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LEAD IDENTIFICATION FOR TREATMENT OF PCOS-A COMPREHENSIVE REVIEW ON CHROMONE ANALOGUES

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ABSTRACT

Polycystic ovarian syndrome (PCOS) affects about one in ten women globally, making it one of the most prevalent endocrine disorders. Its symptoms, such as insulin resistance, hirsutism, hyperandrogenism, and weight gain, vary widely among patients. Despite the variety of treatments available, including lifestyle changes, medications like insulin sensitizers, and surgeries, there is no definitive cure for PCOS. Treatments like ovarian drilling and cosmetic interventions may alleviate specific symptoms but fail to address the root causes.

Additionally, psychological, and occupational stress, coupled with infertility, worsens the condition for many women. This complexity has prompted the exploration of new therapeutic options. Recent attention has turned to coumarins, natural compounds with potential benefits in managing PCOS due to their anti-inflammatory, anti-androgenic, and insulin-sensitizing properties. These properties suggest that coumarins, when combined with existing treatments, could offer more holistic management of PCOS.

Future therapeutic strategies may also involve polyherbal formulations, which could lower costs, reduce side effects, and improve overall treatment outcomes by targeting multiple facets of PCOS. The inclusion of coumarins as a natural, widely available resource highlights the potential for developing novel treatments that integrate traditional herbal medicine with modern medical approaches

KEYWORDS: PCOS, Hyperandrogenaemia, Insulin, Herbal, Nutraceuticals, Coumarin

INTRODUCTION

PCOS is also termed as Stein-Leventhal Syndrome. The actual prevalence of PCOS is unclear, although it varies greatly over the world from 2.2 to 26%. As per Rotterdam's criteria, it has been studied that South India and Maharashtra has prevalence reported as 9.13 and 22.5 %. PCOS has a prelude with noticeable anomalies that existing as the metabolic syndrome like obesity, dyslipidaemia associated with decrease in high density lipoprotein cholesterol and hypertriglyceridemia, high blood pressure, atherosclerosis, gestational diabetes, increased risk of development of type II diabetes, respiratory tract infection with cough and cardiovascular diseases for prolong time. [1] As per the researchers, PCOS largely affects the females of age group of 18-44 years. [4] There are mild to severe variations for each symptom. Hyperandrogenism, a biochemical hallmark for PCOS, is the excessive level of androgens marked in female mainly responsible for PCOS include cutaneous indicators such as male pattern baldness, alopecia and hirsutism which results from disturbances in GnRH pulses that give rise to increased level of LH/FSH ratio. [5][6]

The enhanced testosterone effect is a result of both the overproduction of testosterone and the decreased sex hormone binding globulin (SHBG) levels seen in PCOS, both of which are brought on by excessive insulin. Unusually irregular amount of testosterone hormone in the ovaries block ovulation which leads to infertility. According to the literature, eating high-calorie foods like milk, fruits, and starchy foods during menstruation causes vayu to build up in the uterine cavity. This causes the organ's blood flow to be limited, which in turn causes obesity, abdominal pain, and ultimately conception failure. [2] [3] Aromatase enzyme converts androgen to estrogen so this may be responsible for the syndrome to occur as low aromatase activity has also been demonstrated in women with PCOS. To maintain optimal insulin levels, a low glycemic index diet (GI) is advised, consisting of lentils, fruits, raw pineapple, carrots, cherries, cereals, and whole grain wheat. A fried, spicy, oily, processed, and junk food are to be avoided. [28] Table 1 enlists the common symptoms associated with PCOS.

EPIDEMIOLOGY OF PCOS:

Ethnic prediction and hereditary are one of the factors. The pituitary gland secretes irregularly high amount of Luteinizing hormone in the blood stream interrupting the normal menstruation cycle of a woman ultimately creating imbalance between progesterone, estrogen, FSH and LH leads to PCOS causing anovulation. [9] Cyst or fluid filled sacs is nothing but an undeveloped follicle which remains in undissolved state as illustrated in Figure 1. Hyperandrogenaemia cannot be diagnosed by measuring the blood testosterone levels. [10],[14],[15]

