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The role of cinnamon as an antioxidant in treating Polycystic Ovary Syndrome in humans and laboratory animals: A review

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Abstract

Hormonal derangements, abnormal menstrual patterns, and metabolic impairment are the characteristics of polycystic ovary syndrome (PCOS). It is a frequent endocrine disease among both women and certain small animals. PCOS is associated with oxidative stress, obesity, insulin resistance, and hyperandrogenism, all of which contribute to the complex pathogenesis of the syndrome. Due to the complex procedures of traditional treatment for PCOS by using pharmacologic treatment, surgery like bariatric surgery, and lifestyle modifications, scientists have diverted their attention towards alternatives. An easily available spice, cinnamon has been found to have promising findings in preclinical and clinical trials. Cinnamon extracts have been found to decrease blood pressure, increase insulin sensitivity, alter hormone levels, and reduce oxidative stress in small animals. Several mechanisms, including AMPK (AMP-activated protein kinase) activation, modulation of the insulin signaling pathway, and regulation of key transcription factors are responsible for these effects. Supplementation with cinnamon has been determined through clinical trials to assist patients with their weight control, regulation of their menstrual cycle, and improving insulin sensitivity. This review examines the potential therapeutic application of cinnamon in the treatment of PCOS, examining its effects both in humans and laboratory animals. The present analysis captures cinnamon's role as a treatment supplemental agent through the integration of all data on its multiple benefits in treating the various aspects of PCOS. To fully comprehend the action mechanisms and optimize its therapeutic application to PCOS management, further research is required.

1. Introduction

Polycystic ovary syndrome (PCOS) is one of the main problems in the life of humans and small animals, including rodents (Ren et al. 2024). It is characterized as an endocrine disorder, which shows irregular menstrual cycles, ovulatory dysfunction, and high levels of androgen (Novakovic et al. 2024). It is considered one of the most common diseases in young women with prevalence varying between 2.3-26% (Alawdi et al. 2024). Deswal et al. (2020) reported that one in every ten females shows serious symptoms of PCOS. Signs and symptoms include irregular menstrual cycle, mood swings, continuous weight gain, acne, hirsutism, and infertility (Chaudhuri 2023). Research for PCOS entails the utilization of animal models, particularly those that involve rodents and non-human primates (Mallya et al. 2024). Through the employment of other hormones, such as estrogens and androgens, or other therapies, such as dietary restriction or exposure to toxins, it is possible to induce conditions in these models to mimic PCOS (Mishra and Kakadiya 2023). Scientists are able to study the exact roles of hormones and other factors in the onset of PCOS with these changes (Naseri et al. 2024). The duration of these therapies is carefully controlled to mimic the course of the condition. Primates provide more translatable information because they are more physiologically similar to humans, but rats are useful for initial studies (Scott et al. 2024). The Rotterdam principle emphasizes the presence of at least two of the three following conditions for the diagnosis of PCOS in both human and animal models. These three conditions include polycystic ovaries, hyperandrogenism, and oligo-anovulation (Al-Sobayil et al. 2023).

In the bodies of women with PCOS, levels of many hormones change at an abnormal rate. Hormones like insulin, gonadotropin releasing hormone (GnRH), ghrelin, leuitinizing hormone (LH), follicle stimulating hormone (FSH) ratio, androgen, liver expression antimicrobial peptide-2 (LEAP-2), and estrogen are secreted abnormally (Subih et al. 2024;Yang and Chen 2024). Disturbances in the level of the above-mentioned hormones cause metabolic disorders like diabetes, obesity, insulin resistance, irregular menstrual cycle, and infertility in patients (Ali et al. 2022). Many of the hormonal abnormalities observed in PCOS are precisely mimicked in animal models, including rats, mice, and monkeys (Naseri et al. 2024). For example, scientists demonstrated

