Review Article

INDUCTION AND TREATMENT OF POLYCYSTIC OVARY SYNDROME WITH PLANT EXTRACT IN RATS: A SYSTEMATIC REVIEW

ABSTRACT

Aims: To review the induction and treatment of polycystic ovarian syndrome (PCOS) with plant extract in rats in light of the rising incidence of the condition, its accompanying physical and mental issues, and the role that sex hormone alterations play in its development.

Methodology: An extensive literature search was conducted using relevant publications published between 2012 and 2022, and indexed in Google Scholar, PubMed, Elsevier, Scientific Information Database, and Science Direct were studied.

Results: The review found that 43.75% of the studies induced PCOS with Letrozole, 31.25% with estradiol valerate, 6.25% induced with Testosterone Enanthate (TE) and 6.25% of the studies induced PCOS with Testosterone Propionate (TP). The review reveals that 50, 200 and 600 mg/kg/BW) of saffron petal extract (SPE), and (20, 40 and 80 mg/kg/BW) of saffron petal anthocyanins (SPA) were used for the treatment in TE-induced PCOS. The level of Luteinizing hormone (LH), estrogen and testosterone concentration significantly increased ($P < 0.01$) and the Follicle stimulating hormone (FSH) and progesterone concentration reduced ($P < 0.001$) following TE-treatment as compared with the control.

Conclusion: The health of women is seriously endangered by polycystic ovarian syndrome. The long-term morbidity and danger associated with polycystic ovarian syndrome, particularly for glycemic irregularities and Type 2 diabetes, have previously been misdiagnosed as cosmetic or reproductive issues. Obesity-related problems, mood and/or mental disorders, and cardiovascular disease are additional morbidities. Further investigations into the mechanisms of effect for plant extracts are needed to complete our understanding of the reproductive endocrinological effects for plant extract treatment for polycystic ovarian syndrome.

1. INTRODUCTION

A very prevalent and diverse endocrine disease called polycystic ovarian syndrome (PCOS) causes roughly 75 percent of cases of infertility [1,2]. The Stein-Leventhal syndrome, first published in 1935, was the name given to the polycystic ovary condition at that time. Initially, the clinical triad of hirsutism, amenorrhea, and obesity, as well as pathognomonic ovarian abnormalities, were necessary for diagnosis [3]. In 1986, Brower used a single intramuscular (i.m.) injection of estradiol valerate (EV) in 8-week-old rats to experimentally induce PCOS in the rodents. The rats lost their ability to ovulate and manifested traits similar to those of PCOS in humans, such as big cystic follicles in the ovaries and altered luteinizing hormone concentrations [4]. Premature puberty, hirsutism, atypical menstrual cycles, early adulthood, middle age, and later life (diabetes mellitus and cardiovascular illnesses) are just a few examples of how PCOS symptoms can appear at any age [5]. Its primary characteristics are anovulation, hyperandrogenism, and polycystic ovarian morphology, and its main clinical symptoms are menstrual irregularities, infertility, hypertrichosis, and metabolic syndromes,

which include obesity, dyslipidemia, and type 2 diabetes [6]. While the primary cause of this condition is still unknown, it has been hypothesized that genetics, insulin resistance, obesity, inflammation, and oxidative stress may contribute to its pathogenesis [7,8]. Acne, obesity, hair loss, hypertension, and irregular ovulation are symptoms of this condition in women [9].

Due to underlying metabolic abnormalities, being overweight makes all symptoms of PCOS worse [10]. According to [11], these patients have changed endocrine hormone levels and are at risk for infertility as well as metabolic diseases including type 2 diabetes. Treatment options for moderate syndromes (a situation in which the disease's symptoms are not severe) include the use of oral contraceptives or conventional herbal medicines [12]. Studies on theca cells both *in vivo* and *in vitro* indicated that ovarian theca cells in PCOS-afflicted women are significantly more active than the cells in healthy women in the process of converting androgenic precursors into testosterone. As a result of theca cells producing androgen in response to luteinizing hormone (LH), individuals with PCOS have higher blood levels of androgens [13].

