

## Exploring The Therapeutic Potential Of Herbal Intervention In Polycystic Ovary Syndrome: A Systemic Review And Meta-Analysis

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### ABSTRACT

**Ethnopharmacological Relevance-** PCOS is a hormonal disorder affecting women of reproductive age. Several studies have been carried out on the effect of herbal interventions in improving PCOS patients but these still have not been fully assessed.

**Aim of Study-** This meta-analysis aimed to evaluate whether herbal interventions could promote reproductive health in women with PCOS while providing evidence-based herbal treatment for clinical practice.

**Material and Methods:** This systematic review follows PRISMA guidelines, assessing herbal product's efficacy for PCOS management. In this research, we identified 25 studies for the analysis, including 779 women with PCOS that were defined by using biochemical or ultrasound evidence and followed Cochrane criteria for Risk of Bias (ROB) across domains, considering 7 domains of risk. Meta-analysis utilized continuous data from 11 studies, focusing on substance use and externalizing symptoms, conducted through Review Manager (RevMan version 5.4) for 11 randomized control trials.

**Results:** The forest plot analysis was conducted for Body Mass Index (BMI), hirsutism, insulin levels, blood glucose level, and follicular stimulating hormones (FSH) levels. We utilized a random-effects model to calculate mean differences and standard deviations using the Standard Mean Difference (SMD) scale. For BMI, the overall effect size was -0.16 (CI -0.28 to -0.03), with significant individual study effect sizes. Hirsutism showed an overall effect size of -0.34 (CI -0.62 to -0.05). Insulin analysis revealed an overall effect size of -0.79 (CI -1.28 to -0.34), with two individual study effects favoring the experimental group. Analysis for fasting glucose had an overall value of -0.27 (C.I -0.54 to 0.01) while for FSH it was -0.11 (C.I -0.39 to 0.17). In each analysis, the forest plots demonstrated the benefits of herbal therapy in PCOS treatment.

**Conclusion:** Herbal interventions are a promising therapeutic approach that can be employed in the management of PCOS patients

**Keywords:** Alternative Medicine; Ayurveda; Basti therapy; Herbal Medicines; Medicinal plants; PCOS.

### Highlights

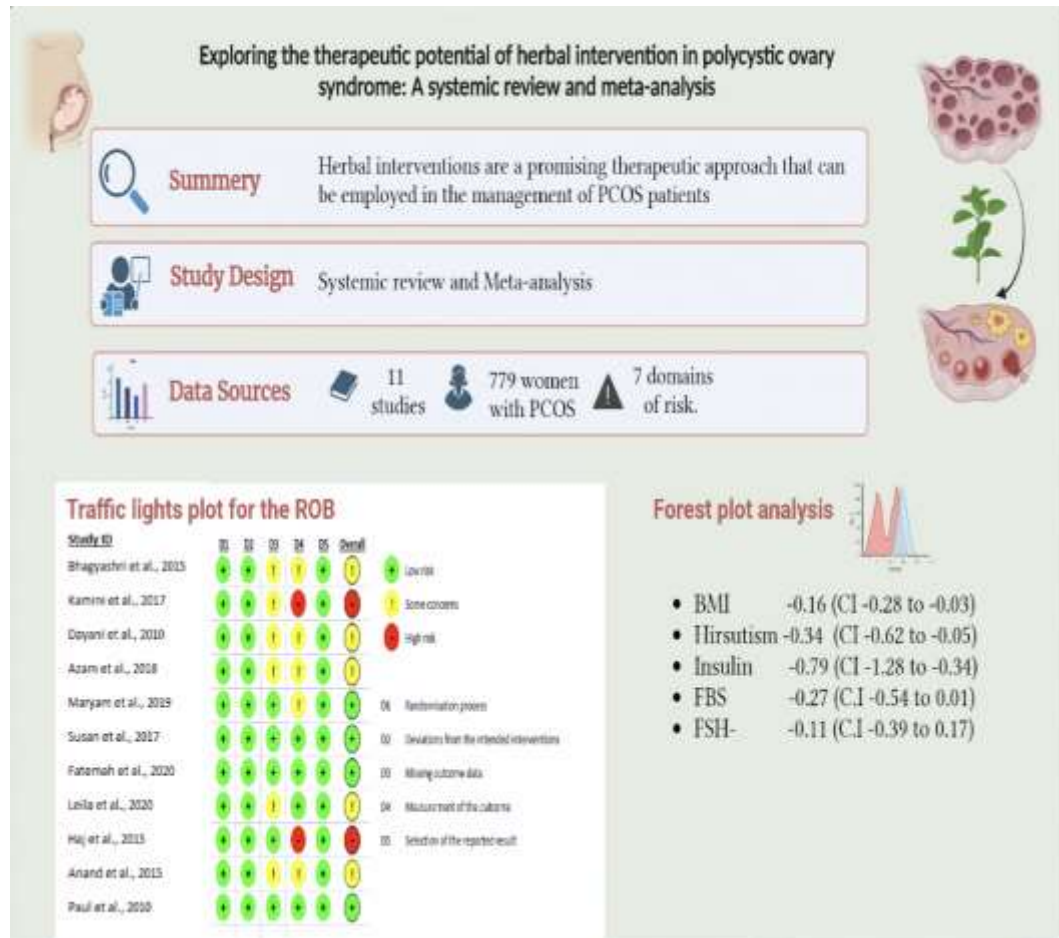
- Identified 25 studies for the analysis, including 779 women, considering 7 domains of risk.
- Based on this systematic review, herbal interventions have a positive impact on all aspects of PCOS; and tend to have more benefits in managing FBS levels, Insulin sensitivity, and Hirsutism, which is found statistically significant based on forest plot analysis.

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### Graphical Abstract:



## 1. Introduction

Polycystic ovary syndrome (PCOS) represents a multifaceted endocrine disorder observed in women of reproductive age, characterized by a diverse array of potential combinations of clinical manifestations and a spectrum of phenotypic variations. (Norman et al., 2007) These manifestations encompass reproductive, metabolic, and endocrine alterations. The clinical features of PCOS encompass amenorrhoea, oligomenorrhoea, obesity, infertility resulting from anovulation and cutaneous manifestations like acanthosis nigricans, acne, and hirsutism. PCOS is also associated with other metabolic disorders including insulin resistance and increased expression of androgens. (Ramanand et al., 2013)

The definitive diagnostic criteria for PCOS encompass three distinct sets, the Rotterdam Criteria 2003, (Fauser, 2004) the Androgen Excess Criteria 2006 (Azziz et al., 2009), and the National Institutes of Health Consensus Criteria 1990 (Zawadzki and Dunaif, 1992). Among these, the Rotterdam criteria (RC) are the most comprehensive and widely employed. RC proposes three specific features for the diagnosis of PCOS which are the presence of clinical and/or biochemical hyperandrogenism, irregular menstrual patterns (oligo-anovulation), and the observation of polycystic ovary morphology through ultrasonography (USG), denoting the existence of 12 or more follicles with a maximum diameter falling within the range of 2–9 mm or an ovarian volume surpassing 10 ml. To validate a PCOS diagnosis by the RC, a woman must exhibit at least two of these three characteristics, while the exclusion of alternative causes of hyperandrogenism, such as nonclassical congenital adrenal hyperplasia and hyperprolactinemia, is imperative (Fauser, 2004).

At present, the primary therapeutic approach for PCOS is tailored to address the patient's foremost concerns. The treatment of PCOS aims to alleviate symptoms related to hyperandrogenism, restore regular menstrual cycles, and facilitate conception. Notably, in the context of addressing infertility attributed to PCOS, letrozole, an aromatase inhibitor, exhibits a higher degree of efficacy compared to clomiphene citrate, which is an anti-estrogen (Ghahiri et al., 2016). Clomiphene citrate exerts its effects by inhibiting estradiol (E2), a hormone involved in the growth and maturation of the endometrial lining, but its use is associated with side effects such as hot flashes, breast discomfort, and gastrointestinal complications. (Takasaki et al., 2018) Combined oral contraceptive pills (OCP) serve as the predominant form of androgen inhibition and are the preferred therapeutic choice for addressing menstrual irregularities in individuals with PCOS. (Bozdaga and Yildizb, 2012) However, OCP is not considered suitable for women who are actively attempting to conceive and may carry potential cardiovascular risks. Metformin, occasionally prescribed to manage hyperglycemia in PCOS, may give rise to gastrointestinal complications and, in rare instances, lactic acidosis (Lashen, 2010).

