

Review Article

A review on the pharmacological potential of Indian spices in polycystic ovarian syndrome

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ABSTRACT

Pharmacological Significance: India has a distinct position in history for using spices from cooking to prevent and cure a variety of illnesses. Numerous studies have been conducted to evaluate the potential of these spices for a variety of conditions such as diabetes, metabolic syndrome, and polycystic ovarian syndrome (PCOS). PCOS is a condition in which women of reproductive age experience common health difficulties such as genetic, metabolic, and endocrine abnormalities. Notably, this may be distinguished by symptoms such as hirsutism, acne, and obesity.

Aim: In this review, we looked at numerous Indian spices that may help to manage PCOS and its symptoms.

Materials and Methods: All data were gathered from the literature using several databases such as PubMed and Europe PMC, publishers such as Springer, Wiley, Elsevier, and Taylor and Francis, and academic libraries such as Google scholar and Sci-Hub.

Results: This study focuses on natural spices and their chemical constituents that have varied therapeutic effects such as anti-inflammatory, anti-oxidant, anti-androgenic, anti-estrogenic, anti-thrombolytic, and anti-diabetic for the treatment of PCOS in women.

Conclusion: In this review, we looked at the effects of several Indian spices on the management of PCOS.

Keywords: Indian spices, Polycystic ovarian syndrome, Inflammation, Food, Women health

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a prevalent hormonal condition observed in reproductive-aged women in which they may be unable to conceive a child, resulting in ovarian enlargement due to the formation of cysts on the outer border.^[1] PCOS was first reported by Stein and Leventhal in 1935.^[2] It is characterized by hirsutism, acne, infertility, balding, fluctuations in endocrine hormones (an increase in androgen, estrogen, and prolactin and a reduction in progesterone), and metabolic dysfunctions (diabetes, insulin resistance, and dyslipidemia,^[3] and Type-2 diabetes).^[4-6] It was initially identified in adults but has since spread to the pediatric population. By examining essential components of normal adolescence, such as irregular periods and ovulation, the diagnosis of PCOS becomes more challenging.^[3,7] Weight control is critical in the treatment of PCOS. Furthermore, McBairty *et al.*^[8] and Atashpour *et al.*^[9] demonstrated the favorable effect of weight loss in PCOS.

Symptoms associated with PCOS have an impact on the patient's quality of life and psychological status.^[10] Evidence suggests that oxidative stress contributes to the advancement of PCOS and its

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accompanying symptoms such as infertility and an increase in androgen levels.^[11] Natural plants can assist in avoiding major illness conditions because of their multi-targeted efficacy. The prevalence of PCOS is estimated to be between 2.2% and 26% worldwide. Several studies were conducted in India to determine the risk associated with PCOS. Hosseinkhani *et al.* conducted a study in South India and Maharashtra and the prevalence of PCOS was found to be 9.13% and 22.5%, respectively.^[12] PCOS is found to be associated with other disease conditions which include sleep deprivation, Type 2 diabetes mellitus (DM-2), and non-alcoholic fatty liver disease^[1,13] thyroid disorders.^[14] However, the association of PCOS with cardiac metabolic disorders is still being debated.^[14] Thus, the natural product could be a possible therapeutic strategy for the management of PCOS [Figure 1].^[15,16]

MATERIAL AND METHODS

All the data and information were collected through various scientific databases including PubMed, Europe PMC, and Google scholar. Apart from this, the data were also collected from various scientific journals and covered various aspects including health, physical life, medicinal plants, traditional medicine, and folk medicines also sought information on Indian herbs and spices.

PCOS-ASSOCIATED PATHOPHYSIOLOGY

PCOS causes irregular menstrual cycles, heavy bleeding, obesity, hirsutism, acne, and acanthosis nigricans. It creates