Mostly due to hormonal imbalance, this disorder affects women's ability to conceive. High plasma androgen concentrations are common in patients. Patients with PCOS may experience increased androgen production due to metabolic abnormalities including insulin resistance that cause high plasma androgen (HPA) axis activation [14] [15]. Multiple cysts develop in PCOS patients' ovarian tissue as a result of hyperandrogenism and high levels of the luteinizing hormone [16] [17]. In contrast to follicular stimulating hormone (FSH), PCOS increased the frequency of gonadotropin-releasing hormone (GnRH) pulses [18]. Theca cells produce more androgens as a result of this rise in LH concentration, but a relative FSH shortage lowers granulosa cells' capacity to convert androgen into estrogen and hinders follicle development and ovulation [19]. PCOS has been treated with a variety of therapeutic approaches, including lifestyle changes, surgery, and medications such as clomiphene citrate, metformin, letrozole, and tamoxifen [20]. Our goal is to review the induction and treatment of PCOS with plant extract in rats in light of the rising incidence of the condition, its accompanying physical and mental issues, and the role that sex hormone alterations play in its development.

2. MATERIAL AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

Design

This was a systematic review which was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

Search strategy

Different databases were searched to get necessary materials needed for this review. A scientific literature search was done using Elsevier, Google scholar, PubMed and Springer link databases. Additionally, literatures were systematically searched from research gate, Cochrane library and Directory of Open Access Journal (DOAL). For studies that may have been missed in the electronic search, cross reference was undertaken using reference lists of all identified articles. The first search took place between October 05 and 07, 2022, while the second took place between October 15 and 20, 2022. Detailed inclusion and exclusion criteria were developed with caution, to make sure that they match the review questions and involve sufficient details to help point out all relevant studies and exclude irrelevant ones (21).

TABLE 1

Search terms used in the literature search

	AND
PCOS*	Rat*
PCOS* Induction*	Plant extract * Rat*
PCOS* Treatment*	Plant extract* Rat*

Inclusion criteria

The inclusion criteria that was used for this review includes both qualitative and quantitative studies on PCOS in low and middle income countries.

Exclusion criteria

Articles were excluded, if no data is presented for the desire outcome, editorials and short commentaries. Other exclusion criteria were papers that were not peer-reviewed and those that the full text could not be assessed.

Data extraction

Standardized forms developed by the authors were used for data extraction to minimize the risk of bias. One of the authors extracted data from the included studies, and two of the other authors checked these data. Discrepancies were resolved by referring to the original studies. Data were extracted on induction and treatment of PCOS plant extract in rats. One of the authors independently considered the potential eligibility of each of the abstracts and titles from the retrieved citations and thereafter requested full-text versions of these potentially eligible studies. Two of the authors separately and independently assessed the full text of the potentially eligible publications. Disagreements were resolved by consensus. Initial agreement was obtained on 80 items (95%), and discrepancies were discussed between authors until 100% agreement was obtained. The following information was extracted from the included studies: authors, tittle, study population, state, objective(s), study design, and findings.

