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A Review on Phytomedicine and Their Mechanism of Action on PCOS

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is characterized by gynaecological endocrine and metabolic abnormality of women at reproductive ages. It is established that hyperandrogenism, insulin resistance, menstrual abnormalities, and chronic absence of ovulation of polycystic ovary are commonly associated with symptoms. It might indicate the multidisciplinary approach for the therapeutic management of PCOS. Conventional medical management concentrated single symptom, is often associated with the side effect, maybe contraindicated and ineffective in some conditions. So far women with PCOS have expressed a desire for alternative medicine. Ayurvedic medicine has been emerging as one of the commonly practised medicines for different health problems, including PCOS.

Objective: In this review, an attempt has been made to study the use and mode of action of potential Ayurvedic drugs for the treatment of PCOS.

Method: This review is mainly based on the scientific literature search. The first search on plant possesses multiple effects against PCOS reproductive and metabolic complications. Selected plants from the first search were used as a keyword for the second search.

Result: They include *Cinnamomum zeylanium*, *Gymnema sylvestre*, *Mentha spicata*, *Pergularia daemia*, *Saraka indica*, *Saw palmetto*, *Tribulus terrestris*, and *Withania somnifera*. The second search sought the reproductive endocrinal and metabolic demonstrated mechanism of the selected plants.

Conclusion: This review supports the alternative Ayurvedic medication as a standard effective and safe drug in the management of PCOS.

Key Words: Medicinal Plants, PCOS, Anti-androgenic, Insulin resistance, Menstrual irregularity, Mechanism of action

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a complex endocrinal reproductive disorder in a coalition with metabolic abnormalities of women at reproductive stages. PCOS characterized by hypergonadotropism, hirsutism, irregular and painful menstrual cycles, amenorrhea, multiple cysts in ovaries, anovulation which is commonly associated with infertility.¹ It is also characterized by multiple metabolic abnormalities, such as insulin resistance, hyperinsulinemia, high incidence of impaired glucose tolerance, obesity, inflammation, endothelial dysfunction, hypertension, and dyslipidemia resulting in an increased risk for diabetes and cardiovascular disease.²⁻⁴ Besides, compromised quality of life, anxiety, and depression is also observed in PCOS.⁵

Existing treatment approaches to PCOS are limited due to the prevalence of contraindication in PCOS women, treatment failure in some circumstances, and may cause some severe side effects. This challenging drawback of current therapy for PCOS in women making an interest in an alternative treatment called Ayurvedic treatment. It is a natural way to treat the diseased condition without causing any serious side effects.⁶⁻⁷ The usage and acceptability of complementary medicine by women has increased from 26% to 91% during the past ten years.⁸⁻⁹ Recent day global health debates getting significant attention towards traditional herbal medicines. However herbal medicines are fighting to be recognized as a standard medication with its own identity. It is become necessary to show that herbal therapy can match

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other fields of medicine in the thoroughness of its pharmacology and standardization of its practical use. Hence the focus of this study was to investigate plants possess multiple pharmacological actions in relevance to PCOS complication and to review its mechanism of action in PCOS condition, to improve its therapeutic wide acceptability and exploration of some standard herbal/ polyherbal formulations in PCOS.

MATERIALS AND METHODS

In this study, we carried out two searches of the scientific literature. The first search on plants reported with multiple reproductive endocrine effects in hyperandrogenism, menstrual irregularity, and multiple cysts in ovaries, and also on metabolic effects in insulin resistance and hyperlipidemia. In the second search sought the reproductive endocrinal and metabolic demonstrated mechanism of the effect of the selected plants.

From the first search, we selected eight plants with multiple pharmacological effects on PCOS. These were *Cinnamomum zeylanicum*, *Gymnema Sylvestre*, *Mentha spicata*, *Pergularia daemia*, *Saraka indica*, *Saw palmetto*, *Tribulus terrestris*, and *Withania somnifera*. The selected plants with a demonstrated mechanism of action were entered as key terms in the second search.