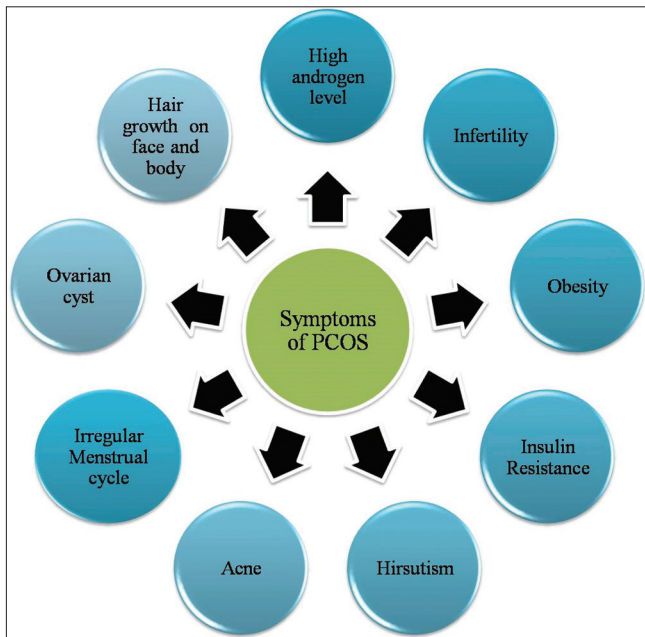


Figure 1: Illustration of symptoms associated with polycystic ovarian syndrome including high androgen level, infertility, obesity, insulin resistance, hirsutism, acne, irregular menstruation, and ovarian cyst.

enlarged ovaries in women, which may include a tiny collection of fluid-filled follicles, also known as cysts, which causes hormonal disruption essential for the onset of ovulation. Ovulation does not occur in PCOS because the sacs are unable to release eggs due to the presence of several harmful follicles in matured sacs.^[1] Women who experience PCOS may have a high level of androgen that can induce chronic obstructive pulmonary disease. However, PCOS diagnosis is critical since it raises the risk of metabolic and reproductive problems. Although PCOS is idiopathic, genetic, environmental, and behavioral factors all play a role in the disease's progression.^[2]

Furthermore, complications such as environmental variables, insulin resistance, and hyperinsulinemia may all contribute to the development of obesity. The reason behind insulin resistance is the impaired insulin receptor signaling pathway that would affect pancreatic β -cell functions. However, a lack of insulin production may have an impact on gonadotropin-mediated ovarian activities, which are more prevalent in PCOS individuals.^[3] High insulin levels may contribute to increased LH/FSH, and hormonal changes in theca as well as granulosa cells (GCs) which further leads to an increase in the synthesis of androgen and a decrease in the synthesis of estradiol which regulates the inhibition of follicle maturation results in PCOS^[4] [Figure 2].

COMMONLY USED INDIAN SPICES

India is well known for its variety of spices all over the world. The word spice is originated from a commonly consumed food in the Middle Ages known as "species,"^[1] Spices are obtained from parts of the plants such as flowers, leaves, seeds, rhizomes, buds, and roots.^[2] They enhance the aroma and appearance of food and are also used in cosmetics, fragrances, and candies. It also carries the essential components of plant products such as protein, carbohydrates, fibers, vitamins, minerals, and tannins.^[3] Spices play an important role in health and illness, including diabetes, cancer, rheumatism, arthritis, and metabolic disorders. Even in today's time, spices are used as medicine and play a significant role in the development of the national economy. The anti-proliferative, anti-hypercholesterolemic, antidiabetic, and anti-inflammatory properties of spices and their active components play both ameliorative and preventive roles in several diseases such as diabetes, arthritis, cancer, and cardiovascular disorders.^[1,2] Some Indian spices, including turmeric, are utilized for medical purposes which are used to treat injuries, gastrointestinal problems, rheumatic pain, and esthetic purposes. According to a report, turmeric has anti-inflammatory, antioxidant, and cholekinetic properties.^[4] Curcumin was discovered to boost detoxification enzymes, promote deoxyribonucleic acid repair, and prevent mutation and the creation of cancerous cells. It is evidenced that curcumin may prevent programmed cell death.^[2]