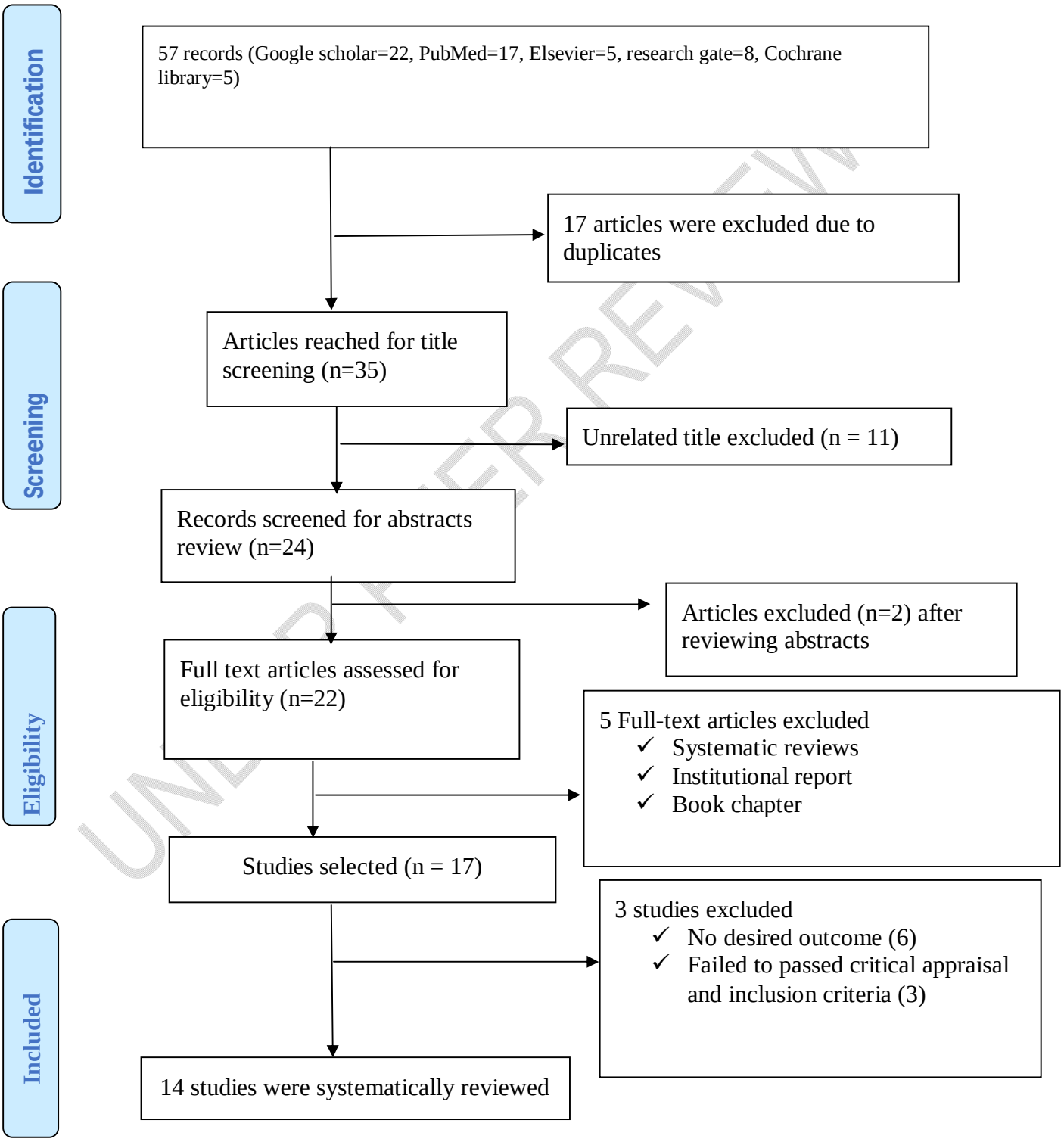
Quality Assessment

The articles used for the review were properly screened. They were firstly screened using the titles and their abstracts. The full papers were screened and the similarities of the papers were determined. The selected papers were manually and automatically de-duplicated. Quality assessment of each study selected was based on the criteria of [22] [23].

Critical appraisal

The qualitative, quantitative, and mixed-method researches were evaluated using the Critical Appraisal Skills Programme [CASP] instrument [24] and Critical Appraisal Framework [25] criteria [26].

Figure 1: PRISMA Flow chat of the study selected



2.2.9 List of Papers Reviewed

The search results are shown in Figure 1, along with a synopsis of the papers consulted (the PRISMA flow chat). Although the databases contained 57 research articles, only 14 of them met the inclusion criteria for this systematic review (Table 2).

Author	Title	Study design	Country of study	Study duration	Objectives/Research question	Findings
[27]	*Crocus sativus* (saffron) petals extract and its active ingredient, anthocyanin improves ovarian dysfunction, regulation of inflammatory genes and antioxidant factors in testosterone-induced PCOS mice	Female NMRI mice (25–35 g, 6 weeks old) (n = 96) were divided into four groups (n = 12 control group, n = 12 testosterone enanthate (TE) group, n = 36 TE + SPE group, n= 36 TE + SPA group,	Iran	60 days	The effects of saffron petal extract (SPE) and saffron petal anthocyanins (SPA) on ovarian hormones, steroidogenic enzymes, ovarian dysfunction, regulation of anti-inflammatory genes, and antioxidant factors in female PCOS mice were studied	These results suggest that SPE and SPA ameliorates symptoms of PCOS by improving dysregulation of ovarian steroids, steroidogenic, antioxidant enzymes and inflammatory markers in PCOS mice.
[28]	Comparison of the effects of Ginger extract with clomiphene citrate on sex hormones in rats with polycystic ovarian syndrome	63 adult female rats (170-200 g) were studied and divided randomly into 9 groups as control, sham, and 7 experimental groups (estradiol valerate used as PCOS inducing agent, intramuscular) orally daily for 60 and 89 days.	Iran		To compare the effectiveness of ginger with clomiphene on sexual hormones such as Luteinizing hormone (LH), Follicle stimulating hormone (FSH), estrogen and progesterone in order to treat PCOS effectively with fewer side effects.	As the long-term administration of clomiphene citrate has some side effects, the use of ginger as a herbal medicine without any side effects at high doses can be an effective and good alternative in improving PCOS
[29]	The ameliorative effects of marjoram in dehydroepiandrosterone induced polycystic ovary syndrome in rats	A 75 postpubertal (42 days old) female Wistar rats were randomly assigned into five groups (control, dehydroepiandrosterone (DHEA) induced-PCOS model, marjoram-treated PCOS rats, metformin-	Jordan		To investigate the ameliorative effects of marjoram extract on hormonal profiles, body and ovaries weight, insulin sensitivity, inflammation, and oxidative stress in a rat	The current study showed that marjoram significantly decreased ovaries' weight and the estradiol levels (P-value < 0.05) compared to the DHEA group. Interestingly, marjoram improved

