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Polycystic Ovarian Syndrome: A brief review on the role of Allopathic and Herbal Treatment

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Abstract

Polycystic ovarian syndrome (PCOS) is the most frequent endocrinopathy in women of reproductive age, characterized by hyperandrogenism and chronic oligo/ anovulation. PCOS is a complex illness that is impacted and complicated by a variety of genetic and environmental factors. The disruption of reproductive hormones such as LH, FSH, oestrogen, and testosterone disrupts the normal menstrual cycle and can result in oligomenorrhoea and amenorrhea-like abnormalities. Although there are significant variations between people, PCOS is characterized by hyperandrogenism, irregular menstruation, and different sized ovarian cysts. Polycystic ovarian syndrome (PCOS) is the most frequent endocrinopathy in women of reproductive age, characterized by hyperandrogenism and chronic oligo/ anovulation. PCOS is a complex illness that is impacted and complicated by a variety of genetic and environmental factors. Additionally, these women most likely have a higher risk of ovarian cancer, venous thromboembolism, cardiovascular and cerebrovascular events, and other illnesses. In addition to its enormous economic burden (an annual health-care expenditure of $5.39 billion in the United States in 2019), PCOS has a negative impact on the long-term health of affected women. The most prevalent endocrine condition, known as polycystic ovary syndrome (PCOS), affects 6%–8% of women globally who are of reproductive age. The first studies to ascertain prevalence in a medically unselected (unbiased) population were started by Azziz and colleagues, who reported PCOS prevalence's ranging from 4% to 6.6% among unselected

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reproductive-age women living in the Southeast of the United States using the NIH 1990 criteria. The demand for herbal medications has developed as a result of high economic costs and a large number of unfavourable side effects linked with the use of allopathic drugs. Herbal plants have been a key source of therapeutic remedies since ancient times. Exceptionally, despite the huge transformation in the pharmaceutical area, the use of herbal treatments is expanding day by day in underdeveloped countries.

Keywords: PCOS, Polycystic ovarian syndrome, endocrinopathy

1. Introduction:

The most common endocrinopathy in women of reproductive age is polycystic ovarian syndrome (PCOS), which is characterised by persistent oligo/ anovulation and hyperandrogenism. Numerous genetic and environmental variables both affect and aggravate PCOS, making it a complex disorder(Johnson, 2014)(Macut et al., 2015)(Daan et al., 2014)(Macut et al., 2019). Menstrual irregularities, polycystic ovaries, and elevated androgen levels (which cause hirsutism and acne) are the biochemical and clinical characteristics that characterise PCOS(Abdalla et al., 2020). The regular menstrual cycle is thrown off when reproductive hormones including LH, FSH, oestrogen, and testosterone are disrupted. This can cause oligomenorrhoea and amenorrhea-like disorders. PCOS is characterised by hyperandrogenism, irregular menstruation, and variously sized ovarian cysts, albeit there are important individual variances. The most common endocrinopathy in women of reproductive age is polycystic ovarian syndrome (PCOS), which is characterized by persistent oligo/ anovulation and hyperandrogenism. Numerous genetic and environmental variables both affect and aggravate PCOS, making it a complex disorder(Johnson, 2014)(Macut et al., 2015)(Daan et al., 2014)(Macut et al., 2019). Menstrual irregularities, polycystic ovaries, and elevated androgen levels (which cause hirsutism and acne) are the biochemical and clinical characteristics that characterize PCOS(Abdalla et al., 2020). The regular menstrual cycle is thrown off when reproductive hormones including LH, FSH, oestrogen, and testosterone are disrupted. This can cause oligomenorrhoea and amenorrhea-like disorders. PCOS is characterized by hyperandrogenism, irregular menstruation, and variously sized ovarian cysts, albeit there are important individual variances. Teenagers who are at a high risk of developing a multitude of comorbidities, such as obesity, type II diabetes, infertility, endometrial dysplasia, cardiovascular illnesses, and mental disorders, initially experience this multifactorial syndrome(Bulsara et al., 2021). PCOS has a detrimental effect on the long-term health of affected women in addition to its significant financial burden ($5.39 billion will be spent on healthcare annually in the US in 2019)(Azziz et al., 2005)(March et al., 2010)(Yildiz et al., 2012)(Stener-Victorin & Deng, 2021). Among the metabolic abnormalities seen in PCOS patients were insulin resistance (IR), hyperinsulinemia, and dyslipidemia(wu et al., 2012)(Wu et al., 2014)(Corbould et al., 2005)(Mu et al., 2021). The metabolic abnormalities in PCOS patients included dyslipidemia, hyperinsulinemia, and insulin resistance (IR)(Xita et al., 2007). Postmenopausal women with PCOS are more prone to develop metabolic and cardiovascular comorbidities, even while menopausal women without PCOS experience an improvement in hyper androgenic symptoms. Endometrial cancer, T2DM, metabolic abnormalities, infertility, obstetrical issues, and mood disorders are more prevalent in women with PCOS. A increased risk of ovarian cancer, venous thromboembolism, cardiovascular and cerebrovascular events, as well as other disorders, is also most likely present in these women(Azziz et al., 2016). Insulin

