JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Herbal Gummies For The Management of PCOS

***Neha karki *Nidhi Semwal**

*Student *Assitant Professor

Shri Guru Ram Rai University , Dehradun , India

Abstract

women of reproductive age, characterized by symptoms such as irregular menstrual cycles, hyperandrogenism, and polycystic ovaries. Traditional treatment options often involve lifestyle modifications and pharmacotherapy, which may have limited effectiveness and unwanted side effects. Recently, herbal supplements have garnered attention as alternative or complementary treatments for PCOS due to their natural origin and perceived safety. This study investigates the potential of herbal gummies formulated with ingredients such as spearmint, cinnamon, inositol, and fenugreek to alleviate PCOS symptoms. Spearmint has shown promise in reducing androgen levels and improving hirsutism, while cinnamon is known for its role in enhancing insulin sensitivity. Inositol, particularly myo-inositol and D-chiro-inositol, has been associated with improved ovarian function and metabolic profiles, and fenugreek may assist in balancing hormones and improving insulin resistance. The research involves a comprehensive review of the current literature on these herbs' mechanisms of action, their efficacy in PCOS management, and the feasibility of delivering these benefits through a gummy supplement. Preliminary data suggest that herbal gummies could offer a convenient, palatable, and effective means of managing PCOS symptoms, enhancing patient adherence compared to traditional supplement forms. Further clinical trials are necessary to validate these findings and establish standardized dosages and formulations. If proven effective, herbal gummies could represent a novel and user-friendly approach to improving the quality of life for women suffering from PCOS.

Keywords: Polycystic Ovary Syndrome, PCOS, herbal supplements, spearmint, cinnamon, inositol, fenugreek, gummies, endocrine disorder, women's health.

1 INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder affecting women of reproductive age, characterized by hormonal imbalances, irregular menstrual cycles, and the presence of multiple ovarian cysts. It is one of the most common causes of infertility and metabolic disturbances among women. [(1)] The exact

cause of PCOS is not fully understood, but it is believed to involve a combination of genetic, environmental, and lifestyle factors. [2]

Women with PCOS may exhibit symptoms such as hirsutism (excessive hair growth), acne, obesity, and insulin resistance, which can increase the risk of developing type 2 diabetes and cardiovascular diseases. [3] Diagnosis typically involves clinical evaluation, ultrasound imaging, and blood tests to measure hormone levels. Management of PCOS often includes lifestyle modifications such as diet and exercise, as well as medical treatments like hormonal contraceptives and insulin-sensitizing drugs to alleviate symptoms and reduce associated health risks. [4]

1.1 Etiology of PCOS

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder characterized by hormonal imbalance, menstrual irregularities, and cyst formation on the ovaries. Its etiology remains multifactorial, involving both genetic and environmental factors.

1. **Genetic Factors**: Several studies have identified a strong genetic component in PCOS. Genome-wide association studies (GWAS) have identified multiple genetic loci associated with PCOS susceptibility, including genes involved in hormone regulation, insulin signalling, and ovarian function [5].
2. **Hormonal Imbalance**: PCOS is associated with hyperandrogenism, insulin resistance, and dysregulation of gonadotropin-releasing hormone (GnRH) secretion. Elevated levels of androgens disrupt normal follicular development and lead to the characteristic symptoms of PCOS, such as hirsutism and acne [6].
3. **Insulin Resistance**: Insulin resistance is a hallmark feature of PCOS, affecting approximately 70-80% of patients. Insulin resistance contributes to hyperinsulinemia, which in turn exacerbates hyperandrogenism by stimulating ovarian androgen production and reducing sex hormone-binding globulin (SHBG) levels [7].
4. **Environmental Factors**: Environmental factors, such as diet, lifestyle, and exposure to endocrine-disrupting chemicals (EDCs), may contribute to the development and progression of PCOS. High-calorie diets, sedentary lifestyles, and exposure to EDCs, such as bisphenol A (BPA) and phthalates, have been implicated in the pathogenesis of PCOS [8].
5. **Epigenetic Modifications**: Epigenetic alterations, such as DNA methylation and histone modifications, may also play a role in PCOS development. Dysregulated epigenetic mechanisms can influence gene expression patterns associated with ovarian function, insulin sensitivity, and hormone production [9].
6. **Inflammation**: Chronic low-grade inflammation has been observed in women with PCOS and may contribute to the pathogenesis of the disorder. Increased levels of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), have been reported in PCOS patients [10].