		treated PCOS rats and the combination of marjoram+metfomin treated PCOS model)			model of PCOS	insulin sensitivity as manifested by a significant increase in the adiponectin serum levels (P-value < 0.05).
[30]	Effect of *Aloe barbadensis* Mill. formulation on Letrozole induced polycystic ovarian syndrome rat model	The PCOS rat model was developed with 12-16 adult virgin Charles Foster female rats weighing 200--225g.	India		To evaluated the efficacy of *Aloe barbadensis* gel formulation in a PCOS rat model.	*Aloe barbadensis* gel formulation exerts a protective effect against the PCOS phenotype by restoring the ovarian steroid status, and altering key steroidogenic activity. This can be attributed to phyto-components present in the extract.
[31]	Effect of *Citrullus colocynthis* hydro-alcoholic extract on hormonal and folliculogenesis process in estradiol valerate-induced PCOs rats model: An experimental study	40 female adult Wistar rats divided into five groups	Iran		To evaluate the effect of CCT hydro-alcoholic extract on hormonal and folliculogenesis process in estradiol valerate-induced PCOS rats' model.	Marked improvemnt in hormonal and histological symptoms of PCOS may be due to CCT effect hence, CCT can potentially be considered as an effective drug for treatment of PCOS.
[32]	Effect of *Vitex agnus-castus* ethanolic extract on hypothalamic KISS-1 gene expression in a rat model of polycystic ovary syndrome	Thirty-two female rats were distributed into: control, Vitagnus-treatment (365 mg/kg for 30 days), PCOS (Letrozole for 28 days) and PCOS animals treated with Vitagnus (30 days of Vitagnus after PCOS induction).	Iran	30 days	To investigate Vitagnus effect on the expression of kisspeptin gene in a rat model of PCOS	The results indicated that Vitagnus extract inhibited downregulation of KISS-1 gene in the hypothalamus of PCOS rats.

[33]	Effects of chamomile extract on biochemical and clinical parameters in a rat Model of polycystic ovary syndrome	Thirty virgin adult cycling Wistar rats, weighting 200 - 220 g were divided into two groups	Iran		To evaluate the effects of Chamomile alcoholic-extract on the biochemical and clinical parameters in a rat model of PCOS.	The histological and hormonal results showed that Chamomile can decrease the signs of PCOS in the ovarian tissue and help LH secretion in rats ($p < 0.05$)
[34]	Effects of *Fagonia indica* on letrozole-jnduced polycystic ovarian syndrome (PCOS) in young adult female rats	Twenty-five healthy female Wistar albino rats (150–200 g)	Pakistan		To investigate the effectiveness of ethanolic extract of *Fagonia indica* in letrozole-induced PCOS young adult female rats	This study validates the potential of *Fagonia indica* for the amelioration of metabolic, as well as, hormonal disturbances that occurred in PCOS.
[35]	Hydroalcoholic extract of flax seed improves polycystic ovary syndrome in a rat model	Twenty four rats divided into four groups including negative control, positive control, PCOS and treatment groups.	Iran		Effect of hydroalcoholic extract of flax seed was evaluated on ovarian hormones and histological changes of uterus and ovary in a PCOS-induced rat model	Hormonal profile and histomorphometric features of ovary that were disturbed by PCOS induction were ameliorated by hydroalcoholic extract of flax seed
[36]	*Phyllanthus muellerianus* (Euphorbiaceae) restores ovarian functions in letrozole-induced polycystic ovarian syndrome in rats.	One hundred and eight adult female Wistar rats (180-200 g) were used.	Cameroon		To investigate the effects of *P. muellerianus* extracts on estrus cyclicity, lipid profile, oxidative stress-related markers, sex hormones, and ovarian architecture in letrozole-induced PCOS in rats.	This plant could be useful in the management/treatment of reproductive and metabolic disorders related to PCOS.
[37]	Licorice ethanol extract improves	Sprague Dawley rats were obtained from	Korea		To examine the effects of GRR	These results suggest that GRR