We searched from the following electronic databases: MEDLINE, EMBASE, PubMed, Google Scholar, Research gate and Science direct from the date of database inception to October 2019. Also, a search was made manually on the references of reviewed articles. First search key terms are title or abstract included 'herbal medicine' or 'herbal extract' or 'phytotherapy' or 'phytomedicine' and title or abstract contains 'androgen' or 'Estrogen' or 'follicle stimulating hormone' or 'luteinizing hormone' or 'prolactin' or 'insulin' or 'glucose' or 'polycystic ovary' or 'PCOS'. Search terms for the second search included the following keywords in the title or abstract, contains; 'Mechanism' 'menstrual irregularity' or 'oligomenorrhoea' or 'amenorrhoea' or 'hyperandrogenism' or 'hirsutism' or 'acne', or 'polycystic ovary syndrome' or 'PCOS' and '*Cinnamomum zeylanicum*' or '*Gymnema sylvestre*' or '*Mentha spicata*' or '*Pergularia daemia*' or '*Saraka indica*' or '*Saw palmetto*' or '*Tribulus Terrestris*' or '*Withania somnifera*'.

Medicinal plants and their mechanism of action on PCOS

A. *Cinnamomum zeylanicum*

Cinnamomum zeylanicum found to be an effective therapeutic agent for PCOS because it has been shown to improve both the reproductive and metabolic aspects of PCOS. Antiandrogenic mechanism: Oral administrations of cinnamon

extract (10mg/100g) downregulate testosterone in dehydroepiandrosterone induced PCOS mice. Insulin resistance in PCOS women with compensatory hyperinsulinemia induces overproduction of androgen in the ovary. This action is mediated through the activation of insulin-like growth factor-1 (IGF-1) receptors on theca and stroma cells. In granulosa cells, IGF-1 stimulates estrogen production and regulates aromatase concentration. IGF-1 also acts synergistically with Luteinizing hormone (LH) to stimulate androgen production on theca cells. Increased serum level of insulin and IGF-1 amplifies the effect of LH on granulosa cell leads to anovulation and affect follicular maturation. Hence the proposed anti- androgenic mechanism of cinnamon is mediated by the downregulation of insulin, insulin-like growth factor-1 (IGF-1), and testosterone serum levels. This downregulation of IGF-1 is associated with an increased level of insulin-like growth factor-binding protein -1 (IGFBP-1) in plasma and ovary.¹⁰⁻¹²

Effect on insulin resistance: Oral administration of the cinnamon extract (one capsule containing 333 mg, three times per day for 8 weeks) would improve insulin sensitivity in PCOS women. The insulin resistance reduction mechanism mediated through an increase in glucose utilization and potentiating phosphatidylinositol 3-kinase (PI-3 kinase) insulin signalling pathway at the post-receptor level. It leads to the translocation of glucose transporter type-4 (GLUT-4) receptor culminate and improved glucose utilization by aiding intercellular glucose transport and increasing glycogen synthesis.¹³⁻¹⁴

Effect on Menstrual irregularity: A clinical study suggests that cinnamon supplementation (1500 mg/day for 6 months) may be a useful adjunct for menstrual dysfunction in women with PCOS. The suspected mechanism is it regulates menstrual irregularity by improving insulin sensitivity.¹⁵ Effect on obesity: Oral supplementation of cinnamon (1500 mg/day for 8 weeks) significantly decreased serum levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and increased high-density lipoprotein cholesterol (HDL-C) levels in women with PCOS¹⁶. The hypolipidemic effect of cinnamon might be due to its polyphenol and cinnamaldehyde content, which inhibits intestinal cholesterol absorption and increases lipolysis in adipose tissues respectively.^{17,18} Anti-hyperlipidemic mechanism of cinnamon mediated through the up-regulation of peroxisome proliferator-activated receptor alpha (PPAR α) expression increased cellular uptake of fatty acid and the expression of lipoprotein lipase gene.¹⁹