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that administering testosterone to Wistar rats (Wuyung et al. 2025) for 29 days resulted in an increase in estradiol (Oktanella et al. 2024), a decrease in FSH, and increase in the development of cystic follicles (Puspitasari et al. 2024). In accordance with these findings, an excess of androgen can disrupt the delicate balance between ovarian morphology and reproductive hormones (Wei et al. 2024). Similarly, scientists discovered that prenatal exposure to testosterone and dihydrotestosterone for 70 days in Sprague-Dawley rats yielded elevated FSH, testosterone, and estradiol levels and abnormal corpus luteum formation (Ji et al. 2024). These studies emphasize the utility of studying animal models to dissect the complex hormonal imbalance of PCOS (Ren et al. 2024).

A set of PCOS-related characteristics was reported by Sánchez-Garrido et al. (2024) in a study using an obese New Zealand mouse model. Apart from increased levels of insulin and estradiol and decreased levels of LH and testosterone, the obese mice also developed moderate diabetes (Ryu et al. 2021). The impaired breeding performance that was observed in this animal model was likely due to these endocrine abnormalities (Gurule et al. 2023). Insulin resistance is also a phenomenon that occurs in PCOS (Stener-Victorin et al. 2024). The mechanism is that there is an abnormal rise in serine phosphorylation and a decrease in tyrosine phosphorylation of insulin receptors (Wei et al. 2022). This leads to reduced metabolic activity because these changes disrupt insulin signaling (Rahman et al. 2024). A study shows that even if metabolic signaling is disrupted, mitogenic signaling is continuous in the cells of females with PCOS (Ahmad and Yousuf 2024). This indicates that insulin still takes non-metabolic processes like androgen production in the ovaries (de Melo Cavalcante et al. 2025). The activity of AMP-activated protein kinase is reduced which is necessary for the regulation of energy (Mićić et al. 2022). Lower activity of AMPK compares with increased levels of testosterone and lower levels of adiponectin. This shows a link between excess androgen and energy sensing in PCOS (Chahal and Kabra 2024; Hong et al. 2024; Jin et al. 2024). The mechanism of insulin resistance in PCOS is not too simple to understand. Variability in the mechanism makes it complicated and complex (Wang and Li 2023). Oxidative stress is identified as an affecting reason for PCOS and other infertility-related problems (Khan et al. 2023a; Vale-Fernandes et al. 2024). It occurs when reactive oxygen species (ROS) exceeds antioxidant capacity. Although ROS has a role in reproductive functioning, a disturbance in the redox signaling can lead to lipid peroxidation, protein oxidation, mitochondrial dysfunction, and DNA damage which affect reproductive function negatively (Kodanch et al. 2024).

PCOS treatment requires a multimodal approach according to the individual needs and symptom presentation of each patient (Sunil et al. 2024). One of the essential elements of PCOS treatment is lifestyle modification, including diet modification and exercise (Różańska-Smuszkiewicz et al. 2024). Low-carbohydrate diets can promote weight control and improve insulin sensitivity, two components that are often critical in the minimization of PCOS problems in humans. Regular exercise is important for minimizing obesity and overall metabolic improvement (Merovci et al. 2024). Pharmacological treatment is necessary when lifestyle changes alone do not suffice. GnRH antagonists, the most frequently administered drugs, help regulate hormonal imbalances; oral contraceptives regulate menstrual periods and reduce testosterone levels; and metformin enhances insulin sensitivity (Ee and Tay 2024). Finasteride and Eflornithine are among the drugs that are administered to alleviate certain symptoms, including hirsutism. All these treatments often fail because they are short-changed by side effects and are not effective in treating etiologies.

