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REVIEW ON EFFECTS OF HERBAL EXTRACT FOR THE TREATMENT OF POLYCYSTIC OVARIAN SYNDROME (PCOS).

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Abstract

Polycystic Ovary Syndrome (PCOS) is a common heterogeneous, endocrinological and metabolic disorder in women which causes infertility or subfertility. Mostly, women of reproductive age are affected with PCOS. Clinical manifestations of PCOS include infrequent or absent menses, abdominal obesity, acanthosis nigricans and signs of androgen excess (hyperandrogenism) which include acne or seborrhea and insulin resistance. Long term consequences include increased risk of endometrial cancer, type 2 diabetes mellitus, dislipidemia, hypertension and cardiovascular disorders. In this review article, the effects of various herbal extracts on the symptoms of PCOS which were characterized by researchers are reviewed.

Key words: PCOS, herbal extracts, infertility, hormones.

Introduction

Polycystic Ovary Syndrome (PCOS) is a common heterogeneous, endocrinological and metabolic disorder in women which causes infertility or subfertility (Reddy P.S., *et al.,* 2016). It is originally called as Stein-Leventhal syndrome. It is serious disorder in women in which the ovaries become enlarged with many cysts which are in fact small undeveloped follicles (Pachiappan S, *et al.,* 2017). It is a common female disorder with prevalence rate of 2.2% to 26% globally and 11.96% in Indian adolescents (Choudhary N., *et al.,* 2011, Singh A., *et al.,* 2018). Clinical manifestations of PCOS include infrequent or absent menses, abdominal obesity, acanthosis nigricans and signs of androgen excess (hyperandrogenism) which include acne or seborrhea and insulin resistance. Long term consequences include increased risk of endometrial cancer, type 2 diabetes mellitus, dyslipidemia, hypertension and cardiovascular disorders (Reddy P.S., *et al.,* 2016).

Women with PCOS have higher risks of endometrial cancer, cardiovascular disease, dyslipidemia and type 2 diabetes mellitus. Primary defects in the hypothalamic – pituitary axis, insulin secretion and action and ovarian function involved in PCOS pathophysiology. PCOS is linked with insulin resistance and obesity. Ovarian function is regulated by the insulin. By producing androgen ovaries respond to the excess insulin which is responsible for the Anovulation (Ndefo U.A., *et al.,* 2013). Anovulation is the most common cause of infertility. Luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the pituitary are implicated in the pathogenesis of PCOS. In PCOS patients, the LH/FSH relation is altered. Higher secretion of LH in relation to FSH can cause increased production of androgens by theca cells and anovulatory cycles. Female hormone regulation can be changed due to excess androgen which causes increased estrogen levels, menstrual irregularity and infertility (Barbosa G., *et al.,* 2016).

Abnormal lipoprotein profile which is characterized by raised concentration of plasma triglyceride, marginally elevated low density lipoprotein cholesterol (LDL-C) and reduced high density lipoprotein cholesterol (HDL-C) is observed in PCOS patients. High concentration of smaller LDL particles often occurs in association with elevated circulating triglyceride concentration, increased hepatic lipase activity and insulin resistance (Pirwany I.R., *et al.,* 2001).

Currently the standard care treatments for the PCOS include changes in current lifestyle and pharmaceutical medications. Such changes in lifestyle include change in food habits, exercise under supervision for weight loss (Pachiappan S, *et al.,* 2017). Orally clomiphene citrate and metformin are given for the treatment of PCOS, but they have certain limitations such as nausea, vomiting and gastrointestinal disturbances (Arentz S., *et al.,* 2014).

To avoid such side effects, herbal medicines in

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combination with chemicals are used to treat the symptoms of PCOS. This review explored the beneficial effects of various herbal extracts on the symptoms of PCOS.

Herbal extracts for PCOS

1. *Ecklonia cava:*

Ecklonia cava is a well known natural substance which reduces the effects of inflammation, allergies and cancer. Eui-Ju Hong, *et al.,* in 2018 investigated the effects of *Ecklonia cava* extract in letrozole induced PCOS rat models. *Ecklonia cava extract* restored the regular estrus cycle, hormone levels, including the levels of testosterone, estrogen, luteinizing hormone (LH), follicle stimulating hormone (FSH) and anti-Mullerian hormone (AMH) were restored to the normal states. In this study they observed that *Ecklonia cava* extract restored the components and morphologies of ovarian follicles to a normal range and suggested that this extract was involved in the regulation of various factors associated with follicular development in the ovary. From histological analysis, authors concluded that *Ecklonia cava* extract significantly reduced the symptoms of PCOS in rats and they are comparable to the normal ovaries (Hong E.J., *et al.,* 2018).