Herbal intervention is defined as a phytopharmaceutical preparation derived from an entire plant or parts of the plant (stem, rhizome, root, leaves, bark, flower, etc.) or its exudates (latex, gums, resins). These preparations are administered either in their crude form or in a purified form like dried powder, decoction, extract, juice, etc., by using extraction, filtration, distillation, etc. (Parasuraman et al., 2014) The pharmacological action of the herbal formulations or drugs is due to their active phytochemical constituents such as polyphenols, tannins, alkaloids, phenols, saponins, polysaccharides, proteins, lipids, flavonoids, terpenoids, peptides etc. Traditional herbal remedies have been employed across generations for their therapeutic attributes, presenting a holistic approach to addressing diverse maladies. Numerous phytochemicals within plants demonstrate several pharmacological properties like anti-androgenic, anti-inflammatory, insulin-sensitizing, antioxidant etc. properties. (Chen and Pang, 2021) Complementary and alternative medicine (CAM) approaches have the potential to alleviate PCOS symptoms and are characterized by greater adaptability and patient-friendliness with a reduced likelihood of side effects. (Rao et al., 2023)

A notable advantage of herbal treatment lies in its favorable safety profile, with fewer side effects in comparison to conventional pharmaceuticals. Furthermore, the presence of multiple bioactive compounds within medicinal herbs can augment their therapeutic efficacy, rendering them a promising alternative to traditional treatment modalities for addressing PCOS. A multidisciplinary approach, encompassing lifestyle modifications, a well-balanced diet, and regular physical activity, can play a pivotal role in reducing adiposity, enhancing metabolic functions, improving insulin sensitivity, and fostering reproductive health. (Akre et al., 2022)

Thus, the primary objective of this study was to furnish an updated scholarly publication substantiating the efficacy of herbal intervention in the therapeutic management of PCOS patients. The purpose of the present systematic review and meta-analysis was to appraise the outcomes from published randomized controlled trials (RCTs) or experimental studies to investigate the impact of pharmaceuticals and therapies on clinical and paraclinical outcomes in women affected by PCOS.

### 1.1 Rationale

The study intends to assess the efficacy and safety of herbal interventions for treating PCOS. Given the limitations and complexity of conventional treatments, exploring CAM approaches is valuable. Herbal remedies have historical relevance in addressing hormonal imbalances, and their holistic nature aligns with PCOS's multifaceted symptoms. With emerging evidence suggesting the anti-androgenic, anti-inflammatory, and insulin-sensitizing effects of certain herbal compounds. This study aims to provide scientific validation for traditional practices. By investigating personalized treatment options rooted

in cultural practices, the study seeks to contribute to a more comprehensive approach to managing PCOS and its diverse manifestations.

## 1.2 Objectives

1. Evaluate the effectiveness and safety profile of herbal formulations or herbal drugs in managing PCOS-related symptoms.
2. Investigate the impact of herbal cleansing and detoxification procedures like Basti therapy (Medicated Enema), Vaman therapy (Therapeutic emesis), and Virechan therapy (Therapeutic Purgation), on promoting reproductive health in PCOS patients.
3. Explore the potential of these herbal formulations or herbal drugs or alternative therapies in improving metabolic markers, insulin sensitivity, androgen levels, and overall well-being of PCOS patients.
4. Provide valuable insights into personalized and holistic approaches to PCOS treatment.

## 2. Materials and methods

We reported this review according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. (Page et al., 2021)

**Table 1: Eligibility Criterion for PCOS Inclusion**

Participants	Intervention	Comparison	Outcomes
Female patients with PCOS (Diagnostic criteria such as the Rotterdam criteria, Androgen excess criteria, and the National Institutes of Health criteria)	single or multiple herbs, herbal classical preparation, patent herbal products, or alternative herbal cleansing therapy. Duration is more than 30 days	Placebo or allopathic Medicine or Lifestyle Modification or combinations of all or without any comparator arm.	Objective nature of the outcomes, such as hirsutism, insulin resistance, weight loss, fasting blood glucose, menstrual irregularities, and BMI. Hormonal outcomes i.e. FSH, LH, testosterone, sex-hormone binding globulin (SHBG), DHEA-S.

### 2.1 Information sources

The published articles were included in the following core databases: Medline via Pubmed, EMBASE via Elsevier, and the Cochrane Central Register of Controlled Trials (CENTRAL).

### 2.2 Search strategy

We found a total of 25 studies (n=140) that were eligible for the inclusion criteria and covered the terms PICO which means a combination of Problem (PCOS), Intervention (Herbal medicines), and Comparison (Oral drugs). Mesh terms for the research included 'Polycystic Ovarian Syndrome' OR 'Ovary Syndrome', 'Polycystic' OR 'Syndrome, Polycystic Ovary' OR 'Stein-Leventhal Syndrome' OR 'Stein Leventhal' OR 'Syndrome', Stein-Leventhal, 'Sclerocystic Ovarian Degeneration' OR 'Ovarian Degeneration', 'Sclerocystic' OR 'Sclerocystic Ovaries', 'PCOS' AND 'Medicine' OR 'Herbal' OR 'Herbal extract' OR 'Ayurved Medicine' OR 'Herbal Medicine' OR 'Formulation' OR 'Medicine, OR 'Ayurved Treatment Procedure', 'PCOS AND Vaman', 'PCOS AND Virechan', 'PCOS AND Basti' AND 'Dimethyl biguanide' OR 'Glucophage' OR 'Metformin Hydrochloride' OR 'Metformin HCl'.

## 2.3 Study selection

A group of 3 researchers searched for literature in peer-reviewed journals and publications by the inclusion criteria. After a thorough selection of the literature, peer-reviewed journals with a strong impact factor were explored to reduce the risk of publication bias. All selected studies were uploaded to the screening software 'Rayyan tool citation' for primary and secondary screening of the literature. Three researchers worked as collaborators to "include" or "exclude" eligible studies based on the inclusion and exclusion criteria. A total of 25 studies (n=140) were considered for the final review and analysis. (Table 1) Studies that did not pass the eligibility for screening were put under "exclusion" or "dispute". The team selected the studies to serve as tiebreakers for a disputed study. Exclusion reasons were put forward before excluding a study from the literature. Studies were excluded because either there was a problem with the population, the study design was not ideal for our analysis, the study measured the wrong outcomes, or we found a high Risk of Bias (ROB). Sometimes, it was a combined effect of multiple reasons for exclusion.

## 2.4 Type of study

In our study, we included randomized controlled trials (RCTs), which are reliable and rigorous in research. We considered both parallel studies, where participants are divided into separate groups, and crossover studies, where participants switch between different treatments. Additionally, we also considered grey literature sources such as dissertations and conference abstracts, which provide valuable insights and perspectives that may not be found in traditional published sources.

## 2.5 Type of intervention

The interventions used were the usage of medicinal plant, polyherbal or Ayurvedic formulations, patent herbal formulations, and some traditional Ayurvedic treatment procedures that are used for cleansing and detoxification i.e. Basti therapy (Medicated Enema), Vaman therapy (Therapeutic emesis), and Virechan therapy (Therapeutic Purgation), in the treatment of PCOS as compared to the use of allopathic oral medication.

