IJPSR (2023), Volume 14, Issue 8 **(Review Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 01 November 2022; received in revised form, 23 March 2023; accepted 20 July 2023; published 01 July 2023

EFFECT OF HERBAL DRUGS ON POLYCYSTIC OVARIAN SYNDROME: A REVIEW

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Keywords:

Polycystic ovarian syndrome, Symptoms, Herbal drugs, Ayurvedic medications

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ABSTRACT: Polycystic ovarian syndrome (PCOS) is a hyper-androgenic disorder that is associated with ovaries that produce an abnormal amount of androgens, male sex hormones that are usually present in small amounts in 5-10% of women at 18-44 years of age women. The numerous small cysts (fluid-filled sacs) form in ovaries in small undeveloped follicles. The chemical-based drugs induce the ovulatory cycle instead of allowing it to restore its original healthy rhythm. This hormone imbalance causes their body to skip menstrual periods, making it harder for them to get pregnant. Many allopathic medications are used for PCOS but also have some side effects. To overcome the adverse impact of chemicals on the body, herbal formulations are preferred. This study explores the efficacy of herbs as a possible therapeutic agent in preventing and managing polycystic ovary syndrome (PCOS). The benefit of herbal therapy compared to conventional therapy is that herbal therapy is safe with lesser side effects, and the presence of multiple active compounds in medicinal herbs provides a potentiating effect.

INTRODUCTION: Polycystic Ovarian Syndrome is a condition that has cysts on the ovaries that prevent the ovaries from performing normally. Symptoms of Polycystic Ovarian Syndrome include Amenorrhea or infrequent menstruation, irregular bleeding, infrequent or no ovulation, multiple immature follicles, increased levels of male hormones, male pattern baldness or thinning hair, excess facial and body hair growth, acne, oily skin or dandruff, dark coloured patches of skin specially on neck, groin, underarms, chronic pelvic pain, increased weight or obesity, diabetes, lipid abnormalities and high blood pressure.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(8).3802-14

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.14(8).3802-14

Polycystic ovary disease is a poorly understood disorder characterized by anovulation, menstrual irregularities (amenorrhea), infertility, and multiple follicular cysts in the ovaries covered by a dense fibrous capsule. *Corpora lutea* and corpora albicantia are absent from the ovaries. Various clinical syndromes have been described in association with polycystic ovary disease. PCOS can be managed with lifestyle modifications by having a healthy diet, adding exercise to the daily routine, and weight loss. Various medications help regulate menstrual cycle, insulin resistance and treat acne and hirsutism.

Causes of PCOS:

1. Genetic predisposition
2. Strong stimulation in adrenals in childhood
3. Raised insulin levels

4. Contraceptive pills
5. Hormonal imbalance
6. Stress

Symptoms of PCOS:

1. Irregular or absence of periods,
2. Ovarian cysts,
3. Acne,
4. Excess body hair (hirsutism),
5. Weight gain or difficulty losing weight,
6. Pain in the Pelvic region,
7. Mood changes,
8. Insulin resistance,
9. Thinning of scalp hair,
10. Elevated Luteinizing Hormone (LH),
11. High testosterone level,
12. Decreased Follicle stimulating hormone (FSH),
13. Insomnia.
14. Trouble or Infertility

Combination of different symtoms which are responsible to cause the PCOS as showed in *Fig. 1* that are environmental factors, genetic predisposition, dyslipidemia, type 2 diabetes mellitus, hyperandrogenism, oxidative strees, *etc*.