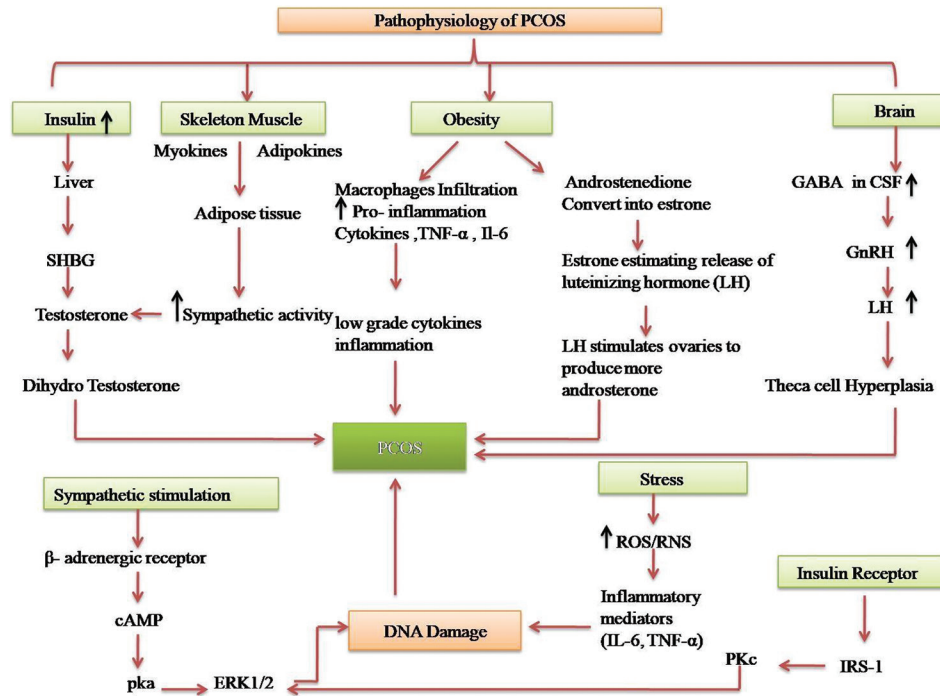


Figure 2: Schematic representation of pathophysiology of the polycystic ovarian syndrome (PCOS). Several factors play a key role in the progression of PCOS which includes insulin level, skeleton muscle, obesity, brain, sympathetic stimulation, stress, and insulin receptors. An increase in insulin level is responsible for damaging the liver which further increases the sex hormone binding globulin protein level that transports the hormones testosterone dihydrotestosterone (DHT), and estradiol in the blood that will lead to develop PCOS. The Skeleton muscle stimulates the sympathetic system which further leads to converting testosterone to DHT which contributes to PCOS pathophysiology. Obesity affects in two ways first is by causing macrophages infiltration that leads to increased pro-inflammation, cytokines, tumor necrosis factor- α , interleukin-6 and causes low-grade cytokines inflammation and second is by androstenedione convert into estrone and then estrone estimating release of luteinizing hormone (LH) and further LH stimulates ovaries to produce more androsterone then after these both processes lead to PCOS. In the brain, GABA increases the level of Cerebrospinal fluid that leads to an increase Gonadotropin releasing hormones which increase the level of LH and contributes to the pathophysiology of PCOS. Sympathetic stimulation and stress lead to an increase in reactive oxygen species/RNS and which intern increases inflammation and deoxyribonucleic acid (DNA) damage that contributes to the progression of PCOS. Insulin receptors stimulation causes DNA damage by activation of the extracellular signal-regulated kinase (ERK1/2) pathway which also may involve in the pathophysiology of PCOS.

It has been reported that spices also have an antimicrobial property that prevents the spoilage of food.^[1] According to the report of the Indian Spice Board, India produces 3.2 million tons of spices. Indian spices have a good reputation in over the world.^[2] Moreover, the cultivation of spices is quite difficult as many factors such as rainfall, soil, cultivation method, altitude, storage, and transport are inevitable in determining the actual role of spices. However, researchers have currently reported on the variant role of spices in the management of PCOS.^[3] They also reported that PCOS patients should intake a protein-rich diet which is generally present in many spices that makes it accessible to the regulation of the menstrual cycle through several

mechanisms such as insulin resistance, lipid profile, and weight.^[4] Some spices are also helpful in hormonal regulation in PCOS patients through decreased androgen levels in the body.^[5] Although studies suggested that a high protein diet is useful for the management of PCOS.^[6] The present study highlighted the therapeutic potential of Indian spices in PCOS.

GARLIC

Garlic (*Allium sativum* Linn) belongs to the family *Alliaceae*.^[7] It is also known as Lahasun,^[8,9] and has a pungent odor due to its oil-soluble organosulfur compounds, such as