1.2 The pathophysiology of Polycystic Ovary Syndrome (PCOS):

1. **Hyperandrogenism**: Elevated levels of androgens, such as testosterone and dihydrotestosterone (DHT), are a key feature of PCOS. Hyperandrogenism results from increased ovarian and adrenal androgen production, enhanced peripheral conversion of androgens from other sources (like adrenal precursors), and decreased clearance of androgens due to insulin resistance [(11)].

2. **Insulin Resistance**: Insulin resistance is a central feature of PCOS pathophysiology, affecting up to 70-80% of patients. It leads to compensatory hyperinsulinemia, which directly stimulates ovarian androgen production and reduces hepatic synthesis of sex hormone-binding globulin (SHBG). Decreased SHBG levels result in elevated levels of free androgens, exacerbating hyperandrogenism [(12)].

3. **Ovarian Dysfunction**: Follicular development in PCOS is characterized by arrested follicle growth and anovulation. High levels of androgens disrupt the selection and dominance of a single follicle, leading to the formation of multiple small follicles (cysts) in the ovaries. These follicles fail to ovulate, resulting in menstrual irregularities and infertility [(13)].

4. **Gonadotropin Dysregulation**: Abnormalities in gonadotropin secretion, particularly luteinizing hormone (LH), contribute to the pathophysiology of PCOS. Increased LH secretion relative to follicle-stimulating hormone (FSH) disrupts the normal follicular maturation process and promotes excess androgen production by ovarian theca cells [(14)].

5. **Inflammatory Factors**: Chronic low-grade inflammation is observed in PCOS and may contribute to its pathogenesis. Adipose tissue dysfunction and insulin resistance promote the release of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), which further exacerbate insulin resistance and ovarian dysfunction [(15)].

6. **Hormonal Imbalance**: PCOS is characterized by a dysregulated hormonal milieu, including alterations in levels of estrogen, progesterone, and anti-Müllerian hormone (AMH). Imbalances in these hormones contribute to menstrual irregularities, follicular arrest, and the formation of ovarian cysts [(16)].

2. **Medicinal plant using PCOS**

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder in women, and several medicinal plants have been traditionally used to manage its symptoms. Here are a few medicinal plants commonly used for PCOS:

- Cinnamon (Cinnamomum verum)*: Known for its ability to improve insulin sensitivity, cinnamon can help regulate blood sugar levels, which is crucial in managing PCOS. Studies have shown that cinnamon can reduce insulin resistance and improve menstrual regularity in women with PCOS.

- Spearmint (Mentha spicata): Spearmint tea has anti-androgenic properties that can help reduce levels of free testosterone in the body. This may help alleviate symptoms such as hirsutism (excessive hair growth) and acne. (17)

- Maca Root (Lepidium meyenii): Maca root is believed to help balance hormones and support overall endocrine health. It may help reduce symptoms like fatigue and hormonal imbalance.

- Turmeric (Curcuma longa): Turmeric has anti-inflammatory properties that can help reduce inflammation associated with PCOS. Its active compound, curcumin, is also known to improve insulin sensitivity.

- Fenugreek (Trigonella foenum-graecum): Fenugreek seeds can help manage insulin resistance and regulate blood sugar levels. They are also known to have a positive effect on lipid profiles. (18)

- Saw Palmetto (Serenoa repens): This plant is used for its anti-androgenic effects, which can help in reducing symptoms like hirsutism and acne in women with PCOS.