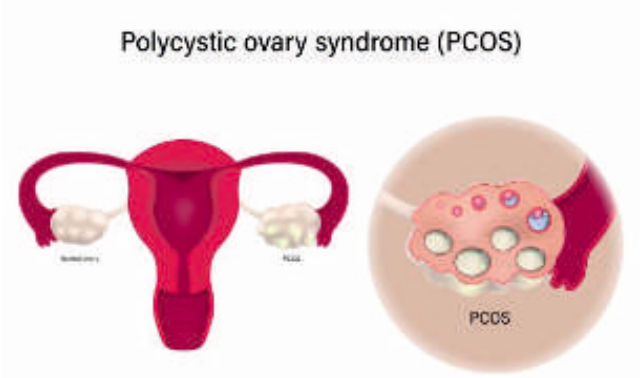

Figure 1: Schematic explanation of polycystic ovarian syndrome [11]

Table 1: Common symptoms of PCOS [14]

Period Problems	Irregular Periods, Period Cramps, Spotting in between Periods, Heavy Bleeding, Scanty Menstrual Flow
Poor Fat Profile	High Cholesterol, High Triglycerides, Fatty Liver
Poor Mental Health	Depression, High stress, Anxiety, Mood swings, Irritability
Hair Health	Hair loss or Alopecia, Hirsutism: Excessive hair on the face, arms, neck
Sleep Problems	Inability to sleep, Waking up in the middle of the sleep, Sleep Apnoea
Skin Problems	Cystic Acne, Dark spots on the skin, Skin Tags, Canker sores, Bleeding gums
Cysts and Lumps	Ovarian cysts, Benign cysts in breast or other body parts, Follicular cysts
Digestive Health	Bloating and Constipation, Uncontrolled hunger, Sugar cravings, Food cravings
Difficulty to get Pregnant	Frequent miscarriage, Inability to conceive, Infertility, Low sexual drive
Weight Problems	Digestive Health

Excess of androgen leads to acne which are very difficult to treat, hirsutism and androgenic alopecia/ baldness. [7] Figure 2 depicts the signs and symptoms associated with PCOS. Long term risk associated with PCOS are Diabetes, Hypertension, Heart disease, Dyslipidemia, Endometrial cancer, Breast cancer and recurrent pregnancy loss. [8] Reduced Melatonin concentration in the follicles and mild sleep disturbances have been found among PCOS women.