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resistance, which manifests most frequently in obese or overweight women but also frequently in lean PCOS women, is now widely accepted as a key contributing component in this complex condition. By collaborating with luteinizing hormone (LH) on ovarian steroidogenic enzymes and the liver's production of sex hormone binding globulin (SHBG), it induces hyperandrogenism(De Leo et al., 2016). PCOS' metabolic problem is connected to continuous low-grade inflammation in addition to ovarian failure(Long et al., 2017). The general public and medical communities have been more aware of polycystic ovarian syndrome in recent years due to the knowledge that these women are predisposed to metabolic syndrome and its accompanying comorbidities(Norman et al., 2007). Although not always present, obesity is a common illness. These traits are often connected to elevated levels of luteinizing hormone and androgen, but normal or low blood follicle-stimulating hormone levels(Stein & Leventhal, 1935). Infertility, irregular menstrual cycles, and hirsutism are the most prevalent illnesses encountered in PCOS patients. PCOS has a variety of clinical traits that vary in severity. Women with PCOS have also been found to have increased risks of endometrial cancer (EC), metabolic syndrome, type 2 diabetes mellitus (DM), and cardiovascular disease (CVD)(Rocca et al., 2015). One crucial aspect of polycystic ovarian syndrome is the temporal progression of the symptoms. Adolescents frequently experience persistent symptoms that get worse with time(Setji & Brown, 2014).

1.1 Risk factor:

Teenagers who are at a high risk of developing a multitude of comorbidities, such as obesity, type II diabetes, infertility, endometrial dysplasia, cardiovascular illnesses, and mental disorders, initially experience this multifactorial syndrome(Bulsara et al., 2021). PCOS has a detrimental effect on the long-term health of affected women in addition to its significant financial burden ($5.39 billion will be spent on healthcare annually in the US in 2019)(Azziz et al., 2005)(March et al., 2010)(Yildiz et al., 2012)(Stener-Victorin & Deng, 2021). Among the metabolic abnormalities seen in PCOS patients were insulin resistance (IR), hyperinsulinemia, and dyslipidemia(wu et al., 2012)(Wu et al., 2014)(Corbould et al., 2005)(Mu et al., 2021). The metabolic abnormalities in PCOS patients included dyslipidemia, hyperinsulinemia, and insulin resistance (IR)(Xita et al., 2007). Although hyper androgenic symptoms improve with menopause, postmenopausal women with PCOS are more likely to develop metabolic and cardiovascular comorbidities. Women with PCOS are more likely to develop endometrial cancer, T2DM, metabolic abnormalities, infertility, obstetrical problems, and mood disorders. Additionally, these women most likely have a higher risk of ovarian cancer, venous thromboembolism, cardiovascular and cerebrovascular events, and other illnesses(Azziz et al., 2016). Insulin resistance is now widely acknowledged as a crucial factor in this complicated illness, presenting up mostly in obese or overweight women but also frequently in lean PCOS women. It causes hyperandrogenism by working in tandem with luteinizing hormone (LH) on ovarian steroidogenic enzymes and the liver's generation of sex hormone binding globulin (SHBG)(De Leo et al., 2016). This syndrome can raise the risk of type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, and even endometrial cancer and probably breast cancer in premenopausal and postmenopausal women(Jalilian et al., 2015).Along with ovarian failure, Additionally connected to the persistent low-grade inflammation is PCOS' metabolic problem (Long et al., 2017). The general public and