allicin, alliin, and ajoene. The main sulfur compound in both raw garlic and garlic powder is alliin^[10] and a key constituent of garlic is allicin, which has therapeutic effects such as antioxidant, and anti-inflammatory. The study revealed that allicin-containing compounds prevent oxidative stress.^[11] Garlic is generally used for various medicinal properties such as anticancer, cardioprotective, antithrombotic, and antioxidant properties.^[12] Raw garlic or powdered garlic is a part of the daily diet as its prolonged use can be beneficial as an antioxidant.^[13] It has the potential to lower the lipid profile and can prevent atherosclerosis.^[14] Due to its antioxidant properties, garlic can inhibit the production of reactive oxygen species such as OH⁻, NO, H₂O₂, O₂⁻ which can cause organelle damage.^[15] Another study also suggested that garlic could reduce total blood cholesterol and triglyceride (TG) while another study contradicted this statement.^[14] The reason behind contraindication could be the different dosage of garlic, duration of the test, and characteristics of an enrolled subject. It also possesses an anti-inflammatory effect which may provide relief in PCOS.^[16] Studies clarified that the risk ratio of PCOS is high in adult women who are suffering from DM-2 at their reproductive age as compared to normal women.^[17] Hence, as it is reported that garlic cures diabetes mellitus; hence, it could be the better therapeutic approach against PCOS in diabetic women as well.

GINGER

Ginger (*Zingiber officinale*) belongs to the family *Zingiberaceae*.^[7] However, ginger is well known for its flavoring and pharmacological properties (carminative, anti-seizures, and anti-inflammatory), apart from this, it is also used for the management of rheumatoid arthritis.^[7] Gingerol and Shogaols are the active compounds of ginger which are responsible for its antioxidant properties.^[8] It is reported that ginger also has an important role in the management of an altered menstrual cycle and can inhibit the unwanted growth of ovarian cells.^[9,10] However, studies also suggested that the regular conception of ginger can prevent anti-fertility activity and increase the fertility index and level of serum testosterone.^[11] Moreover, it is a safe spice used as natural medicine, especially in pregnant women for ease of nausea and vomiting.^[12] Moreover, it has an antiemetic, antipyretic, anti-ulcer, antioxidant, and anxiolytic activities.^[13] Ginger's pharmacological properties differentiate from Non-steroidal anti-inflammatory drugs (NSAIDs) as it suppresses the synthesis of prostaglandin through the inhibition of Cyclooxygenase (COX)-1 and COX-2^[14] [Figure 3].

It has also been reported to have anti-clotting, and analgesic property.^[15] Regular consumption of ginger does not affect blood glucose level, but it can alter the serum TG, total cholesterol (TC), increased insulin level, and prevent the loss of body and kidney weight in DM-2-associated animals.^[16]

Another study suggests that ginger is also effective in the improvement of the endocrine functions.^[17,18]

CINNAMON

Cinnamon (*Cinnamomum zeylanicum*) also known as Dalchini is a commonly used spice for many years; it belongs to family *Lauraceae*.^[19] The study revealed that cinnamon having insulin-sensitizing effects in animals as well as in humans.^[20] The flavonoids and polyphenols isolated from cinnamon have free-radical-scavenging activity.^[21] These compounds have also been reported to inhibit 5-lipoxygenase in a dose-dependent manner which results in decreased oxidative stress.^[22] Its anti-hyperlipidemic activity has been reported along with its antioxidant property. Moreover, several studies demonstrated that the consumption of an aqueous extract of cinnamon improves the level of antioxidant enzymes.^[23] In addition, cinnamon is also known to decrease the TC and TG levels in a diabetic patient.^[24] *In vitro* study revealed that cinnamon showed anti-inflammatory responses through the inhibition of NO, COX-2, and decrease the production of prostaglandin E2^[25] [Figure 3].

It has been found that cinnamon could be utilized as insulin-sensitizing agents for the management of PCOS. Oral administration of cinnamon helps to tolerate and improved insulin sensitivity in non-diabetic women associated with PCOS.^[26] According to a survey, the level of insulin in women with average body weight is 65% which elevates up to 95% in obese women.^[27] Insulin resistance or hyperandrogenism in women having PCOS has been implicated in the abnormal function of a hypothalamic-pituitary-ovary axis, which leads to menstrual irregularity and ovulation.^[28]

Although it is evidenced, cinnamon has favorable effects against oxidative stress and lipid profile in several diseases.^[23] However, the pharmacological properties of cinnamon against serum antioxidant levels and the lipid profile in PCOS-associated women have not been studied yet.