	symptoms of polycytic ovary syndrome in Letrozole-induced female rats.	Daehan Biolink and divided into three groups of six rats each. For the PCOS rat model, a 90-day release pellet containing Letrozole (1.8 mg/pellet) was implanted subcutaneously for 4 weeks under anesthesia [Zoletile (30 mg/kg)–Rompun (5 mg/kg)–saline mixture (2:1:2)] in 6-week-old female rats.			(Glycyrrhizae radix et rhizome) extract on PCOS-like symptoms in female rats.	extract inhibits the symptoms of PCOS by regulating imbalanced hormonal levels and irregular ovarian follicles
[38]	*Ocimum kilimandscharicu*m L. restores ovarian functions in letrozole - induced polycystic ovary syndrome (PCOS) in rats: comparison with metformin	Adult virgin female Wistar Albino rats (6 weeks old, weighing 150–200 g; total n = 54, n = 6)	Egypt		To investigate therapeutic merits of *Ocimum kili-* *mandscharicum* (Ok), in a letrozole PCOS rat model, and compare it to metformin	These results suggest that Ok extract and EA (ethyl acetate) fraction halt letrozole-induced reproductive dysfunctions and restore normal morphological and physiological functions in PCOS rats, even superior to metformin.
[39]	A novel potential reproductive effects of *Pterocarpus marsupium* methanolic extract on testosterone propionate Induced Polycystic Ovary Syndrome in Female Albino Rat	Cyclic, virgin female albino rats (weighing 180-200g), All the experimental animals except control group were injected with Testosterone Propionate (TP) intraperitoneally at a dose of 1mg/100gm b.w	India	15 days.	To investigate potential reproductive effects of *Pterocarpus marsupium* methanolic extract on testosterone propionate induced PCOS in female albino rats	*Pterocarpus marsupium* showed potential reproductive effects on testosterone propionate induced PCOS female albino rats and could be used as an alternative therapy in the treatment of PCOS
[40]	The effect of hydroalcoholic extract of *Nigella Sativa* seed on	36 female Wistar rats (60 ± 10 g, aged 21 days)	Iran		To investigate the therapeutic effect of hydroalcoholic	The histopathological results which are in accordance with

	dehydroepiandrosterone-induced polycystic ovarian syndrome in rats: An experimental study				extract of *N. sativa* seed on dehydroepiandrosterone (DHEA)-induced PCOS rats.	biochemical findings imply that *N. sativa* seed could be useful in the treatment of PCOS, the higher doses of the extract being more effective.
[41]	The effects of *Urtica dioica* extract on lipid profile, insulin resistance index and liver histology in polycystic ovary syndrome-induced Wistar rats	144 adult Wistar rats were divided into control, PCOS and nettle-treated groups. The group PCOS was injected subcutaneously with 2 mg estradiol valerate, after 60 days	Iran		To examine the *Urtica dioica* moderator effect on liver function in PCOS rats	The results show that *Urtica dioica* by increasing insulin sensitivity and reducing hepatic necrosis may reduce inflammation and improve metabolic symptoms in PCOS and has significant protective effect on liver.
[42]	The leaf aqueous extract of *Myrianthus arboreus* P. Beauv. (Cecropiaceae) improved letrozole-induced polycystic ovarian syndrome associated conditions and infertility in female Wistar rats	Sixty female Wistar rats were used to evaluate the effects of the aqueous extract of M. arboreus leaves on PCOS- bassociated symptoms and PCOS-related infertility.	Camero on		To evaluate the effects of such an extract on an animal model of infertility caused by polycystic ovary syndrome (PCOS), in order to bring scientific evidence to the curative action of this plant against female infertility	the traditional use of M. arboreus against female infertility and suggest that this plant could be a promising alternative treatment to improve symptoms associated with different PCOS phenotypes.

Table 2. **Literature Review database**

3. RESULTS AND DISCUSSION

[(All of the publications reviewed were published between 2010 and 2022, with 21.42% published in 2017 (Fig.3), and 42.85% were carried out in Iran (Fig. 2).