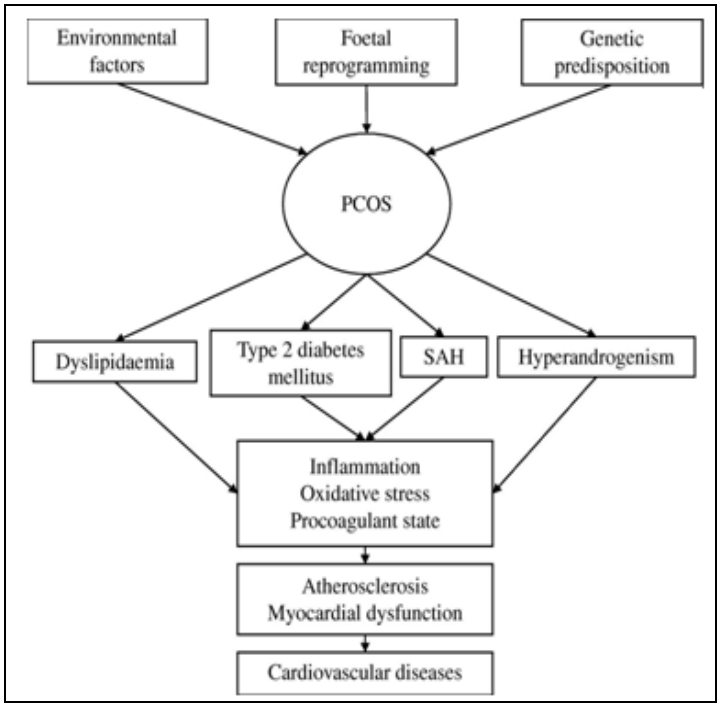

FIG. 1: PATHOGENESIS OF PCOS

Diagnosis: There is no single test to diagnose polycystic ovary syndrome (PCOS) specifically. Depending upon the symptoms, medications, and any other medical conditions, menstrual periods, weight changes, signs of excess hair growth, insulin resistance, and acne diagnosis will be carried out.

- **Physical Examinations:** These include weight, height, blood pressure measurement, and unwanted hair growth.
- **Pelvic Exam:** Checking of reproductive organs for masses, growths or other changes.
- **Blood Tests:** Blood tests can measure hormone levels. Blood testing, such as fasting cholesterol and triglyceride levels. A glucose tolerance test can measure body's response to sugar (glucose). Thyroid hormone testing,
- **Ultrasound:** An ultrasound can check the appearance of ovaries and the thickness of the

lining of your uterus. A transducer is placed in the vagina. The transducer emits sound waves translated into images on a computer screen. Ultrasound may show enlarged ovaries and cysts. Normal ovary and PCOS ovary is shown in **Fig. 2.**

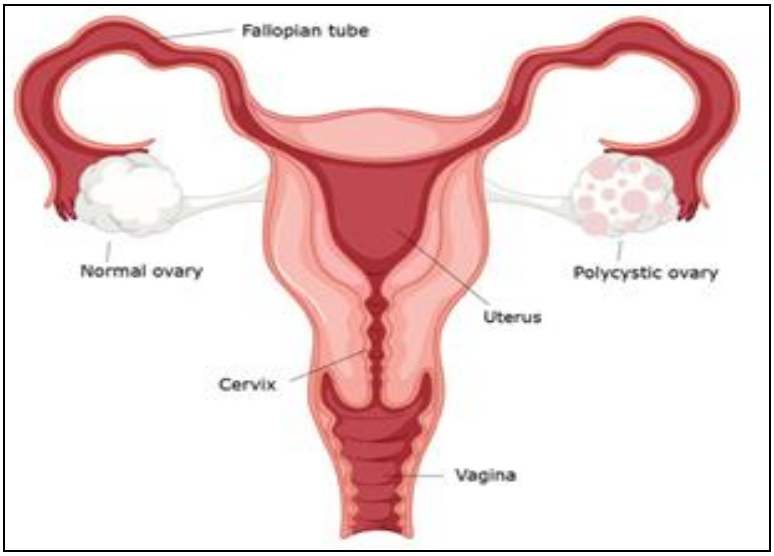

FIG. 2: NORMAL OVARY AND PCOS OVARY

Oral Contraceptive Pills: Estrogen (ethynly-lestradiol), progestin are mostly used. Nafarelin, a specific gonadotropin-releasing hormone agonist, include a decrease in hirsutism but total and LDL cholestrol increased by both formulations

Antiandrogens: Medications to block androgens, Spironolactone is mostly used and only given when oral contraceptive pills measures are guaranteed.

Metformin: Metformin use has increased over the last 10 years despite not being licensed for PCOS. Observational studies demonstrated short-term beneficial effects of metformin in PCOS. Adolscent who were mostly overweight or obese and very few in non obese with dose 850mg/day, which causes improved BMI.