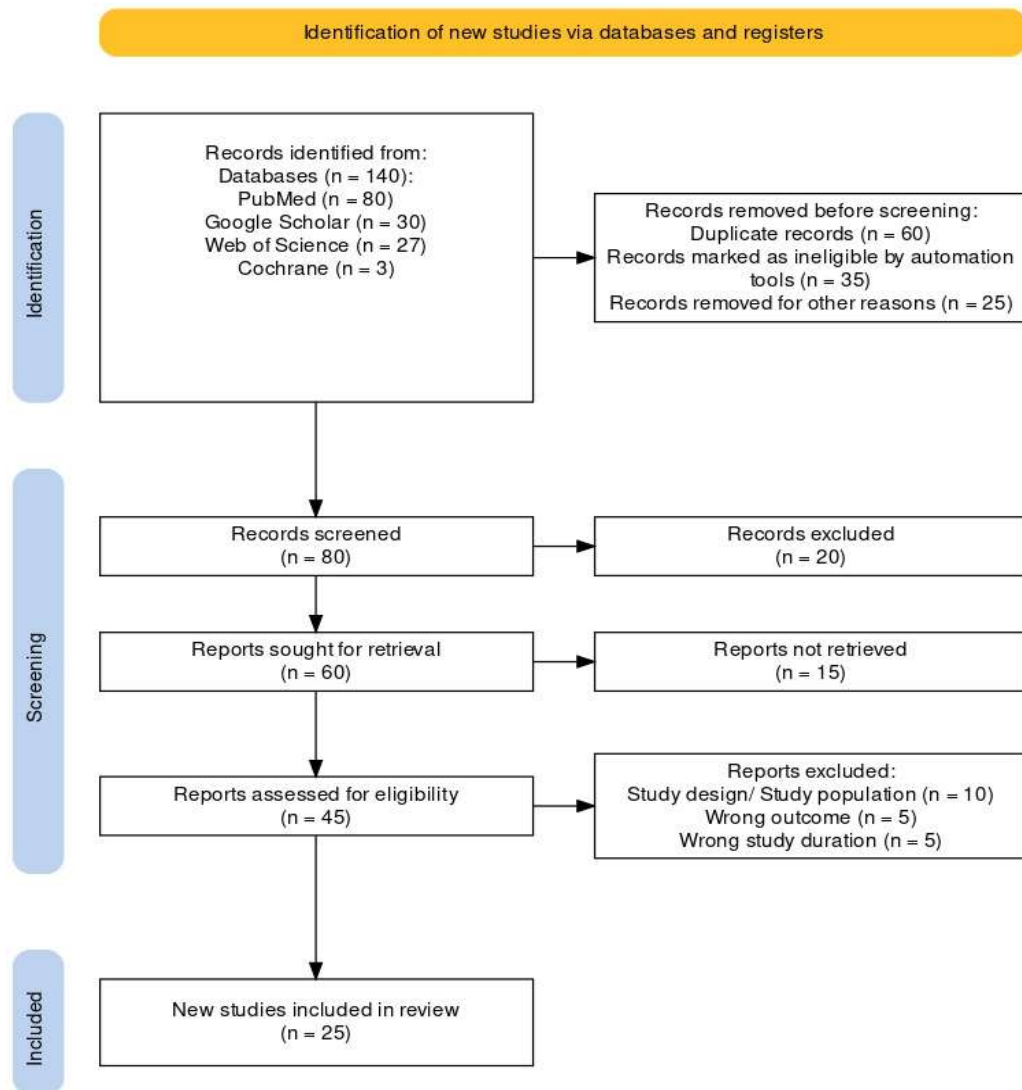
## 2.6 Type of outcomes

### 2.6.1 Data Extraction

Working separately, two researchers used predefined extraction forms to collect data from the studies included in the analysis. The collected data encompassed a range of information, such as the name of the first author, publication year, sample size, participant age, pattern identification, interventions in the experimental and control groups, treatment duration, outcomes, results, adverse events, and methodological aspects like randomization method, allocation concealment, and blinding method. The researchers ensured that the data extraction process was performed independently to maintain accuracy and reliability.

### 2.6.2 Data items

The total sample size for the selected literature (n=140) was scrutinized after the secondary screening protocol was completed. We used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) standards to create a flow diagram for the selected studies from journals and other independent resources. (Figure 1)



**Figure 1:** Prisma flow diagram for selection of studies reporting the number of records identified from each database or register searched

After the study selection process, we tabulated the study interventions one by one against the study population and the outcomes studied. Only the relevant themes of the outcome were mentioned in the synthesis table. Bias in the analysis was minimized by selecting high-quality research and thorough literature review, eliminating the double standard concerning peer review and informed consent applied to clinical research and practice, requiring peer reviewers to acknowledge conflicts of interest, and replacing ordinary review articles with meta-analyses. Systematic reviews and narrative reviews were frequently excluded from the literature to maintain the standards of the study. These guidelines detect and remove bias in the study protocol following Chalmers et al. 1990 stages of removing publication bias. (Chalmers et al., 1990) All the studies chosen for the meta-analysis were found to have a “low” overall ROB. A “traffic light” figure was plotted using this data for randomization. A summary of the ROB was also mentioned for collaborator convenience.

### 2.7 Quality assessment and Risk of Bias for systematic review:

All the studies selected for quality assessment were analyzed for publication bias. All the studies were manually checked for intervention characteristics, population demographics, and outcomes domains. All the studies eligible for the analysis were independently selected based on the Cochrane criteria for ROB. We calculated the ROB via the Cochrane Risk-of-Bias (version 2019) online tool. (Higgins et al., 2011) According to the Cochrane protocol,

the ROB algorithm assessed 5 domains of potential ROB. These domains were biased due to the randomization process, deviation from the intended intervention, missing outcome data, measurement of the outcome, and selection of the reported result.

Two researchers decoded all relevant data for risk assessment for meta-analysis. We sought digital/ online tools for ROB assessment of the studies selected for the meta-analysis. Cochrane Risk-of-Bias (version 3.5.1) online tool was used to assess 7 domains of the risk occurring in the primary studies. [ROBv2 Tool] These domains were random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias.

Continuous data was extracted. This data measured similar outcomes like substance use and externalizing symptoms. Using the data we created a “forest plot” using Review Manager (RevMan version 5.4) for the meta-analysis. Meta-analysis of 11 primary studies, was done using Revman (version 3.5.1).

### 3. Results

#### 3.1 Study Characteristics

The final sample for the systematic analysis included 25 studies, all of these studies used randomization out of which 23 favored herbal therapy while 2 did not favor our study. Sample sizes ranged from small to large. Follow-up data collection time points ranged from 2 months to 24 months. Outcomes for each study were averaged and Cohen’s d (effect size used to indicate the standardized difference between 2 means.) was calculated based on weighted averages across the studies. Combined outcomes favored Systemic Therapy. (Table 1)

**Table- 1. Introductory table showing study characteristic**

S. N.	Study design	Sample size (n) and duration	Experimental group	Control group	Outcomes	Ref No
1	randomized single-blind study	n=60, 60 days	Patients of Group A (n=20) were given Satapushpa-Shatavari (Anethum sowa & Asparagus racemosus) Powder, 5 grams thrice a day (t.d.s) per oral (p.o.). Patients of Group B (n=20) were given Anuvasan basti (medicated oil enema) of Satapushpa-Shatavari Ghrita (butter) 60 ml for 2 weeks with 1-week gap in between, Group C (n=20) received both the	No control group	The effectiveness of therapy is evident in its ability to consistently lower the ovarian volume and endometrial thickness in all three groups, Hirsutism and Quantity of menstrual flow showed significant improvement in Group C as compared to groups A and B.	(Mangalika et al., 2018)

