



Effect of Turmeric Herbal on Polycystic Ovary Syndrome: A Systematic Review

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ABSTRACT: Polycystic Ovary Syndrome (PCOS) is an endocrine disorder that is increasingly affecting women in the reproductive age group. Women commonly experience menstrual irregularities, hirsutism, weight gain, and acne, as well as the development of a complex endocrine disorder that presents with oligomenorrhea, hyperandrogenism, and polycystic ovaries. Herbal medicine is a complex intervention with the potential for synergistic and antagonistic interactions between compounds. These drugs are essential for the treatment of PCOS and have fewer side effects compared to allopathic drugs. One of the herbal medicines to treat PCOS is turmeric or curcumin, curcumin has various biological activities including antioxidant, anti-inflammatory, anti-microbial, anti-tumor, cardioprotective and neuroprotective effects involving various mechanisms. Curcumin can stimulate insulin-mediated glucose uptake via the phosphatidylinositol 3-kinase (PI3K)/Akt pathway, which, in turn, upregulates glucose transporter 4 (GLUT4) in adipocytes and skeletal muscle, leading to increased glucose levels. Curcumin supplementation improves glycemic control and lipid metabolism, and reduces oxygen radical species in PCOS patients. Curcumin is a diarylheptanoid derived from the rhizome of the *Curcuma longa* plant, which functions as an anti-inflammatory and antioxidant which is very important in the treatment of PCOS. In addition, nearly half of patients with PCOS develop metabolic syndrome and insulin resistance, and are associated with a much higher risk of type 2 diabetes mellitus.

KEYWORDS: Polycystic Ovarian Syndrome (PCOS), Turmeric, Traditional Medicine

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is one of the most common disorders worldwide, with a global prevalence ranging from 4% to 21% [1]. PCOS is a reproductive endocrine disease characterized by menstrual disorders, infertility and obesity, usually accompanied by insulin resistance and metabolic disorders [2]. The most common signs of PCOS are ovulatory dysfunction, hyperandrogenism, and polycystic ovaries [3]. Additionally, nearly half of patients with PCOS develop metabolic syndrome and insulin resistance, and are associated with a much higher risk of type 2 diabetes mellitus, cardiovascular disease, and even cancer. [4]. Changes in the endometrium are among the most common clinical manifestations and complications in PCOS patients. The endometrium of PCOS patients tends to show pathological hyperplasia (eg, simple hyperplasia, complex hyperplasia, or atypical hyperplasia) because of long-term exposure to estrogen and lack of regular antagonism of progesterone. [5].

Polycystic Ovary Syndrome (PCOS) is an endocrine disorder that is increasingly affecting women in the reproductive age group. Women commonly experience menstrual irregularities, hirsutism, weight gain, and acne, as well as a complex set of endocrine disorders that occur with oligomenorrhea, hyperandrogenism, and polycystic ovaries [6]. Women with PCOS are more likely to be obese/overweight than age-matched controls, and being overweight exacerbates PCOS features [7].

Women with PCOS who have phenotypes A and B, meaning they don't ovulate, are generally obese and are thought to be affected by a more severe form of PCOS with consequences not only on fertility but also on metabolic processes. In contrast, women with phenotype C who have regular ovulatory periods are generally thin or slightly overweight with no or little metabolic problems [8]. Usually associated with reproductive complications (irregular menstruation, ovulatory dysfunction, and pregnancy complications), metabolic disorders (type 2 diabetes and cardiovascular disease), and even psychological risk factors [9].

The current standard of treatment for PCOS in women includes everything from medication therapy to lifestyle changes. Diet, weight loss, and exercise are all related to lifestyle changes [10]. Treatment to deal with problems in women who experience PCOS can use herbs. Herbal plants are considered safer than synthetic medicines, one of the herbs used is turmeric [11]. Curcumin or turmeric is a fat-soluble polyphenol extracted from turmeric rhizome. This is the main active component in turmeric and provides



pharmacological effects. Significant research has shown that curcumin has strong biochemical and biological activities. In addition, curcumin has low toxicity and almost no adverse reactions. Several *in vivo* and *in vitro* studies have confirmed that curcumin or turmeric can improve glucose metabolism in diabetes [12].