Combination Treatments: Triple low dose of combination of insulin-sensitizing and antiandrogens normalises cardiovascular risk and body composition

Alternative Herbal Remedies for Pcos:
Aloe Vera (Botanical Name: *Aloe barbadensis*, **Family:** Liliaceae

It maintains menstrual cycle and regulates hormones responsible for menstruation. *Aloe vera* **Fig. 3** clears the digestive tract and facilitates the active removal of toxins. Aloe vera helps to correct hormonal balances, and can increase the estrogen level. Also its anti- inflammatory and antimicrobial property help with pain and irritation in cysts. In the present study, the efficacy of Aloe vera gel formulation in a PCOS rat model was checked. Five-month-old Charles Foster female rats were orally fed with letrozole, a non-steroidal aromatase inhibitor, to induce PCOS. The rats were then treated orally with the Aloe vera gel formulation (1 ml dose daily for 45 days). This restored their estrus cyclicity, glucose sensitivity, and steroidogenic activity. Co-treatment of the inductive agent (letrozole) with the Aloe vera gel A prevented the development of the PCOS phenotype. Aloe vera gel formulation protects against the PCOS phenotype by restoring the ovarian steroid status and altering key steroidogenic activity. This can be attributed to phyto-components present in extract [15].

FIG. 3: ALOE VERA

Cinnamon (Botanical Name: *Cinnamomum zeylanicum*.
Family: Lauraceae

Cinnamon is a promising drug to reduce insulin resistance which is cause for increasing the body weight which affects the PCOS. Also cinnamon is loaded with natural antioxidants, anti-inflammatory properties and also responsible for reducing the blood sugar level. Cinnamon **Fig. 4** increases the hormone progesterone and decreases testosterone production in women, helping to balance hormones. Cinnamon extract has been shown to reduce insulin resistance in *in-vitro* and *in-vivo* studies by increasing phosphatidylinositol 3-kinase activity in the insulin signaling pathway, thus potentiating insulin action. Fifteen women with polycystic ovary syndrome (PCOS) were randomized to daily oral cinnamon and placebo for 8 weeks. Comparisons of post-treatment to baseline insulin sensitivity indices using fasting and 2-hour oral glucose tolerance tests showed significant reductions in insulin resistance in the cinnamon group but not in the placebo group [10].

FIG. 4: CINNAMON

Liquorice (Botanical Name: *Glycyrrhiza glabra*
Family: Leguminosae

Liquorice is helpful for lowering the body weight and menopausal symptoms. The effect of liquorice was investigated on androgen metabolism in nine healthy women 22–26 years old, in the luteal phase of the cycle. They were given 3.5 g of a commercial preparation of licorice (containing 7.6% W/W of glycyrrhizic acid) daily for two cycles [31]. They were not on any other treatment. Plasma renin activity, serum adrenal and gonadal androgens, aldosterone, and cortisol were measured by radioimmunoassay. Total serum testosterone decreased gradually within two months. It returned to pretreatment levels after discontinuation. Licorice can reduce serum testosterone probably due to the 17- hydroxysteroid dehydrogenase block and 17–20 lyase. Licorice could be considered an adjuvant therapy of hirsutism and polycystic ovary syndrome [6]. Ashoka **Fig. 5** means no grief in Sanskrit language. So it is also called as friend of women.

FIG. 5: LIQUORICE

Flaxseed (Botanical Name: *Linum usitatissimum*
Family: Linaceae

It has promising weight reducing properties, reducing the triglyceride level in blood and reducing the hirsutism and androgen levels in women. It reduces the insulin resistance and improves the menstrual cycle. Flaxseed **Fig. 6** contains omega-3 fatty acids and antioxidants called lignans. Flax seed rank near the top as estrogenic foods. They have the highest amount of phytoestrogen. These are the great source of dietary fibre, which helps to lower cholesterol and regulate the digestive tract.