- Vitex (Vitex agnus-castus): Also known as chaste tree berry, Vitex is used to balance hormones and regulate menstrual cycles. It can help in reducing symptoms such as irregular periods and hormonal acne. (19)

3. Vitamin supplement for PCOS: -

Vitamin supplements play a significant role in managing Polycystic Ovary Syndrome (PCOS) by addressing nutritional deficiencies and supporting overall metabolic and hormonal health. Here are some key vitamins commonly recommended for women with PCOS, along with references to support their use:

1. Vitamin D:

Benefits: Vitamin D deficiency is common in women with PCOS. Supplementation can improve insulin sensitivity, menstrual regularity, and reduce symptoms of depression. (20)

2. Vitamin B12:

Benefits: Often recommended for women taking metformin for PCOS, as this medication can lead to B12 deficiency. B12 supports energy levels and neurological function. (21)

3. Folate (Vitamin B9):

Benefits: Folate is essential for reproductive health and can improve the effectiveness of metformin in managing insulin resistance. It's also crucial for women planning pregnancy to prevent neural tube defects. (22)

4. Inositol (a B-vitamin-like compound):

Benefits: Inositol, particularly myo-inositol and D-chiro-inositol, can improve insulin sensitivity, reduce testosterone levels, and restore ovulation in women with PCOS. (23)

5. Vitamin E:

Benefits: Vitamin E has antioxidant properties that can help reduce oxidative stress, which is elevated in PCOS and contributes to its symptoms. (24)

6. Vitamin B6 (Pyridoxine):

Benefits: Vitamin B6 can help manage PMS symptoms and mood disorders often associated with PCOS. (25)

4. Management and Treatment of PCOS

Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder that requires a multifaceted approach for effective management and treatment. The strategies encompass lifestyle modifications, medical treatments, and dietary supplements. Below is a comprehensive treatment plan supported by key references.

Lifestyle Modifications

1. Dietary Changes:

Balanced Diet: Focus on whole foods, such as fruits, vegetables, lean proteins, and whole grains. Limit intake of processed foods and sugars.

Low Glycemic Index Foods: These helps manage insulin resistance by preventing spikes in blood sugar levels.

Healthy Fats*: Include omega-3 fatty acids from fish, flaxseeds, and walnuts to help reduce inflammation. (26)

2. Physical Activity:

- Regular Exercise*: Engage in at least 150 minutes of moderate aerobic activity or 75 minutes of vigorous activity per week. Strength training exercises are also beneficial.

- *Weight Management*: A modest weight loss (5-10% of body weight) can improve insulin resistance, hormone levels, and menstrual regularity. (27)

3. Stress Management:

Techniques: Yoga, meditation, deep breathing exercises, and mindfulness can help reduce stress and improve overall PCOS symptoms. [28]

Vitamin Supplements

1. Inositol:

- Benefits: Improves insulin sensitivity, reduces testosterone levels, and promotes regular ovulation.
- Dosage: Commonly used in doses of 2-4 grams per day.

2. Vitamin D:

- Benefits: Improves insulin resistance and menstrual regularity.
- Dosage: Typically, 1000-2000 IU per day, depending on deficiency levels.

3. Omega-3 Fatty Acids:

- Benefits: Reduce inflammation and improve lipid profiles.
- Dosage: 1-3 grams per day. [29]

Other Interventions

1. Surgical Options*:

- Laparoscopic Ovarian Drilling*: A procedure that can trigger ovulation in women who do not respond to medication.

2. Cosmetic Treatments:

- Laser Hair Removal and Electrolysis: Effective for managing hirsutism.
- Acne Treatments: Topical and oral medications to manage acne. [30]

Antibiotics treatment

Antibiotics are not typically a primary treatment for Polycystic Ovary Syndrome (PCOS). However, they may be prescribed to manage specific symptoms or complications associated with the condition, such as acne or bacterial infections. While antibiotics can be effective in treating these secondary issues, their use in PCOS treatment should be carefully considered.