			combination of Group A and B			
2	randomized single-blind controlled study	n=60, 90 days	Patients of Group B (n=20) received a 700 mg capsule p.o. daily containing an herbal mixture of Spearmint (250 mg), ginger (200 mg), cinnamon (150 mg), and <i>C. sinensis</i> (100 mg).  Group C (n=20) received both herbal mixture capsules with clomiphene Citrate (50–150 mg) daily	Group A (n=20) were given clomiphene citrate (CC) (50–150 mg) for 3 menstrual cycles	herbal mixture along with CC (Group C) has more beneficial effects on glycemic biomarkers of infertile PCOS (insulin, fasting blood sugar, glutathione peroxidase, malondialdehyde, Catalase, superoxide dismutase,), menstrual regulation, pregnancy rate, and serum antioxidant levels.	(Ainehchi et al., 2019)
3	randomized, triple-blinded, controlled trial	N=60, 56 days	Group A (n=30) <i>Salvia officinalis</i> (Sage) was given at 330 mg per day p.o.	Group B (n=30) placebo was given	Administering <i>S. officinalis</i> extract effectively reduces BMI and systolic blood pressure and improves insulin resistance markers in euglycemic PCOS patients.	(Amini et al., 2020)
4	randomized controlled trial	n=122, 90 days	Group A (n=60) 2 tablets of herbal medication (Tablet 1: <i>Cinnamomum verum</i> , <i>Glycyrrhiza glabra</i> , <i>Hypericum perforatum</i> , and <i>Paeonia lactiflora</i> . (750 mg extract of each tablet p.o.) Tablet 2: <i>Tribulus terrestris</i> 13500 mg extract) With Lifestyle intervention (calorie-controlled diet and exercise for at least 150 minutes/week including 90 minutes of aerobic activity)	Group B (n=62) Lifestyle intervention only	Group A estimated significant improvements were found compared with controls, for quality of life, body mass index, LH, insulin, blood pressure, anxiety, depression, stress, pregnancy rates, and PCOS symptoms.	(Arentz et al., 2017)
5	randomized clinical trial	N=150, 90 days	Group A=50 herbal medication combination containing <i>Vitex agnus castus</i> , <i>Foeniculum vulgare</i> . and <i>Daucus carota</i> - 2 capsules twice a day	Group B (n=50) (Metformin 500 mg Tablet t.d.s alone)	herbal medications (Group A) exhibit similar effects compared to metformin (Group B) for PCOS symptoms, BMI, menstruation bleeding, and regulation of menstrual cycle, Combination of both	(Bahman et al., 2019)



			(b.d) (166 mg extract of each herb p.o.) Group C=50 (herbal medication capsule 2 b.d. and metformin 1 tablet 500 mg t.d.s)		(Gropup C) did not show better results.	
6	Prospective, Single-arm, non-randomized clinical trial	n=15, 60 days	All Patients (n=15) received Vamana Karma (therapeutic vomiting) followed by Shatapushpadi Ghanavati 2 tablets (each 500 mg) b.d.	No control group	The combination of Vamana Karma (therapeutic vomiting) followed by Shatapushpadi Ghanavati proves highly effective in managing obesity, FBS, regulation of hormones in PCOS patients, and enhancing the likelihood of conception.	(Kamini et al., 2017)
7	Prospective randomized clinical trial	n=84, 56 days	Group A(n=42) 1 cinnamon capsule t.d.s (each one contained 500 mg cinnamon)	n=42 (placebo)	Cinnamon improved antioxidant status, malondialdehyde, and serum lipid profile in women with PCOS, suggesting its potential application in reducing risk factors associated with PCOS.	(Azam et al., 2018)
8	Non-randomized, single-arm clinical trial	n= 80, 60 days	All patients received polyherbal capsules of 500 mg b.d using extracts of Saraca indica, Vitex agnus castus, Embelica officinalis, and Symplocos racemosa., all extracts were used in equal ratio	No control group	Herbal capsule regularized menstruation and ovulation with improvement in FBS levels. Changes in free testosterone levels and ovarian morphology were also measured as secondary outcomes.	(Ishaq et al., 2021)
9	Prospective randomized control trial	n=47, 90 days	Group A (n=19) Chinese patent medicine Tian Gui Capsule (containing extract of Uncaria rhynchophylla, Cyathula officinalis, Gastrodia elata, Scutellaria baicalensis, Eucommia ulmoides, Leonurus japonica)- 500 mg b.d  Group B (n=11) was given Diane-35 tablet containing Ethinylestradiol (35	Group C (n=17) was given metformin 500 mg once at night	Group A patients showed decreased serum testosterone, FBS, sex hormone binding globulin and dehydroepiandrosterone sulfate (DHEA-S) levels, free androgen index fasting insulin, and left and right ovary volumes.	(Kuek et al., 2011)

			µg) and cyproterone acetate (2 mg) 1 tablet daily			
10	Open-labeled controlled clinical trial	n=48, 84 days	Group A(n=24) received flaxseed powder (30 g/day) plus lifestyle modification p.o	n=24 lifestyle modification alone	Group A showed a significant reduction as compared to group B in body Triglycerides, high-CRP, leptin, adiponectin, Body weight, and insulin compared to the baseline.	(Fatemeh et al., 2020)
11	Prospective randomized clinical Trial	n=35, 60 days	Group A(n=18) was given Dashamoola Taila Matra Basti (oil enema) Group B (n=17) was given Tila Taila Matra Basti (oil enema of sesamum oil). (Each 60 ml per day in the morning for 7 days in mid of menstrual cycle for 2 consecutive cycle were administered)	No control group	Dashamoola Taila effectively manages symptoms of PCOS as compared to Tila Tail.	(Karunagoda et al., 2010)
12	Prospective randomized clinical Trial	n= 40, 180 days	All 40 patients were given ayurvedic intervention. Day 1-14: Triphala Kwatha (Decoction of Terminalia chebula, Terminalia bellerica and Emblica officinalis) 30 ml b.d Day 15- 120: Shatavari, Shatapushpa and Guduchi (Tinospora) powder 5 gm each twice a day. Day 120-180: Powder of Shatpushpa and Atibala 5 gm each and 20ml Sahachara oil b.d	No control group	At the end of the treatment, show highly significant results on symptoms of PCOS including dysmenorrhea, Hirsutism, and skin discoloration. BMI was normal.	(Dayani et al., 2010)
13	Prospective randomized clinical Trial	n=45, 180 days	Group A(n=23) received Cinnamon 1.5 gm per day b.d	Group B (n=22) received a placebo	Data indicates that cinnamon enhances menstrual regularity, suggesting its potential as an effective treatment for certain PCOS cases. Insulin resistance or	(Kort and Lobo, 2014)

					serum androgen levels did not change for either group.	
14	Prospective randomized clinical Trial	n=28, 30 days	Group A (n=15) given Origanum majorana Tea- 50 ml twice a day	Group B (n=13) placebo	Marjoram tea significantly reduced DHEA-S, fasting glucose and insulin levels of PCOS.	(Haj-Husein et al., 2016)
15	Prospective randomized clinical Trial	n=60, 90 days	Group A (n=30) was given a combination of oral herbal-mineral drugs (Rajapravartini vati 2 tablets twice a day, Pushpdhanva Ras 2 tablets twice a day, Phalghrita: 15 ml b.d with milk) Group B (n=30) was given a combination of oral herbal-mineral drugs, Phalaghrita along with Yogbasti (Anuvasana basti with tila oil and Nirooha basti with Dashamoola decoction) for 8 days for 3 consecutive cycles after cessation of menstruation.	No Control Group	Group B showed statistically very significant results in improving Hirsutism, menorrhagia, oligomenorrhoea, dysmenorrhoea, serum LH & FSH.	(Bhagyashri and Ramesh, 2015)
16	open-label, single-arm, Non-randomized Trial.	n=58, 90 days	All patients received a patent herbal drug ovaryl tablet (containing Dashmool and Triphala)-1 tablet b.d	No control group	The treatment successfully addressed PCOS symptoms, including weight, hirsutism, and irregular cycles, while reducing cyst formation, serum insulin levels, and ovarian volume.	(Manish R et al., 2015)
17	Prospective randomized clinical Trial	n=32, 60 days	Patients of Group A (n=12) were given 60 ml of Shatapushpa Taila Matra Basti (STMB) once and 30 ml of Pathadi kwatha orally b.d for 7 days after cessation of menses in two consecutive cycles. Patients of group B	Group C (n=6) was given a placebo	The combined treatment of Pathadi Kwatha and STMB exhibits additional effectiveness in managing PCOS symptoms, promoting regular menstruation, weight reduction, follicular growth, and ovulation.	(Patel et al., 2012)