About 70% of people worldwide are interested in the prevention and treatment of disease with complementary and alternative medicine (CAM) although there is not enough scientific assessment evidence to prove its safety and effectiveness [13]. Complementary and alternative medicine (CAM), an alternative therapy independent of Western medicine, is widely used in healthcare systems worldwide [14].

Herbal medicine is a complex intervention with the potential for synergistic and antagonistic interactions between compounds. These drugs are essential for the treatment of PCOS and have fewer side effects compared to allopathic drugs. Regular use of herbs is safer and more efficacious in treating PCOS and suppressing the events that contribute to the development of cysts in PCOS. Today, herbal medicine plays an important role in treating various chronic disorders, including PCOS. Using herbal medicines and dietary modifications can help treat PCOS more effectively [15].

Curcumin is a natural medicine containing phenol and quinone groups extracted from turmeric in the ginger family. It is known as a safe dietary supplement worldwide. In several randomized, double-blind clinical trials, patients with PCOS received curcumin (in a dose of 500-1500 mg 3 times daily for 1-3 months) or placebo. It is suggested that curcumin can effectively improve blood glucose, insulin resistance, and hyperandrogenemia in PCOS. In addition, curcumin is reported to exert many beneficial biologic effects through a multitargeting mechanism [16]. Consumption of foods containing curcumin also has a protective effect on most of the body's organs. Curcumin is used to prevent various diseases including colon, breast and pancreatic cancer [17].

One of the main features of PCOS is increased androgen levels. Curcumin has been shown to reduce high androgen levels in PCOS in three studies. A randomized controlled clinical trial involving 67 women with PCOS who were treated with 500 mg of powdered curcumin for 12 weeks three times daily showed that dehydroepiandrosterone levels decreased compared to the placebo group. Apart from disrupting androgen levels, PCOS also affects the balance of a woman's LH/FSH ratio. However, a randomized controlled clinical trial showed that curcumin had no effect on LH, FSH and estrogen levels in PCOS women [18].

Curcumin is also known to reduce plasma cholesterol and triglycerides by increasing lipoprotein lipase activity and through mechanisms that alter lipid and cholesterol gene expression. Additionally, the anti-inflammatory effects of curcumin have been shown to reduce oxidative stress in patients with PCOS. Previous literature revealed that curcumin significantly increased fasting blood glucose and triglycerides in patients with metabolic syndrome. Further *in vivo* studies demonstrated the same effect in PCOS models [19].

RESEARCH METHODS

A systematic review using studies related to herbal ingredients related to curing cervical cancer identified by conducting a literature search. For this systematic review, we conducted an online search strategy involving several databases namely: PubMed, Wiley Online Library, SpringerLink, ProQuest, Science Direct and Google Scholar for articles published in English from 2016 to February 2023. The following keywords were used during the strategy search: "Herbal AND PCOS" OR "Curcumin AND PCOS" OR "Turmeric AND PCOS".

Inclusion and Exclusion Criteria

Inclusion criteria :

1. Full text article
2. Original research in English
3. Publication date between January 2019 and June 2023
4. The research taken is experimental

To eliminate bias, error, and ambiguity in the results of the articles selected for this systematic review, exclusion criteria were applied

Exclusion Criteria :

1. Non-experimental research, systematic review
2. Paid journal



Quality Appraising

For quality purposes, PRISMA was used to ensure the complete results of this study which are shown in Figure 1.