Alternative treatments are gaining increasing popularity aside from conventional medicine (Dalal et al. 2023; Tan et al. 2024). With its tailored methodology, botanicals have shown potential in symptom relief and restoration of menstrual regularity (El-Dawy et al. 2023; Bagheri et al. 2024; Ryandini et al. 2024). Furthermore, some nanoparticles and plant extracts containing beneficial phytochemicals have proven to be useful in the management of a variety of diseases especially PCOS symptoms (Sai et al. 2024; Ahmad et al. 2023; Maqsood et al. 2023). While there are numerous benefits of these different methods of treatment, it is important to keep individualized care as a top priority (Khan et al. 2023b; Azam et al. 2023). Cinnamon is of potential as an adjuvant treatment based on its potential insulin-sensitizing, anti-inflammatory, and lipid-lowering activities; however, while there exist encouraging preclinical and some clinical evidence, more rigorous investigation is necessary to clarify optimal dose, long-term efficacy and safety, and potential interactions, especially in light of the heterogeneity of response and the necessity of standardized high-quality preparations of cinnamon.

2. Contributing factors of PCOS

There is a multifactorial interaction of environmental, hormonal, and genetic factors that causes PCOS. Key hormonal influences are insulin resistance, hyperandrogenism, and genetic susceptibility (Kurniawati et al. 2024). Environmental factors like obesity, unhealthy diet, and lack of exercise exacerbate the disease (Różańska-Smuszkiewicz et al. 2024). Recent studies are highlighting the role of gut microbiota in this etiology. Stress and chronic inflammation may also disrupt the hormonal equilibrium. Due to hormonal imbalance and weight control-associated problems, PCOS exerts a tremendous burden on the health and well-being of females (Dagenet et al. 2025). Although complexity

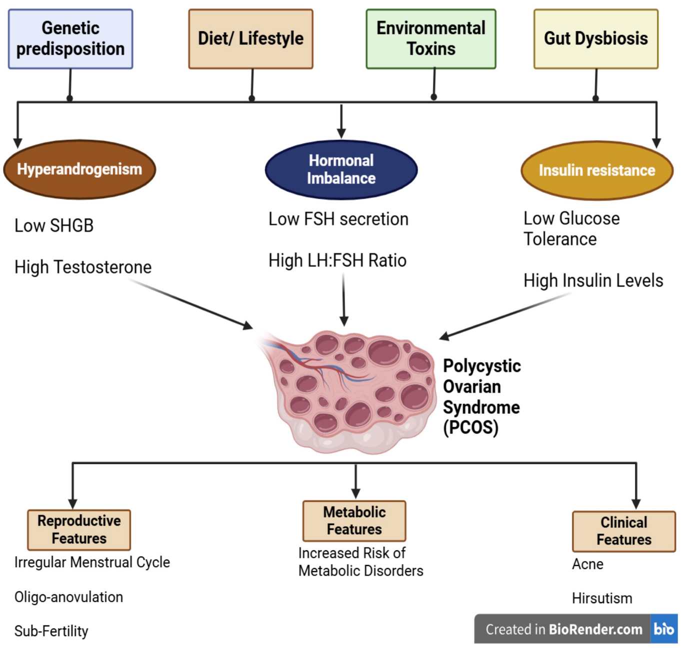

Fig. 1. *Various factors contributing to PCOS and its different features*

exists in long-term consequences, metabolic abnormalities can lead to cardiovascular diseases. PCOS also contributes to increased rates of anxiety and depression that need to be treated at mental health facilities. The necessity of personalized treatment to address the heterogeneity of women with PCOS is well justified by the recognition of the heterogeneity of symptoms. Fig. 1 highlights the overall factors contributing to PCOS and also the outcomes.