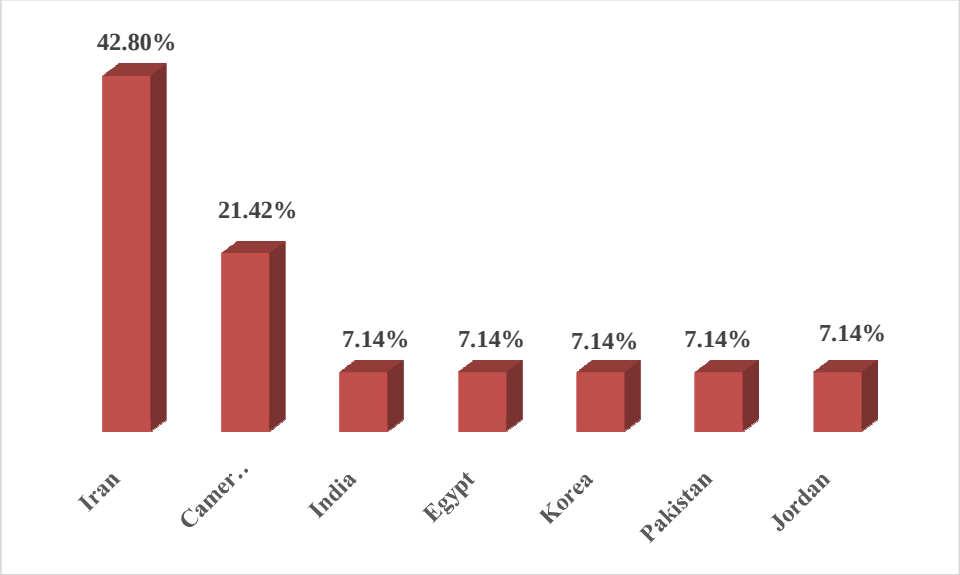


Fig. 2: study location

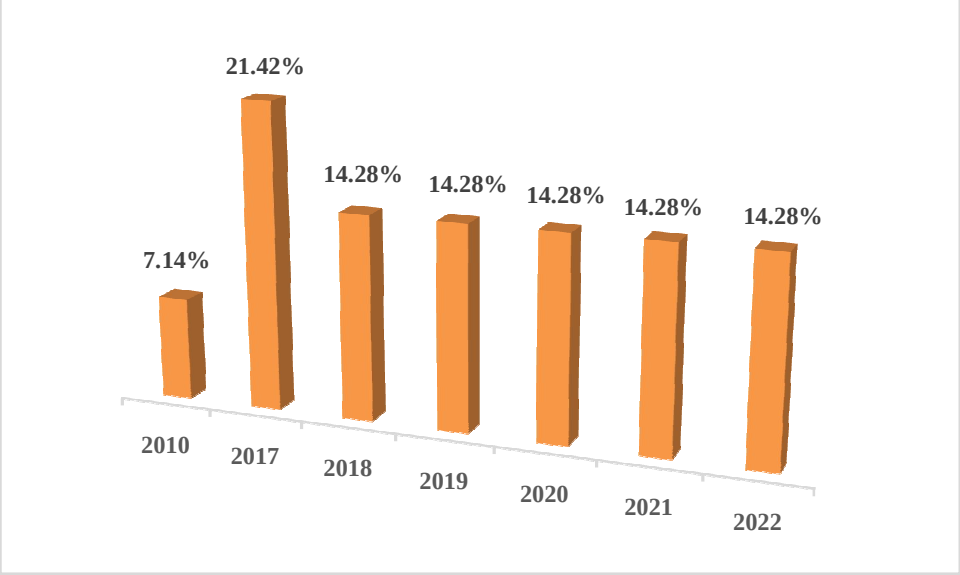


Fig. 3: Study Year

3.1 THE INDUCTION OF PCOS WITH PLANT EXTRACT IN RATS

Among the studies reviewed, it was found out that 43.75% of the studies induced PCOS with Letrozole [30] [34] [36] [37] [38] [42] [32]. 31.25% of the studies induced PCOS with estradiol valerate [28] [31] [33] [35] [41], 12.5% induced with Dhea [29] [40], 6.25% induced with Testosterone Enanthate (TE) [27] and 6.25% of the studies induced PCOS with Testosterone Propionate TP) [39].

3.2 The treatment of PCOS with plant extract in rats

A study [27] reveals that in SPE (50, 200 and 600 mg/kg/BW) and SPA (20, 40 and 80 mg/kg/BW) treatment in TE-induced PCOS mice, the level(s) of LH, FSH, and steroid hormones, i.e., estrogen, progesterone, and testosterone, were estimated. The LH, estrogen and testosterone concentration significantly increased ($P < 0.01$) and the FSH and progesterone concentration reduced ($P < 0.001$) following TE-treatment as compared with the control.

According to [28], the results of this study showed that LH serum level was significantly increased in the sham group (89 days) compared to control groups and sham group (60 days) ($p<0.001$). These results showed that clomiphene and ginger extract could have positive and dose- dependent effect in PCOS treatment. In addition, the experimental group 5 showed a higher increase in FSH serum level compare to the experimental groups 4. The results of serum concentration measurement of FSH showed that in experimental groups 1 and 2, FSH significantly reduced compared to control and sham groups ($p<0.001$). It was seen in the experimental groups 3, 4 and 5 that there was significant decrease in serum estrogen and progesterone level, compared to experimental groups 1 and 2.