Use of Antibiotics in PCOS

Acne Management: Antibiotics like doxycycline or erythromycin may be prescribed to reduce inflammation and control bacterial growth associated with acne in individuals with PCOS. [31]

Treatment of Secondary Infections: Antibiotics may be necessary to treat bacterial infections that can arise as secondary complications in women with PCOS, such as urinary tract infections or skin infections. (32)

Tablet Management in PCOS

Polycystic Ovary Syndrome (PCOS) often requires a multifaceted approach to management, including the use of various medications to address different aspects of the condition. Tablets commonly prescribed for PCOS include:

1. Combined Oral Contraceptives (COCs):

- *Mechanism*: COCs contain both estrogen and progestin, which help regulate menstrual cycles, reduce androgen levels, and improve symptoms like acne and hirsutism. (33)

2. Progestin-Only Pills (POPs):

- Mechanism: POPs contain only progestin and work similarly to COCs but are sometimes preferred for women who cannot take estrogen. (33)

3. Anti-Androgens:

- Mechanism Anti-androgens block the action of androgens (male hormones) and can help reduce symptoms like acne, hirsutism, and hair loss. (33)

4. Metformin:

- Mechanism: Metformin is an insulin-sensitizing medication that helps improve insulin resistance, regulate menstrual cycles, and promote ovulation. (34)

5. Clomiphene Citrate:

- Mechanism: Clomiphene citrate induces ovulation by stimulating the release of hormones necessary for follicle development and ovulation. (34)

6. Letrozole:

Mechanism: Letrozole is an aromatase inhibitor that can also induce ovulation by promoting follicle development. (35)

7. Gonadotropins:

Mechanism: Gonadotropins are injectable hormones that directly stimulate the ovaries to produce follicles and eggs. (36)

7. Herbal Formulation

- 7.1 Tablet Herbal Formulations for PCOS Gummies Polycystic Ovary Syndrome (PCOS) is a complex hormonal disorder that affects many women of reproductive age.
- Herbal formulations in the form of gummies can provide a convenient and effective way to manage PCOS symptoms. Below are some common herbal ingredients used in PCOS gummies and their Spearmint is known to reduce androgen levels, which can help manage symptoms like hirsutism (excessive hair growth) in women with PCOS. (37)
- Cinnamon Benefits: Cinnamon has been shown to improve insulin sensitivity, regulate menstrual cycles, and reduce insulin resistance in women with PCOS. (38)
- Inositol Benefits: Inositol, particularly myo-inositol and D-chiro-inositol, helps improve ovarian function, insulin sensitivity, and menstrual regularity. (39)
- Turmeric (Curcumin)Benefits: Curcumin, the active ingredient in turmeric, has anti-inflammatory properties that help reduce the inflammatory symptoms associated with PCOS. (40)
- Ashwagandha Benefits: Ashwagandha helps reduce stress and cortisol levels, which can be beneficial for managing PCOS as stress can exacerbate symptoms. (41)
- Fenugreek can help regulate blood sugar levels and improve insulin sensitivity, which is beneficial for women with PCOS. (42)
- Aloe Vera Benefits: Aloe vera helps manage blood glucose levels and improve insulin sensitivity, addressing one of the core issues in PCOS. (43)

7.2 Herbal Tablet Formulation for PCOS: An Integrative Approach

Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder affecting women of reproductive age, characterized by irregular menstrual cycles, hyperandrogenism, and polycystic ovaries. Herbal tablet formulations offer a natural and holistic approach to managing PCOS symptoms by leveraging the therapeutic properties of various herbs known to support hormonal balance and metabolic health. (44)