B. *Gymnema sylvestre*

Gymnema sylvestre is the most widely used ayurvedic medicine for diabetes mellitus and the lowering of serum cholesterol.²⁰ It also effective in reducing the elevated androgen and regulate the menstrual irregularity in PCOS. Antiandrogenic

mechanism: The ethanolic leaf extract of *Gymnema sylvestre* decreases the elevated androgen level in estradiol valerate induced PCOS rats. Till there is no possible anti-androgenic mechanisms were explored.²¹ Effect on insulin resistance: The leaf extract of *Gymnema sylvestre* (400mg/kg) was reported to reduce hyperglycemia in both insulin-dependent and non-insulin-dependent diabetic patients.²² *Gymnema sylvestre* posse multiple antihyperglycemic mechanisms like increases in insulin secretion and glucose utilization through the insulin-dependent pathway by increased the activity of phosphorylase and decrease in gluconeogenic enzymes and sorbitol dehydrogenase. It also promotes the regeneration of islet cells. Gymnemic acid in *Gymnema sylvestre* prevents excess glucose absorption in the intestine by binds with glucose receptor.^{23,24}

Effect on Menstrual irregularity: A preclinical study demonstrated that ethanolic leaves extract of *Gymnema sylvestre* 400mg/kg/ day regularizes the menstrual irregularity in estradiol valerate induced PCOS rats. But the study fails to explain the mechanistic approach.²⁵

Effect on obesity: The different solvents leave extract of *G. Sylvestre* reported to possess significant hypolipidemic activities in experimentally induced obesity models. Hexane extract at 250 mg/kg/day for 28 days²⁶, hydroalcoholic extract at 200 mg/kg/ day for 7 days²⁷ and methanolic extract 1gm/kg/day for 4 weeks significantly decreased the body weight gain and lowered serum total cholesterol, triglycerides (TG), very low-density lipoprotein cholesterol (VLDL), LDL, leptin and increases HDL levels.²⁸

C. *Mentha spicata*

Mentha spicata indicated for PCOS women. Because of *M. spicata* effective in both the reproductive and metabolic complications of PCOS.

Antiandrogenic effect: *Mentha spicata* essential oil (spear-mint oil) 300mg/kg treatment daily for 20 days effectively reduced the body weight, serum testosterone level, number of atretic follicles, ovarian cyst and also increased the Graafian follicle in letrozole induced PCOS rats.²⁹ Clinical studies also demonstrated that spearmint tea (a cup of *M. Spicata* 5gm/250ml) taking twice a day for 30 days decreased the free and total testosterone and increase LH and FSH. It might be concluded that *M. spicata* acts as an effective antiandrogenic agent in female patients with PCOS by decreasing free and total androgens and reduces the number of ovarian cysts.^{30,31}

Hypoglycemic & Hypolipidemic effect: *M. spicata* aqueous leaf extract (300 mg/kg for 21 days) has efficient hypoglycemic, hypolipidemic, and lipid peroxidation activities in alloxan-induced diabetic rats.³² Similarly, 14-day treatment of aqueous ethanolic fresh leaf extracts of *M. spicata* 400 mg/kg showed an efficient anti-diabetic and moderate hypolipidemic effect in alloxan-induced diabetic rats. Those study

results suggested that the anti-diabetic effect of *M. spicata* is mainly due to its secondary metabolites. Flavonoids, phenol, glucoside terpenoids, and steroids in *M. spicata* reduce the serum glucose level by stimulating the beta cells for insulin production and utilization. Carbohydrate increases glucose tolerance and release, alkaloids reduces intestinal glucose transport by inhibiting the alpha- glycosidase.³³ Hence *M. spicata* acts as anti-diabetic medication by stimulating insulin production, and increase the release and utilization, also acts by reduces the intestinal glucose absorption.

D. *Pergularia daemia*

The fresh leaf extract of the *Pergularia daemia* is an effective medicine in normalizing the hormonal levels of the PCOS induced rats. It acts by normalizing the elevated Testosterone and Luteinizing hormone level and decreases Progesterone and Follicle-stimulating hormone (FSH) in induced PCOS.³⁴ *P. daemia* has the potential to normalize menstrual irregularities and regularize the estrous cycle. Subsequently, the restoration of the estrous cycle reduces the development of follicular cyst.³⁵ Besides, *P. daemia* also possess effective hypoglycemic and hypolipidemic properties in PCOS induced conditions.^{36,37} The mechanisms of action of *P. daemia* are not clear at this time; more work is required on a molecular level to delineate the process on PCOS.