Another study [29] found out that after 21 days of treatment, progesterone, and estradiol levels were significantly higher in the DHEA group in comparison with the control group P-value < 0.01). The serum progesterone level was significantly reduced in the metformin-treated group (group 4) compared to the DHEA group (P-value < 0.05). Furthermore, the levels of estradiol were significantly reduced following administration of marjoram (group 3), metformin (group 4), or the combination treatment (group 5) in comparison to DHEA group (P-value < 0.05). Conversely, the current study showed no significant changes in testosterone levels detected among different study groups (P-value > 0.05).

In a study by [31], it was revealed that there was a significant reduction in luteinizing hormone and testosterone in III-V groups compared to Sham group, whereas follicle stimulating hormone in III-V groups was not significantly changed in comparison with Sham group.

It observed that vitagnus treatment in the PCOS group resulted in a raise in progesterone, estrogen and FSH levels and a reduction in the levels of testosterone and LH [32].

A study [33] found out that the serum levels of estradiol and gonadotropins, LH and FSH, were significantly decreased in the Chamomile group relevant to the control group ($p < 0.05$).

In a study by [34], it was seen that group II (PCOS) showed significant increase ($p < 0.05$) in LH levels as compared to group I (normal control). LH levels decreased significantly in group III ($p < 0.05$) and group V, ($p > 0.05$) while a decrease was observed in group IV, when compared with group II. A significant ($p < 0.0001$) reduction was observed in FSH, estradiol,

and progesterone concentrations in group II, when compared with group I. Estradiol levels were significantly improved ($p < 0.0001$) in all treated groups as compared with group II).

According to [35], it was also reported that the level of estradiol in the PCOS and treatment groups increased compared to the positive and negative controls ($P<0.05$). While, there was no significant difference in estradiol level between the PCOS and treatment groups. Progesterone concentration in the PCOS group decreased compared to the control and treatment groups ($P<0.05$); however, the level of progesterone in the treatment group did not have significant difference with the control groups ($P>0.05$). In addition, mean testosterone level in the PCOS group was higher than the control and treatment groups ($P<0.05$). On the other hand, there was no significant difference in testosterone level between the control and treatment groups. There was no significant difference between the groups regarding the level of DHEA ($P<0.05$).

In a study [39], it was observed that the hormonal parameters such as FSH, LH and estrogen levels in standard clomiphene citrate and *Pterocarpus marsupium* methanol extract treatment with low and high dose groups have exhibited a significant increase ($p<0.01$) in their levels and significant decrease ($p<0.01$) in testosterone levels on Day 30. However, it was reported that the serum level of FSH was reduced only in the letrozole treatment group (PCOS), whereas significant recovery of FSH level was observed in the letrozole and GRR co-treatment group (PCOS + GRR). Serum LH levels were not altered in any of the groups. Furthermore, the LH/FSH ratio (known biomarker for PCOS) was elevated only in the letrozole treatment group (PCOS), whereas it was significantly reduced in the letrozole and GR co-treatment group (PCOS + GRR) [37].

Furthermore, the results in a study revealed deleterious effects of letrozole on the hormonal profile, where significant elevation in testosterone and significant reduction in estrogen and progesterone levels by 153%, 27%, and 9%, respectively, were reported, compared to control animals. Treatment of PCOS rats with metformin (Gp IIb), Ok extract (Gp IIc), and EA fraction (Gp IId) decreased testosterone levels by 40%, 42%, and 73%, significantly increased estrogen levels by 225%, 579%, and 94%, and also increased progesterone levels by 321%, 500%, and 813%, respectively, compared to PCOS untreated rats (Gp IIa). [38]. A study [36] reported that *P.muellerianus* significantly decreased ($p<0.001$) LH and testosterone (both extracts; 30, 60, and 120 mg/kg) levels, but increased ($p<0.01$) estradiol (aqueous extract; 60 mg/kg) concentration.

A study [40] also observed that the treatment of PCO animals with metformin and doses of 50, 100, and 200 mg/kg of the *N. sativa* extract decreased LH levels ($p < 0.001$ and $p = 0.05$ respectively). The level of FSH decreased in PCOS rats, while FSH increased in other groups. The testosterone levels elevated in PCOS rats ($p< 0.001$) and treatment with metformin and a dose of 200 mg/kg *N. sativa* reduced it. A dose of 200 mg/kg of *N. sativa* extract increased the progesterone level ($p = 0.03$). Data of the present study showed that the level of estrogen upregulated in the PCOS group while it decreased in all treatment groups.