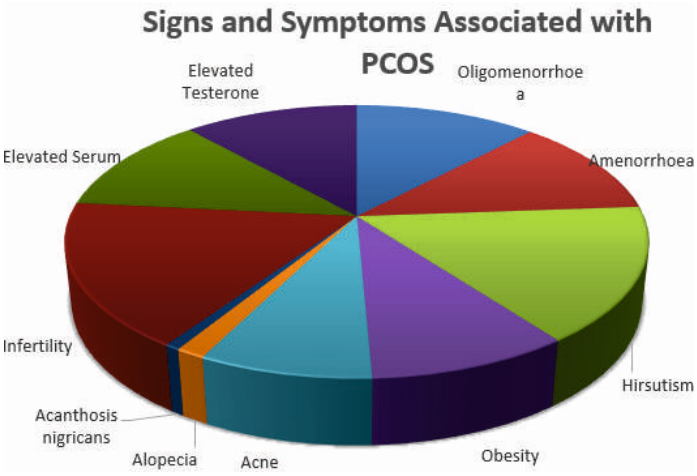

Figure 2: Signs and Symptoms associated with PCOS

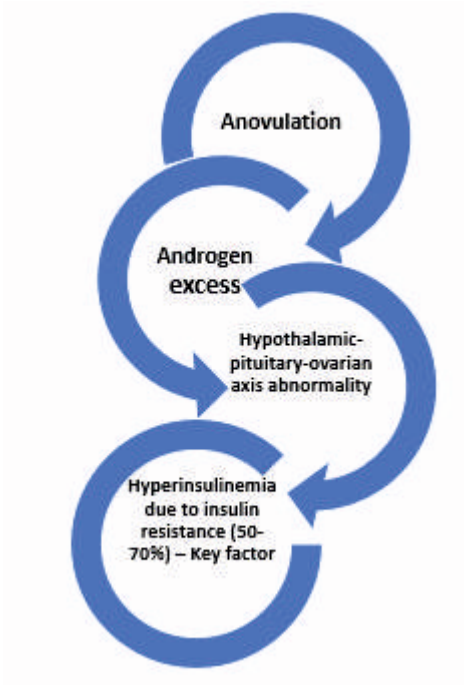

Figure 3: Factors responsible for PCOS

Allopathic: The Allopathic remedies available for PCOS are enlisted in Table 2. Surgical methods like Laparoscopic ovarian drilling by Laser, Cyst Aspiration and Oophorectomy also available as one of the treatment methods. [6]

Table 2: Treatment Available for PCOS [38]:

MOA	Drugs
A specific gonadotropin-releasing-hormone agonist	Nafarelin
Insulin sensitizing and ovulation improving agent	Troglitazone
Non-steroidal selective estrogen receptor modulator, ovulation improving agent	Tamoxifen
Partially selective estrogen receptor modulator	Clomiphen citrate
Inhibits hepatic gluconeogenesis, decreases serum lipids and androgen	Metformin
Blocks androgen receptor and prevent testosterone from binding and exerting hirsutism	Spironolactone
Blocks Estrogen receptor by inhibiting negative estrogen feedback	Estrogen
Inhibits GnRH and decreases the LH secretion	Progestins
Hirsutism treatment	Eflornithine

The GnRH agonist like Nafarelin is typically used in severe cases where other treatments fail. Its prolonged use reduces ovarian hormone production, addressing both menstrual irregularities and hyperandrogenism, although it is often a second-line treatment due to side effects like menopausal symptoms. An insulin sensitizer (Troglitazone) that addresses the underlying insulin resistance in PCOS. However, glitazone derivatives have been withdrawn in many countries due to concerns over liver toxicity. Alternatives like metformin are now more commonly used. Tamoxifen and Clomiphene Citrate induce ovulation in women with PCOS, especially those seeking fertility treatments. Clomiphene is more commonly used than tamoxifen, but tamoxifen can be an alternative for clomiphene-resistant cases. For managing hirsutism and acne in women with PCOS Spironolactone is used to provides symptomatic relief However its anti-androgenic effects are cause for concern. Another alternative is Eflornithine used topically and / or systemically. Though it reduces hair growth but does not affect the underlying hormonal

imbalance Often used in hormonal therapies progestin and estrogen regulates the menstrual cycle, preventing endometrial hyperplasia in PCOS patients. Such combination of progestins and estrogen is prescribed for long-term management.

Herbal: Natural alternatives available for treatment of PCOS are adequate intake of Calcium, Vitamin D, and Magnesium (low levels of Mg associated with Diabetes). It also includes increased intake of Chromium & Turmeric (essential for insulin and blood glucose level), omega-3 supplements (decreases Androgen level in women with PCOS), rich fibre diet, anti-inflammatory foods like olive oil, tree nuts, tomatoes, leafy green vegetables, fatty fish like Mackerel and Tuna, totally cut off the coffee as it causes changes in estrogen level.[39],[40],[41] Auraptene is a natural bioactive monoterpene coumarin isolated from Citrus aurantium and Aegle marmelos (family Rutaceae) has clinically proven acting via anti-inflammatory effect as the inflammatory mediators like TNF α increases in PCOS patients and eventually induces apoptosis in antral follicles granulosa cells. [29], [30] Vitamin B12 and Vitamin B9 are mostly prescribed as the level of homocysteine has been found increased in the blood eventually causing damage to the lining of arteries, increases formation of blood clots in blood vessels and high chances of blockage of blood vessel.[12] Vitamin B12 and Vitamin B9 (folate) helps to lower the inflammation by breaking down amino acid homocysteine level in the blood. Vitamin C and Vitamin E are also prescribed to protect the blood from clotting.[13] Poppy seeds one of the home remedies contains Magnesium, Calcium, Vitamin D, Zinc provides nutrition and acts as anti-inflammatory.[16] Mohammed Azeemuddin et al reported in the study that a multiherbal preparation "DXB-2030" formulation consisting of Trigonella foenum-graecum, Aloe vera, Sphaeranthus indicus, Nardostachys jatamansi, and Symplocos racemosa extracts was found to be successful in managing PCOS and can be suggested as a line of treatment.[67] Eating healthy, balanced diet rich with green vegetables, getting good sleep, and keeping oneself away from stress is recommended as a best effective medicine by Gynaecologist. The hepatic synthesis of the sex hormone binding globulin is decreased by hyperinsulinemia, which increases the levels of circulating androgens. Insulin resistance affects both adipose tissue and skeletal muscle. The hepatic synthesis of the sex hormone binding globulin is decreased by hyperinsulinemia, which increases the levels of circulating androgens. Insulin resistance affects both adipose tissue and skeletal muscle. [17]