3. Role of cinnamon in PCOS management

Cinnamon (*Cinnamomum zeylanicum* and *C. cassia*) is a spice commonly used, valued not only for its distinctive flavor and aroma but also for its potential medicinal properties (Ribeiro-Santos et al. 2017; Suriyagoda et al. 2021). Essential oil obtained from cinnamon contains active constituents such as trans-cinnamaldehyde and cinnamonaldehyde (Lin et al. 2019; Lee et al. 2020; Wang et al. 2020; Meilawati et al. 2023; Patil et al. 2024). Similarly, cinnamon leaves contain plenty of trans-cinnamaldehyde (Weerasekera et al. 2021) while cinnamon bark contains procyanidins, catechins, and antioxidants. Cinnamaldehyde also possesses anti-tyrosinase properties (Ullah and Hassan 2022). Studies reported that the fragrance and spicy taste are due to the presence of cinnamaldehyde (Zeng et al. 2024). Cinnamaldehyde is the compound that gives cinnamon its characteristic flavor and aroma (Kliszcz et al. 2021; Gul et al. 2024). Aside from its use in perfumery, cinnamon possesses significant therapeutic properties, including immunomodulatory, anticancer, antibacterial (Caserta et al. 2023), anti-inflammatory, and antioxidant activities (Mohapatra et al. 2020). It is appropriate for controlling type 2 diabetes (Musaddaq et al. 2024), one of the prevalent comorbidities of PCOS, because it also serves to reduce blood cholesterol levels (Pulungan and Pane 2020) and appears to replicate the action of insulin (Santoso et al. 2024), stimulating glucose metabolism (Silva et al. 2022) and perhaps reducing blood glucose levels (Suriyagoda et al. 2021; Hossain et al. 2022). Some of the major compounds obtained from cinnamon and their primary effects are shown in the Table 1.

4. Insulin resistance and diabetic control

Several studies on insulin resistance and glucose metabolism confirm cinnamon's useful therapeutic aspect of being effective in the treatment of diabetes (Shang et al. 2021; Mohsin et al. 2023). Cinnamaldehyde also proved highly effective in clinical trials in diabetic patients by reducing blood sugar and stabilizing cholesterol levels by inhibiting carbohydrate absorption. In PCOS, cinnamon can also be used as a second drug to treat diabetes. Extracts of cinnamon can prove beneficial in decreasing insulin resistance, according to animal studies (Wang et al. 2024). Not only glucose but it also regulates the lipid and cholesterol levels in the blood and proved that cinnamon can be used in diabetes as an alternative medicine in PCOS to control diabetes (Choudhary and Tahir 2023; Zarezadeh et al. 2023).

Several animal models have indicated that cinnamon extracts possess a lot of potential to manage insulin resistance. As an example, rats treated with 300 mg/kg/day of cinnamon extract for a period of three weeks has improved insulin sensitivity with enhanced insulin receptor substrate 1 (IRS1) or phospho-inositide 3-kinase (PI3K) and skeletal muscle insulin receptor (IR) β and IR substrate-1 (IRS1) tyrosine phosphorylation (Peivandi et al. 2024). For example, the extract of cinnamon improved the insulin sensitivity and connected signaling pathways of rats. Cinnamonaldehyde enhances glucose uptake by activating glucose absorption by enhancing glucose transporter type 4 (GLUT4) gene expression, and cinnamon extract elevates GLUT4 and uncoupling protein 1 (UCP-1) expression to improve glucose regulation in diabetic mice (De La Vega-Moreno and Suárez-Cuenca 2024). Activation of AMPK, which is responsible for mediating GLUT4 translocation, is probably involved in the mechanism. Recent evidence indicates that cinnamon may decrease blood sugar through increasing