			(n=14) were treated with only STMB.			
18	Prospective single-arm, non-randomized clinical Trial	n=60, 180 days	3 Ayurvedic classical formulations, Rajahpravartini Vati (250 mg), Kanchanar Guggulu (500 mg.), and Varunadi Kashaya (20 ml with 40 ml lukewarm water) were given twice a day.	No control group	There was a negligible reduction in the mean score of the size of the cysts in the ovary but significant effects were observed in reducing the number of ovarian cysts, hirsutism, oligomenorrhea, and overall quality of life improvement in women with PCOS.	(Sannd et al., 2017)
19	open-label, parallel-group, randomized controlled clinical trial	n=110, 90 days	Group A(n=35) A patent drug polyherbal powder Dingkun 7 gm daily (containing Radix Ginseng, pilose antler, Radix notoginseng, Stigma croci, Radix angelica sinensis, Radix rehmannia preparata, and Asini corii colla, etc.) Group C (n=39) Polyherbal powder 7 gm and Diane-35 tablet 1 daily p.o.	Group B (n=36) Diane-35 tablet containing Ethinyl estradiol (35 µg) and cyproterone acetate (2 mg) 1 tablet daily	Group C produces a slight improvement in insulin sensitivity compared with groups A and B. Fasting glucose was significantly decreased in all 3 Groups.	(Deng et al., 2019)
20	Prospective randomized clinical trial	n=95, 180 days	Group A (n=48) Received a Chinese patented herbal medicine capsule (Heyan Kuntai) consisting of Radix rehmanniae, Rhizoma coptidis, Radix paeoniae Alba, Radix scutellariae baicalensis, Colla corii asini.- 4 capsules t.d.s	Group B (n=47) Placebo	BMI, waist-hip ratio, and blood glucose levels of all the patients of Group A significantly declined and also lowered the LH/FSH ratio, and testosterone levels.	(Liang et al., 2019)
21	Prospective randomized clinical Trial	n=80, 56 days	Group B (n=20) Persian herbal medicine 5 g per day (containing Foeniculum vulgare, Urtica dioica, Curcuma longa, and Daucus carota, all in equal ration)	Group A (n=20) 500 mg metformin hydrochloride bd	Body fat, BMI and fasting insulin, triglycerides, aspartate aminotransferase, and alanine aminotransferase were decreased the most in group D (herbal medicine + electroacupuncture), and Insulin sensitivity check	(Maryam et al., 2019)

			Group C (n=20) acupuncture-20 sessions Group D (n=20) herbal medicine with acupuncture		index decreased in all groups.	
22	Prospective, single- arm, Non- randomized clinical Trial	n=30 , 90 days	all patients (n=30) were given Daśmūla Niruha Basti (medicated decoction enema) followed by 5 ml Śatāvadhī Tail Uttar Basti (Intrauterine instillation of medicated oil). (After menstruation Niruha Basti for 3 days has been given on the 5 <sup>th</sup> , 6 <sup>th</sup> 7 <sup>th</sup> day and Uttara Basti for 3 days (on the 8 <sup>th</sup> , 9 <sup>th</sup> , and 10 <sup>th</sup> days) in every month	No control group	Basti appears effective in managing PCOS by locally influencing ovarian cysts and reducing ovarian volume, with limited impact on hormonal levels without any adverse reaction.	(Katkar et al., 2016)
23	open- label, single- arm, non- randomized clinical trial	n=50, 90 days	All patients (n=50) received Trigonella foenum graecum seed extract- 2 capsules of 500 mg per day p.o	No control group	Herbal capsules caused significant decrease effects on ovarian volume, cyst reduction, and hormonal markers assessed through sonographic scans and also showed significant results on LH, FSH, LH/FSH ratio, and menstrual cycle regulation in PCOS patients.	(Anand et al., 2015)
24	randomized clinical Trial	n=84, 112 days	Group A (n=42) Nigella sativa oil soft gel capsules (500 mg, 2 capsules at night p.o)	Group B (n=42) placebo group	N. sativa capsules led to a decrease in insulin levels, serum androgen, LH, and LH/FSH ratio with an increase of sex hormone binding globulin and serum estradiol level that led to improved menstrual cycles with normal ovulation.	(Naeimi et al., 2019)
25	Prospective randomized clinical Trial	n=42, 30 day	Group A (n=21) All patients were given Spearmint herbal Tea 50 ml twice a day	Group B (n=21) Placebo	Free and total testosterone levels were significantly reduced in group A. Increased LH and FSH, self-reported degree of hirsutism also	(Paul, 2010)

					reduced in PCOS patients.	
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### 3.2 ROB Plot

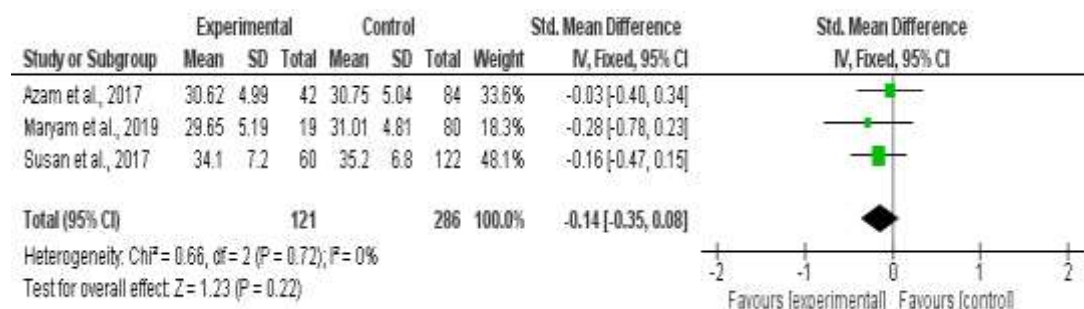
As mentioned (Anand et al., 2015) earlier, ROBv2 was used to assess the risk for all the primary studies selected for meta-analysis. The studies with a “low” overall ROB were then selected. We used the ‘Cochrane Risk-of-Bias tool’ to create a “traffic lights” plot for the final assessment of 11 studies. (Figure 2)



**Figure 2:** Traffic lights plot for the ROB for the reviewed studies.

#### 3.2.1 Forest plot for BMI

Three individual studies were plotted for continuous data. A random effect model was selected to calculate the deviation and differences in the mean (m) and standard deviation (SD) using the Standard Mean Difference (SMD) scale. We calculated the confidence interval (CI =95%) on the horizontal axis while the “point estimation” was represented by green squares on the plot. The total sample size (n=84,80,122) changed to (42,19,60) due to the exclusive involvement of the people taking the herbal medication. The central vertical line refers to a state of “no effect”. This forest plot summarizes each study and provides an estimated overall quantitative value for all the combined effects. The overall effect size was calculated in terms of Cohen’s d, CI=95% (-0.03,-0.28,-0.16). The individual effect size was found to be significant. The heterogeneity was calculated to be: Tau<sup>2</sup> =0.00, Chi-square =0.66, df =2 (p-value =0.72) I<sup>2</sup>= 0%. The analysis for the overall effect was found to be Z=1.23 (p=0.22). The individual effect of all the studies favored the experimental group, i.e. The population receiving one or more herbal therapies. The mean difference was found to be -0.03 with a CI of 95% (-0.40,0.34) for the study conducted by Azam et al. 2018; whereas the Mean Difference (MD) was -0.28 with a CI of 95% (-0.78,0.23) for Maryam et al., 2019 and the MD of -0.16 with a CI of 95% (-0.47,0.15) by Susan et al., 2017. We calculated SD from SMD using the SMD standardization in Revman and basic statistical tools for variance. The results of these studies were found to favour herbal therapy interpreting herbal products a significant role in decreasing BMI for the treatment of PCOS. (Figure 3)

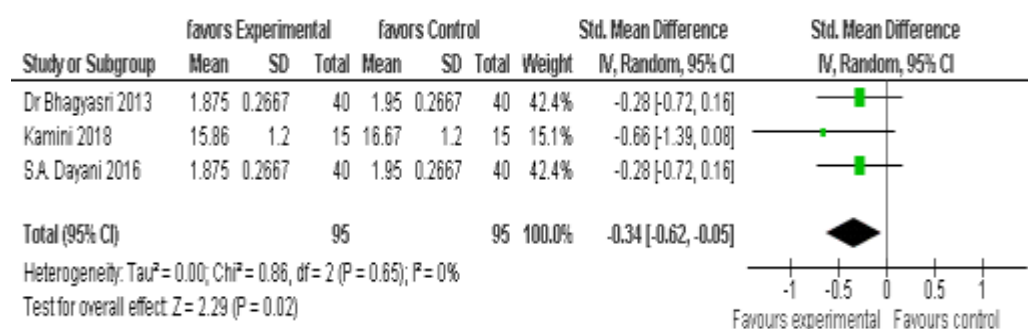


**Figure 3:** Forest plot for (BMI) shows the effect of herbal products on BMI [CI=95% (0.35,0.15), p=0.22]

The forest plot for BMI shows the effect of herbal products on BMI in women with PCOS, a hormonal disorder that affects fertility and metabolism. The plot indicates that herbal products have a significant and favorable effect on reducing BMI in women with PCOS, compared to placebo or no treatment. This suggests that herbal products may be a useful adjunct therapy for PCOS, as lower BMI may improve hormonal balance and ovulation