As per Ayurvedic literature, similar kind of features are observed in Pushpadhni jataharini (disease like polycystic ovarian syndrome with hyperandrogenism and irregularity in menstrual cycle) and Nashtartva (improper growth of follicles and frequent anovulatory cycle). It encompasses the inequality ratios of dosha, dhatu and upadhatu. [18]

NUTRACEUTICALS AVAILABLE FOR TREATING PCOS:

Allopathic treatment, despite of causing severe side effects, is used majorly in the society for women suffering from PCOS. To overcome these problems, many Research Scientists from the industry are working on nutraceuticals and recently some nutraceuticals are available in the market as a symptomatic treatment. A Nutraceutical powder formulation launched by Unived industry containing D-chiro Inositol (DCI) and Myoinositol with the composition of 1:40. Myoinositol is a natural source obtained from carob seeds responsible for reducing Insulin resistance. D-chiro Inositol can be synthesized from Myoinositol. Vegan capsules/powder as a nutraceutical contains D-chiro Inositol: Myoinositol in the range of 1:40, key supportive nutrients like alpha lipoic acid for obesity, chromium picolinate to reduce glucose level, Vitamin D3, folates for cellular metabolism, natural calcium from algae to increase the bone density. [31] Higher DCI concentration is used to compensate epimerase inactivity. Epimerase is the enzyme responsible for properly release of insulin

after signalling. For the fertility treatment, regularization of menstrual cycle and healthy ovarian functioning D-chiro Inositol (Caronositol): Myoinositol capsules in the ratio of 1:3.6 can be used as its clinically tested, proven, and has shown 65.52% fertility success rate in the clinical trials. A nutraceutical named Lipifuse contains L-Carnitine Tartrate, Alpha Cyclodextrin, Phaseolus vulgaris extract, Coffee bean extract tablets under its brand name. [32]

COUMARIN

Plant origin of Coumarin [23][21]: Scientist Vogel (1820) separated coumarin first from tonka beans (Dipteryx odorata) using extraction technique. Then subsequently it was identified in many plants belonging to different families such as Apiaceae, Caprifoliaceae, Clusiaceae, Guttiferae, Nyctaginaceae, Oleaceae, Rutaceae and Umbelliferae.

Table 3: List of Plants Containing Coumarin

Botanical Name	Plant	Family
Coumarouna odorata	tonka bean	*Leguminosae*
Anthoxanthum odoratum	Vanilla grass	*Poaceae*
Melilotus alba and Melilotus officinalis	sweet clover	*Fabaceae*
Glycyrrhiza glabra	liquorice	*Fabaceae*
Cinnamomum cassia	cassia cinnamon	*Lauraceae*
Asperula odorata	sweet woodruff	*Rubiaceae*
Myroxylon pereirae	balsam of Peru	*Fabaceae*
Justicia pectoralis	chamba	*Acanthaceae*
Prunus serrulata	cherry blossom	*Rosaceae*