Table 1 Components presents in the different parts of the cinnamon plant

Parts of cinnamon plants	Active compounds	Primary effects	Traditional use	Reference
Root	Camphor	Analgesic, anti-inflammatory	Pain relief	(Li et al. 2023)
Bark	Eugenol and cin	Antimicrobial, antioxidant, antidiabetic	Flavoring, spices, and traditional remedies for digestive issues	(Gogoi et al. 2021)
Leaves	Eugenol and cin	Antimicrobial, antioxidant	Tea, flavoring, and traditional medicine	(Addai et al. 2022)
Fruit	Caryophyllene and trans-cinnamyl acetate	Anti-inflammatory, Antioxidant	Flavoring and spice	(Lin et al. 2019)
Buds	Copaene, terpenoids,	Anti-inflammatory, aromatic	Traditional medicine, flavoring, and spice	(Hawwal et al. 2021)
Flower	Caryophyllene	Anti-inflammatory, aromatic	Perfume, flavoring, and spice	(Tsigoriyna et al. 2024)
Stem	Cinnamaldehyde	Antimicrobial, antioxidant	Flavoring and essential oil extract ion	(Ramos et al. 2023)
Seeds	Fatty Acids, essential Oils	Anti-inflammatory, antioxidant	Oil extraction and cooking	(Omar et al. 2024)
Roots (Inner bark)	Tannins	Antimicrobial, astringent	Traditional remedy for skin disorders	(Shoaib et al. 2022)
Essential oil	Cinnamaldehyde, eugenol, linalool	Antimicrobial, antioxidant, anti-inflammatory	Flavoring, aromatherapy, and pharmaceutical preparations	(Damasceno et al. 2024)
Bark (Powdered)	Polyphenols, flavonoids	Antioxidant, antidiabetic	Traditional medicine, cooking uses, and	(Sariwati et al. 2024)
Young shoots	Various volatile compounds	Aromatic, culinary use	Spice and pickling	(Li et al. 2022)

nerve growth factor (NGF) levels, which increase insulin levels and modulate the homeostasis of pancreatic β-cells (Ray et al. 2023). Also, Mild et al. (2023) highlighted that the cinnamon extract is known to act on transcription factor or forkhead box1 (FOXO1), affecting lipid distribution and the formation of GLUT4.

5. Hormonal regulation

One of the most important contributing factors to PCOS pathophysiology is excess ovarian androgen secretion, which is associated with raised insulin levels secondary to insulin resistance (Ding et al. 2021). Due to its role in modulating insulin resistance, cinnamon might indirectly benefit women's testosterone regulation and levels of ovarian hormones (Valizadeh et al. 2022). Dou et al. (2018) and Noreen et al. (2022) showed that cinnamon intake has been shown to help PCOS patients stabilize their menstrual cycle along with levels of testosterone and LH, which may help the ovaries work normally again. Extracts of cinnamon have also been found to block folliculogenesis and the concentration of anti-Mullerian hormone (Wiweko and Susanto 2017), which tends to increase normally in PCOS (Stracquadanio et al. 2018). Excess production of advanced glycation end products (AGEs) (Novakovic et al. 2024), which persist to play a role in encouraging the overproduction of testosterone in PCOS, could be lessened by cinnamon *via* increased sensitivity to insulin. Studies on PCOS mouse models provide evidence for the beneficial effects of cinnamon on hormone balance, showing its ability to increase insulin sensitivity, modify insulin-like growth factor (IGF-1) (Rafian et al. 2024) and IGF binding protein-1 (IGFBP-1), and normalize FSH, LH, and testosterone levels (Ren et al. 2024). The Fig. 2 shows different regulatory effects produced by cinnamon.