2. *Glycyrrhiza glabra:*

Glycyrrhiza glabra is prescribed in many Korean medicinal formulas for its potential effects in the regulation of inflammation, immune response, hepatic failure, spasms and women's metabolic disorder. Hye Won Lee, *et al.,* in 2018, examined the effect of *Glycyrrhiza glabra* ethanol extracton letrozole induced PCOS like symptoms in female Sprague Dwaley rats. The significant recovery of FSH level and significant decrease in LH/FSH ratio was observed in the licorice and Letrozole co-treatment group. Administration of licorice extract resulted in successful elimination of PCOS-associated symptoms, including thickening of the theca layer, thinning of the granulosa layer of antral follicles, reduction of number of antral follicles and induction of number of follicular cysts (Lee H.W., *et al.,* 2018).

3. *Aegle marmelos*:

C. Dhivya, *et al.,* in 2018, evaluated the antiandrogenic effect of hydroalcoholic extract of *Aegle marmelos* in the treatment of PCOS induced by Letrozole in female wistar rat model. In this study, they observed the effect of hydroalcoholic extract of *Aegle marmelos* on physical and biochemical parameters and histopathology of ovary. They observed significant increase in serum LH and decrease in serum FSH level. Also they observed the presence of more number of developing follicles and corpus luteum, oocyte surrounded by granulose cells (Dhivya C., *et al.,* 2018).

4. *Bougainvillea spectabilis*:

Ebrahim N.A., *et al.,* in 2018, observed the assessed protective potency of *Bougainvillea spectabilis* leaves (BSL) extract on ovarian folliculogenesis in a rat model of estradiol valerate (EV) induced PCOS. They observed significant reduction in LH, estrogen and glucose serum levels and increase in serum FSH and the antioxidant serum levels in estradiol valerate and *Bougainvillea spectabilis* extract treated group. In this group they also observed the ovarian cortex contained pre-antral, antral follicles and corpora lutea (Ebrahim N.A, *et al.,* 2018).

5. *Matricaria chamomila*:

According to traditional herbal medicine, chamomile has been considered as one of the herbal remedies for patients with PCOS. In 2018, Heidary M., *et al.,* observed the effects of *Matricaria chamomile* (chamomile) on lipid and hormonal parameters in PCOS women of reproductive age. They observed significant decrease in total testosterone levels after oral administration of chamomile capsule (370 mg) in PCOS women. However, they did not observed any significant change in lipid parameters, the ratio of LH/FSH and dehydroepiandrosterone sulfate level (Heidary M., *et al.,* 2018).

6. *Cinnamomum zeylanicum*:

Maryam Rafraf, *et al.,* in 2018, were studied the effects of cinnamon supplementation on oxidative stress including serum total antioxidant capacity (TAC), malondialdehyde (MDA) and serum lipids in women with polycystic ovary syndrome. They observed significant increase in serum total antioxidant capacity and significant improvement in serum level of total cholesterol, low density lipoprotein cholesterol and high density lipoprotein cholesterol. They also observed decreased in malondialdehyde levels (Rafraf M., *et al.,* 2017).

7. *Galega officinalis*:

Majid Shokoohi *et al.,* in 2018, investigated the protective effect of *Galega officinalis* on metabolic as well as hormonal parameters in a rodent model of estradiol valerate induced PCOS. They observed significant decrease in the levels of fasting blood sugar, insulin, testosterone, LH and FSH levels and significant increase in serum aromatase level and serum estrogen level. In *Galega officinalis* treated group they observed significant increase in pre-antral and antral follicles and significant decrease in number of cystic follicles. From this study they conclude that *Galega officinalis* have beneficial effects due to the presence of antioxidant and insulin like

agents such as Bygvanydyn, resin, glycoside and saponins (Shokoohi M., *et al.,* 2018).