E. *Saraka indica*

Saraka indicia dried barks and flowers are one of the most widely using Unani and Ayurvedic medications for several female disorders principally in gynaecological disorders and menorrhagia. *S.indica* bark has an excellent uterine and endometrial tissue stimulant effect. It is also useful in treating female disorders like painful periods, internal bleeding, haemorrhoids, menometrorrhagia, amenorrhoea, menorrhagia particularly due to uterine fibroids, leucorrhoea and pimples.^{38,39}

S. indica methanolic extract (200 mg/kg) in female rats reported to possessing anti-estrogenic properties because of its phytoestrogens constituents. Hence it is effective in PCOS hormonal and reproductive complications by block the over-expression of estrogen in PCOS women.⁴⁰ Phenolic glycoside P2 isolate from *S. indica* also reported producing oxytocic activity in both animal and human myometrial tubes.⁴¹ *S. indica* leaves, flowers, and bark extract reported to possess hypoglycemic and hypolipidemic activity in induced diabetic conditions. Lack of molecular level findings to explore its exact mechanisms.⁴²⁻⁴⁴

F. *Saw palmetto (Serenoa repens)*

Saw palmetto indicated for PCOS, hormone imbalances (estrogen/testosterone), and benign prostatic hyperplasia. It also used to improve the genitourinary health in both sexes; this means it promotes the sexual vigour and chronic nonbacterial

prostatitis and pelvic pain syndrome.^{45,46} The saw palmetto berries containing fatty acids liposterols indicated to produce significant anti-androgenic action in PCOS condition. It produces anti-androgenic action by inhibiting the 5- α reductase enzyme responsible for the conversion of testosterone into its active form dihydrotestosterone (DHT) in the adrenal gland. It also reduces the 40% tissue uptake of androgens including DHT and testosterone.^{47,48} These mechanisms illustrated that *Saw palmetto* may aid in PCOS hyperandrogenism by reducing the 5- α reductase activity inhibits DHT production and increases DHT breakdown.

Animal studies showed that *Saw palmetto* regularizes the elevated prolactin-induced suppression of follicle maturation, ovulation, and formation of cysts in the PCOS ovary. *Saw palmetto* suppresses the elevated prolactin-induced ovarian changes by inhibiting the ovarian prolactin receptor by reducing the K⁺ channels and protein kinase C basal activity involved in the prolactin transduction signals.⁴⁶ Additionally, the anti-inflammatory properties of *Saw palmetto* extract can also be helpful to combat bloating, pelvic pain, and low-grade systemic inflammation in women with PCOS.⁴⁹

G. *Tribulus terrestris*

The aerial parts and fruits of *Tribulus terrestris* indicated in PCOS to promote regular ovulation and reduce the ovarian cyst.⁵⁰ The hydroalcoholic extract of *T. terrestris* 10 mg treatment normalizes the menstrual irregularity, hormonal alterations, and efficiently removes the ovarian cysts and resumes the ovarian normal activity in the estradiol valerate induced PCOS rats. It might be due to its luteinizing effect related to its gonadotropin like activity or luteinization of follicular cysts.^{51,52} The proposed mechanism of *T. terrestris* on normalizing the hormonal level and induction of ovulation in PCOS is mainly due to its antiestrogenic action. The phytoestrogens (diosgenin, gitogenin, chlorogenin, ruscogenin, and essential oil) present in *T. terrestris* binds with estrogen receptor ER α and ER β , and act as a pure estrogen antagonist by stimulating the Gonadotropin-releasing hormone secretion.⁵³ A randomized control study reported that 1000 mg/day treatment of hydroalcoholic *T. terrestris* extract showed promising hypoglycemic effect and significantly reduced the total cholesterol and low-density lipoprotein in women with diabetes mellitus type 2. These results further add up its therapeutic efficacy in PCOS.⁵⁴