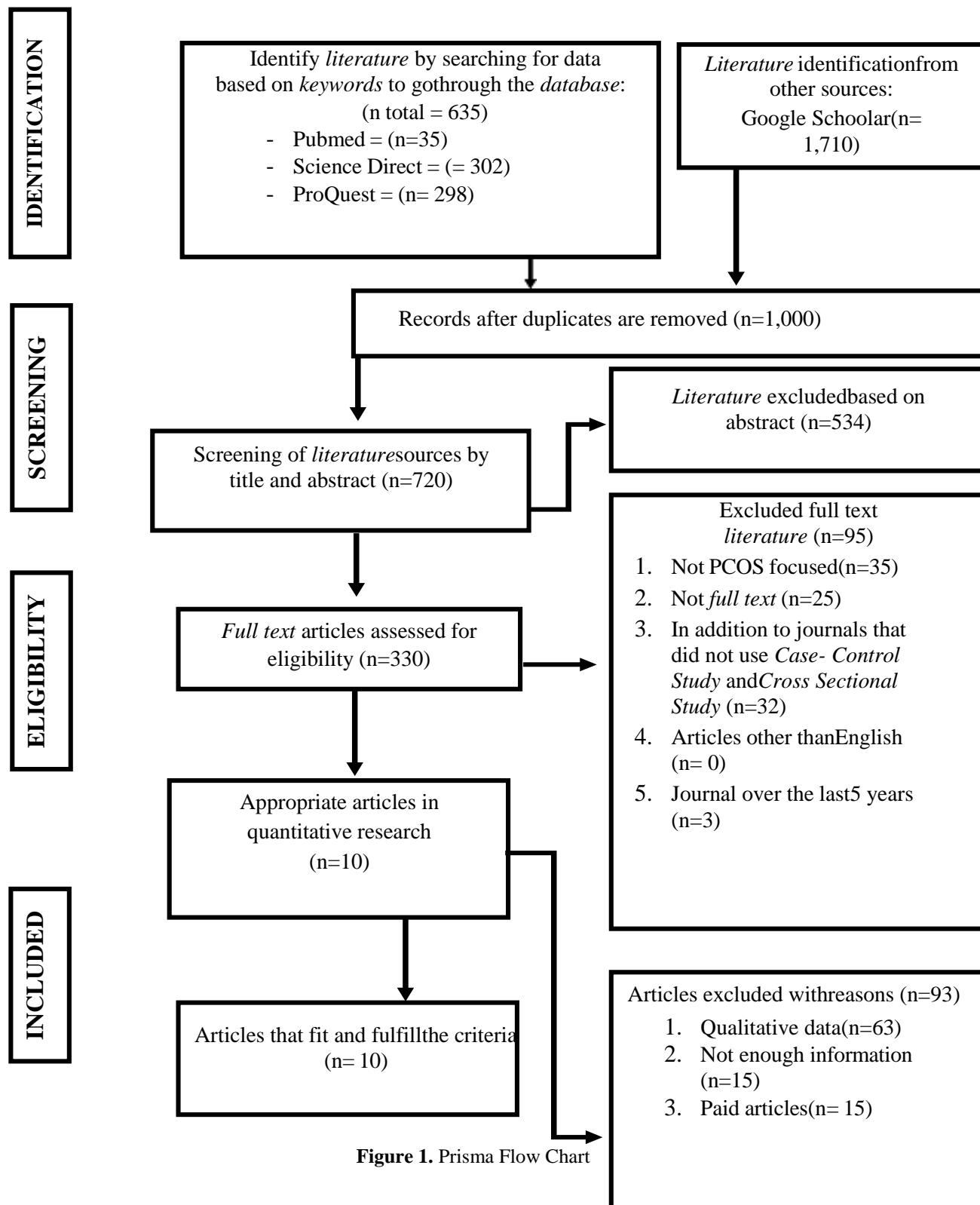


Figure 1. Prisma Flow Chart



RESULTS

Based on 10 articles discussing the benefits of herbal ingredients that have an effect on curing cervical cancer, they come from various countries, such as Iran, Turkey, Egypt, India. The results of this analysis reported in 10 articles that herbal therapy has a positive effect on healing PCOS as an anti-inflammatory. Journals were obtained from pubmed, science direct, proquest databases (635) and Google Scholar (1710). Article removed due to duplicates (1000). Literature screening by title and abstract (720). Literature excluded for abstract (534). Eligible full text articles (330), published full text literature (95). Article removed for reasons (93). Quantitatively suitable articles (10). Articles that are appropriate and meet the criteria (10).