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medical communities have been more aware of polycystic ovarian syndrome in recent years due to the knowledge that these women are predisposed to metabolic syndrome and its accompanying comorbidities(Norman et al., 2007). Although not always present, obesity is a common illness. These traits are often connected to elevated levels of luteinizing hormone and androgen, but normal or low blood follicle-stimulating hormone levels(Stein & Leventhal, 1935). Infertility, irregular menstrual cycles, and hirsutism are the most prevalent illnesses encountered in PCOS patients. PCOS has a variety of clinical traits that vary in severity. Women with PCOS have also been found to have increased risks of endometrial cancer (EC), metabolic syndrome, type 2 diabetes mellitus (DM), and cardiovascular disease (CVD)(Rocca et al., 2015). One crucial aspect of polycystic ovarian syndrome is the temporal progression of the symptoms. Adolescents frequently experience persistent symptoms that get worse with time(Setji & Brown, 2014).

1.2 Prevalence or Epidemiology:

Polycystic ovarian syndrome (PCOS), the most common endocrine disorder, affects 6%–8% of women worldwide who are of reproductive age. Adolescent PCOS prevalence ranges from 0.81% to 18.5%(Azargoon et al., 2020). In a survey of 277 women undergoing a pre-employment physical at a university in the Southeast of the United States, we first reported an overall prevalence of PCOS diagnosed by the NIH 1990 criteria of 4.0%, with no discernible difference between Whites and Blacks(Knochenhauer et al., 1998). The prevalence of clinically evident PCOS in unselected women of reproductive age ranges from 6.5 to 8.0%, according to the 1990 NIH criteria. Given that 62 million women between the ages of 15 and 44 live in the United States(Goodarzi & Azziz, 2006). Compared to White or African American women, Mexican American women appear to have a higher prevalence of PCOS(Goodarzi et al., 2005). First-degree relatives with high prevalence of PCOS or associated symptoms suggest inherited impact(Sirmans & Pate, 2013). Azziz and colleagues conducted the first research to determine prevalence in a medically unselected (unbiased) sample, reporting PCOS prevalences of 4% to 6.6% among reproductive-age women living in the Southeast of the United States using the NIH 1990 criteria(Belenkaia et al., 2019). The reported prevalence of PCOS ranges between 5% and 20% to date, depending on factors like the diagnostic criteria used, how the study population was identified, the methods used to define each phenotypic feature, and how thoroughly the phenotypic assessment and recruitment process of the populations were conducted(Maya et al., 2018). A analysis of records from a large managed care organisation revealed that the prevalence of PCOS for women between the ages of 20 and 39 was 2.2%, which is much lower than the rate discovered in systematic screens(Sirmans et al., 2014).

2. Treatment

2.1 Allopathic treatment

Management of women with PCOS depends on the symptoms. These could be ovulatory dysfunction-related infertility, menstrual disorders, or androgen-related symptoms. Treatments

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focus on relieving your signs and symptoms and preventing or managing chronic conditions that may occur with aging(Badawy & Elnashar, 2011).

Table: 2. Allopathic treatment used for PCOD (Polycystic ovary syndrome)

S.no.	Medication	Characterization	Manifestation Treated	FDA Pregnancy Category	Adverse Effects	Dosage	Reference
1.	Clomiphene (Clomid)β	Ovulation induction agent	Infertility	X	Multiple pregnancy/ ovarian hyper stimulation, thromboembolism, visual disturbances	50-100 mg/kg/day orally	(Atay et al., 2006)(Dehbashi et al., 2006)(Barnes, 2006)
2.	Eflornithine (Vaniqa)‡	Inhibits hair growth	Hirsutism	C	Mild skin irritation	13.9% cream applied to face twice per day	(Kang et al., 2021)
3.	Metformin (Glucophage)¥	Insulin-sensitizing agent	Hirsutism; infertility; insulin resistance; menstrual irregularities	B	GI upset, lactic acidosis, increase in homocysteine levels	1,500 to 2,250 mg/kg/per day	(Glueck et al., 1999)(Moghetti, Castello, et al., 2000)(Nestler & Jakubowicz, 1997)(Önalan et al., 2005)(Ortega-González et al., 2005)(Şahin et al., 2004)
4.	Oral contraceptives ¥α	-	Hirsutism; menstrual irregularities	X	Nausea, headache, spotting, thrombophlebitis, deep	Varies	-