H. *Withania somnifera*

Stress is one of the major factors that affect female reproductive health by modulating ovarian physiology and reproductive hormones. This may lead to menstrual irregularity, amenorrhea, and anovulation.^{55,56} Many of preclinical and clinical studies proved the potent anti-stress property of *Withania somnifera*. It also poses a positive influence on the endocrine system.⁵⁷ *Withania somnifera* root indicated to sup-

port all endocrine functions in PCOS women. The proposed mechanism links the antioxidant features and its positive effect on hormonal imbalances of testosterone, LH, and FSH. However, the gamma-aminobutyric acid (GABA) mimetic feature of *Withania somnifera* extract plays a major role in the inducing gonadotropin-releasing hormone secretion and improving hormonal balance.⁵⁸ *W. somnifera* root hydroalcoholic extract treatment increases the number of days in the estrus phase and decreases the duration of the diestrus phase. Also, it increases the FSH and decreases LH, testosterone, and estradiol in letrozole induced PCOS rats.⁵³ Supporting finding such as hypoglycemic potency by increased insulin secretion and improved insulin sensitivity in muscles and hypolipidemic effect mediated through an increased bile acid synthesis for the elimination of body cholesterol shows the efficiency of *W. somnifera* in PCOS.^{59,60}

CONCLUSION

Based on the available previous preclinical and clinical reported data we have selected eight plants with multiple promising effects on PCOS complications. All the selected plants were not completely screened for all PCOS complications. Still the available preliminary data revealed the therapeutic potential of the selected herbs in PCOS. The selected list of herbs is merely outnumbered in the unexplored domain of medicinal herbs having pharmacological potential. There is a need for therapeutic standardization to improve its acceptability and applications on PCOS. Further rational investigations are needed to explore deeper and extensive mechanisms of selected herbs on both reproductive and metabolic PCOS complications. This extensive review will support the researchers and phytotherapist to explore more standard herbal polyherbal formulations/remedies for PCOS.

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Table 1: Phytopharmacological data of the selected plants

Medicinal plants & Scientific name	Family	Commonly used Plant Parts	Traditional climes	Reported activities	References
<i>Cinnamomum zeylanicum</i> L. (Cinnamon)	Lauraceae	Steam bark, Leaves	Increases the blood circulation in the uterus and advances tissue regeneration, As tooth powder to treat toothaches, dental problems, oral microbiota, and bad breath. It can also improve the health of the colon, thereby reducing the risk of colon cancer.	Antidiabetic, Cardio-protective, Anti-oxidant, Neuroprotective, Anti Alzheimer's, Anti-inflammatory, Hepatoprotective, Antimicrobial, and Anticancer activity.	61, 62, 63
<i>Gymnema sylvestre</i>	Asclepiadaceae	Leaves, Flowers and bark	Diabetes, Malaria, antihelminthic, antipyretic, astringent, cardiotonic, digestive, diuretic, cough, dyspepsia, hemorrhoids, hepatosplenomegaly, laxative, stimulant, stomachic, uterine tonic, intermittent fever, jaundice, leucoderma. Snakebites, urinary disorders, and respiratory diseases.	Anti-arthritic, Antihyperlipidemic, Antidiabetic, Immunostimulatory, Hepatoprotective, Wound Healing, Antiarthritic, Anti-inflammatory Anticancer, and Cytotoxic.	64, 24, 22
<i>Mentha spicata</i> L. (spearmint)	Labiatae	Fresh or dried plant, Leaves, spearmint oil	Colds, fever and flu, respiratory tract problems, gastralgia, hemorrhoids, and stomachache, also used as carminative to treat digestive disorders	Antispasmodics, anti-platelets, antioxidant, anti-microbial, Hypoglycemic, Hypocholesterolemic, Anti-androgen, Reverse hormonal, and folliculogenesis disturbances in PCOS.	65, 66, 29, 31, 32
<i>Pergularia daemia</i> (Forsk.)	Apocynaceae	Arial parts, Stem bark, Leaves, Roots, fruit, Latex	Gastric ulcer, uterine and menstrual complaints (Amenorrhoea, dysmenorrhoea), hemorrhoids, abortifacient, Uterine tonic infantile diarrhoea, bronchitis, whooping cough, cold, heals cuts and wounds, antipyretic and appetizer.	Uterine stimulant, analgesic, antipyretic, anti-inflammatory, CNS depressant, hepatoprotective, Anti-fertility, anti-oxidant, anti-cancer, Antidiabetic, anti-bacterial, anti-fungal and anti-malarial activity.	67, 68, 69