8. *Moringa oleifera*:

Budi Santoso *et al.,* in 2018, proved the effect of *Moringa oleifera* leaf extract in various doses on insulin levels and folliculogenesis in PCOS model with insulin resistance.They observed significant decrease in accretion of body weight. They also observed significant decrease in insulin levels in *Moringa oleifera* treated group and increase in folliculogenesis in ovary model of PCOS and decrease in androgen (Santoso B., *et al.,* 2018).

9. *Nigella sativa*:

Mojgan Tansaz *et al.,* in 2018, assessed the effect of processed *Nigella sativa* on oligomenorrhea and amenorrhea in patients with polycystic ovary syndrome. In this study, ten women diagnosed with PCOS having oligomenorrhea were participated. They observed significant decrease in the levels of serum cholesterol, triglycerides, FBS, insulin, AST, LH and HOMA-IR index after intervention of *Nigella sativa* (Tansaz M., *et al.,* 2018).

10. *Vitis*:

Salmabadi Z., *et al.,* in 2017, assessed the effect of grape seed extract (GSE) on triglyceride (TG), total cholesterol (TC), high density lipoproteins cholesterol (HDL-C), low density lipoprotein- cholesterol (LDL-C) and interleukin 6 (IL-6) in estradiol valerate induced PCOS wistar rats. They observed significant decrease in the levels of LDL-C, TC and IL-6 in grape seed extract treated group. According to the findings of this study, they concluded that the selected doses of GSE with its effects on serum TC, LDL-C and IL-6 could reduce the effects of dyslipidemia and inflammation in PCOS rats and improve systemic symptoms of PCOS (Salmabadi Z., *et al.,* 2017).

11.*Bambusa bambos*:

V. Soumya, *et al.,* in 2016, evaluated the effect of bamboo seed oil in decreasing the major metabolic symptoms associated with letrozole induced polycystic ovarian disease using female rat model. They observed marked reduction in glucose and levels of total cholesterol, very low density lipoprotein, triglyceride. They find the traditional use of bamboo seed on its hypoglycemic and hypolipidemic effects in rats. They concluded that beneficial effects of the bamboo seed along with its potent antioxidant activity contribute to the treatment of major metabolic symptoms of PCOD such as irregular estrus cycle and polycystic ovaries to normal level (Soumya V., *et al.,* 2016).

12. *Commiphora weightii*:

Kavitha A., *et al.,* in 2016 evaluated the effects of *Commiphora weightii* on hyperandrogenism in dehydroepiandrosterone (DHEA) induced PCOS in female wistar rats. From the obtained results, they observed the significant increase in hormone profile (estradiol, testosterone, progesterone, luteinizing hormone, follicle stimulating hormone) and significant decrease in glucose levels in PCOS rats. From this study they conclude that commiphora weightii significantly reduced the morphological abnormalities of the ovarian follicles and normal hormone levels in DHEA induced PCOS rats (Kavitha A., *et al.,* 2016).

13. *Corylus avellana*:

Demirel M.A, *et al.,* in 2016, assessed the activity of hazelnut oil in the treatment of polycystic ovary syndrome in Sprague Dwaley rats. From the obtained the results, they observed remarkable decrease in body weight as well as LH and FSH levels to the normal and increase in uterine weight. They also observed significant increase in estrogen and progesterone and decrease in testosterone levels. From this study, they found the beneficial effects of *Corylus avellana* oil in the treatment of PCOS via regulating gonadotropins, steroids and serum lipid parameters and possess antioxidant activity (Demirel M.A, *et al.,* 2015).

14. *Curcumin*:

In 2016, Reddy P.S., *et al.,* observed the beneficial effects of curcumin in letrozole induced PCOS female wistar rats. Curcumin was able to normalize serum testosterone levels and successfully restored the decreased levels of progesterone to the normal. Oral administration of *curcumin* was able to prevent the rise in HbA1c, which indicates beneficial effects of *curcumin* in preventing insulin resistance and diabetic complication. In this study, curcumin was able for disappearance of cysts. From this study they concluded the curcumin as a promising drug for the treatment of clinical and pathological abnormalities in PCOS condition (Reddy P.S., *et al.,* 2016).