These can help control excess estrogen production, leading to bloating, mood swings, cramping, breast tenderness, and even acne in women with PCOS. Not just that, flaxseed also helps to improve ovulation and in reducing common PMS symptoms such as breast pain and cramping. This study observed the impact of flaxseed supplementation (30 g/day) on hormonal levels in a 31-year old woman with PCOS. During four months, the patient consumed 83% of the flaxseed dose. Height, weight measurement and fasting blood samples taken at baseline and 4-month follow-up

indicated a significant decrease in Body Mass Index (BMI), insulin, total serum testosterone and free serum testosterone levels. The patient also reported a decrease in hirsutism after the study period. The clinically-significant decrease in androgen levels with a concomitant reduction in hirsutism was reported in this case study [8].

FIG. 6: FLAXSEED

***Gymnema sylvestre* (Gymnema):** Gymnema is a traditional Ayurvedic herb used as an antidiabetic, hypogylcemic, lipid-lowering agent and to support weight reduction. Gymnema possibly has a trophorestorative action of the beta cells of the pancreas.

The plant part used as medicine is the leaf. Gymnema is well indicated for PCOS, due to its insulin-modulating activity and the added benefits of reducing the elevated triglycerides associated with PCOS [21-23].

Key constituents of Gymnema **Fig. 7** include saponins, especially the gymnemic acids. Gymnemic acid suppresses the sweet taste on the taste buds, so if taken before food masks the sweet sensation. Gymnema has demonstrated hypoglycemic activity in experimental models of diabetes and regulated blood sugar in hyperglycemia.

The mechanism of action also includes inhibiting glucose absorption in the intestine. The daily dose of Gymnema is 3.5 to 11 mL of 1:1 liquid extract. Since conventional medical models focus on pharmaceutical agents such as metformin to control PCOS, Gymnema may prove to be one of the most significant herbs in treating the underlying factor of insulin resistance [44].

FIG. 7: *GYMNEMA SYLVESTRE*

Fennel Seeds (Boatnical Name: *Foeniculum valgarae*

Family: Apiacea

The efficacy of oral fennel oil in the management of dysmenorrhea, premenstrual syndrome, amenorrhea, menopause, lactation, and polycystic ovary syndrome were confirmed according to results of clinical studies. The results of clinical efficacy of fennel oil on menstrual bleeding is complicated, but results of one meta-analysis study revealed that fennel oil significantly increased means of bleeding in the first menstrual periodic cycle Fennel seeds are said to help cycle Fennel seeds **Fig. 8** are said to help in n treating PCOS as they have anti-hirsutism properties and help decrease androgen (male hormones) levels [49].

FIG. 8: FENNEL SEEDS

Chaste berry (Botanical Name: *Vitex agnus-castus*
Family: Lamiaceae

This herb has been used for centuries for hormone imbalances and is considered an adaptogen. Chaste berry berry **Fig. 9** is one of the most common herbs

is one of the most common herbs used to treat PCOS, because it helps to stimulate and stabilize the function of the pituitary gland. The pituitary gland releases a luteinizing hormone that can reduce estrogen and androgen levels while raising progesterone levels. Side effects: This herb is not associated with major side effects but can cause dizziness, rash and stomach issues. Since, it affects the hormones, pregnant women or taking birth control pills should avoid this herb. People taking dopamine-related drugs such as Parkinson's medications or antipsychotics should also not take chaste berry [42].

FIG. 9: CHASTE BERRY

Green Tea (Botanical Name: *Camellia sinensis* **Family:** Theaceae

The potent antioxidants present in green tea, namely catechins, are responsible for lowering the hormone levels that are causing ovarian cysts and related symptoms. Insulin levels are also brought under control by green tea antioxidants. Drinking green tea **Fig. 10** daily also impacts the weight gain commonly seen in PCOS and helps you shed this excessive weight [28].

FIG. 10: GREEN TEA

Amla (Botanical Name: *Emblica officinalis* **Family:** Phyllanthaceae

It is very effective in weight loss and improves the antioxidants. Amla **Fig. 11** is a wonderful detoxifying and cholesterol-reducing agent. Its free radical scavenging and anti-inflammatory effects can help restore the body's hormonal balance.

It flushes out toxins, regulates the menstrual cycle and causes hormonal balance. It also fights against the negative effects of PCOS like obesity, unwanted hair growth, *etc.* [43].