However, it was reported that the aqueous extract of *M. arboreus* leaves induced a similar effect at doses of 20 mg/kg (37% induction; $p < 0.001$) and 110 mg/kg (95% induction; $p < 0.001$). The serum levels of LH increased by 310% ($p < 0.001$) in the LTZ group as compared with the normal control group. The combined administration of clomiphene citrate and metformin decreased this parameter by 77% ($p < 0.001$) in comparison with the LTZ group. The aqueous extract of *M. arboreus* leaves induced a similar effect at tested doses. It was shown that serum levels of estradiol dereased by 84% ($p < 0.001$) in the LTZ group as compared with the normal control group. The combined administration of clomiphene citrate

and metformin increased this parameter by 764% ($p < 0.001$) as compared with the LTZ group. The aqueous extract of *M. arboreus* leaves also induced a similar effect as it increased serum levels of estradiol by 74%, 219% and 87% at doses of (20, 110 and 200) mg/kg, respectively [42].

DISCUSSION

We carried out this review to introduce plants that have recently been studied for their effects on PCOS with animal models, as well as to give evidence on the induction and treatment of PCOS. The majority of research examined the levels of sex hormones in the serum, induction of PCOS and the treatment on animal models.

Majority of the studies reviewed, successfully administer letrozole to induce PCOS in rat model. It is a nonsteroidal and highly potent aromatase inhibitor [37]. Among the other studies, estradiol valerate was used for induction of PCOS [35] as reviewed. Following the induction of PCOS, estradiol and testosterone levels significantly increased, while level of progesterone significantly decreased in these group; however, no significant change in levels of DHEA was observed. Similar results were also reported by other researchers following induction of PCOS by estradiol valerate [43] [44]. In this present review, the level(s) of LH and FSH in the serum of TE-induced mice [27] was observed. Elevated level(s) of LH, estrogen, and testosterone significantly decreased following treatment with SPE. In addition, a decrease in progesterone and FSH level(s) following treatment with TE was observed, and their reduction was restored by SPE treatment in TE-induced mice. According to research, premenstrual syndrome is caused by changes in the amount of estrogen and progesterone, such that the amount of progesterone compared to estrogen decreases. SPE causes a natural balance between estrogen and progesterone during menstruation. In fact, the saffron petal plant, with its physiological-pharmacological effects, balance the decrease or increase of hormones in the body [45].

In the present review, previous studies reported the enhancement in serum level of LH and estrogen hormone and reduction in the level of FSH and progesterone. On the other hand, any agent that could reduce estrogen and LH and increase FSH and progesterone level can be used to treat PCOS disorder. Previous studies stated that hyperandrogenism and increased serum levels of LH are very common in PCOS [46]. Some other reviews demonstrated that PCOS could increase secretion of testosterone and LH and reduce FSH hormones secretion [47]. One possible mechanism for an explanation of sex hormones changes in PCOS is relative lack of aromatase enzyme in the ovary which could increase androgen concentration [48]. Herbal medicine usage by women has increased over the past decade. Herbal remedies are known to contain pharmacologically active constituents with physiological effects on female endocrinology and have been shown to be positively associated with reduced incidence of breast, bone, and cardiovascular diseases [49] [50]

Previous studies demonstrated that inducing PCOS with letrozole, led to the production of higher amounts of testosterone, elevated ratio of LH/FSH, higher numbers of follicular cysts, elevated thickness of the theca layer and decreased thickness of granulosa layer (Sun *et al*., 2013). All these key symptoms were observed in the current study, indicating successful induction of PCOS in our experimental animals. Increased level of LH causes the increased production of testosterone that consequently leads to follicular arrest and increased AMH levels [51]. Polycystic ovarian syndrome is very complex endocrine disorder that is most frequently encountered gynecological endocrinopathy among reproductive aged women [52]. Many genetic and environmental factors are responsible for the etiology of this syndrome. Unhealthy lifestyle and diet or any infectious mediators elevate the probability of PCOS.

4. CONCLUSION

In conclusion, the health of women is seriously endangered by PCOS. The long-term morbidity and danger associated with PCOS, particularly for glycemic irregularities and T2DM, have previously been misdiagnosed as cosmetic or reproductive issues. Obesity-related problems, mood and/or mental disorders, and CVD are additional morbidities.

Further investigations into the mechanisms of effect for plant extracts are needed to complete our understanding of the reproductive endocrinological effects for plant extract treatment for PCOS.

CONSENT (WHERE EVER APPLICABLE)

Not applicable

ETHICAL APPROVAL (WHERE EVER APPLICABLE)

Not Applicable

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