FENNEL

Fennel (*Foeniculum vulgare*) also referred to as Saunf is a famous aromatic plant that lies under the family *Apiaceae*,^[29] which has been used for the past years as traditional medicine and as a spice, having a fragrant odor and a pleasant aromatic taste.^[30] It is reported to have antioxidant, anti-inflammatory, analgesic, and diuretic properties.^[31] The fennel seeds are used to promote menstruation and decrease the symptoms of female climacteric and enhancement of libido.^[32] The fennel seeds can be used for the management of PCOS. The fennel is rich in phytoestrogen which helps to decrease insulin resistance and results in a reduction of PCOS-associated inflammation.^[33] Similarly, it acts as an estrogen, which aids in the treatment of PCOS.^[30] It can also

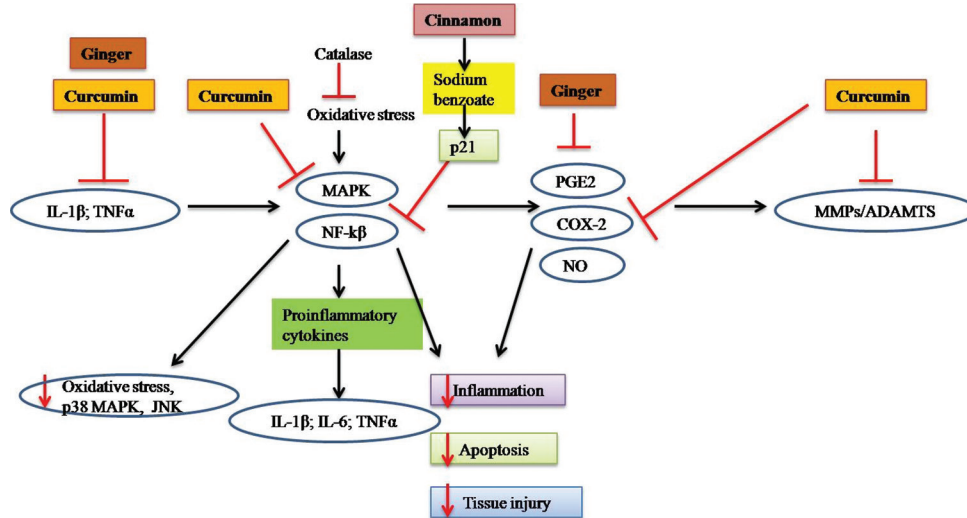


Figure 3: Anti-inflammatory and antioxidant mechanism of various spices is shown in the figure. The effect is shown by inhibiting several inflammatory cytokines, inflammatory mediators such as interleukins, cyclo-oxygenase, prostaglandin, and oxidative stress thereby, inhibiting polycystic ovarian syndrome-mediated inflammation and stress.

enhance the milk flow, libido, and help to relieve menopausal symptoms in PCOS patients.^[34] The cellular imbalance is markedly reduced with the phytoestrogen. Hence, it may be beneficial in the management of PCOS-associated metabolic disturbances.^[33] Nowadays, different parts of the plants are used in the management of several complications such as vomiting, nausea, kidney stone, bronchitis, diabetes, and chronic cough.^[33]

NUTMEG

Nutmeg (*Myristica fragrans*) is also known as Jaiphal and it belongs to the family *Myristicaceae*.^[29] Its external cortex is also known as mace, which is having variants of flavonoids, phytoestrogen, and minerals.^[30] Nutmeg has aphrodisiac effects as well as antifungal, antibacterial, hepatoprotective, anti-inflammatory, and immunomodulation activities.^[31] The study clarified that the levels of magnesium and calcium in the blood reduced at the time of stimulation of ovulation and downregulation of estrogen levels in infertile women.^[32]

TURMERIC

Scientifically, turmeric is known as *Curcuma longa* belonging to the family *Zingiberaceae*.^[33] The principal constituent of turmeric is curcumin which gives the yellow color to turmeric and is responsible to modulate several signaling pathways.^[34] Turmeric is a water-soluble spice having a low molecular weight that has been used for many years as a flavonoid and coloring agent, it has also been used as Indian herbal medicine.^[35] Curcumin has various biological activities such as anti-inflammatory, antioxidant, hypoglycemic, and

antihyperlipidemic activity.^[36] It is reported that curcumin selectively inhibits COX-2, lipoxygenase, and inducible nitric oxide synthase (iNOS) due to its anti-inflammatory property. The disrupted regulation of COX-2, lipoxygenase (LOX), and iNOS can lead to developing PCOS and associated symptoms.^[37]

Mohammadi *et al.* reported the dual effects of curcumin as an anti-inflammatory and antioxidant in PCOS possibly due to its inhibition activity of tumor necrosis factor- α , interleukin-6, and C-reactive protein levels^[38] [Figure 3]. PCOS is common in endocrinopathies in 5–8% of premenopausal women, which is characterized by hyperandrogenism and ovulation dysfunction.^[38] The pathophysiological aspect of PCOS seems to involve insulin resistance.^[39] Curcumin possesses an antioxidant property that can be determined using superoxide dismutase and catalase.^[40]