Coumarin was found to be present in majorly in certain herbs particularly Thuja occidentalis, Tephrosia purpurea, Camellia sinensis, Labisia pumila, Nardostachys jatamansi, Tribulus terristris, Symplocos racemosa, Aloe barbadensis, Commiphora mukul, Mentha piperita, Corylus avellana, Commiphora wightii, Cimicifuga racemosa, Cinnamomum cassia, Curcuma longa, Glycyrrhiza spp., Matricaria chamomilla, Paeonia lactiflora, Silybum marianum, and Vitex agnus-castus [9], [19], [20] Coumarin is from plant origin and oils are rich source of coumarins like cinnamon bark oil (0.1-1.6% or 7000 ppm (mg/kg)), cassia leaf oil (0.03-0.08% or 17000-87300 ppm), peppermint oil (20 ppm), cinnamon leaf oil (40600 ppm), also found in lavender oil, sweet clover oil, woodruff, whereas Australian cassia recorded 15.3% of coumarin. [22] Approximately 1200 coumarin has been recognized from different plant origins till date. According to the studies conducted in Pakistan on fresh mature seeds of Ferula foetida indicates mixture of coumarins approximately 7.5-7.8%. It has a very good skin penetration ability. [23]

To establish the relationship between these herbal components and anti-PCOS action, a literature survey led to very less yet convincing data pertaining to utility of coumarin. A preliminary study on rat models' liquorice had been found to alleviate the symptoms of PCOS hinting connection with regulation of imbalanced hormonal levels. [24]

Utility of Cinnamon powder had been proved to be effective in PCOS through Clinical trials. [25] Among other related compounds, Auraptene had been found to be effective in improvement of oocyte maturation and fertilization rate in PCOS Mouse Model. [26]

Synthesis of Coumarin:

Coumarin is widely distributed in plant kingdom, so extraction techniques can be used to obtain coumarins; but for commercial use it has been mostly synthesized in the laboratory. Various methods can be used to synthesize coumarins like from (Phenol) Pechmann reaction- green synthesis, (Salicylaldehyde) Knovengel condensation (Salicylaldehyde) Perkin reaction, (O-hydroxyaryl ketones) Kostanecki acylation, (Phenol) Pschorr synthesis, Reformatsky, Wittig reaction. By using different means several numbers of coumarins can be synthesized. [27] Coumarin possesses immunomodulatory, antitumour, antifungal, antiviral, antibacterial, antitubercular, anticoagulant, anti-inflammatory, anticonvulsant, antiadipogenic, antihyperglycemic, antioxidant, antioedematous, anti-HIV and neuroprotective activity. [23]

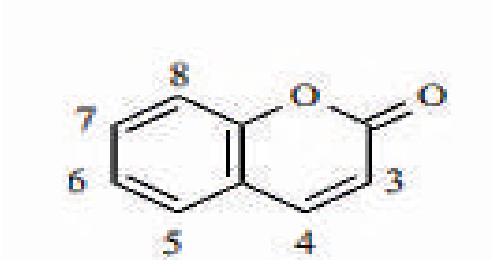

Figure 4: Structure of Coumarin

Challenges and Opportunities while treating PCOS-

Although coumarins may be manufactured in a wet lab using a number of synthetic processes, there are certain challenges in using coumarins as ligands to treat PCOS.

a) The research does not yet show evidence of target-specific treatment. The illness is managed by keeping an eye on the symptoms and the ovarian structure.

b) No biological testing is mentioned in the literature for synthetic chromone counterparts. Chromone extraction and activity have been documented in the literature. The development of appropriate animal models has emerged as an important area of research to better understand the genesis and association of metabolic factors to the outcome of chronic disease in PCOS

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c) Computer simulations: Chromones are not investigated in computer simulations for managing PCOS. No information was discovered in the older records.

d) No reports have been discovered about the use of synthetic analogues to treat PCOS.

Certain herbs can be used to screen for PCOS are classified as follows in Table 4

In PCOS, uncharacteristically high amount of Luteinizing hormone was released by the pituitary gland in blood stream which eventually upsets the normal menstruation cycle of a patient. Consequently, it affects the maturity of the follicle and subsequently ovulation which leads to anovulation. The undissolved immature follicle remains as fluid filled sacs or cysts. These cysts bring about a hormonal imbalance due to an increased amount of testosterone. The outcome is production of acne in facial and body hair. Table 2 illustrates the list of various herbs to be used with their appropriate body parts containing coumarin for the management of PCOS.