### 3.2.2 Forest Plot for Hirsutism

Three individual studies were plotted for continuous data. The total sample size (40,15,40) remained the same. The overall effect size was calculated in terms of Cohen’s d, CI=95% (-0.62,-0.05) with a mean difference of -0.34. The individual effect size was found to be significant for all 3 research. The heterogeneity was calculated to be: TAU<sup>2</sup> =0.00, Chi-square =0.86, df=2 (p-value =0.65) I<sup>2</sup>= 0%. The analysis for the overall effect was found to be Z=2.29 (p=0.02). The individual effect of all studies (Bhagyashri et al. 2015, Kamini et al. 2017, and Dayani et al. 2010 ) favored the experimental group. The mean difference was found to be -0.28 with a CI of 95% (-0.72,0.16) for the study conducted by Bhagyashri et al. 2015, whereas MD was -0.66 with a CI of 95% (-1.39,0.08) for Kamini et al. 2017 and the MD of -0.66 with CI of 95% (-0.72,0.16) by Dayani et al. 2010. The results of these studies were found to favour herbal therapy interpreting herbal products a significant role in decreasing Hirsutism during the treatment of PCOS. ( Figure 4)

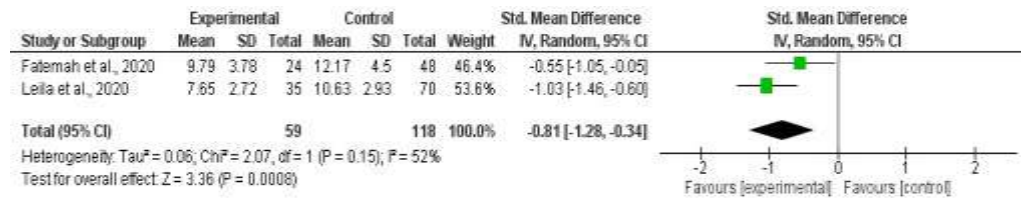


**Figure 4:** Forest plot for hirsutism [CI=95% (-0.62, -0.05), p=0.02]

### 3.2.3 Forest plot for insulin resistance

Two individual studies were plotted for continuous data. The total sample size (48,70) changed significantly to (24,35) due to the exclusive involvement of the people taking herbal medication. The overall effect size was calculated in terms of Cohen’s d, CI=95% (-1.28,-0.34). The individual effect size was found to be significant for both research. The heterogeneity was calculated to be: TAU<sup>2</sup> =0.06, Chi-square =2.07, df =1(p-value =0.15) I<sup>2</sup>= 52%. The analysis for the overall effect was found to be Z=3.36 (p=0.0008). The individual effect of two studies (Fatemeh et al.,2020 and Laila et al.,2020) favored the

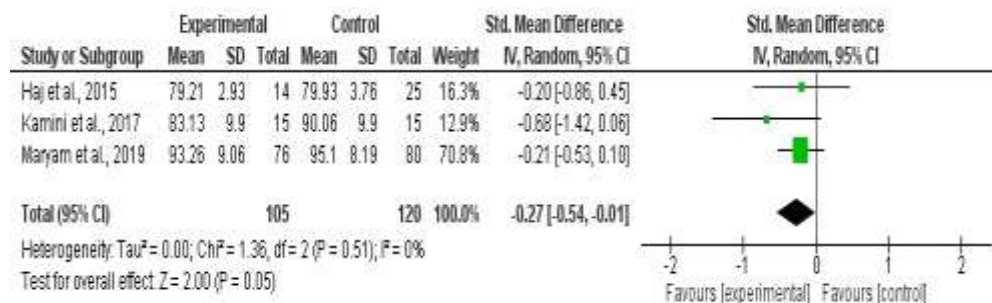
experimental group i.e. the population receiving one or more herbal therapies. The mean difference was found to be -0.55 with a CI (CI) of 95% (-1.05,-0.05) for the study conducted by Fatemeh et al. 2020; whereas MD was -1.03 with a CI of 95% (-11.46,-0.60) for Laila et al .2020. The results of these studies were found to favor herbal therapy interpreting herbal products a significant role in decreasing insulin levels and decreasing insulin resistance for the treatment of PCOS. (Figure 5)



**Figure 5: Forest plot for insulin resistance [CI=95% (-1.28, -0.34) p=0.0008]**

3.2.4 Forest plot for Glucose:

Three individual studies were plotted for continuous data. The total sample size (25,15,80) changed to (14,15,76). The overall effect size was calculated in terms of Cohen’s d, CI=95% -0.54, -0.01) with a mean difference of -0.27. The individual effect size was found to be significant for all three research. The heterogeneity was calculated to be: TAU2 =0.00, Chi-square =1.36 , df =2(p-value =0.51) I2= 0%. The analysis for the overall effect was found to be Z=2.00 (p=0.05). The individual effect of all studies (Haj et al.,2015 Kamini et al. 2017, Maryum et al) favored the experimental group. MD was found to be -0.20 with a CI of 95% (-0.86,0.45) for the study conducted by Haj et al., 2015; whereas MD was -0.68 with a CI of 95% (-1.42, 0.06) for Kamini et al. 2017 and the MD of -0.21 with CI of 95% (-0.53,0.10) by Maryam et al., 2019. The results of these studies were found to favour herbal therapy interpreting herbal products a significant role in decreasing fasting blood glucose levels. (Figure 6)



**Figure 6: Forest plot for fasting blood glucose [CI=95%, (0.54, -0.01), p=0.05]**

3.2.5 Forest plot for FSH

Three individual studies were plotted for continuous data. The total sample size (50,25,42) changed to (50,14,21). The central vertical line refers to a state of “no effect”. This forest plot summarizes each study and provides an estimated overall quantitative value for all the combined effects. The overall effect size was calculated in terms of Cohen’s d, CI=95% -0.39,0,17) with a mean difference of -0.11. The individual effect size was found to be significant for two of three researchers (Anand et al 2015, Paul et al., 2010) favoring the experimental group while one was showing results towards the control group (Haj et al., 2015). The heterogeneity was calculated to be Tau<sup>2</sup> =0.00, Chi-square =0.88 , df =2 (p-value =0.64) I2= 0%. The analysis for the overall effect was found to be Z=0.76 (p=0.45). The individual effect of two studies (Paul et al.,2010 and Anand et al.,2015) favored the experimental group while one (Haj et al.,2015) favored the control group. MD was found to be -0.22 with a CI of 95% (-0.61,0.18) for the study conducted by Anand et al 2015;



whereas MD was 0.15 with a CI of 95% (-0.51,0.80) for Haj et al .2015 and the MD of -0.09 with CI of 95% (-0.61,0.44) by Paul et al., 2010. The results of these studies were found to favour herbal therapy interpreting herbal products a significant role in decreasing FSH levels. (Figure 7)

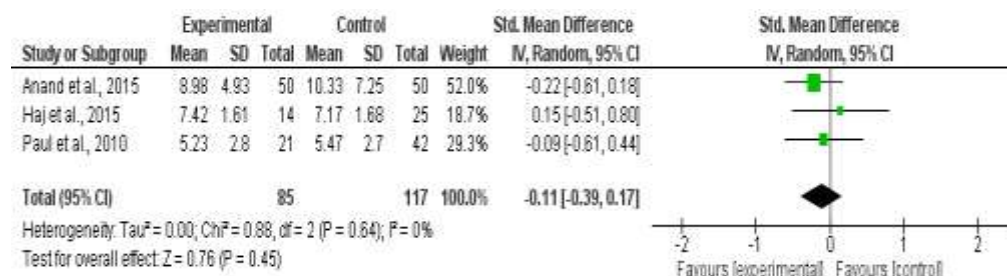


Figure 7: Forest plot for FSH [CI=95% (-0.39, 0.44), p=0.45]