CORIANDER

Scientifically, coriander is known as *Coriandrum sativum* also referred to as Dhania, it belongs to the family *Umbelliferae*.^[41] It is reported to have several therapeutic effects against burning sensations, flatulence, indigestion, headache, colic pain, pyrexia, indigestion, and thirst.^[42] The active chemical constituent of coriander is linalool (coriandrol 60–70%) and also includes borneol, p-cymene, α -pinene, camphor, geraniol, limonene, and coumarins.^[43] Due to the presence of active components, that is, echinulin, and aristictin B, coriander tends to have, antioxidant, antihyperlipidemic, and antihyperglycemic properties.^[43] Coriander also has antioxidant constituents such as flavonoids, terpenes, catechins, and polyphenolic

compounds that inhibit the increased oxidation in the body.^[44] The study suggested that coriander has anti-diabetic properties thus, it can inhibit the complication that arises due to PCOS.^[45] Quercetin which is obtained from coriander, has free radical scavenging, anti-inflammatory, anticancer, antihyperlipidemic, and antiplatelet activity. However, it also regulates steroidogenic activity which further modulates ovarian function, helping in correcting hormonal indices.^[46,47] Quercetin was found to have inhibitory activity of phosphatidylinositol 3-kinase (PI3K). Thus, quercetin is found to act on PI3K and tends to produce beneficial effects in women with PCOS.^[48] Another study demonstrated the efficient role of quercetin in inhibiting PI3K in ovarian theca cells which further leads to decreased androgen production through the down-regulation of Cytochrome P enzyme gene expression.^[49]

CARDAMOM

The biological name of cardamom is *Elettaria cardamomum* (L.) Maton it is also known as Elaichi and belongs to the family *Zingiberaceae*.^[50] It can be found in India (Tamil Nadu, Karnataka, and Kerala). Each pod of cardamom contains 15–20 brownish-black colored seeds. Cardamom seeds are used since ancient times for the treatment of vomiting, excessive thirst, burning sensation, pyrexia, and weakness because of their refreshing properties. The active chemical constituents present in cardamom are cineol, terpineol, terpene, and volatile oil which show anti-inflammatory, carminative, antipyretic, and aromatic properties.^[51]

SPEARMINT

Various plant species are well utilized in the treatment of fertility-related diseases. The spearmint (*Mentha spicata*) is one of them belongs to the family *Lamiaceae*.^[41] *Mentha piperita* is another species of the genus *Mentha* that has anti-inflammatory, antibacterial,^[42] and antifungal activity.^[43] Several studies demonstrated that spearmint has antioxidant properties as well as antiandrogenic properties in females.^[44-46] The previous study revealed that spearmint has a protective effect against PCOS.^[46] Spearmint is also used for its non-pharmacological benefits.^[44] The Study suggested that spearmint has been found to decrease the level of free testosterone and increase the level of FSH, LH, and estradiol.^[47]

The study demonstrated that spearmint leaves can be used in the treatment of PCOS-associated mild hirsutism women. It decreases the level of free testosterone in the blood due to its anti-androgenic properties while there was no decrease seen in overall testosterone level.^[48] The study explored that spearmint can reduce body weight and also reduce the production of androgen. The study revealed that spearmint

can also reduce DM-2-associated symptoms, level of cholesterol, and oxidative stress.^[44,46]

CONCLUSION

Nowadays, PCOS has become one of the greatest concerns in women's life which greatly affects their health and fertility. It may cause several health complications such as mood disorders, irregular menstruation, obesity, and cardiovascular diseases. Several factors may contribute to the pathogenesis of PCOS such as insulin resistance, obesity, and sympathetic stimulation. Several studies evidenced that several Indian spices including *E. cardamomum*, *M. spicata*, *C. longa*, *M. fragrans*, *F. vulgare*, *C. zeylanicum*, *Z. officinale*, and *A. sativum* Linn play a crucial role in the management of PCOS and associated symptoms. It is suggested that PCOS patient should consume a high protein diet that is present in most of the spices. However, it is also suggested that spices may decrease insulin resistance, regulate the menstrual cycle, improves lipid profile, and also decrease the weight in PCOS patients. This review highlighted the therapeutic potential of Indian spices for the management of PCOS.

Availability of data and materials

Data have been collected from Google scholar, PubMed, Europe PMC, and Sci-Hub.

Declaration of patient consent

Patient consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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