Literature survey of various related studies of coumarins acting as anti-PCOS agent reveals some possibilities of mechanism of actions. Coumarins could act as insulin sensitizers, like metformin or thiazolidinediones (e.g., troglitazone). Several studies have shown that coumarins improve insulin sensitivity by modulating glucose uptake, enhancing insulin signaling pathways, and reducing insulin resistance, which is central to the pathology of PCOS. Studies on certain coumarin derivatives, such as esculetin and umbelliferone, have demonstrated their ability to lower blood glucose levels and improve insulin sensitivity in diabetic animal models. [33]

PCOS is associated with chronic low-grade inflammation and oxidative stress, both of which contribute to insulin resistance and hyperandrogenism. Coumarins have well-documented anti-inflammatory and antioxidant effects, which could mitigate these underlying issues in PCOS. Coumarins like scopoletin and 7-hydroxycoumarin may inhibit the nuclear factor-kappa B (NF-κB) pathway, reducing the production of pro-inflammatory cytokines like TNF-α, IL-6, and IL-1β, which are elevated in PCOS. Furthermore, they could upregulate antioxidant enzymes such as superoxide dismutase (SOD) and catalase, neutralizing reactive oxygen species (ROS). [34] Coumarins could potentially act as anti-androgenic agents, modulating the synthesis and action of androgens. This could be particularly relevant for women with PCOS, as hyperandrogenism leads to symptoms like hirsutism, acne, and anovulation. Although direct evidence of coumarins' effect on

androgen synthesis in PCOS is limited, compounds such as coumarin derivatives from Angelica sinensis have been shown to reduce testosterone levels in animal models, providing a basis for further exploration. In this connection there is a report of coumarin analogue with new aromatase inhibitors will be worth mentioning. [35]

There is a possibility that coumarins may help regulate ovarian function by restoring hormonal balance, particularly the levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). In fact, Coumarin based selective estrogen receptor modulators (SERMs) and coumarin-estrogen conjugates have also been described as potential anti-breast cancer agents, advocating this prospect. [36]

Coumarins may have a role in modulating lipid metabolism and providing cardiovascular protection. Coumarins such as esculin may inhibit lipid peroxidation, improve cholesterol metabolism, and reduce serum triglyceride and LDL cholesterol levels, which are often elevated in women with PCOS. [37]

The coumarins have been known to have a vast number of pharmacological effects and reach to systemic circulation. Hence, possibility that it is acting on many systematic targets including the hormonal sites, CNS sites and offshore sites cannot be negated. In future more would be explored about the targets in PCOS and hence design of coumarin analogues or testing of known analogues on them will be possible through all computational, in-vitro and in-vivo models.

Among many challenges to treatment of PCOS by herbal components is one misconception of complete safety of herbal products, especially in Indian subcontinent. With the complex nature of disease it can be speculated that it will involve long-term treatments, hence long-term safety of herbal treatments for PCOS, particularly when combined with conventional medications, would be a cause of concern. Herbal compounds can interact with conventional medications used to treat PCOS, such as metformin, clomiphene, or spironolactone. These interactions may either enhance or inhibit the effects of these drugs, leading to adverse reactions. For example, Angelica sinensis (Dong Quai) has coumarin derivatives, which have mild anticoagulant effects. When combined with medications like spironolactone, it may increase the risk of bleeding. The coumarins are known to have inducer abilities to cytochrome P450 system, potentially reducing effectiveness of co-administered drugs. Another hiccup with Herbal remedies is lack of standardization, which may lead to inconsistent dosages. Third cause of concern will be side effects like liver toxicity or exacerbate hypertension if used long-term or in high doses. For example, berberine, while helpful for insulin resistance, may lead to gastrointestinal upset and affect liver enzyme levels when used chronically. Hence it implies that long-term clinical trials to assess their safety in treating chronic conditions like PCOS will be required which is unavailable as of now. Also, Regulatory Oversight over herbal remedies can result in contamination, poor-quality ingredients, or variations in active compounds, leading to unpredictable outcomes when used with PCOS medications. If consultation, standardization, and ADR monitoring is observed a safer usage can be ensured.