Table -2. Results table tabulating RCT used in meta-analysis

S.N	Author name (Study)	Mean Favoring experiment	S.D	(n)	Tau <sub>2</sub>	Chi-square	Z	df	P value	I <sup>2</sup>	CI	Mean difference
1	Azam et al., 2018	30.62	4.99	84	0.00	0.66	1.23	2	0.22	0	-0.40, 0.34	-0.03
2	Maryam et al., 2019	29.65	5.19	80	0.00	0.66	1.23	2	0.22	0	-0.78, 0.23	-0.28
3	Susan et al., 2017	34.1	7.2	60	0.00	0.66	1.23	2	0.22	0	-0.47, 0.15	-0.16
4	Bhagyashri et al., 2015,	1.875	0.27	40	0.00	0.86	2.29	2	0.02	0	-0.72, 0.16	-0.28
5	Kamini et al., 2017	15.86	1.2	15	0.00	0.86	2.29	2	0.02	0	-1.39, 0.08	-0.66
6	Dayani et al., 2010	1.875	0.26	40	0.00	0.86	2.29	2	0.02	0	-0.72, 0.15	-0.28
7	Fatemeh et al., 2020	9.79	3.78	48	0.06	2.07	3.36	1	0.008	52%	-1.05, 0.05	-0.55
8	Leila et al., 2020	7.65	2.72	70	0.06	2.07	3.36	1	0.008	52%	-1.46, -0.60	-1.03
9	Haj et al. 2015	79.21	2.93	25	0.00	1.36	2	2	0.05	0%	-0.86, 0.45	-0.20

1	Anand et al., 2015	8.98	4.93	50	0.00	0.88	0.76	2	0.45	0%	-0.61, 0.18	-0.22
1	Paul et al., 2010	5.23	2.8	42	0.00	0.88	0.76	2	0.45	0%	-0.61, 0.44	-0.09

**(Abbreviations:** S.D- Standard Deviation, n-sample size, Tau<sup>2</sup> =Variance, df- degree of freedom, Z value-Percentage of observation that falls between two points, p value-probability value, I<sup>2</sup>-Heterogeneity, CI-Confidence interval)

#### 4. Discussion

##### 4.1 Findings for Clinical Outcomes

This study explored all the possible relationships between PCOS and clinical outcomes like hirsutism, insulin resistance, weight loss, Body mass index, hormones, and fasting blood glucose. We included all RCTs in the analysis and from a broad search we were able to find out the poolable data of 25 studies. This study showed the importance of herbal products in PCOS. We found out that herbal therapies have minimal side effects with maximum advantages. Based on this systematic review, herbal interventions tend to have more benefits in managing FBS levels, Insulin sensitivity, and Hirsutism, which is found statistically significant. The outcomes, such as BMI and FSH, were not statistically significant. Herbal products proved to reduce BMI, insulin resistance, fasting blood glucose levels, hirsutism, and balance levels of hormones (FSH and LH).

The study's results also indicated a notably large quantity of RCTs on herbal medicine's use for PCOS over the last decade. These RCTs displayed a bias toward favorable conclusions. This inclination could be attributed to the selective reporting of positive outcomes in original research on this intervention. Additionally, most of the primary studies included in the systematic reviews were poorly designed RCTs, significantly compromising the quality of evidence. This might be due to the complexity and severity of the disease and there is a strong demand for evidence regarding potential alternative medicines

We plotted 5 forest plots to assess the beneficial effects of herbal products in the treatment of PCOS. Table 3 indicates the results of the meta-analysis for all the outcomes measured in this study. We found out that many herbal interventions like herbal medications, acupuncture, herbal detoxification procedures like Basti therapy, etc. proved to be beneficial in managing the patients of PCOS when compared to placebo or allopathic drugs like metformin.

In our analysis for BMI, we concluded that treatment with herbal products can significantly reduce obesity [CI=95% (-0.35. 0.08), p=0.22], and consequently provide a safety window to women suffering from PCOS. Weight loss and prevention of PCOS-related metabolic abnormalities, like insulin resistance, are crucial for managing PCOS. Excess weight worsens hormonal imbalances and insulin resistance.(Beydoun et al., 2009) In this research, we found that by adopting dietary changes and regular physical activity, individuals can improve insulin sensitivity, regulate menstrual cycles, lower androgen levels, and enhance metabolic health.

In the context of PCOS, the prevalence of insulin resistance is notably high. This condition results in elevated blood glucose levels, heightening the risk of developing type 2 diabetes and cardiovascular complications. Moreover, it triggers a continuous surge in estrogen production by the ovaries, exacerbating the symptoms experienced by women with PCOS(Purwar and Nagpure, 2022). However, the adoption of lifestyle modifications such as adhering to a well-balanced diet, engaging in regular physical activity, and maintaining a healthy body weight can significantly enhance insulin sensitivity and impede

the progression of metabolic irregularities in PCOS.(Zhao et al., 2023) Analysis shows that herbal interventions can significantly reduce insulin resistance and increase insulin sensitivity [CI=95% (-1/28, -0.34),  $p < 0.0008$ ], improving patient prognosis and providing long-term relief.

Women with PCOS are at risk of developing T2DM and impaired glucose tolerance(Xia et al., 2023). The current study showed that herbal interventions can decrease high blood sugar levels [CI=95% (-0.54, -0.01),  $p = 0.05$ ], providing beneficial effects in women with PCOS.

Associate with the poor ovulatory response, the LH/FSH ratio is increased in PCOS.(Zhu et al., 2013) Investigating the effects of herbal treatment on FSH levels in patients with PCOS, we found that herbal therapy resulted in a significant decrease in FSH levels suggesting its effectiveness in managing hormonal imbalances associated with PCOS. With herbal treatment, this ratio was shown to decrease, improving PCOS symptoms in the studied populations in our meta-analysis [CI=95% (-0.39, 0.17),  $p = 0.45$ ]. The findings highlight the promising role of herbal therapy as a viable treatment option for PCOS offering potential benefits in terms of hormone regulation and weight management.

Hirsutism is the manifestation of hyperandrogenism in women with PCOS. Elevated levels of androgens can cause vellus hair follicles to produce larger, darker, terminal hair, which leads to hirsutism. Acne and female pattern hair loss are also clinical manifestations. (Spritzer et al., 2016). The results of this study were found to favor herbal therapy interpreting a significant role in decreasing hirsutism during the treatment of PCOS [CI=95% (-0.62,-0.05),  $p = 0.02$ ].

This systematic review represents the most updated and comprehensive analysis of the data on the herbal approach for PCOS to date. One limitation of this study is that certain investigations were characterized by their small sample sizes and methodological shortcomings. In this analysis, few findings were limited by a small sub-group sample size i.e. Kamini, et al. 2017 ( $n = 15$ ) and Haj et al.. 2015 ( $n = 28$ ) the study was underpowered for the small number of PCOS women and was assessed as low-quality due to not reporting baseline characteristics of subgroups. Due to the nature of the interventions, participants couldn't be blinded. However, the objective nature of the outcomes, such as hirsutism, insulin resistance, weight loss, hormone levels, and fasting blood glucose, ensured that they remained unaffected by the lack of blinding of participants. Additionally, the diversity of interventions posed challenges in making some comparisons, making it challenging to conclude. The sample sizes in the included studies were also relatively small, emphasizing the need for a large-scale multicenter study on herbal interventions for PCOS. Consequently, most studies had a follow-up duration of just two months. Lastly, the limited number of studies included in the meta-analysis raises the possibility of a type I error.

#### 4.2 Interventions for PCOS

In contemporary times, PCOS is continuously rising, primarily attributable to sedentary lifestyles, environmental contamination, excessive consumption of unhealthy dietary choices etc. Herbal drugs are multifaceted interventions with antagonistic and synergistic interactions between molecules. The consistent utilization of herbal interventions offers a safe and more efficacious approach to the treatment of PCOS, effectively suppressing the underlying pathophysiological events that contribute to cyst formation in PCOS. The integration of herbal interventions emerges as a promising strategy for enhancing the effectiveness of PCOS treatment. Distinct herbal agents employ diverse mechanisms of action to address PCOS, encompassing the modulation of prolactin levels, facilitation of FSH, reduction in LH, ovulation induction, anti-androgenic properties, restoration of glucose sensitivity, normalization of menstrual cyclicity, and modulation of enzyme activity(Lakshmi et al., 2023).