FIG. 11: AMLA

Sesame Seeds (Botanical Name: *Sesamum indicum*
Family: Pedaliaceae

Sesame seeds **Fig. 12** are helpful for regularizing periods. Sesame seeds contain nutrients beneficial for PCOS patients. Its healthy fats help to regulate blood glucose levels. It also contains minerals like calcium, magnesium, and zinc [52].

FIG. 12: SESAME SEEDS

Pumpkin Seeds (Botanical Name: *Cucurbita maxima*

Family: Cucurbitaceae

Pumpkin seeds boost the estrogen for healthy egg production; it tones and strengthens the uterus and improves ovulation. Pumpkin seeds **Fig. 13** also contain healthy omega-3 fatty acids that can help manage the high cholesterol and insulin levels in PCOS. They also contain beta-sitosterol that can remove excess androgens and treat the hirsutism, acne, and weight gain symptoms of PCOS. Pumpkin seeds (also called pepitas) provide many PCOS-fighting nutrients, including magnesium, phosphorus, manganese, copper, iron, and zinc. Pumpkin seeds provide a good source of monounsaturated fats, protein, B vitamins, and vitamin A. They also contain beta-sitosterol, a plant sterol that reduces cholesterol and boosts the immune system. Having these seeds will allow you to slash down the chances of osteoporosis after menopause also [52].

FIG. 13: PUMPKIN SEEDS

Tulsi (Botanical Name: *Ocimum sanctum*
Family: Lamiaceae

The androgens are not utilized because the ovulation process does not take place. Also, the SHBG protein produced by liver is also pretty low. This is why women have excessive facial hair growth, acne, and trouble conceiving. Tulsi **Fig. 14** can control androgens and moderate insulin levels.

It's also an excellent antioxidant. Chew at least 10 leaves early in the morning on an empty stomach. Consume boiled tulsi water regularly. Tulsi can control androgens and moderate insulin levels.

Tulsi has also been shown to counter metabolic stress through normalization of blood glucose, blood pressure, and lipid levels, and psychological stress through positive effects on memory and cognitive function and through its anxiolytic and anti-depressant properties [20].

FIG. 14: TULSI

Spearmint Tea (Botanical Name: *Mentha spicata*
Family: Labiatae

It reduces the testosterone level in patients with PCOS. Spearmint tea **Fig. 14** is high in antioxidants and helpful for reducing facial hair, stress hirsutism symptoms and provides natural glowing skin. The study was carried out in Turkey in a two-centre as 30-day randomized controlled trial. Forty-two volunteers were randomized to take spearmint tea twice a day for a 1 month period and compared with a placebo herbal tea. At 0, 15 and 30 days of the study serum androgen hormone levels and gonadotropin were checked; the degree of hirsutism was clinically rated. 41 out of 42 patients completed the study. Free and total testosterone levels and degree of hirsutism were reduced over the 30 day period in the spearmint tea group. LH and FSH were increased. It was demonstrated and confirmed that spearmint has antiandrogen properties [16].

FIG. 15: SPEARMINT TEA

Ginseng Saponin (Botanical Name: *Panax ginseng*

Family: Araliaceae

FIG. 16: GINSENG SAPONIN

Female Sprague-Dawley rats (190-210 g) were induced polycystic ovary with intramuscular injection of Estradiol Valerate (EV) and separated into three groups: EV control (n=10), EV plus Ginseng Total Saponins (n=10), and oil control (n=10). Ovarian morphology and Nerve Growth Factor (NGF) protein expression were observed. Increased expression of Nerve Growth Factor was noted in the ovaries and the brain of rats with Poly Cystic Ovary. Ginseng Total Saponis administration attenuated NGF expression in the ovaries [7].

Curcumin (Botanical Name: *Curcuma longa*
Family: Zingiberaceae

Turmeric **Fig. 15** is an amazing medicinal spice that can also act as a potent hormone balancer and fertility promoter. The anti-inflammatory, liver detoxification, and antioxidant properties can help support our hormone balance and fertility, reducing aging effects on our bodies. Curcumin showed beneficial effects in Letrozole-induced PCOS in female Wistar rats. Its effect was comparable to Clomiphene citrate, the most widely used treatment for ovulation induction in PCOS condition [35].