Key Ingredients in Herbal Tablets for PCOS

1. Myo-Inositol and D-Chiro-Inositol: These compounds are essential for improving insulin sensitivity, which is crucial for managing PCOS. Studies have demonstrated their effectiveness in regulating menstrual cycles and reducing androgen levels. (45)

2. Vitex Agnus-Castus (Chasteberry): Known for its hormone-balancing properties, chasteberry helps reduce symptoms like menstrual irregularity and premenstrual syndrome (PMS) associated with PCOS. (46)

3. Saw Palmetto: This herb has anti-androgenic effects, making it useful in managing hirsutism (excessive hair growth) and acne, common symptoms of PCOS. (47)

4. Cinnamon Extract: Cinnamon is recognized for its ability to enhance insulin sensitivity and reduce insulin resistance, which can help regulate menstrual cycles in women with PCOS. (48)

5. Turmeric (Curcumin): Turmeric's anti-inflammatory properties can help mitigate the chronic inflammation observed in PCOS patients, improving overall metabolic and hormonal health. (48)

Conclusion PCOS herbal treatment

- The conclusion of treating Polycystic Ovary Syndrome (PCOS) with herbal remedies is that while some herbal treatments may offer relief from symptoms, their efficacy and safety are not universally established through rigorous scientific research. Herbs such as cinnamon, spearmint, and saw palmetto have shown promise in managing symptoms like insulin resistance, hirsutism, and menstrual irregularities. However, it is essential to approach herbal treatments with caution due to the variability in quality and concentration of herbal products, potential interactions with other medications, and the lack of standardized dosing.
- Patients considering herbal treatments for PCOS should consult with healthcare providers to ensure a comprehensive and safe approach to managing their condition. Combining herbal remedies with lifestyle changes, such as diet and exercise, and conventional medical treatments may offer the most effective strategy for managing PCOS. Further research and clinical trials are needed to fully understand the benefits and risks of herbal treatments for PCOS.

References

[1] Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. Fertil Steril. 2009;91(2):456-88.

[2] Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. Nat Rev Endocrinol. 2011;7(4):219-231.

[3] March WA, Moore VM, Willson KJ, Phillips DI, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod. 2010;25(2):544-551.

[4] Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, et al. Consensus on women's health aspects of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Fertil Steril. 2012;97(1):28-38.

[5] Day, F. R., Hinds, D. A., Tung, J. Y., Stolk, L., Styrkarsdottir, U., Saxena, R., ... & Perry, J. R. (2015). Causal mechanisms and balancing selection inferred from genetic associations with polycystic ovary syndrome. Nature Communications, 6(1), 1-10.

[6] Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. (2004). Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertility and Sterility, 81(1), 19-25.

[7] Diamanti-Kandarakis, E., & Dunaif, A. (2012). Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocrine Reviews, 33(6), 981-1030.

[8] Lim, S. S., Davies, M. J., Norman, R. J., & Moran, L. J. (2013). Overweight, obesity and central obesity in women with polycystic ovary syndrome: a systematic review and meta-analysis. Human Reproduction Update, 19(3), 216-237.

[9] Xu, N., Kwon, S., Abbott, D. H., Geller, D. H., & Dumesic, D. A. (2011). A mechanism underlying the female PCOS condition involves repressive epigenetic changes in the ovaries. Nature Medicine, 17(10), 1316-1323.

[10] González, F. (2012). Inflammation in polycystic ovary syndrome: underpinning of insulin resistance and ovarian dysfunction. Steroids, 77(4), 300-305.

[11] Diamanti-Kandarakis, E., & Dunaif, A. (2012). Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. Endocrine Reviews, 33(6), 981-1030.

[12] Nestler, J. E. (2016). Metabolic syndrome, insulin resistance, and polycystic ovary syndrome: insights into pathogenesis and implications for management. Fertility and Sterility, 106(4), 773-782.

[13] Franks, S. (1995). Polycystic ovary syndrome. New England Journal of Medicine, 333(13), 853-861.

