian secretion of Androgens [32]. The cold aqueous extract of *Asparagus officinalis L.* stems contains active components that affect the regulation of Luteinizing Hormone and Hormone-Stimulating Follicle Growth. This plant contains arginine, which converts to nitric oxide, an essential element in regulating these hormones [33].

The active compounds in *Asparagus officinalis L.* plant increase hormone levels in female white rats, specifically (FSH, LH, Prog, Testo, and E2). The highest increase was observed in the group that received a dose of 300 mg/kg of cold aqueous extract from fresh, tender *Asparagus officinalis L.* stems [34]. *Asparagus officinalis L.* is rich in Amino Acid compounds such as Aspartic Acid and Arginine, which stimulate the secretion of Gonadotropin-Releasing Hormones and Luteinizing Hormones [35,36].

Phytoestrogen compounds in *A. officinalis* extract also increase Ovarian Hormone levels. Additionally, Steroidal Saponins extracted from *A.officinalis* act as precursors to Progesterone and increase its secretion [37-39].

Asparagus officinalis L. stems are rich in Minerals and Vitamins Olas, [40], which act as cofactors in Various Enzymatic activation systems for Oocyte growth and maturation, affecting ovarian function and fertility [41,42]. The histological analysis in this study revealed an increase in number of Ovarian Follicles and Corpus Luteum, as well as a non-significant increase in number of Atretic Follicles in the group treated with *A. officinalis* extracts. These findings are consistent with an increase in hormones of Hypothalamic-Pituitary Axis and Gonads. During the early stages of follicular development (Initial and Primary), granulosa cells proliferate slowly, but the granulosa cells of the pre-antral follicles respond to (FSH) stimulation and secrete large amounts of Estradiol [43]. An increase in number of Corpus Luteum is also accompanied by an increase in (LH), which affects the cells of Corpus Luteum and subsequently leads to increased synthesis of progesterone [43]. Therefore, the increase in Progesterone level was not unexpected given the increased Corpus Luteum number in the study (Jashni et al., 2016).

3.2 Histological Studies

1. **Control Group:** Ovarian tissue from the control group displayed a normal histological structure with Outer Cortex, Inner Medulla, Graafian Follicles, abundant Corpus Luteum, presence of Primordial Follicles, and some Aretic Follicles (Fig. 1).
2. **PCOS Group:** Ovarian tissue from Female rats with induced Polycystic Ovaries showed numerous expanded Cysts or Cystic Follicles on ovary surface. There were also Primordial Follicles, abundant Atretic Follicles, and minimal or no Corpus Luteum present (Fig. 2).
3. **Metformin Drug Group:** Ovarian tissue from rats treated with Metformin exhibited limited or non-existent dilated Cyst Follicles. It also showed Primordial Follicles, Primary Follicles, Graafian Follicles, Corpus Luteum, and a significant amount of vesicular Atretic Follicles (Fig. 3).
4. ***Asparagus officinalis L.* Stems Group:** Ovarian tissue of rats treated with Fresh Green *Asparagus officinalis L.* stems extract displayed Primordial Follicles, Primary Follicles, Graafian Follicles, and Corpus Luteum, with no presence of Cyst Follicles (Fig. 4).

Fig. 1. Shows a histological section of ovary of female Albino rats from Control Group
The image displays a normal histological structure, including Outer Cortex (OC) and Central Medulla (CM). Additionally, it depicts Graafian Follicles (GF), Corpus Luteum (CL), Primordial Follicles (PF), and Atretic Follicle (AF). (H&E 10X)

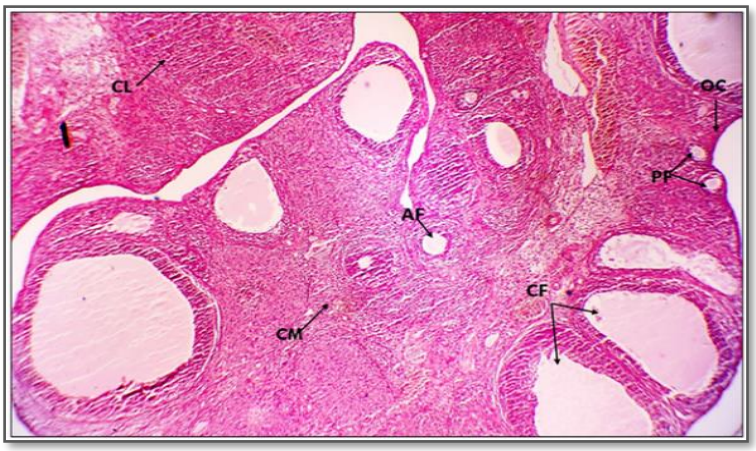

Fig. 2. Shows a histological section of ovaries of female Albino rats
The experiment induced Polycystic Ovary Syndrome, which is represented by Outer Cortex (OC) and Central Medulla (CM). In some cases, the presence of Corpus Luteum (CL) was noted. Additionally, there were Cysts or Cystic Follicles present. Cyst Follicle (CF) was greatly expanded, and there was a presence of both Primordial Follicles (PF) and a large number of Atretic Follicles)10X H&E