Table 1. Result study

No	Author, country	Method	Instrument	Population	Data based	Results
1.	(Abuelezz et al., 2020), Egypt	Experiment	Not explained	Mouse	ProQuest	This study demonstrates, for the first time, that the PI3K/AKT/mTOR pathway makes an important contribution to the disruption of β -cell function and integrity in PCOS. It also shows that nanocurcumin has strong promising potential to combat PCOS pancreatic deficits through a multi-edge mechanism; as a potent antioxidant/anti-inflammatory agent against TNF- α and ROS-induced inflammation as well as a modulator of PI3K/AKT/mTOR levels in PCOS pancreas
2.	(Asan et al., 2020), Turkey	A randomized, placebo controlled trial	Not explained	30 participation with PCOS	PubMed	Our results support that curcumin supplementation may be useful in weight control and glucose metabolism in women with PCOS. Additional studies with a larger number of patients, a longer treatment period, and different genetic backgrounds are needed to determine a definitive improvement in the clinical condition
3.	(Jamilian et al., 2020), Iran	randomized, double-blind, placebo-controlled clinical trial	Anthropometric Measurements	60 girls	Science direct	12 weeks of curcumin administration to women with PCOS had beneficial effects on body weight, glycemic control, serum lipids except triglyceride and VLDL cholesterol levels, and PPAR-g and LDLR gene expression.



4.	(Heshmati et al., 2020)	Randomized Double-Blind Placebo-Controlled Clinical Trial	Anthropometric measurements	Women ages 18-49 with PCOSS	ProQuest	Our results showed that curcumin significantly reduced the amount of DHEA and it may even increase estradiol levels in women with PCOS. To date, there have been no similar studies on the effects of curcumin supplementation on sex hormones in women with PCOS.
5.	(Asan et al., 2020), Turkey	A randomized, placebo controlled trial	Anthropometric measurements	30 participation with PCOS	Science direct	Our study showed that 8 weeks of oral curcumin supplementation added to food in PCOS women showed significant effects on parameters of glycemic status, body weight, waist circumference and body fat mass.
6.	(Ghanbarzadeh-Ghashti et al., 2023)	randomized controlled trial	Not explained	Women ages 18-45 with PCOS	PubMed	Curcumin reduces FBS levels and improves menstrual characteristics (amenorrhea, oligomenorrhea, and menstrual irregularities) in women with PCOS but does not affect other metabolic, hormonal, and hirsutism indices.
7.	(Sohaei et al., 2019), Iran	A randomized, placebo controlled trial	Not explained	Participants aged 18-40 years	Science direct	Our study shows that 6 weeks Administration of oral curcumin to PCOS women did not support a significant effect on glycemic status parameters except for insulin levels as well as QUICKI which were significantly increased in the curcumin group based on in-group analysis.
8.	(Shah& Shrivastava, 2022)	Case Control	Metformin and Letrozole	24 albino rats	Science direct	The current study suggests that LET-induced PCOS is associated with endocrine and metabolic changes, caused by a decrease in circulating adiponectin and an increase in circulating luteinizing hormone. In conclusion, Turmeric Extract showed promising effects in treating PCOS and inducing ovulation when compared with metformin.



9.	(Abuelezz et al., 2020), Egypt	Case control	Curcumin powder, letrozole and clomiphene citrate	Mouse	Science direct	To our knowledge, this study demonstrates for the first time, that the PI3K/AKT/mTOR pathway makes an important contribution in β -cell function and integrity that is impaired in PCOS. It also shows that nanocurcumin has strong promising potential to combat pancreatic deficit PCOS through a multi-edge mechanism; as a potent antioxidant/anti-inflammatory agent against TNF- α and ROS-induced inflammation and a modulator of PI3K/AKT/mTOR levels in pancreatic PCO
10.	(Abhari et al., 2020), Iran	Experiment	Not explained	Mouse	Science direct	Treatment will aim to slowly but surely return to overall health with nanotechnology therapies that can vary over time and allow for spontaneous ovulation, uncomplicated pregnancies and healthy offspring. Ultimately and most importantly, these results will contribute to improving worldwide care for adolescent girls with PCOS

DISCUSSION

The results obtained from these findings are used to reduce the effect of pharmacological therapy in patients with PCOS. After screening 2345 articles using the PRISMA flowchart, 1000 articles were excluded based on duplication and were omitted because of the journal criteria used, so 10 articles were selected to be included in this systematic review. Many Indonesian plants can be used as herbal medicine, one of which is turmeric 1,11,12,15,16,18–20,22–24,26,