FIG. 15: CURCUMIN

Chamomile (Botanical Name: *Matricaria chamomilla*

Family: Asteraceae

Chamomile **Fig. 16** is effective for menstrual pain. Thirty virgin adult cycling Wistar rats, weighing 200 - 220 g were divided into two groups and housed every six mice into cage under standard conditions (21 ± 2°C, 12-hour light/ 12-hour dark cycles) for at least one week before and throughout the study. The estrous cyclicity of 30 virgin adult cycling rats was monitored by vaginal smears obtained between 0800 and 1200 hours. After about 4 days, each rat received an i.m. injection of Estradiol Valerate), 2 mg in 0.2 ml of corn oil, to induce PCOS. Corn oil was injected to the rats in the control group. All the rats in the experimental group were evaluated for follicular cysts 60 days after the injection. Rats with PCOS were treated by multiple doses (25, 50, 75 mg/kg) of intraperitoneal injections of Chamomile alcoholic extract for ten days. The histological and hormonal results showed that Chamomile can decrease the signs of PCOS in the ovarian tissue and help LH secretion in rats [12].

FIG. 16: CHAMOMILE

Astragalus (Botanical Name: *Astragalus membranaceous*
Family: Fabaceae

In this study, 32 women with PCOS were administered with combined application of astragalus polysaccharides and diane-35 for 3 months. Sex hormones, insulin sensitivity and blood lipid were evaluated before and after the therapy. After the treatment, fasting serum insulin levels, LH/FSH ratio was reduced and the insulin sensitivity index increased significantly. Astragalus **Fig. 17** polysaccharides plus diane-35 can

effectively improve insulin resistance, high androgen hormone status and lipid metabolism in patients with PCOS and may be an alternative for PCOS [32].

FIG. 17: ASTRAGALUS

Shatavari (Botanical Name: *Asparagus racemosus*
Family*:* Liliaceae

Shatavari is the powerhouse of antioxidants, prevents collagen breakdown and also manages blood sugar level in blood/Shatavari **Fig. 18** is one of the major health tonics and most popular rasayana drugs to treat reproductive ailments of women, the underlying mechanism of Shatavari action at the level of ovary remains poorly understood. Based on the existing studies, we propose that Shatavari may improve female reproductive health complications, including hormonal imbalance, polycystic ovarian syndrome (PCOS), follicular growth and development, oocyte quality and infertility possibly by reducing OS level and increasing antioxidants level in the body [45].

FIG. 18: SHATAVARI

Kanchanar (Botanical Name: *Bauhinia variegate*
Family: Fabaceae

Kanchanar **Fig. 19** is a valuable herb with an abundance of benefits. It has a vast reserve of vitamin C, iron, calcium, magnesium, vitamin B, as well as dietary fibres, proteins, and carbohydrates. Rich in bioactive chemicals that have strong antioxidant, anti-inflammatory, anti-tumour, pain-relieving, and detoxifying properties, kanchanar guggulu rectifies thyroid issues like goitre, blood clots, irregular periods, overweight conditions, respiratory illnesses, and skin disorders [30].

FIG. 19: Kanchanar

Chia Seeds (Botanical Name: *Salvia hispanica* L.
Family: Labiate

Chia seeds **Fig. 20** are rich in omega fatty acids and fiber and can help with hormonal fluctuation, mood swings, and metabolic syndrome. These magical seeds can also aid in regularizing one's periods. In addition, chia seeds are rich in calcium, magnesium, iron, and zinc which are good for your overall health. A great thing about chia seeds is that they are so filling. Just 1 tablespoon of these nutty seeds provides 5 grams of fiber. When mixed with water, chia seeds form a gel-like texture that's good to use in smoothies, soups, oatmeal, and even as a substitute for eggs in many baked goods. Chia seeds are rich in calcium, magnesium, iron, and zinc. They also provide a good dose of omega-3 fats [52].

FIG. 20: CHIA SEEDS

Ginger (Botanical Name: *Zingiber officinale*
Family: Zingineraceae

Ginger **Fig. 21** restores the healthy levels of estrogen in the body. It is consumed worldwide as a flavoring agent and medicine for thousands of years. In Ayurveda, ginger has been used as a carminative, sweat-inducing, anti-seizure, and blood circulation stimulator for treating inflammation and rheumatoid arthritis 10.