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					venous thrombosis		
5.	Pioglitazone (Actos) ¥	Insulin-sensitizing agent	Hirsutism ; infertility ; insulin resistance	C	CHF, may cause weight gain	30 mg/kg/ day orally	(Ortega-González et al., 2005)(Brettenthaler et al., 2004)(Glintborg et al., 2006)
6.	Rosiglitazone (Avandia) ¥	Insulin-sensitizing agent	Hirsutism ; infertility ; insulin resistance ; menstrual irregularities	C	CHF, hepatotoxicity, edema, increase in homocysteine levels	2 to 8 mg/kg/day orally	(Cataldo et al., 2006)(Dereli et al., 2005)(Lemay et al., 2006)
7.	Spironolactone (Aldactone) ¥	Antiandrogenic antimineralocorticoid	Hirsutism ; menstrual irregularities	C	Hyperkalemia, nausea, breast tenderness	50 mg per day to 100 to 200 mg/kg/day orally	(Ashraf Ganie et al., 2004)(Moghetti, Tosi, et al., 2000)
8.	Acarbose (Precose) ¥	Insulin-sensitizing agent	Hirsutism ; menstrual irregularities	B	GI upset	150 mg/kg/day(for menses regulation)	(Penna et al., 2005)
9.	Desogestrel/ ethinyl estradiol (Apri) ¥£	Oral contraceptive	Hirsutism	X	Increased total cholesterol and low-density lipoprotein cholesterol; thromboembolism, stroke, MI	0.15 mg desogestrel plus 30 mcg ethinyl estradiol per day	-
10.	Finasteride (Propecia) ¥	5-alpha-reductase inhibitor	Hirsutism	X	Hypersensitivity reaction, decreased libido	5 mg/kg/day orally	(Falsetti et al., 1999)

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11.	Flutamide (formerly Eulexin) ¥	Nonsteroidal antiandrogen used mostly in prostate cancer	Hirsutism	D	Thrombocytopenia, leukopenia, liver toxicity, hot flashes	250 mg/kg/day orally	(Falsetti et al., 1999)
12.	Letrozole (Femara) ¥	Nonsteroidal competitive inhibitor of aromatase; inhibits conversion of adrenal androgens	Infertility	C	Osteoporosis, thromboembolism, MI, hot flashes, arthralgias	2.5 mg/kg/day orally	(Atay et al., 2006)
13.	Sibutramine (Meridia)¥	Centrally acting appetite suppressant	Hirsutism	C	Tachycardia, hypertension, headache, dry mouth	10 mg/kg/day	(Sabuncu et al., 2003)

CHF = congestive heart failure; FDA = U.S. Food and Drug Administration; GI = gastrointestinal; MI = myocardial infarction; PCOS = polycystic ovary syndrome

β— FDA-approved for female infertility caused by PCOS.

‡— Not studied specifically in women with PCOS; therefore, effectiveness is unknown.

¥— Not FDA-approved for treatment of manifestations of PCOS.

α— Based mostly on anecdotal evidence; cyproterone acetate plus ethinyl estradiol (drug not available in the United States) has been extensively studied.

£— studied in adolescents with PCOS

2.2 Role of Herbal Medicine:

Due to high financial expenditures and a significant number of unfavourable side effects associated with the use of allopathic treatments, there is an increased demand for herbal medications. Since ancient times, herbal plants have been a significant source of therapeutic medicines(Arentz et al., 2014). Exceptionally, despite a significant advancement in pharmaceuticals, the use of herbal remedies is rising steadily in developing nations(Iqbal et al., 2022). Despite the pharmaceutical chemistry revolution that took place in the early 20th century and made it easier to synthesise a huge variety of medicinal drug molecules that also allowed the treatment of previously incurable diseases, thousands of medicinal plants that have potent effects on PCOS symptoms are still in use throughout the world(Badawy & Elnashar, 2011)(Moini Jazani et al., 2019).