CONCLUSION:

PCOS, being a multifactorial disorder, number of symptoms at a time in the patients. Patients with PCOS experience undergoing repeated fertility treatments like IVF, IUI with poor pregnancy outcomes. Not all PCOS symptoms can be managed with birth control pills. Many women have discovered natural remedies for PCOS and other restorative concerns, which have improved their long-term health. Despite being a condition, evidence suggests that reducing inflammatory reactions and apoptosis rates in PCOS ovaries can improve the oocytes' capacity for IVF and in vitro maturation. Despite being a condition, evidence suggests that reducing inflammatory reactions and

apoptosis rates in PCOS ovaries can improve the oocytes' capacity for IVF and in vitro maturation. This study focuses on several herbs that can be used to treat PCOS depending on the symptoms. Coumarin is widely utilized in the global market and is of natural origin. Table 1 lists the number of herbs utilized for the symptomatic and centrally acting therapy of PCOS. Future research can be planned by executing biological activities on animal models and determining the mode of action for centrally and peripherally acting coumarins. Given the opportunities and challenges, there should be plenty of potential for pharmaceutical discovery and development.

NA1:D12ame of the Herb	Botanical name	Parts used	Pharmacological activities
Centrally acting			
Ashwagandha	*Withania somnifera*	Leaves	Stress levels are minimised by balancing Cortisol levels [42]
Maca Plant	*Lepidium meyenii*	Roots	Hormonal balance and in Depression [43]
Liquorice	*Glycyrrhiza glabra*	Roots	Antiandrogenic and reduces blood glucose level [44], [76]
Cinnamon	*Cassia cinnamon*	Bark	Reduce Insulin resistance, help to regulate menstruation [45], [77]
Fenugreek	Trigonella foenum	Seeds	Reduce Insulin resistance, Lowers the Cholesterol, reduce the size of ovarian cysts, Regularize the menstrual periods [46], [78]
Shatavari	*Asparagus racemosus*	Leaves, Powder	Regulates Menstrual cycle [56]
Holy Basil	*Ocimum sanctum*	Leaves, Seeds	Antiandrogenic [47], [79]
Black Cohosh	*Actaea racemose*	Roots	Induce ovulation [48]
Peppermint	*Mentha piperita*	Leaves	Antiandrogenic [49], [80]
Maitake Mushroom	*Grifola frondose*	Extract	Induce ovulation and in management of Diabetes [51]
Varuna	*Crataeva nurvala*	Powder	Helps to reduce cyst size, and normalize the menstrual cycle [52]
Flax seeds	*Linum usitatissium*	Seeds	Suppression of Testosterone levels and Hirsutism [53]
Sunflower	*Helianthus annuus*	Seeds	Promote progesterone development [54]
Turmeric	*Curcuma longa*	Powder	Antiandrogenic [53]
Shatapushpa	*Anethum graveolens*	Seeds	Reduce insulin resistance [54]
Chamomile	*Chamomilla recutita*	Flower	Reduces Luteinizing hormone and Improves Ovarian Morphology [55]
Stinging Nettle	*Urtica dioica*	Roots	Reduces level of free Testosterone by increasing production of sex hormone binding globulin [57]
Fennel	*Foeniculum vulgare*	Extract	Reduces Testosterone level, increases the serum levels of FSH and decreased the LH hormones [58]
Pumpkin	*Cucurbita pepo*	Seeds	Manage Cholesterol Level, Anti-androgen, and Treat Hirsutism and prevent hair loss [65]
Peripherally acting			
Guduchi	*Tinospora cordifolia*	Herb	Hypoglycemic [56]
Bael/ Bilva	*Aegle marmelos*	Fruits	Helps in producing more amount of Insulin, provide nourishment to hair, Improves lactation [59]
Sesame	*Sesamum indicum*	Seeds	Regulate blood glucose level [61]
Amla	*Phyllanthus emblica*	Extract	Hormonal balance and Reduces Cholesterol [60]
Red Clover	*Trifolium pratense*	Flower	Purify blood and treat Acne associated with PCOS [62]
Green Tea	*Camellia sinensis*	Extract	Controls Insulin Level [63], [81]
Punarnava	*Boerhaavia diffusa*	Powder	Used to reduce obesity and regulates blood sugar level [64]
Chia	*Salvia hispanica*	Seeds	To inhibit or normalize insulin resistance [66]

Table No.4: List of herbs used in PCOS treatment with their role

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DECLARATION OF INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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