15. *Palm pollen*:

Jashni H.K., *et al.,* in 2016, evaluated the effect of *Palm pollen* extract on estradiol valerate induced PCOS in rats. They observed decrease in levels of LH, estrogen and number of cystic follicles and increase in levels of FSH, progesterone and number of corpus luteum after administration of *Palm pollen* extract. From this study, they concluded that *Palm pollen* extract can improve the symptoms of PCOS (Jashni H.K., *et al.,* 2016).

16. *Pushpadhanwa rasa*:

Dash M. K., *et al.,* in 2016, trialed *Pushpadhanwa rasa*, a herbo-mineral compound formulation containing *Rasasindoora, Abhraka bhasma, Lauha bhasma, Vanga bhasma, Naga bhasma, Dhatura, Bhanga, Yastimadhu, Shalmali, Nagavalli* to check its role in the psychological symptoms of PCOD. They observed that, trial groups significantly relieved the psychological symptoms like headache, irritability, mood swings, depression, and sleep disturbances, lack of confidence, forgetfulness, and loss of libido (Dash M. K., *et al.,* 2016).

17. *Sargassum ilicifolium*:

Anbu J., *et al.,* in 2016, conducted this study to evaluate the effect of *Sargassum ilicifolium* on testosterone induced PCOS in female albino wistar rats. In this study they observed that due to the administration of ethanolic extract of *Sargassum ilicifolium* estrus cycle was restored to the regular and caused an elevation of serum concentration of FSH, LH, estrogen, progesterone and decrease in testosterone also it was more effective in reducing elevated glucose and cholesterol levels. Thus, they concluded that the test drug had potential effect on PCOS bringing the reproductive cycle and other related complications to normal by reducing the risk of type 2 diabetes mellitus or insulin resistance (Anbu J., *et al.,* 2016).

18. *Withania somnifera* and *Tribulus terrestris:*

Saiyed A., *et al.,* in 2016, investigated the effect of the combination of hydroalcoholic extract of *Withania Somnifera* and *Tribulus terrestris* on letrozole induced PCOS in female wistar rats. They observed significant effects of combination of *Withania somnifera* and *Tribulus terrestris* in normalizing the estrus cycle after being altered by letrozole and significant increase in FSH levels and decrease in LH, estradiol and testosterone levels after administration of the combination of the *Withania somnifera* and *Tribulus terrestris*. They also observed significant decrease in serum total cholesterol (Saiyed A., *et al.,* 2016).

19. *Trigonella foenumgraecum*:

Anand Swarroop, *et al.,* in 2015, assessed the efficacy of novel, patent pending fenugreekseed extract enriched in furostanolic saponins (Furocyst) to determine its efficacy in an open label, one arm, non randomized, post marketing surveillance study in 50 premenopausal women (age: 18-45 years, BMI: 23.88 ± 4.72 kg/m^2, diagnosed with PCOS) and they conducted this study over a period of 3 consecutive months. In this study, they asked the patients to consume 2 capsules of Furocyst over a period of 3 consecutive months. They observed significant improvement in menstrual cycle after Furocyst treatment. In this study they observed 3 pregnancies after 30 days, one after 39 days, one after 70 days and another after 84 days of treatment respectively. Also, at the end of the study, 46% subjects showed reduced cyst size while 36% showed no cysts. They also observed significant increases in LH and FSH levels (Swaroop A., *et al.,* 2015).

20. *Mentha piperita*:

Amoura M., *et al.,* in 2015, evaluated the protective effect of peppermint on Letrozole induced PCOS in female wistar rats. After administration of peppermint, they observed significant decrease in body weight and ovarian weight and significant decrease in LH and testosterone levels and significant increase in estrogen level. They did not observed significant change in the level of FSH. Necrosis in stromal mesenchymal cells manifests massive alterations in the uterine tissue in PCOS group.

By giving supplementation of peppermint, all these alterations in the ovarian and uterine tissues were ameliorated. From this study they found peppermint as the potential alternative for the treatment of PCOS (Amoura M., *et al.,* 2015).

21. *Pergularia daemia*:

Bhuvaneshwari S, *et al.,* in 2015, analyzed the estrous cycle in the testosterone propionate induced PCOS in female albino wistar strain rat models and its treatment with a common trellis vine called *Pergularia daemia*. After the treatment with *Pergularia daemia* for 7 days, they observed the reversible process of the irregular estrous cycle. From this they conclude that *Pergularia daemia* is most effective in the treatment of PCOS and active potential herbal medicine to save human kind to save from infertility (Bhuvaneshwari S, *et al.,* 2015).