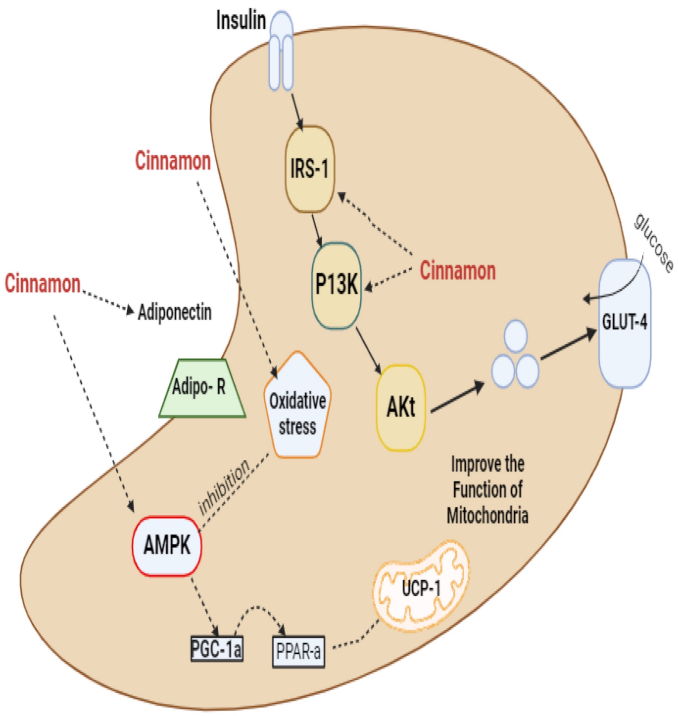

Fig. 2. Regulatory effects of cinnamon (IRS-1: Insulin receptor substrate-1; PI3K: phosphoinositide 3-kinase; AKt/PKB: Protein kinase-B; Adipo-R: Adiponectin-R; AMPK: AMP-activated kinase; PGC-1α: Peroxisome proliferator-activated receptor gamma coactivator-1 alpha; PPAR-α: Peroxisome proliferator-activated receptor alpha; GLUT-4: Glucose transporter type 4)

6. Blood pressure regulation

The bark of cinnamon has effects against cardiovascular diseases like high blood pressure (Shang et al. 2021). This property of cinnamon is used to control blood lipid and glucose levels, which helps in lowering blood pressure. Systolic blood pressure is very effectively controlled by adding cinnamon to the diet (Moncada et al. 2022). It increases the level of atrial natriuretic factor (ANF) (Farooq et al. 2023). ANF helps reduce the load of water, adipose, and sodium from the circulatory system and lowers blood pressure (Hall et al. 2024). In PCOS animal models, cinnamon is also hypotensive. Activity of *C. cassia* bark was correlated with increased plasma levels of ANF in mice (Riaz et al. 2022). By lowering the volume of fluid, sodium, and fat in the blood, ANF thus lowers blood pressure. In a Letrozole-induced PCOS rat model, Rizk et al. (2024) showed that a dose of 200 mg/kg of hydroalcoholic *C. zeylanicum* extract inhibited lipid peroxidation and offered protection against oxidative stress.

7. Obesity

Obesity is one of the main problems associated with PCOS (Zhang et al. 2024). Patients suffer a lot from high weight gain (Mathur 2024). Studies show that cinnamon has an effect on controlling the weight of females who are suffering from PCOS (Rao et al. 2024). Cinnamon is given in powder form to control weight (Onder et al. 2024). Various clinical trials were carried out to check the role of cinnamon in weight loss, and the supplementation of cinnamon gave remarkable results in reducing the weight of women suffering from PCOS (Nemati et al. 2024). Animal models have also been employed to explore cinnamon's efficacy in managing obesity. Ion channel protein transient receptor potential ankyrin 1 (TRPA1), found on gastrointestinal epithelial cells, is critical for this function (Kumar et al. 2022). Researchers found that the primary active compound in cinnamon, cinnamonaldehyde, acts as a TRPA1 agonist and decreases visceral fat in mice consuming a diet rich in fat and sugar. By serotonergic mechanisms, TRPA1 activation also influences gastrointestinal function, such as cholecystokinin secretion, gastric emptying, and overall motility (Oh et al. 2023). Furthermore, by inducing an increase in UCP-1 production in brown adipose tissue, TRPA1 activation aids autonomic thermoregulation. The co-localization of ghrelin, enteroendocrine cells, and TRPA1 in the duodenum was observed by researchers, indicating that cinnamonaldehyde activation of TRPA1 suppresses ghrelin release, thereby reducing appetite (Abd Eldaim et al. 2021). On top of all these mechanisms, scientists demonstrated that cinnamon improves lipid profiles in mice by enhancing the expression of peroxisome proliferator-activated receptor alpha (PPAR-α) and related lipid homeostasis genes in adipocytes, such as CD36 and lipoprotein lipase (LPL) (Handayani et al. 2023). Finally, through inhibition of acetyl-CoA-carboxylase and activation of malonyl-CoA-dehydrogenase, cinnamon's AMPK activation also assists with lipid metabolism regulation through enhanced beta-oxidation and decreased fatty acid synthesis. All these mechanisms suggest a complex but perhaps beneficial role of cinnamon in weight regulation (Oh et al. 2023). Obesity heavily exacerbates metabolic derangements and infertility in PCOS.