Table 1: (Continued)

Medicinal plants & Scientific name	Family	Commonly used Plant Parts	Traditional climes	Reported activities	References
<i>Saraca indica</i> L.	Leguminosae	Leaves, Flowers, Barks, Seeds	Useful in several feminine disorders like internal bleeding, hemorrhoids, ulcers, uterine affections, menorrhagia especially due to uterine fibroids, menometrorrhagia, leucorrhoea, and pimples.	Anti-inflammatory, Analgesic, Antipyretic, Antioxidant, Immunomodulatory, Antimenorrhagic, Uterine tonic, Antioxytotic, Antidiabetic, CNS depressant, Cardioprotective and Anticancer activity.	38, 70,71
<i>Saw palmetto</i> (Serenorepens)	Arecaceae	Berries, oil	To cure genitourinary disturbances, relieve mucous membrane irritations, increase testicular function, the breast size.	Antiandrogen, anti-proliferative and anti-inflammatory, Effective in Androgenetic alopecia, Prostate hypertrophy.	72, 73, 74
<i>Tribulu terrestris</i> L.	Zygophyllaceae	Arial parts, Fruits	Used in infertility, impotence, erectile dysfunction, low libido, tonic, aphrodisiac, diuretic, urinary disorders, hyperuricemia, expectorant, improves eyesight and to relieve rheumatic pain.	Libido enhancing activity, Effective in erectile dysfunction, Fertility improver, Hypoglycemic, Hypolipidemic, Anti urolithiatic, analgesic, antioxidant, anti-inflammatory, Anti-aging, cardio-protective, neuroprotective, diuretic and uricosuric.	75, 76, 77
<i>Withania somnifera</i> Dunal (Ashwagandha)	Solanaceae	Root, Leaves, Flowers, seeds	Treatment of tumors and tubercular glands, a tonic for vitality and longevity, Adaptogen, aphrodisiac, narcotic, diuretic, anthelmintic, astringent, ulcers and painful swellings, thermogenic and stimulant.	Abortifacient, aphrodisiac, Anti-hyperglycemic, Hypolipidemic, Immunomodulatory, Cardioprotective, Antiparkinsonian, Nootropic, Anticonvulsant, Anti-aging, Antioxidant, Anti-stress, anti-arthritis and anti-inflammatory	60,78, 79