Many herbs (*Urtica dioica*, *Curcuma longa*, and *Daucus carota*) have anti-inflammatory and antioxidant properties. Studies claimed its role in weight loss and improved glucose and insulin levels (Yatoo et al., 2018).

Shatavari (*Asparagus racemosus*) has gained medicinal popularity and is considered to be a potent drug of choice for improving reproductive health in women. Shatavari is used to correct hormonal imbalances and enhance follicular maturity. The studies suggest that Shatavari leads to normalizing the physiology of the ovary, reduction of ovarian volume, and prompt growth and development of ovarian follicles. (Moini Jazani et al., 2019)

Shatpushpa is a commonly used ayurvedic medicine, with ingredients of many ayurvedic formulations like Shatpushpa Ghan Vati, Shapusha Churna, Shatpushpa Tail Basti etc. It is called Indian dill or Sowa (*Anethum sowa*) Shatpushpa exhibits phytoestrogenic activity. Due to its adaptogenic activity, it can be useful in both hypo-estrogenic and hyper-estrogenic states in the body, so it could be useful to maintain menstrual cyclicity. It also induces ovulation and is effective in the management of infertility. (Patel et al., 2012)

Fennel (*Foeniculum vulgare*), is one of the important herbal medicines used for reproductive health (called 'Mishreya' in Ayurveda). It is known as an estrogenic compound and is used to treat several menstrual irregularities and provide effective measures to manage PCOS symptoms. Fennel also acts as an antioxidant and anti-diabetic agent.

*Limium usitatissimum* (Flax seed), has been also introduced as an estrogenic and anti-diabetic agent. It decreases androgen levels and reduces the increased testosterone level in the blood and also regulates the frequency of menstrual cycles, which is useful for treating PCOS [46]. Studies proved its benefit in reducing ovarian volume and follicle size. (Nowak et al., 2007)

*Trigonella foenum-graecum* commonly known as "fenugreek". Clinical trials demonstrated that it is effective in reducing the cyst size, as well as ovarian volume, balancing the LH/FSH ratio, and regulating menstrual cyclicity. It also acts as a hypoglycemic agent and reduces insulin sensitivity. (Hassanzadeh et al., 2013)

The *Vitex agnus-castus* corrects high estrogen-dependent hormonal irregularities or premenstrual syndrome and reduces the associated symptoms. The extract of the *Vitex agnus-castus* changes the amount of sex hormones and their balance. It reduces the LH levels which reverses the LH / FSH ratio and reverses the overproduction of androgen. (Saul, 2017)

Cinnamon is useful for regulating the menstrual cycle and improving reproductive health. Cinnamon increases glucose uptake and glycogen production and increases insulin receptor phosphorylation, increasing insulin sensitivity. Cinnamon has antioxidant properties, it reduces body fat and glucose level. (Dou et al., 2018)

Herbal tea offers benefits to those suffering from PCOS, from correcting hormonal imbalances to reducing insulin resistance. Recent scientific investigations have unveiled that *Mentha spicata* (spearmint) herbal tea possesses antiandrogenic attributes in females presenting hirsutism. It exerts regulatory control over the LH and FSH blood ratio, thus exhibiting potential utility in the therapeutic management of PCOS. (Mehraban et al., 2020) Consumption of *Salvia officinalis* (sage) tea may exert an influence on oxidative status, culminating in a reduction of blood glucose levels and atherogenic indices. Consequently, it may manifest cardioprotective effects among women afflicted by PCOS (Ghowsi et al., 2020). *Origanum majorana* (marjoram) tea effectively modulates the hormonal profile of women with PCOS, it was found to improve insulin sensitivity and reduce the levels of adrenal androgens (Rababa'h et al., 2020).

There are several Ayurvedic formulations that claim a promising role in managing symptoms of PCOS. In this analysis, Rajapravartini vati, Pushpdhanva Ras, Phalghrita and

Kanchnar guggulu proved its efficacy in managing PCOS. They encourage ovulation and remove ovarian cysts, thus showing fertility benefits.

Alternative medicine presents a promising approach to treating PCOS. In Ayurvedic therapy of medicine, basti therapy is gaining recognition nowadays for the treatment of PCOS and is well practiced with substantial results. In basti therapy liquid form of medicines (either decoction or/medicated oil of herbs) is delivered through the rectal route, is absorbed through a mucosal layer of the rectum, and enters into systemic circulation.(Auti et al., 2013) According to the research, this rectal administration of medicine stimulates the enteric nervous system, triggering stimulatory signals for the Central Nervous System. These signals activate  $\beta$ -endorphin within the gastrointestinal tract, which subsequently inhibits the release of GnRH and aids in regulating the HPO axis, ultimately leading to the normalization of the ovarian cycle.(Chouhan and Garg, 2023)

Ayurveda also presents another way of detoxification called Vamana (therapeutic emesis). Vamana is a procedure in which toxins and waste products are eliminated through the oral route. Studies claim that eliminating toxins clears the obstruction of channels and improves female reproductive health.(Asmabi and Jithesh, 2022; Best et al., 2017) It helps in balancing hormones, boosts fertility, and helps in reducing BMI. PCOS is a metabolic condition, Vamana aids in enhancing the body's metabolism, resulting in weight reduction. It particularly targets liver metabolism, which plays a crucial role in hormone production. Furthermore, there is a direct relationship between obesity and estrogen. Weight loss not only reduces glucose levels and circulatory androgens but also helps with ovulation and thus increases the pregnancy rate in obese women with PCOS(Best et al., 2017).

The use of acupuncture (involving the insertion of needles into the skin) in PCOS has recently gained increased popularity worldwide. Acupuncture potential to impact  $\beta$ -endorphin production, which may lead to GnRH and then consequently impact ovulation, fertility, and the menstrual cycle. Clinical data has also revealed its importance in regulating FSH, and LH, improving insulin sensitivity, and decreasing testosterone in patients with PCOS(Wu et al., 2020).

Lifestyle modification (LSM), must be the first-line treatment for PCOS patients with obesity. Many studies proved that LSM, such as a healthy diet and exercise has a positive effect on reproductive function regarding menstrual irregularity, and hormonal results. LSM helps to lower blood sugar and prevent insulin resistance, as well as reduce weight and BMI(Moran et al., 2006). Weight reduction also confers notable benefits in hyperandrogenism, and hirsutism, ultimately leading to their complete resolution(Best et al., 2017).

## **5. Conclusion**

According to the present meta-analysis, herbal interventions have a positive impact on all aspects of PCOS. The analysis looks deeply into a condition called PCOS, which affects different conditions like reproduction, hormones, and how they process energy. Because PCOS is so complicated, it's important to use many different ways to understand and overcome PCOS. In this review, a total of 25 studies involving herbal interventions exhibited beneficial effects on PCOS. Meta-analysis was done on 11 primary studies, including 779 women with PCOS. Based on this systematic review, herbal interventions tend to have more benefits in managing FBS levels, Insulin sensitivity, and Hirsutism, which is found statistically significant. It's also really important to make changes in how we live, like lifestyle. Traditional treatments like Ayurveda and plant-based remedies have shown good results, in managing PCOS. By using all these different ways, we can make better ways to treat PCOS and help women to be healthier.

## **6. Limitations**

The limited number of studies could affect the generalizability of findings. The diversity in herbal formulations, dosages, and participant attributes introduces substantial variability in

treatment outcomes, limiting the study's ability to draw consistent conclusions. This heterogeneity complicates the establishment of clear recommendations for clinical practice and underscores the need for cautious interpretation of findings. Subgroup analyses might help address this limitation but could add complexity to the result interpretation. Publication bias may influence the availability of studies in databases, skewing the overall picture. Additionally, the short-term nature of some studies may not fully capture long-term effects. Lack of standardization in outcome measures and potential confounding variables could undermine result validity. Finally, cultural and regional differences in herbal usage might limit applicability across populations.

## 6. Conflict of Interest – Nil

## 7. Author contribution

Visualization, conceptualization, formal analysis, writing- Chouhan P.; Data curation, review, editing- Garg A.K.

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