8. Mechanism of action of cinnamon in mice

By mediating increased insulin sensitivity (Mishra and Kakadiya 2023), cinnamon affects ovarian hormones, androgens, estrous cycle, gonadotrophins, and morphology of ovaries in model systems, and aids in maintaining hormone equilibrium (Khodaeifar et al. 2019). Cinnamon increases PI3K, IR, and IRS-1 tyrosine phosphorylation within rat skeletal muscle. Cinnamon may increase muscle tissue glucose uptake in mice through increased GLUT4 gene expression, possibly via AMPK activation (Peivandi et al. 2024). Activated AMPK can be derived from LKB1 activation by cinnamon via phosphorylation. In addition to stimulating GLUT4, AMPK suppresses gluconeogenesis, which has a bearing on glucose metabolism (Nguyen and Liu 2024). With the induction of high levels of nerve growth factor (NGF), cinnamon is capable of lowering blood sugar. Cinnamon can ameliorate PCOS in mice by rescuing endocrine disorders and insulin resistance. Cinnamon supplementation had substantially lowered blood insulin, testosterone, and LH levels in mice having PCOS, which indicated increased insulin sensitivity and hormonal equilibrium. It also improved ovarian morphology and follicular growth, which were shown to be associated with the changes in IGF-1 and IGFBP-1 levels. Although these results are encouraging, further studies need to be conducted to determine the therapeutic effects of cinnamon in PCOS, especially in humans (Aras and Sari 2021).

9. Limitations and future perspectives

Despite the promise that cinnamon holds as a therapy for PCOS due to its anti-inflammatory and insulin-sensitizing properties, there are different limitations that render it unable to be used everywhere in clinics. Its efficacy is threatened by uneven results from research in the shape of contradictory meta-analyses on its influence on fasting plasma glucose as well as insulin. Its clinical use is also hindered by a lack of standard dosage and treatment duration protocols, suggesting that longer treatments and higher doses may be required to achieve a measurable clinical effect. Perhaps most importantly, further intense research is required because the precise mechanisms through which cinnamon works to change the metabolic indices in the PCOS cases are unknown. To overcome such limitations, future research will need to lay considerable stress on carefully designed clinical trials with standardized dosing and long duration of treatment in a bid to finally establish the efficacy and safety of cinnamon. Furthermore, in a bid to harness the full medicinal power of cinnamon, mechanistic studies that clearly characterize the metabolic pathways on which it operates are a necessity. Apart from lifestyle change and traditional drugs, studies on the application of cinnamon as an add-on therapy might also be a superior and better alternative means of PCOS treatment that can ultimately close the gap between effective preclinical results and robust clinical practice.

10. Conclusion

As a natural medication with many benefits for PCOS therapy, cinnamon holds promise. Favorable impacts on significant PCOS traits, including insulin sensitivity, hormone balance, oxidative stress, and perhaps weight, are indicated by clinical trial data and animal studies. Available evidence indicates that cinnamon can be an effective supplementary treatment, although the mechanisms are still under research. To validate these findings, to maximize dose, and to fully understand its long-term effectiveness and safety, additional research is needed, especially clinical trials. Yet current research suggests that cinnamon is an extremely promising natural therapeutic option for improving hormonal and metabolic well-being in individuals with this prevalent endocrine disorder.

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