FIG. 21: ***ZINGIBER OFFICINALE***

The main medicinal value of ginger is due to gingerol and shogaol, which have potent antioxidant activity. In addition, it contains zingerone and some oily resin called gingerin. It has been shown that ginger could have a good effect in menstrual irregularities treatment and can inhibit ovarian cancer cells [39].

Red Clover (Botanical Name: *Trifolium pretense*
Family: Zingineraceae

Red clover **Fig. 22** contains phytoestrogens, a plant-based estrogen, which helps improve the hormonal imbalances caused by menopause. It decreases testosterone levels and shows a significant increase in estrogen level in women.

FIG. 22: RED CLOVER

Fenugreek (Botanical Name: *Trigonella foenum graceum*
Family: Fabaceae

Fenugreek **Fig. 23** decreases insulin resistance and weight gain by lowering cholesterol levels. Preliminary animal and human trials propose possible hypoglycemic, antiplasmodiac, anticarcinogenic, anti-hyperlipidemic, prevent hair loss, antinociceptive, help losing weight. and gastroprotective properties of fenugreek seeds.

FIG. 23: FENUGREEK

Because of fenugreek's estrogen content and its ability to stimulate the uterus. Historically fenugreek has been used in Chinese and Ayurvedic medicine. The application involved several medical conditions like indigestion, labor induction, immune booster. Intake of fenugreek seeds for three months positively affected the regularity of menstrual cycle, egg maturation, and ovarian volume and infertility [19].

Ashwagandha (Botanical Name: *Withania somnifera*
Family: Solanaceae

Patients with PCOS are more prone to high blood pressure levels, stress, anxiety, and depression. It could also correct irregular menstrual cycles and reduce. Patients with PCOS are more prone to high blood pressure levels, stress, anxiety, and depression.

Ashwagandha **Fig. 24** may address the issues by acting on many fronts that can affect women with PCOS. Ashwagandha has been a traditional remedy to ease stress and anxiety in ancient cultures. The same benefits contribute to relieving the stress, anxiety, and depression associated with PCOS. The

root extract improves insulin sensitivity in the body and stimulates glucose uptake by the muscle cells.

FIG. 24: ASHWAGANDHA

Cumin Seeds (Botanical Name: *Cuminum cyminum*
Family: Apiaceae

Cumin seeds **Fig. 25** are rich in antioxidants which help nourish the skin. It also regulates blood pressure as well as blood sugar. It also boosts immunity, detoxifies the body, and positively affects the menstrual cycle.

It is a very effective immune system boosting agent which helps to balance cortisol levels i.e., stress and also corrects the hormonal imbalance and regularizes the periods.

FIG. 25: CUMIN SEEDS

Star Anise: Star anise if helps to prohibit viral contamination, reinforces cardiac output, provides defense against Human Flu, regulates insulin sensitivity, menstrual cramps, "dysmenorrhea" or painful uterine contractions is the result of excessive prostaglandin production in secondary endometrium during the first 48 h of menstruation. The pain and feeling of pressure in the abdominal cavity, headache, pain in the hips, lower back, and tights, upset stomach, vomiting and loose stools are the common symptoms of dysmenorrhea. Aniseed treats primary dysmenorrhea (bleeding and menstrual pain) [55].

CONCLUSION: PCOS is an ovarian cyst, a health condition becoming very common nowadays. Nature has given us so many herbal remedies for ovarian cysts, which can be used in both benign and malignant cases along with the other remedies you are taking. These herbs help other treatments to work better, and sometimes these herbs are so effective that they alone are good enough to care for ovarian cysts naturally.

ACKNOWLEDGEMENT: We would like to thank Dr. Birajdar Arunadevi, HOD Quality Assurance Department, K.T. Patil College Of Pharmacy, Osmanabad, for their continuous support and guidance.

CONFLICT OF INTEREST: There is no conflict of interest.

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How to cite this article:
Mulay KV and Birajdar AS: Efect of herbal drugs on polycystic ovarian syndrome: a review. Int J Pharm Sci & Res 2023; 14(8): 3802-14. doi: 10.13040/IJPSR.0975-8232.14(8).3802-14.