22. *Punica granatum*:

Hossein K. J., *et al.,* in 2015, investigated the effect

Table 1: Hormonal parameters and their effects in PCOS.

Hormonal Parameters	Effect in PCOS
LH	Increase (Barbosa G., *et al.,* 2016)
FSH	Decrease (Barbosa G., *et al.,* 2016)
Weight	Increase (Reddy P.S., *et al.,* 2016).
LDL-C	Increase (Pirwany I.R., *et al.,* 2001)
HDL-C	Decrease(Pirwany I.R., *et al.,* 2001)
Insulin	Increase (Ndefo U.A., *et al.,* 2013)
Androgen	Increase (Barbosa G., *et al.,* 2016)
Estrogen	Increase (Barbosa G., *et al.,* 2016)
Triglyceride	Increase (Pirwany I.R., *et al.,* 2001)

Table 2: Herbal extract used for the treatment of Polycystic Ovarian Syndrome (PCOS).

Sr. No.	Plant	Effects	Reference No.
1	*Curcuma longa*	Normalize serum testosterone levels and successfully restored the decreased levels of progesterone to the normal.	Reddy P.S., et.al, 2016.
2	*Ecklonia cava*	Restored regular estrus cycle and hormone levels to the normal.	Hong E.J., et.al, 2018.
3	*Glycyrrhiza glabra*	Significant recovery of FSH level and significant decrease in LH/FSH ratio.	Lee H.W., et.al, 2018.
4	*Aegle marmelos*	Significant increase in serum LH level and decrease in serum FSH level.	Dhivya C., et.al, 2018.
5	*Bougainvillea spectabilis*	Significant decrease in serum LH level and increase in serum FSH level.	Ebrahim N.A, et.al,2018.
6	*Matricaria chamomila*	No significant change in LH/FSH ratio	Heidary M., et.al, 2018.
7	*Cinnamomum zeylanicum*	Significant increase in serum total antioxidant capacity and improvement in serum level of total cholesterol	Rafraf M., et.al, 2017.
8	*Galega officinalis*	Significant decrease in LH and FSH level	Shokoohi M., et al., 2018.
9	*Moringa oleifera*	Significant decrease in insulin levels and increase in folliculogenesis	Santoso B., et.al, 2018.
10	*Nigella sativa*	Decrease in LH, FBS and insulin	Tansaz M.,et.al, 2018.
11	*Vitis*	Significant decrease in LDL-C, TC and IL-6	Salmabadi Z., et.al, 2017.
12	*Bambusa bambos*	Reduction in glucose and levels of total cholesterol, very low density lipoprotein, triglycetide.	Soumya V., et.al, 2016.
13	*Commiphora weightii*	Increase in hormone profile and decrease in glucose levels.	Kavitha A., et.al, 2016.
14	*Corylus avellana*	Decrease in LH and FSH levels	Demirel M.A, et.al, 2015.
15	*Palm pollen*	Decrease in levels of LH and increase in levels of FSH	Jashni H.K., et.al., 2016.
16	*Pushpadhanwa rasa*	Significantly relieved the psychological symptoms like headache, irritability, mood swings, depression, and sleep disturbances, lack of confidence, forgetfulness, and loss of libido	Dash M. K., et.al, 2016.
17	*Sargassum ilicifolium*	Elevation of serum concentration of FSH, LH, estrogen, progesterone and decrease in testosterone	Anbu J., et.al. 2016.
18	Combination of *Withania somnifera Dunal and Tribulus terrestris Linn.*	Significant increase in FSH levels and decrease in LH levels.	Saiyed A., et.al, 2016.
19	*Trigonella foenumgraecum*	Significant increases in LH and FSH levels	Swaroop A., et.al, 2015.
20	*Mentha piperita*	Significant decrease in LH and testosterone levels and significant increase in estrogen level. No significant change in the level of FSH.	Amoura M., et.al, 2015.
21	*Pergularia daemia*	Reversible process of the irregular estrous cycle	Bhuvaneshwari S, et.al, 2015.
22	*Punica granatum*	Reduction in the concentration of estrogen, free testosterone and andrestandion hormone.	Hossein K. J., et.al, 2015.
23	*Vitex negundo L*	Significant decrease in serum testosterone levels and serum glucose levels	Shetty D.K., et.al, 2015.
24	*Foeniculum vulgare*	Decrease in serum urea levels and significant improvement in bowman's space and acute tubular necrosis towards normal.	Sadrefozalayi S., et.al, 2014.
25	*Alium cepa*	Increase in total antioxidant capacity levels and decrease in number of cyst.	Ghasemzadeh A., et.al, 2013.
26	*Aloe barbadensis*	Decrease in ovary atretic cysts	Nampoothiri L., et.al, 2010.