Table 2: Selected medicinal plants and their mechanism of action on PCOS

Medicinal plants	Reported activities in relation to PCOS	Mechanism of action	References
<i>Cinnamomum zeylanicum</i>	Antiandrogenic, Normalize the disrupts folliculogenesis and menstrual cyclicality Improves insulin sensitivity Antihyperlipidemic	Cinnamomum acts by down-regulate serum levels of testosterone, insulin and decreases IGF-1 level while increase IGFBP-1 level in plasma as well as in the ovary of patients with PCOS. Reduced insulin resistance mediated through an increase in glucose utilization, by potentiating insulin signaling at the post-receptor level, increasing PI-3 kinase activity. This leads to the translocation of GLUT-4 receptors and the attenuation of the tonic inhibition on glycogen synthase, culminating in improved glucose utilization by facilitating intracellular glucose transport and increasing glycogen synthesis. Cinnamon regulated lipid metabolism via the up-regulation of Peroxisome proliferator-activated receptor alpha (PPAR α) expression increased the cellular uptake of fatty acids liberated from fat tissues. PPAR α ligands also increased the expression of the lipoprotein lipase gene, resulting in the anti-hyperlipidemia effect.	11, 12 13, 14 19
<i>Gymnema sylvestre</i>	Antiandrogenic and regularize the menstrual irregularity Improves insulin sensitivity Hypolipidemic	Decrease the elevated androgen level in induced PCOS. But the possible mechanism was not explored. It increases glucose utilization shown by increase the activities of enzymes responsible for the utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, a decrease in gluconeogenic enzymes and sorbitol dehydrogenase. It also increases insulin secretion and promotes the regeneration of islets cells. It possesses significantly reduces the total cholesterol, TG, LDL, VLDL, and leptin in induced condition.	21 23, 24 26, 27, 28
<i>Mentha spicata</i>	Anti androgenic, Reduce atretic follicles, ovarian cyst and also increased the Graafian follicle in PCOS Hypoglycemia, Hypolipidemia and lipid peroxidation activities	By decrease the free and total testosterone and an increase in luteinizing hormone and follicle-stimulating hormone. The present secondary metabolites flavonoids reduce the serum glucose level and stimulate beta cells for insulin production. Phenol and flavonoids increase the utilization of insulin and reduce glucose level, alkaloids inhibit α -glucosidase by decreasing glucose transport through the intestinal epithelium.	29, 30, 31 32, 33

Table 2: (Continued)

Medicinal plants	Reported activities in relation to PCOS	Mechanism of action	References
<i>Pergularia daemia</i>	Normalizing the hormonal levels in PCOS	Decrease elevated Testosterone and LH level and Increase the decreased Progesterone and FSH level in PCOS.	34
	Normalizing menstrual irregularities and regularizing the estrous cycle		35
	Hypoglycemic and Hypolipidemic	By restoration of the estrous cycle, <i>Pergularia daemia</i> reduces the development of follicular cysts.	
<i>Saraca indica</i>		Possess hypoglycemic and hypolipidemic in PCOS induced condition.	36, 37
	Antiestrogenic, Oxytocic Hypoglycemic and Hypolipidemic	Phytoestrogens in <i>Saraca indica</i> suppress the estrogen-induced endocrine and reproductive systems associated with malfunctions of reproductive organs.	38, 39
<i>Saw palmetto</i>	Anti androgenic	Liposterols in Saw palmetto produce anti-androgenic effects by inhibits 5 α -reductase to reduce the uptake of androgens, also by increases DHT breakdown and inhibits DHT production and binding to androgen receptor sites.	47, 48
	Inhibit prolactin level		46
	Anti-inflammatory	Saw Palmetto inhibits prolactin receptors on ovarian cells and reduces the basal activity of K (+) channels and protein kinase C involved with the transduction of prolactin signals.	
<i>Tribulu sterrestis</i>		Reduce low-grade systemic inflammation in women with PCOS.	49
	Normalize the hormonal level, Promote regular ovulation and reduce ovarian cyst in PCOS	Phytoestrogens present in <i>Tribulus terrestris</i> binds with estrogen receptors ER α and ER β and acts as a pure estrogen antagonist by stimulating Gonadotropin-releasing hormone secretion. Such this mechanism it normalizes the hormonal level and induction of ovulation in PCOS.	53
<i>Withania somnifera</i>	Anti stressor, Antioxidant, Anti androgenic, Improves follicular development	Increase the level of stress hormone cortisol may reduce estradiol-17 β biosynthesis in the ovary. It results in amenorrhea, anovulation, and menstrual irregularities in females. WS regulate this condition by reducing this stress hormone.	56, 57
	Hormone regulation in PCOS		
	Hypoglycemic activity	GABA mimetic feature of WS extract is thought to play the main role in inducing gonadotropin-releasing hormone secretion and improving hormonal balance.	58
	Hypocholesterolemic effect	Increased insulin secretion and improved insulin sensitivity in muscle cells.	59
		Mediated through an increased bile acid synthesis for the elimination of body cholesterol in PCOS.	60