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Table 3: Herbal Medicine used for PCOD (Poly cystic ovary disesase)

S.no.	Plant Name/Biological Name/Family Name/Plant Part	Extract and Dose	Mechanism of Action	Responsible Constituents	Reference
1.	Liquorice ***Glycyrrhiza glabra*** Leguminosae (roots)	(containing 7.6% W/W of glycyrrhizic acid) 100 – 150mg/kg/day	Licorice can reduce serum testosterone probably due to the block of 17-hydroxysteroid dehydrogenase and 17-20 lyase. Licorice could be considered an adjuvant therapy of hirsutism and polycystic ovary syndrome.	triterpenoids, polyphenols, and polysaccharides	(Gajanan Khanage et al., 2019)
2.	Aloe-vera ***Aloe barbadensis*** Liliaceae (leaves)	ALOE BARBADENSIS EXTRACT (1 ml dose daily for 45 days)	Cotreatment of the inductive agent (letrozole) with the Aloe vera gel prevented the development of the PCOS phenotype. Aloe vera gel formulation exerts a protective effect in against the PCOS phenotype by restoring the ovarian steroid status, and altering key steroidogenic activity.	Amino Acids Anthraquinones Enzymes Hormones Lignin Minerals	(Dopson, 1999)
3.	Flax seed ***Linum usitatissimum*** Linaceae (seed)	Flax seed oil 1 or 2 table spoonfuls of liquid flaxseed oil daily	It has protective effects by decreasing inflammation in the body as an omega-3 fatty	Alpha-linolenic acid (ALA), an omega-3 fatty acid Linoleic acid (LA),	(Almaguer et al., 2008)

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			acid, inhibits aromatase activity, binds weakly to estrogen receptors, and increases the weaker 2-hydroxyestrones.	an omega-6 fatty acid Oleic acid, an omega-9 fatty acid Fiber Lignans, glycosides, and peptides	
4.	Gymnema sylvestre ***Apocynaceae*** Gurmar (Leaf)	3.5 to 11 mL of 1:1 liquid extract daily	The mechanism of action includes the inhibition of glucose absorption in the intestine.	Key constituents of Gymnema include saponins, especially the gymnemic acids	(Gajanan Khanage et al., 2019)
5.	Fennel Seeds ***Foeniculum vulgare*** Apiaceae (seed)	5 to 7 g and 0.1 to 0.6 mL Fennel seed and Fennel seed oil Oral essential fennel oil (30%) capsules and fennel extract vaginal cream (5%) have been used to improve symptoms in postmenopausal women at 200 mg/day and 5 g/day	The mechanism seems to involve the inhibition of uterine contraction induced by prostaglandin E2 and oxytocin.	Trans-anethole (31.49%), 2-pentanone (25.01%), fenchone (11.68%) and benzaldehyde-4-methoxy (8.01%).	(Harris, 2003)
6.	Cinnamon ***Cinnamomum zeylanicum*** Lauraceae (bark)	Cinnamon powder 1.5 g /day (3 cinnamon capsules; each one contained 500 mg)	The underlying mechanism for cinnamon effects on PCOS may contribute to its improvement in insulin sensitivity.	cinnamaldehyde and trans-cinnamaldehyde (Cin)	(Wang et al., 2007)
7.	Chaste berry ***Vitex agnus-castus***	Fluid extract: 40 gtt/d PO	It inhibits basal- and thyrotropin-releasing hormone–	Flavonoids (i.e., casticin, kaempferol, orientin,	(Gajanan Khanage et al., 2019)