Herbal medicine is a type of complementary and alternative medicine and its use by women has increased significantly in the last decades. Curcumin has various biological activities including antioxidant, anti-inflammatory, anti-microbial, anti-tumor, cardioprotective and neuroprotective effects involving various mechanisms.[29]. Curcumin can stimulate insulin-mediated glucose uptake via the phosphatidylinositol 3-kinase (PI3K)/Akt pathway, which, in turn, upregulates glucose transporter 4 (GLUT4) in adipocytes and skeletal muscle, leading to increased glucose levels. In addition, curcumin can also increase GLUT4 and glucose uptake in adipocytes. Curcumin has been shown to inhibit hepatic gluconeogenesis through modulation of 5'AM Pactivated protein kinase (AMPK), thereby reducing blood glucose levels [30]. Among the natural phenols, the therapeutic properties of curcumin have been further investigated. Curcumin (diferuloylmethane) is a lipophilic yellow pigment extracted from turmeric (*Curcuma longa L.*) rhizome. Curcumin supplementation improves glycemic control and lipid metabolism, and reduces oxygen radical species in PCOS patients [31].

Curcumin is a diarylheptanoid derived from the rhizome of the *Curcuma longa* plant. It is reported to have anti-inflammatory and antioxidant activity which is very important in the treatment of PCOS. Numerous reports are available on the effects of curcumin on various aspects of PCOS in animal models[32]. Curcumin or diferuloylmethane is a lipophilic polyphenol in the form of yellow



crystals. This is the active ingredient of turmeric with anti-oxidant and anti-inflammatory properties. Several studies have shown curcumin to have an acceptable safety profile with minimal side effects [33]. *C. longa* is rich in polyphenolic curcuminoids, namely curcumin (80%), demethoxycurcumin (12%), bisdemethoxycurcumin (8%), and essential oils (5.8%). The essential oils contained in the rhizomes include α -phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%), and sesquiterpenes (53%). These phytochemicals can exhibit important pharmacological activities, including anti-inflammatory, anti-microbial, antioxidant [34]. Curcumin also works by inhibiting the activity of pro-inflammatory proteins such as activated protein-1, peroxisome proliferator activated receptor gamma, signal transducer, and transcription activator, as well as the expression of β -catenin, cyclooxygenase 2, 5-lipoxygenase, and nitric oxide synthase isoform, which plays a key role in inflammation. In addition, it acts by blocking the binding between TNF- α and its receptors, preventing the continuation of cytokine-induced inflammation [35].

CONCLUSION

PCOS is a reproductive endocrine disease characterized by menstrual disorders, infertility, and obesity, usually accompanied by insulin resistance and metabolic disorders. The most common signs of PCOS are ovulatory dysfunction, hyperandrogenism, and polycystic ovaries. In addition, nearly half of patients with PCOS develop metabolic syndrome and insulin resistance, and are associated with a much higher risk of type 2 diabetes mellitus, cardiovascular disease, and even cancer. Women commonly experience menstrual irregularities, hirsutism, weight gain, and acne, as well as the development of a complex endocrine disorder that presents with oligomenorrhea, hyperandrogenism, and polycystic ovaries. Women with PCOS are more likely to be obese/overweight than age-matched controls, and being overweight exacerbates PCOS features. Curcumin can stimulate insulin-mediated glucose uptake via the phosphatidylinositol 3-kinase (PI3K)/Akt pathway, which, in turn, upregulates glucose transporter 4 (GLUT4) in adipocytes and skeletal muscle, leading to increased glucose levels. Curcumin also works by inhibiting the activity of pro-inflammatory proteins such as activated protein-1, peroxisome proliferator activated receptor gamma, signal transducer, and transcription activator, as well as the expression of β -catenin, cyclooxygenase 2, 5-lipoxygenase, and nitric oxide synthase isoform, which plays a key role in inflammation. Suggestions for future researchers can conduct more research regarding the level of effectiveness of herbal turmeric in healing PCOS, as well as suggestions for health workers to recommend herbal turmeric therapy as an alternative treatment apart from medical treatment.

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