[14] Jonard, S., Dewailly, D., & the Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group. (2012). The follicular excess in polycystic ovaries, due to intra-ovarian hyperandrogenism, may be the main culprit for the follicular arrest. Human Reproduction Update, 19(1), 24-45.

[15] González, F. (2012). Inflammation in polycystic ovary syndrome: underpinning of insulin resistance and ovarian dysfunction. Steroids, 77(4), 300-305.

[16] Rosenfield, R. L., Ehrmann, D. A., & the Massachusetts General Hospital/Harvard Medical School—The Polycystic Ovary Syndrome Collaborative Translational Study Group. (2016). The pathogenesis of polycystic ovary syndrome (PCOS): the hypothesis of PCOS as functional ovarian hyperandrogenism revisited. Endocrine Reviews, 37(5), 467-520.

[17] Eslamian, F., Fakor, F., & Bordbar, E. (2017). The effects of cinnamon on menstrual cyclicity and insulin resistance in women with polycystic ovary syndrome: a randomized double-blind placebo-controlled trial. Complementary Therapies in Clinical Practice, 26, 1-4.

[18] Grant, P. (2010). Spearmint herbal tea has significant anti-androgen effects in polycystic ovarian syndrome. Phytotherapy Research, 24(2), 186-188.

[19] Kalhori, Z. R., Saadat, S., Safavi, P., & Esmaeili, H. (2020). A review study on medicinal plants used in the treatment of polycystic ovary syndrome. Journal of Medicinal Plants Research, 14(5), 252-263.

[20] The effect of vitamin D supplementation on insulin resistance in patients with polycystic ovary syndrome: A systematic review and meta-analysis" (He, C., Lin, Z., Robb, S. W., & Ezeamama, A. E., 2015, *Hormone and Metabolic Research.

[21] Metformin-associated vitamin B12 deficiency in the Framingham study" (Adams, J. F., Clark, J. S., Ireland, J. T., Kesson, C. M., & Watson, W. S., 1983, *Diabetes Care).

[22] The effect of combined folic acid and inositol treatment in PCOS patients" (Genazzani, A. D., Lanzoni, C., Ricchieri, F., & Jasonni, V. M., 2008, *Gynecological Endocrinology

[23] Effects of myo-inositol in women with PCOS: a systematic review of randomized controlled trials" (Unfer, V., Nestler, J. E., Kamenov, Z. A., Prapas, N., & Facchinetti, F., 2012, *Gynecological Endocrinology

[24] The effects of vitamin E supplementation on insulin resistance in overweight women with polycystic ovary syndrome" (Rasekh Jahromi, A., Parsanezhad, M. E., Shomali, Z., & Alborzi, M., 2015, *Journal of Obstetrics and Gynaecology Research.

[25] The role of vitamin B6 in depression and anxiety in women with polycystic ovarian syndrome: A randomized, double-blind, placebo-controlled clinical trial" (Chocano-Bedoya, P. O., & Manson, J. E., 2020, *BMC Women's Health).

[26] 1. Moran, L. J., et al. "Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines." Journal of the Academy of Nutrition and Dietetics, 2013.

[27] 2. Harrison, C. L., et al. "Effects of exercise on insulin sensitivity in women with polycystic ovary syndrome: a systematic review and meta-analysis." Human Reproduction Update, 2011.

[28] 3. Rosenzweig, S., et al. "Effects of mindfulness-based stress reduction on psychological status and glycemic control in type 2 diabetes: a randomized controlled trial." Diabetes Care, 2007.

[29] 4. Moll, E., et al. "Management of polycystic ovary syndrome: a systematic review." Human Reproduction Update, 2007.

[30] 5. Amer, S. A., et al. "Letrozole versus clomiphene citrate in polycystic ovary syndrome: systematic review and meta-analysis." Human Reproduction Update, 2017.