pomegranate juice extract on changes of active hormones in patients with estradiol valerate induced polycystic ovary syndrome in female wistar rats. From this study they concluded that consumption of pomegranate extract improves changes of female sex hormones by reducing the concentration of estrogen, free testosterone and andrestandion hormone in patients with PCOS (Hossein K. J., *et al.,* 2015).

23. *Vitex negundo*:

In 2015, Shetty D.K., *et al.,* observed the testosterone lowering effect of vitex negundo in PCOS induced hyperandrogenised female Sprague Dwaley rats. They observed significant decrease in excessive androgen levels after administration of hydroalcoholic extract of vitex negundo on daily basis. They observed significant decrease in serum testosterone levels and serum glucose levels after administration of nirgundi extract. They also found least follicular cysts and lesions in nirgundi group (Shetty D.K., *et al.,* 2015).

24. *Foeniculum vulgare*:

Sadrefozalayi S., *et al.,* in 2014, studied the renoprotective effect of the aqueous extract of *Foeniculum vulgare* (AEF) in experimental PCOS female wistar rats. In this study they observed that serum urea levels were decreased in PCOS rats. After administration of *Foeniculum vulgare*, they observed significant improvement in bowman's space and acute tubular necrosis towards normal (Sadrefozalayi S., *et al.,* 2014).

25. *Alium cepa*:

Khaki A., *et al.,* in 2013, assessed the effect of ethanolic extract of *Alium cepa* seeds on modulation of apoptosis in experimental induced Polycystic Ovarian Syndrome (PCOS) in wistar albino female rats. After administration of *Allium cepa*seed extract they observed increase in total antioxidant capacity levels and decrease in number of cyst as compared to control and PCOS group. They also observed decrease in granulosa apoptotic cells after administration of *Alium cepa* seed extract in PCOS rats (Ghasemzadeh A., *et al.,* 2013).

26. *Aloe barbadensis Mill. (Liliaceae)*:

It is popularly known as Aloe Vera. Laxmipriya Nampoothirti, *et al.,* in 2010 evaluated the efficacy of Aloe vera gelformulation in Letrozole induced PCOS rat model. They did not observed increase in body weight and also observed decrease in ovary atretic cysts after administration of aloe vera gel. The aloe vera gel formulation given by oral route (1ml dose daily for 45 days) restored their estrus cyclicity, glucose sensitivity and steroidogenic activity and exerts a protective effect in against a PCO phenotype by restoring the ovarian steroid status and altering key steroidogenic activity (Nampoothiri L., *et al.,* 2010).

Conclusion

PCOS is a common heterogenous, endocrinological and metabolic disorder in women of reproductive age leading to infertility or subfertility. Medicinal plants have been found to be used in many ways either directly or in form of extracts for management of several diseases including PCOS due to the presence of different phytoconstituents. After induction of PCOS, treatment with different herbal extract causes reduction in blood testosterone levels and LH levels and increase in blood progesterone and FSH level. Also, in different stages of growth in treatment group, many follicles such as primary follicles, antral follicle, preantral follicle, large oocyte, grafian and corpesluteum were observed. Studies reported that most of the herbal extract are effective in treatment of PCOS and they are able to normalize blood hormones levels, levels of sex hormone, disappearance of cyst, able to reduce insulin levels and other PCOS symptoms. Also some studies revealed that the medicinal plants used for the treatment of PCOS have no major adverse effects since phytoestrogens are present in them which are weak antagonists of estrogen and they exhibit more potent estrogenic effects when estrogen level of the body is low in PCOS patients and hence they are safe and therefore can be widely used for the treatment of PCOS.

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