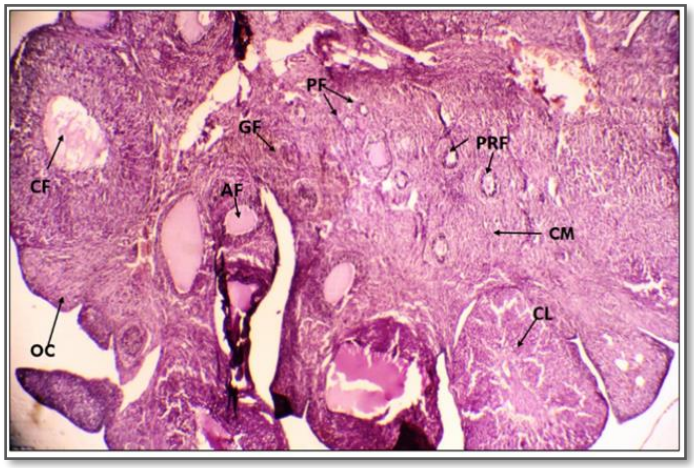

Fig. 3. Shows depicts a tissue section of Ovaries of female Albino rats

These rats were induced with Polycystic Ovary syndrome and treated with Metformin. The image shows Outer Cortex (OC) and Central Medulla (CM), as well as the presence of dilated Cystic Follicles (CF). There is very little or no presence of Primordial Follicles (PF) and Primary Follicles (PrF), but there is an indication of Graafian Follicles (GF) and the corpus luteum (CL). Additionally, a significant number of Atretic Follicles (AF) are observed (10X H&E)

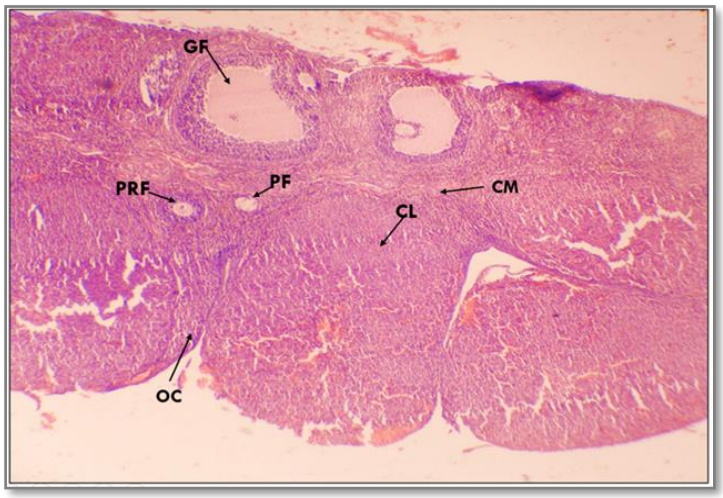

Fig. 4. Shows a histological section of the ovaries of female Albino rats with PCOS

These rats were induced with Polycystic Ovary syndrome and treated with an extract of fresh Green Asparagus officinalis L. stems. The image shows Outer Cortex (OC) and Central Medulla (CM), as well as the little or not found of Cystic Follicles (CF). There is containing Primordial Follicles (PF) and Primary Follicles (PrF), Graafian Follicles (GF), and the presence of Corpus Luteum (CL). Additionally, a significant number of Atretic Follicles (AF) are observed (10X H&E)

The results of this study, in which Polycystic Ovary Syndrome was induced, showed a significant appearance of Cystic Follicles. This is consistent with pathological changes in the ovaries of women with Polycystic Ovary Syndrome, due to the use of Letrozole, an effective aromatase inhibitor [44]. Letrozole leads to the accumulation of excess androgen in ovary, affecting the growth and function of Ovarian Follicles, ultimately causing their destruction and the formation of Cystic Follicles. Al-Masoudi [8] conducted a study that supports these findings, as histological sections from female albino rats treated with Metformin 500 mg/kg showed improved growth and development of Ovarian Follicles, egg maturation, and a decrease in the number of Cystic Follicles in Ovaries, ultimately improving fertility. This improvement is attributed to the active components of Metformin, which work to Regulate Insulin levels in the body, increasing insulin sensitivity and preventing weight gain [45].

Thus, it reduces obesity, which is one of the symptoms of Polycystic Ovary Syndrome, and it also works to reduce the percentage of Low-Density Lipoprotein Cholesterol in the body. All of these results do not appear accurate, some agree that it is a cause of Polycystic Ovary Syndrome, and others do not agree, according to what was stated in the article. Study Lord et al., [15], but according to the study conducted, we note that the weight of female white rats was reduced, while the results of histological sections in all female white rats treated with fresh asparagus stem extract, 300 mg/kg, show a significant increase in the growth and development of the follicles. And faster than in the group treated with Metformin, the maturation of the eggs and the complete disappearance of Cystic Follicles leads to an increase in fertility, as this plant is used to treat impotence and infertility. This is due to Biologically active components that are found in the stems of the asparagus plant, which contains high levels of flavonoids, Phenolics, and essential nutrients Motoki et al., 2019, Lee et al., [9]. Including vitamins, amino acids, minerals, salts, and the compound Quercetin (Staruschenko, 2018), which is one of the plant estrogen compounds, Phytoestrogen, which is similar in its action to Estrogen and therefore binds to hormone receptors and increases the secretion of (FSH), which leads to the maturation of follicles and improvement of fertility, and this study agreed. Several studies of many plants that contain flavonoids, such as mint [46], dates, and other plants [47-49].

4. CONCLUSIONS

In our current study, we found that both the drug metformin and asparagus stems have an effect in treating polycystic ovary syndrome. However, we observed that fresh green *Asparagus officinalis L.* stems have a faster effect than Metformin Drug in treating Polycystic Ovary Syndrome induced in female Albino rats.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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