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	Lamiaceae (dried fruit and leaves)	Dried fruit extract: 1.6-3 mg PO BID Tincture: 35-45 gtt PO TID	stimulated prolactin release	quercetagetin, and isovitexin), iridoid glycosides (i.e., agnuside and aucubin), and essential oils (i.e., limonene, cineol, pinene, and sabinene).	
8.	Stinging Nettle ***Urtica dioica*** Urticaceae (root)	770 mg dried extract orally twice daily 4 g whole herb steeped 10 minutes hot water, three to four times daily	Stinging nettle (Urtica dioica) is a common supplement and has the potential to induce galactorrhea. The proposed mechanisms of this galactorrhea are through effects on sex hormone-binding globulin, histamine-induced prolactin release, and serotonin-induced release of thyrotropin-releasing hormone.	Formic acid, histamine, and acetylcholine	(Gajanan Khanage et al., 2019)
9.	Red Clover ***Trifolium pretense*** Legume (flower)	A usual dosage is 40 to 80 mg/day of total isoflavones Crude plant extract 240 mg approximates to 40 mg of isoflavones.	Isoflavones in red clover interact with and activate estrogen receptors to initiate gene transcription	calcium, chromium, magnesium, niacin, phosphorus, potassium, thiamine, and vitamin C, rich source of isoflavones (chemicals that act like estrogens and are found in many plants).	

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10.	Bamboo ***Bambusa Vulgaria*** Poaceae (seeds)	21-day administration with letrozole and 3-week treatment with the extract	Improving estrous cycle and exerting hypolipidemic and hypoglycemic effects. Decreasing blood glucose and the levels of cholesterol, LDL, and triglyceride, improving cystic ovaries and ovulation.	cellulose 41–44%, pentosans 21–23%, lignin 26–28%, ash 1.7–1.9%, and silica 0.6–0.7%	(Soumya et al., 2016)

2.3. Non-Pharmacological Treatment

2.3.1. Reduction in weight

There is some evidence that central obesity with a high waist/hip ratio is brought on by PCOS-related hyperandrogenism independently of body mass index (BMI). Obesity is known to increase the risk of anovulation, miscarriage, and late pregnancy problems such pre-eclampsia and gestational diabetes(Pasquali et al., 2003). Obesity is seen in 35%–60% of PCOS patients and is associated with a lack of or delayed response to several therapies, including clomiphene citrate (CC), gonadotropins, and surgical laparoscopic diathermy(Gjønnaess, 1994).

2.3.2. Diet

The 5%–10% weight loss required to restore ovarian function in obese PCOS patients can be achieved with any variation of the low-calorie, low-carbohydrate diets that are advised. Reaven proposed in 2005 that low-fat diets result in a decline in hyperinsulinemia, which enhances metabolic benefits(GM, 2005).

2.3.3. Exercise

To determine the effect of exercise in the treatment of obese PCOS patients, several research have been conducted. A longer weight loss maintenance time did seem to be associated in these patients, but no significant differences were discovered when various diets, whether or not connected with activity, were examined. Patients with PCOS are advised to improve their physical activity, however there are frequently obstacles to this(Moran et al., 2006). There is a lack of information on the best kind, amount, and frequency of exercise.

2.3.4. Weight loss surgery

Recently, bariatric surgery has been recommended as a weight loss method for morbidly obese people. Bariatric surgery is another option if diet and exercise are unable to cause spontaneous weight loss. There are two main strategies—restrictive and combination restrictive—as well as malabsorptive techniques such adjustable gastric bands and the Roux-en-Y gastric bypass. Not surprisingly, bariatric surgery led to improvements in ovulation, insulin resistance,

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hyperandrogenism, and hirsutism in 17 women with PCOS and a mean BMI of 50.7 kg/m2 over the course of a year. Twelve PCOS patients who were eligible for follow-up after undergoing bariatric surgery for severe obesity all saw the return of normal periods(Escobar-Morreale et al., 2005). Notably, nutritional deficits in protein, iron, vitamin B12, folate, vitamin D, and calcium are more common in women who have undergone bariatric surgery; however, there is no agreement on the best methods for nutritional assessment and treatment.

3. Conclusion:

The treatment of PCOS is complex, and there is no one-size-fits-all approach. Allopathic treatment aims to address specific symptoms and underlying hormonal imbalances. Birth control pills and anti-androgen medications are commonly used to manage symptoms, while insulin-sensitizing agents can help with metabolic aspects. On the other hand, herbal treatments have gained popularity as complementary options to manage PCOS symptoms. However, it's important to note that the scientific evidence supporting the efficacy of herbal remedies for PCOS is limited and mixed. The best approach to managing PCOS often involves a combination of both allopathic and herbal treatments, along with lifestyle modifications such as a balanced diet, regular exercise, and stress management. Therefore, this review suggests that the herbal drug have more benefits in treating PCOS than allopathic treatment.

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