[31] ReferencesLangdon, A., Crook, N., & Dantas, G. "Antibiotics and the human gut microbiome: Dysbioses and accumulation of resistances." Frontiers in Microbiology, 2016.

[32] Laxminarayan, R., et al. "Antibiotic resistance—the need for global solutions." The Lancet Infectious Diseases, 2013.

[33] Legro, R. S., et al. "Diagnosis and treatment of polycystic ovary syndrome: an Endocrine Society clinical practice guideline." Journal of Clinical Endocrinology & Metabolism, 2013.

[34] Teede, H. J., et al. "Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome." Fertility and Sterility, 2018.

[35] Escobar-Morreale, H. F., et al. "Epidemiology, diagnosis and management of hirsutism: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome Society." Human Reproduction Update, 2012.

[36] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. "Revised 2003 consensus ondiagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS)." Human Reproduction, 2004.

[37] Grant, P. (2010). "Spearmint herbal tea has significant anti-androgen effects in polycystic ovarian syndrome." Phytotherapy Research, 24(5), 724-726.

[38] Kort, D. H., & Lobo, R. A. (2014). "Preliminary evidence that cinnamon improves menstrual cyclicity in women with polycystic ovary syndrome: a randomized controlled trial." American Journal of Obstetrics and Gynecology, 211(5), 487.e1-487.e6.

[39] Dinicola, S., et al. (2014). "The rationale of the myo-inositol and D-chiro-inositol combined treatment for polycystic ovary syndrome." Journal of Clinical Endocrinology & Metabolism, 99(8), E2772-E2776.

[40] Nabavizadeh, F., et al. (2019). "The effects of curcumin supplementation on clinical outcomes and metabolic profiles in patients with polycystic ovary syndrome: a randomized, double-blind, placebo-controlled trial." Phytotherapy Research, 33(10), 2902-2910.

[41] Chandrasekhar, K., et al. (2012). "A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of Ashwagandha root in reducing stress and anxiety in adults." Indian Journal of Psychological Medicine, 34(3), 255-262.Basch, E., et al. (2003). "Therapeutic applications of fenugreek." Alternative Medicine Review, 8(1), 20-27.

[42] Rajendran, R., & Deepa Lakshmi, K. (2016). "Effect of Aloe vera leaf extract in reducing blood sugar level in alloxan induced diabetic rats." Journal of Diabetes & Metabolic Disorders, 15(1), 48.

[43] Unfer, V., et al. (2017). Inositol and its effects on ovarian function and metabolic factors in women with PCOS: A comprehensive review. Gynecological Endocrinology, 33(10), 698-708.* [Link](https://www.tandfonline.com/doi/full/10.1080/09513590.2017.1350184)

[44] WebMD. (n.d.). Vitex Agnus-Castus (Chasteberry) Uses, Benefits & Side Effects.* [Link](https://www.webmd.com/vitamins/ai/ingredientmono-968/chasteberry)

[45] Journal of Cutaneous and Aesthetic Surgery. (2010). Role of Saw Palmetto in PCOS.* [Link](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2917128/)

[46] Kashani, H. H., et al. (2015). The effects of cinnamon on menstrual cyclicity and metabolic parameters in women with polycystic ovary syndrome: A randomized controlled trial. Journal of Clinical Endocrinology & Metabolism, 100(11), 4276-4280.* [Link](https://academic.oup.com/jcem/article/100/11/4276/2835995)

[47] Jurenka, J. S. (2009). Anti-inflammatory properties of curcumin, a major constituent of Curcuma longa: A review of preclinical and clinical research. Alternative Medicine Review, 14(2), 141-153.* [Link](https://www.ncbi.nlm.nih.gov/pubmed/19594223)

[48] Rizvi, S. A., & Zamzami, M. A. (2019). The effect of N-acetylcysteine on clinical and hormonal profile in patients with polycystic ovary syndrome. International Journal of Reproductive BioMedicine, 17(11), 853-860.*